Assessing neurotoxicity of working children between the ages of 10-17 in Lebanon

Author:
Saddik, Basema

Publication Date:
2005

DOI:
https://doi.org/10.26190/unsworks/13241

License:
https://creativecommons.org/licenses/by-nc-nd/3.0/au/
Link to license to see what you are allowed to do with this resource.

Downloaded from http://hdl.handle.net/1959.4/68626 in https://unsworks.unsw.edu.au on 2024-05-03

UNSW
>013408119

ASSESSING NEUROTOXICITY OF WORKING CHILDREN BETWEEN THE AGES OF 10-17 IN LEBANON

B. SADDIK

THE UNIVERSITY OF NEW SOUTH WALES
Thesis/Dissertation Sheet

Surname or Family name: Saddik

First name: Basema **Other name/s: Ahmed**

Abbreviation for degree as given in the University calendar: PhD

School: Public Health and Community Medicine **Faculty: Medicine**

Title: Assessing neurotoxicity of working children between the ages of 10-17 in Lebanon

Abstract 350 words maximum: (PLEASE TYPE)

Children working in vehicle spray painting, mechanical and other trade workshops in Lebanon are at significant risk of exposure to organic solvents and, as a result, may be at significant risk of developing clinical and sub-clinical signs of neurotoxicity. This study aimed to investigate the association between exposure to solvents and neurobehavioural performance of 10-17 year old working children in comparison to groups of non-exposed working children and non-exposed children at school. A convenience cross-sectional sample of 100 working children (10-17 years) exposed to organic solvents at work (spray painting, mechanical, and furniture painting), a positive control of 100 non-solvent exposed working children, and a negative control of 100 non-working, non-exposed school children were recruited to the study. The exposed and non-exposed groups were matched, on geographic location of residence and age.

Neurotoxic effects were assessed using a questionnaire and the child's performance on a selection of computerised and non-computerised neurobehavioural tests. Exposure levels to solvents were measured using personal indirect passive samplers. Analysis of the computerised neurobehavioural tests showed that, working exposed children had significantly slower mean reaction time than children in the working exposed and school-groups. Analysis of the non-computerised tests demonstrated that working exposed children performed significantly worse than the two non-exposed groups on the motor dexterity and memory tests. These differences between working exposed children and the other two groups remained when the analysis controlled for potential confounding variables such as age and education. Analysis of workplace exposure measures showed that working exposed children had significantly higher levels of solvents than the working non-exposed and school children. Analysis of the relationship between workplace exposure and performance on the neurobehavioural tests showed that children with exposure levels above the hygienic effect threshold performed significantly worse on a number of tests, specifically those which assessed functional domains in reaction time and memory functions.

This study has identified that there is an association between exposure to solvents and lower neurobehavioural performance with significant neurobehavioural deficits in children exposed to solvents. Reaction time, memory and motor dexterity appear to be particularly affected in solvent exposed working children.

Declaration relating to disposition of project thesis/dissertation

I hereby grant to the University of New South Wales or its agents the right to archive and to make available my thesis or dissertation in whole or in part in the University libraries in all forms of media, now or here after known, subject to the provisions of the Copyright Act 1968. I retain all property rights, such as patent rights. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

I also authorise University Microfilms to use the 350 word abstract of my thesis in Dissertation Abstracts International (this is applicable to doctoral theses only).

Signature	Witness	6-04-06 Date

The University recognises that there may be exceptional circumstances requiring restrictions on copying or conditions on use. Requests for restriction for a period of up to 2 years must be made in writing to the Registrar. Requests for a longer period of restriction may be considered in exceptional circumstances if accompanied by a letter of support from the Supervisor or Head of School. Such requests must be submitted with the thesis/dissertation.

FOR OFFICE USE ONLY Date of completion of requirements for Award:

Registrar and Deputy Principal

THIS SHEET IS TO BE GLUED TO THE INSIDE FRONT COVER OF THE THESIS

N:\FLORENCE\ABSTRACT

B. SADDIK

STACK

PhD

2005

MBT 613.62/80

Assessing neurotoxicity of working children between the ages of 10-17 in Lebanon.

B.SADDIK

A thesis submitted in fulfilment
of the requirements for the degree of
Doctor of Philosophy

The University of New South Wales
Faculty of Medicine
School of Public Health and Community Medicine
September 2005

UNSW
13 SEP 2006
LIBRARY

ABSTRACT

Introduction: The potential for exposure to neurotoxicants in Lebanon is high, especially in the absence of strict control and regulatory measures in workplaces. Children working in vehicle spray painting, mechanical and other trade workshops are at significant risk of exposure to organic solvents and, as a result, may be at significant risk of developing clinical and subclinical signs of neurotoxicity. To date, there has been no research available on occupational toxic exposures in working children, despite working children being exposed to a range of toxic substances.

Aim: This study aimed to investigate the association between exposure to solvents and neurobehavioural performance of 10-17 year old working children in comparison to groups of non-exposed working children and non-exposed children at school.

Subjects: A convenience cross-sectional sample of 100 working children (10-17 years) exposed to organic solvents at work (spray painting, mechanical, and furniture painting), a positive control of 100 non-solvent exposed working children, and a negative control of 100 non-working, non-exposed school children were recruited to the study. All the children were males. The exposed and non-exposed groups were matched, as far as possible, on geographic location of residence and age.

Materials and Methods: Neurotoxic effects were assessed using both a standardised questionnaire derived from the Swedish Q16 Neurotoxic questionnaire and the child's performance on a selection of computerised and non-computerised neurobehavioural tests. Exposure levels to solvents were measured using personal indirect passive samplers (3M Brand Organic Vapour Monitors). Exposure levels for hexane, MEK, benzene, toluene, xylene and styrene, were analysed using gas chromatography. In addition to the individual solvent exposure levels found, cumulative hygienic effect levels of exposure were calculated for each sample.

Results: Analysis of the computerised neurobehavioural tests showed that, working exposed children had significantly slower mean reaction time on the PIPS Choice Reaction Time, PIPS Dual Tracking Task, PIPS Symbol Digit and the NES2 Continuous Performance Test than children in the working non-exposed and school-groups. The average length of sequence in the PIPS Spatial Memory Search was also significantly shorter for children in the working exposed group than the other two groups indicating poorer memory performance. Analysis of the non-computerised tests demonstrated that working exposed children performed significantly worse than the two non-exposed groups (working and non-working) on the motor dexterity (Grooved Pegboard) and memory (WISC-R Digit Span) tests. These differences between working exposed children and the other two groups remained when the analysis controlled for potential confounding variables such as age and education.

Analysis of workplace exposure measures showed that working exposed children had significantly higher levels of hexane, MEK, benzene, toluene, xylene and styrene, than the working non-exposed and school children. In the working exposed children, almost two thirds (67%) were found to have a cumulative hygienic effect level of more than 1.0. Analysis of the relationship between workplace exposure and performance on the neurobehavioural tests showed that children with exposure levels above the hygienic effect threshold performed significantly worse on a number of tests, specifically those which assessed functional domains in reaction time and memory functions. Working children with higher solvent exposure showed significantly higher reporting of neurotoxic symptoms with specific solvents of MEK, toluene, xylene and styrene found to be associated with more symptoms. Furthermore, multiple regression models revealed significant dose-response relationships, with poorer performance on the neurobehavioural tests with increasing cumulative exposure for the PIPS Choice Reaction Test, PIPS Symbol Digit, NES2 CPT, WISC-R Digit Span, and the Grooved Pegboard. Specifically, benzene, xylene and styrene exposure significantly predicted slower reaction time and lower accuracy and hand-eye /motor coordination in a number of measures of these tests.

Conclusion: This study has identified that there is an association between exposure to solvents and lower neurobehavioural performance with significant neurobehavioural deficits among children exposed to solvents in comparison to working children not exposed to solvents and non-working school children. Reaction time, memory and motor dexterity appear to be particularly affected in solvent exposed working children. This study suggests that urgent action needs to be taken to address the effects of exposure in this group of children before further deterioration in performance. A large percentage of solvent exposed working children in Lebanon are at high risk of developing neurobehavioural deficits that are likely to compromise their capacity to respond quickly and safely to new demands and to learn new information, especially since long-term effects are unknown.

ACKNOWLEDGEMENTS

This thesis would not have been possible without the cooperation and support of many people.

I would like to extend my warmest thanks and appreciation to my supervisor Associate Professor Deborah Black and my co-supervisor Associate Professor Ann Williamson. Deborah and Ann provided me with the utmost support and encouragement throughout the duration of this project. Their patience, persistence and insightful feedback are gratefully acknowledged.

I would like to also extend a special thank you to Professor Iman Nuwayhid from the American University of Beirut, who co-supervised this project during the data collection phase in Lebanon. Iman's guidance, enthusiastic support and good-natured encouragement were invaluable.

I would also like to thank Dr John Frith for his assistance and support during the initial phase of this study.

I would like to acknowledge the ILO (International Labor Organisation)-Beirut office, and the American University of Beirut Research Board for their partial funding of this project.

I would also like to thank the staff at the American University of Beirut Environmental Core Laboratory for their assistance in analysing the exposure measures used for this project.

I am grateful to my work colleagues for their continued support and sympathetic ear in times of need.

I would also like to acknowledge the assistance and invaluable contributions made by all the people involved in the data collection phase of this study.

My deepest appreciation and gratefulness are extended to the children who participated in this study, their families and employers.

I would like to thank my immediate and extended family, my brothers and sisters and my friends for their continued support and for giving me the strength to keep going. I am indebted to my parents Ahmed and Khadejah for their lifelong support and encouragement. Without their commitment and encouragement this thesis would not have been possible.

Finally, I wish to extend my gratitude to my husband Dr. Samir El-Masri for his love, support and patience throughout the duration of this project, especially his persistence and determination in ensuring that I remained on track and completed this thesis.

DEDICATION

This thesis is dedicated to my son Adam who is a constant source of inspiration and joy.

ORIGINALITY STATEMENT

"I hereby declare that this submission is my own work and to the best of my knowledge it contains no materials previously published or written by another person, or substantial proportions of material which have been accepted for the award of any other degree or diploma at UNSW or any other educational institution, except where due acknowledgement is made in the thesis. Any contribution made to the research by others, with whom I have worked at UNSW or elsewhere, is explicitly acknowledged in the thesis. I also declare that the intellectual content of this thesis is the product of my own work, except to the extent that assistance from others in the project's design and conception or in style, presentation and linguistic expression is acknowledged."

Signed...

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER ONE: INTRODUCTION

Child labour is a problem around the world and one of the social problems in Lebanon, especially in underserved urban neighbourhoods of the major cities and in rural areas. This phenomenon is attributed to poverty, loss of or injury to parents during the civil war, low educational status of parents, lack of recreational activities for the children, divorce and loss of work opportunities for the parents, along with the increasing number of students leaving their schools for economic reasons or lack of interest. It has been reported that in spite of several national laws and international agreements which ban child labour, more than 40 thousand children less than 18 years of age are active participants of the labour force in Lebanon (4.6% of the labour force) (Issa and Houry, 1998). In the absence of workplace control measures, children working in mechanical and other trade workshops are at significant risk of exposure to organic solvents and as a result at significant risk to develop clinical and subclinical signs of neurotoxicity

Previous studies have investigated the magnitude of developmental neurotoxicity and the effects of environmental exposure of children to lead, methylmercury, pesticides and other toxins. However, there have been no published studies that have investigated the association between neurotoxicity and solvent exposure of children in the workplace. Research on solvent exposure among children is still limited to glue sniffers and solvent abusers, who often have other confounders, such as alcohol use and malnutrition.

Most research, which has been conducted on adults and more recently adults exposed to low concentrations of solvents, suggests that solvents have an effect on the central nervous system and neurobehavioural performance and exposure to solvents has been associated with several neurobehavioural effects, such as loss of dexterity, delayed reaction time, lack of concentration and loss of memory (Xiao and Levin, 2000; Tsai et al., 1997). Many studies conducted have shown clear dose-effect relations between the degree of exposure and the magnitude of the associated neurobehavioural deficits (White and Proctor, 1997).

There have been no published studies that address occupational solvent exposure in children. This thesis will investigate the effects of child labour and in particular will address the issue of the significant gap in evidence on the consequences of toxic exposures in working children and the underlying effects manifest in adulthood. This study will also examine the neurotoxic effects of exposure to relatively high concentrations of solvents in a younger more susceptible population for the first time.

1.1 AIM OF THE STUDY

The study aims to investigate the association between exposure to solvents and neurobehavioural performance of 10-17 year old working children in comparison to groups of non-exposed working children and non-exposed children at school.

1.2 STUDY OBJECTIVES

1. To measure the exposure levels to solvents in working children in Lebanon.
2. To identify the major types of solvents working children are being exposed to.
3. To examine the neurobehavioural and neuropsychological effects of chronic exposure to solvents in working children
4. To evaluate whether some neurobehavioural functions in working children are affected more than others on different neurobehavioural and neuropsychological tests.
5. To assess the relationship between duration of exposure and performance on selected neurobehavioural and neuropsychological tests

1.3 STUDY HYPOTHESIS

There is an association between solvent exposure levels and neurobehavioural effects in working children exposed to solvents in Lebanon.

1.4 OVERVIEW OF THE STUDY

Chapters One, Two and Three will present the introduction and literature reviews for this study. Chapter Two will present the literature on child labour and discuss the effects of child labour, whilst Chapter Three will introduce toxic exposures and the effects of toxic exposures on adults and children. Chapter

Four will provide a discussion on the methodological issues which need to be addressed in conducting sound neurobehavioural research and the attempts which will be made to address these issues in the development of this study. Chapter Five will introduce the research methods and materials this study will undertake. Chapter Six will present the analysis of the results of the study and Chapter seven will undertake to discuss these results. The final chapter, Chapter Eight will present the conclusions drawn from the study and recommendations will be presented.

CHAPTER 2: CHILD LABOUR

2.1 Overview of the Chapter

The following section sets the scene and outlines the extant literature pertaining to child labour, the factors contributing to child labour and the effects of child labour on the health and well-being of children with a focus on child labour in Lebanon. The definition of child labour will be presented as well as global estimates and figures.

2.2 What is Child Labour?

Children work around the world, especially in developing countries where they play a major economic role for the family and the economy of the country. The literature on working children is extensive and highlights the reasons children are working and the negative consequences of specific work situations children are working under.

Working per se is not the problem for children, especially older children, where work such as babysitting or grocery bagging is seen to encourage the development of the child's self discipline and independence. A study conducted by the NSW Commission for Children and Young People in Australia, found that children aged between 12 and 16 years who were working in jobs such as babysitting, newspaper deliveries or general farm hand work, found work rewarding and saw it as an opportunity to exercise autonomy, develop skills and obtain some form of income (Fattore, 2005). However when the job a child does becomes exploitative and potentially harmful to the child's health, this becomes a problem. There is an ongoing concern that exploitative work for children is a growing phenomenon throughout the world. This issue will be tackled in this thesis. In particular the thesis will address the issue of the significant gap in evidence on the consequences of toxic exposures in working children and the underlying effects manifest in adulthood.

International authorities on safety and health at work such as the International Labour Organisation (ILO) and the World Health Organisation (WHO) have focused on the adverse impacts of children working and have used the term "child labour" to describe this problem, however, no clear definition of child labour has yet been conceptualised and definitions differ somewhat between different organisations. The United Nations (UN) defines child labour as "all forms of economic exploitation, any work that is likely to be hazardous or interfere with the child's physical, mental, spiritual, moral or social development" (United Nations, 2003). The International Labour Organisation (ILO) has a broader definition and states, "Child labour is remunerated or unremunerated work by a young person under a certain age, the work of which impairs their personal development, health, safety, well being physically, mentally and psychologically, impairment of which is in violation of national or international law" (ILO, 1997). The International Labour Organisation International Programme on the Elimination of Child Labour (ILO/IPEC) defines child labour more categorically and comprehensively as "work situations where children are compelled to work on a regular basis to earn a living for themselves and their families, and as a result are disadvantaged educationally and socially; where children work in conditions that are exploitative and damaging to their health and to their physical and mental development; where children are separated from their families; often deprived of educational and training opportunities; where children are forced to lead prematurely adult lives" (ILO/IPEC, 2002). Although these definitions are not the same, they have notable similarities in that they identify the exploitation of children, the denial of their human rights and well-being, deprivation of their right to health, education and childhood and the denial of a decent future (Nkurlu, 2000; Forastieri, 2000).

Definitions of the child also differ. UNICEF (2003), has defined children in the convention on the rights of the child, "as all human beings under the age of 18, unless the relevant national laws recognize an earlier age of majority". UNICEF also highlights the distinction between "child work" and "child labour".

"Child" and "childhood" are also defined differently in different cultures — and the definition is not necessarily delineated by age. Social scientists point out that children's abilities and maturities vary so much that defining a child's maturity by calendar age can be misleading (Boyden et al., 1998). For instance: International conventions adopted by the United Nations and the International Labour Organization define "child" as anyone below the age of 18, and "child labour" as some types of work performed by children below age 18 (United Nations, 2003). And yet governments adding to the confusion variously define the appropriate minimum age of work as age 15 or under 14 in developing nations (Images of child labour (date unknown)).

Overall, the issue of child labour and the protection of children from hazardous work has been one of the aims of the International Labour Organisation since its creation in 1919 as stated in its constitution (ILO, 1997). Hazardous work by children has been defined by the ILO convention Nos. 138 and 182, as "work likely to jeopardize and/ or harm the health, safety or morals of children" (Nkurlu, 2000). The International Programme on the Elimination of Child Labour (IPEC) and the Statistical Information and Monitoring Programme on Child Labour (SIMPOC) (2002) also explain that hazardous work by children constitutes any activity or occupation which, by its nature or type has, or leads to, adverse effects on the child's safety, health (physical or mental), and moral development. Hazards could also derive from excessive workload, physical conditions of work, and /or intensity in terms of the duration or hours of work even where the activity or occupation is known to be non-hazardous or 'safe'.

Although many restrictions exist in most nations and the 175 member states of ILO have pledged to abide by ILO restrictions, many children still work (ILO, 2002). The ILO Minimum Age Convention, 1973 (No. 138) together with the ILO resolution concerning the progressive elimination of child labour (1979) and the ILO Worst Forms of Child Labour Convention, 1999 (No. 182) set the framework for international policies on the elimination of child labour. The minimum age convention (No.138) expresses that the minimum age for entry into employment should not be less than the age of completion of compulsory schooling whereas the Worst Forms of Child Labour Convention (No. 182) passed in 1999, specifies that persons carrying out work in circumstances which are hazardous and likely to jeopardize the health, safety, or morals of young persons may not be less than 18 years of age (ILO, 2002).

2.3 Global Estimates of Child Labour

In order to address the impact of child labour, it is important that global estimates are established. The ILO has attempted to establish global estimates of the number of children at work but has faced serious difficulties due to inconsistencies in the definition of child labour and to the lack of reliable national statistics (Forastieri, 2002). These estimates have been reported and used by most studies on child labour in the absence of more accurate and reliable data. Recent data published by the International Programme on the Elimination of Child Labour (IPEC) and Statistical Information and Monitoring Programme on Child Labour (SIMPOC) (2002), have categorised estimates of working children into three groups including, "economically active children", "children in hazardous work" and "children in unconditional worst forms of child labour that requires elimination".

"Economically active children" is a broad category that encompasses most productive activities by children whether paid or unpaid in the formal and informal sectors including illegal work (IPEC/SIMPOC, 2002). It is, however, not the same as "child labour which needs to be eliminated" as per the ILO Minimum Age Convention, 1973 (No. 138) and the ILO Worst Forms of Child Labour Convention, 1999 (No. 182) which includes estimates of only the number of children involved in the worst types of exploitative work for example; trafficking, forced and bonded labour, armed conflict, prostitution, pornography, and illicit activities.

"Children in hazardous work", has been explained earlier and includes work which by its nature or type may lead to adverse effects on the child's safety, health and moral development. The category, "children in unconditional worst forms of child labour that requires elimination", includes all forms of slavery, trafficking of children, debt bondage, forced or compulsory labour, prostitution, pornography and engaging the child in illicit activities including the production and trafficking of drugs (ILO/SIMPOC, 2002).

Based on these definitions and criteria IPEC and SIMPOC (2002) have estimated that there were 211 million children between the ages of 5 and 14 at work in economic activity in the world in the year 2000. This accounts for a little less than one-fifth of all children in this age group with approximately 73 million economically active children being less than 10 years old. The total economically active child population 5-17 years old is estimated at 352 million children as displayed in Table 2.1 below.

Table 2.1: Global estimates of economically active children ages 5 to 17 in 2000.

Age Group	Total Population (000's)	Number at work (000's)	Work ratio (%)
5-14	1,199,400	210,800	17.6
15-17	332,100	140,900	42.4
Total	1,531,100	351,700	23.0

Source: IPEC and SIMPOC (2002)

The IPEC/SIMPOC (2002) study also provides estimates on the category "Child labour" which has been defined as a narrower concept than "economically active children", excluding all those children 12 years and older who are working only a few hours a week in permitted light work and those 15 years and above whose work is not classified "hazardous". It is estimated that there were about 186 million child labourers below the age of 15 in the world in 2000. About 110 million were below the age of 12 whilst among the children in the larger age group 5-17, there were approximately 246 million children in child labour that requires elimination (ILO/SIMPOC, 2002).

An estimated 171 million children ages 5-17 were estimated to work in hazardous situations or conditions in 2000. Therefore children in hazardous work make up about half the number of economically active children and more than two thirds of those in child labour. IPEC/SIMPOC also found almost 55 per cent of very young child labourers (i.e. those below 12 years of age) were already working in a hazardous occupation or situation. Although not presented in the table below, an estimated 8.4 million children are working in unconditional worst forms of child labour (ILO/SIMPOC, 2002)

Table 2.2: Global estimates of working children using three different definitions

Age Group	Economically Active Children ('000s)	Child Labour ('000s)	Children in Hazardous work ('000s)
5-14	210,800	186,300	111,300
15-17	140,900	59,200	59,200

Source: IPEC and SIMPOC (2002)

In terms of gender differences, IPEC and SIMPOC (2002) estimates show that there are no significant gender differences in the global incidence of children in economic activity. In both the 5-9 and 10-14 age brackets, boys and girls are equally likely to be engaged in economic activity however this changes when examining the more narrowly defined group of child labourers. On average, more boys tend to be exposed to child labour than girls and this pattern becomes more pronounced with increasing age. In the 5-14 age brackets, the gender distribution of child labour is roughly even, however it then tilts towards boys particularly so in the 15-17 age group (57 per cent boys versus 43 per cent girls) where estimates show that child labour is automatically equated with hazardous work (IPEC and SIMPOC, 2002). According to these estimates, this suggests that older boys may be at risk of working in hazardous work. Hadi (2000) illustrates this trend in a study conducted on working children in Bangladesh where more boys than girls were in the workforce and older children and boys suffered more child abuse including exposure to hazardous work than younger children and girls.

For all categories, the Asian-Pacific region harbours the largest number of child workers in the 5-14 age category, 127.3 million in total. This is followed by Sub-Saharan Africa, Latin America and the Caribbean with 48 million and 17.4 million respectively (IPEC and SIMPOC, 2002). The highest proportion of working children however was noted in Sub-Saharan Africa with 29% of children in this age group working. The number of children in the 5-14 age category in the Middle East and North Africa has been estimated at 13.4 million with 15% working. Not surprisingly, the incidence of child labour is lowest in developed countries; however this is not to say that it does not exist and that child labour is limited to developing countries. Estimates have indicated that more than 5 million children and adolescents in the United States (US) are legally employed either part-time or full-time (Woolf et al., 2001; Landrigan and McCammon, 1997) with an estimated 1 to 2 million employed in violation of provisions of the Fair Labour Standards Act (FLSA) (Widome 1996 cited in Woolf 2001). Conley (2000), reports that 60 000 children working in the US are under the age of 14 and migrant workers make up the majority of child labourers. While an estimated 32.6% of German and 43% of United Kingdom teens 15-19 years old are employed (Woolf, 2002).

The above statistics exemplify that the scope of child labour is global involving significant numbers of children in both developing and developed countries; however, the ratio of children active in the labour force is worse in some regions than others as displayed in Table 2.3 (Woolf, 2002; IPEC and SIMPOC, 2002). The worst estimates were found in Sub-Saharan Africa followed by Asia and the Pacific regions. Developed nations have the lowest work ratio of economically active children.

Table 2.3: Regional estimates of economically active children ages 5-14 in 2000

Region	Number of children (in millions)	Work Ratio (%)
Developed economies	2.5	2
Transition economies	2.4	4
Asia and the Pacific	127.3	19
Latin America and Caribbean	17.4	16
Sub-Saharan Africa	48.0	29
Middle East and North Africa	13.4	15
Total	**211**	**18**

Source: IPEC and SIMPOC (2002)

All the data that has just been discussed are global estimates supplied by the IPEC and SIMPOC report and are limited to 29 national household surveys mostly conducted in the late 1990s. Only ten of these surveys were specifically designed to measure child labour and were conducted under the ILO, SIMPOC project: Kenya 1999, Namibia 1999, Nigeria 2000, Pakistan 1996, Portugal 1998, South Africa 1999, Sri Lanka 1999, Turkey 1994, Ukraine 1999 and Zambia 1999. The other 19 surveys were a mixture of broad-based household and community surveys which were conducted as part of the World Bank's programme of Living Standards Measurement Surveys and included Azerbaijan 1995, Bolivia 1999, Brazil 1998, Cambodia 1996, Cameron 1996, Colombia 1998, Costa Rica 1998, Egypt 1998, El Salvador 1999, Ghana 1997, Kazakhstan 1996, Mauritania 1995, Mexico 1996, Paraguay 1999, Philippines

1998, Senegal 1995 and national statistical programmes in Bangladesh 1999, India 1994 and Yemen 1997. Whilst these estimates are the most recent and most commonly used and cited in child labour research, caution in generalisability and accuracy of these estimates needs to be undertaken. With only 29 countries participating in the household surveys, these estimates may not truly be reflective of the factual global and regional estimates. Moreover, the reliability of these results is not ensured since only 10 of these countries collected data specifically for child labour within the ILO, SIMPOC project. However in the absence of more reliable data and global estimates, these statistics are sufficient for the purposes of this thesis.

2.4 Child labour in Lebanon

In spite of several national laws and international agreements which ban child labour, more than 40 thousand children less than 18 years of age are active participants of the labour force in Lebanon (4.6% of the overall labour force) (Issa and Houry, 1997). Whilst Table 2.3 earlier indicated that the magnitude of child labour may be less devastating in the Middle East than in other developing countries, child labour has been reported as one of the social problems in Lebanon of increasing magnitude especially in underserved urban neighbourhoods of the major cities and in rural areas (Issa and Houry, 1997; CAS and UNICEF, 2002). The civil war in Lebanon between 1975 and 1990 left the country with a shattered economy, disintegrated and paralysed infrastructure and an impoverished middle class (Fischbach, 1998). Following the war, the phenomenon of working children began to increase mainly due to poverty, loss of or injury to parents, low educational status of parents, lack of recreational activities for the children, divorce and loss of work opportunities for the parents, along with the increasing number of students leaving their schools for economic reasons or lack of interest (Nuwayhid et al., 2001).

There have been various reports in the last decade estimating the number of working children in Lebanon. An earlier National report on child labour in Lebanon found that working children between 10-14 years and 15-19 years of age constituted 0.6 percent and 5.5 percent of the Lebanese labour force (estimated at 944,281), respectively. Most of the 10-14 year old working children were full time paid workers and the majority of the males in the report were employed in metal works, handicrafts, and artisan production (Hamdan, 1997).

In total, working children in Lebanon constitute 6.4 percent of the labour force and 8.3 percent of the total number of children aged 10-17 years (Diab, 2001). However, there are variations between the age groups 10 to 13 and those aged 14 to 17 years. The working children in the first group (10-13 years) represent 1.9 percent of the total number of children in that age group whereas working children of the second age group (14-17 years) represent 14.5 percent (Diab, 2001). A more recent national survey also reported similar estimates in that 1.8% of the 10-14 year old children and 11.3% of those aged 15-18 years work (CAS and UNICEF, 2002). The age distribution of working children in Lebanon is presented in Table 2.3. Whilst it should be noted that cases of working children below 10 years of age are rarely reported in Lebanon they do exist. CAS and UNICEF (2002) have for the first time covered the situation of children in the age group 5-9 years of age where it was found that 4.6% of children in this age group helped their family in their work. Around two thirds (67.5%) worked for less than 4 hours and 6.8% worked for 4 hours or more per day. Similarly a study conducted by UNICEF on working children (1995) indicated that 43 per cent of working children recorded an early entry into the labour market (10-13 years), whereas 21 percent began work before they were 10 years. As reported earlier by Hamdan (1997), and consistent with earlier global estimates, the majority of the working children are males (89.4 percent). A smaller proportion of working girls were reported in Lebanon either because fewer of them were sent to work especially at an early age (Diab, 2001) or because girls mostly worked in the informal sector and were not captured by surveys.

Table 2.4: Age distribution of working children in Lebanon

Age group	Number of working children	Total number of children	Percentage of working children
10-13	5,108	262,360	1.9
14-17	38,307	263,466	14.5
Total	43,415	525,826	8.3

Source: Diab, 2001

Child labour in Lebanon is not equally distributed across the country, but clearly associated with the poor outskirts of the country (CAS and UNICEF, 2002). The distribution of working children over the different regions in Lebanon coincides with the spread of poverty conditions (ILO/IPEC, 2002). The region of North Lebanon has the highest proportion of working children with respect to the two age groups 10-13 years and 14-17 years. It is followed by the region of Bekaa, then Beirut, Mount Lebanon and the South for the 10-13 age groups and the south, Bekaa, Mount Lebanon and Beirut for the 14-17 year age group (CAS and UNICEF, 2002). Overall the districts of Tripoli, Minyeh, Akkar, Baabda, Baalbeck, Zahleh, Saida and Tyre have about 80% of working children aged 10-13 years (Issa and Houry, 1997).

Unfortunately not many studies exist on child labour in Lebanon and therefore the scope and reasons for employment are limited to a number of descriptive studies. However from the studies available, it is clear that the majority of working children have low school enrolment rates, consequently dropping out of school as a result of failure in their studies. UNICEF (1995) reported that 37.5% of working children in Lebanon were illiterate or had not finished their elementary education, compared to national illiteracy levels of 1.6 percent and 2.4 percent for the 10-14 year age group and 15-19 year age group respectively (Central Administration of Statistics, 1997). The more recent national survey found that 3.8% of working children in the age group 10-14 years were illiterate and 70% had a primary level education whereas in the 15-18 year age group 1.6 % were illiterate and 61.2% had primary level education (CAS and UNICEF, 2002). Furthermore, the educational level of the children was found to be similar to that of their parents. UNICEF (1995) and ILO/IPEC (2002), found that working children mainly came from poor families having a low educational level. Children were usually employed in the same kind of work as their fathers and had a lower educational level than non-working children of the same age. Issa and Houry (1997) also reported that almost all (92%) of the working children in their study aged 10-13 years lived in families whose head of household had received only primary education or was illiterate. Similarly, Hamdan, (1997), found that 50 percent of children were working due to economic reasons, 33 percent in order to gain a profession and 14 percent because they had failed in their studies.

The majority of working children were paid very low salaries, all of them earning rates below the minimum wage rate declared by the Government (UNICEF, 1995). Hamdan (1997), also revealed that 65 percent of children get less than half the minimum wage rate. The same study found that 90 percent of working children worked for more than ten hours a day and were not registered by employers in the National Social Security Fund (NSSF); therefore they were not covered by health or medical insurance. In the 10-14 year age group, most working children were employed in artisan production (49 percent) followed by trade and service (23 percent) whereas 56.5% worked in artisan production and 18.9% as unskilled employees in the 15-18 year age group (CAS and UNICEF, 2002). Eleven percent of working children were reported to be employed in the agriculture sector, and 5 percent were working in construction (ILO/IPEC, 2002). The report also found that children in urban areas worked in jobs predominantly trade-related whereas in the rural sector, agricultural work predominated. The kind of work a child did was probably linked to the availability of employment for children, rather than intended selection of sectors. Although, it may also be argued that children preferred specific sectors because of their own or their parents desire for them to learn a trade.

Most of children work in small industrial workshops with minimal control of hazards and practically total absence of protective measures or equipment. An investigation of the work environment and work activities of children working in mechanical, carpentry, autobody repair and spray-painting workshops in Lebanon (Nuwayhid et al., 2001), found that the workplaces visited lacked basic hygienic principles including washing basins, soaps and toilets. Children reported using chemicals to "wash" grease and paints from their hands, while control measures and the use of protective personal equipment was almost non-existent and missing from the majority of the 98 workplaces visited. Furthermore, a more recent investigation of the physical and mental health of working children in Lebanon (Nuwayhid et al., 2005) revealed that working children are disadvantaged compared to non-working children. It was found that the nutritional intake of the working children was poorer than non-working children. Working children also reported more health problems and injuries. Physical examination and laboratory tests showed that more working children were anaemic and had a higher blood lead level than non-working children and the condition of their skin reflected the jobs they were involved in showing a clear indication of working with tools or chemicals.

2.5 Lebanese Labour Laws

In 1996, Lebanon adjusted its labour law by increasing the legal age at which children are allowed to work from 8 to 14 years. More recently, Lebanese legislation pertaining to child labour has undergone tremendous positive developments, although many gaps still remain in the level of implementation. Lebanon ratified ILO convention 136 pertaining to the prevention of intoxication hazards resulting from benzene in 1999 where the government undertook various technical measures that ensured effective protection of exposed workers to benzene and its products. Employment of youth under 18 years of age is considered an infringement of the conventions articles. Lebanon also ratified ILO Convention No 138 in 2002 which sets the minimum age for child labour, whereby the minimum set age should not be less than the age required to complete compulsory education, (i.e. 15 years of age). Other Lebanese labour law decrees addressing the physical, mental and social protection of working children were suggested for amendment to include: (OHCHR, 2003; US Department of Labour 2003)

- Ensuring that the number of working hours per day do not exceed 6 hours with one hour break after each consecutive 4 hours for those below 18 years of age
- Requiring a minimum of 13 hours of rest between every two work shifts

- Giving the working child, after one year of employment, the right for 21 days of vacation with full payment
- Prohibiting in an absolute manner, assigning overtime work to youth, or making them work during their daily and weekly rest period, during holidays and occasions and forbidding night employment from 7 in the evening until 7 in the morning
- Performing a medical examination on working children to establish their ability to perform the tasks of the job
- Providing a minimum of 36 consecutive resting hours each week
- Requiring the employer to register the working child in the National Social Security Fund after three months of employment
- Prohibiting children's employment in dangerous occupations such as mining, cooling and electrical industries, demolition, dying, chemical materials, soap and copper production, or in occupations that require lifting heavy objects or using fuel

However, the laws are not strictly applied and children are still working in hazardous conditions in Lebanon (Nuwayhid et al., 2005; Nuwayhid et al., 2001; Saddik and Nuwayhid, 2003). Furthermore working children less than 20 years of age are disadvantaged because of law No. 36/67, which states that the minimum wages for employees and workers apply only to those who are over 20 years of age (Diab, 2001), therefore providing no protection for children in terms of sufficient and fair remuneration for their services. Nuwayhid et al.,

(2005) found that 80% of children who had been working for two or more years were receiving less than half the Lebanese minimum wage of about US$50 (equivalent to 70000 Lebanese pounds) per week which would barely meet the family's basic needs like house rent, food or education.

More information is still needed about the work hazards, work exposures and conditions to which working children in Lebanon and other developing countries are exposed to and about the types and frequency of physical activities they do at work. These are important to guide any policy action that aims to prevent child labour and to promote awareness of it. Moreover, there is a need to investigate particular problems among working children be it mental health, exposure to heavy metals, neurophysiological and neurobehavioural impairment, injuries and the like.

2.6 Motivators for Child Work and Labour

Children work for a variety of reasons, the most important being poverty and the induced pressure upon them to escape from this plight. (Gharaibeh and Hoeman, 2003; Kapinga, 2000). Case studies cited in Del Rosario and Bonga (2000), and more recent studies by Lim (2002) and Alonza and Edillon (2002) argue that poverty is the foremost determinant of child labour in the Philippines. Though children are not well paid, they still serve as major contributors to family income in developing countries and are often prompted to work by their parents (Nkurlu, 2000). Children may provide 25% or more of a family's total income, and many traditional cultures include child labour as an integral part of the child's socialization and achievement of status in the local community (Woolf, 2002). Income from child labour, therefore, is welcome to very low-income households, whether it is in the rural or urban setting. Because of poverty, households need their children's earnings to augment their household's incomes therefore; children are forced or pressured by their parents or head of household to work, interfering with their education and potentially exposing them to health risks (Aldaba et al., 2002). Syed et al., (1991) found that parents represented 62% of the source of induction into employment, whereas only 8% of children contributed to this decision.

Schooling problems also contribute to children working, whether it is the inaccessibility of schools owing to distance or the lack of quality education which spurs parents to enter their children into more profitable and long term pursuits (Siddiqi and Patrinos, 1996; Edralin, 2002). The high cost of education for poor families is also an overriding factor in why children of poor households do not attend school (Aldaba et al., 2002). Alonzo and Edillion (2002) have reported on the vicious cycle that occurs between the lack of education and child labour which impacts on future generations. They state that the heads of poor households are likely to have low levels of education and often household poverty can be ascribed to the heads having low education attainment themselves therefore not realising the benefits of education for their children. Similarly, Lim (2002) points out that the educational levels of the parents, household head or mother of the family have a strong bearing on the decision whether to send children to school or to allow the children to work. The need to survive on a day-to-day basis far outweighs the long-term benefit of education at least in short-term decision making.

There is also the factor of children being favoured over unskilled adults in some lines of work because of their physical characteristics (Aldaba et al., 2002). It has been reported that drug traffickers prefer to use children in their operations because they are harder to detect (ILO/IPEC, 2002), employers in the hand-woven carpet industry prefer the nimble fingers of child workers (Lansky, 1997) and fishing expeditions favour children because of their small sizes which means they take up less room (Aldaba et al., 2002). Moreover, children may be favoured over adults because using children is cheaper than using adults (Nkurlu, 2000). That is, with adults, employers have to enter into employment contracts whereas with children, the employer is able to dictate the terms and the conditions of work including wages, working hours and rest periods. Furthermore (Lim, 2002), states that children are easier to manage, control and discipline; they know less about their rights and do not know where to turn to for complaints, help and rescue. It is argued therefore that children may be favoured over adults because more work can be extracted from them owing to their greater docility and lack of awareness of and ability to claim their rights (ILO, 2002).

2.7 Effects of Child Labour

It is clear that children at work are a special risk category for health and safety purposes (WHO, 1987; O'Donnell, 2002) although few studies are available concerning the health status of working children, and these are mainly descriptive and are not comparable with each other. Furthermore, only limited information is available on how different kinds of work affect children's health and development. There seems little doubt that the interrelationship between physical characteristics, working environment and emotional development is little understood (Heptinstall et al., 1997) and that understanding is the key to preventing accidents and injury (White and O'Donnell, 2001). Table 2.5 provides a summary of the limited published studies available from the Ovid Medline Database on the different effects of child labour in developing countries.

In total there were 12 studies reviewed on the effects of child labour in developing countries. Ten of these studies were cross-sectional; one was a case control and one a convenience qualitative study. All the children in the studies were between the ages of 5-17 years and had suffered the effects of working. Eight of the studies reported a generally lower level of health status in working children compared to that of non-working and reported health problems such as malnutrition; anaemia and stunted growth while four of the studies reported work related injuries. Only four of these studies adjusted for confounding variables such as age, education, parental education and father's occupation.

The majority of the studies showed that adverse effects were associated with working even though a number of the studies were not well-designed. The overall findings suggest that work-related children are much worse off than non-working children however, significant confounding effects cannot be excluded.

Table 2.5: Studies of child labour in developing countries

Reference	Study design	Sample size	Country	Age range	Findings
Nuwayhid et al. (2005)	Cross-sectional	78 working 60 non working	Lebanon	10-17 years	▪ Working children reported a higher number of injuries and recent skin, eye and ear complaints & changes in skin and nails. ▪ No differences noted in height or weight or reports of anxiety, hopelessness and self-esteem ▪ Regression analysis adjusted for age, years at school, education of mother and father and occupation of father.
Omokhodion & Omokhodion (2004)	Cross-sectional	223 working 230 non-working	Nigeria	8-15 years	▪ No difference in the occurrence of disease between working and non-working ▪ Malnutrition more prevalent in working children & sig. underweight & stunted compared to non-working ▪ More working children reported fever, visual problems, skin lesions, muscular and joint pain, diarrhoea and Schistosoma ova.
Gharaibeh & Hoeman (2003)	Qualitative descriptive	41 working	Jordan	<15 years	▪ Children in child labour were poor and dropped out of school to assist their families ▪ Working children exposed to health hazards such as inhaling chemical fumes and paints, injury from metal parts falling and cutting them, cold hands and feet, eyes burning and hand injuries ▪ Verbal, physical and sexual abuse also reported by children in the study
Venkateswarlu et al. (2003)	Descriptive	100 working children in cottonseed fields	India	7-14 years	▪ Most of the children interviewed were in debt bondage to pay off a family loan or advance and had dropped out of school or had never attended. ▪ Children earned 18 rupees for 12 hr days ▪ Children reported exposure to pesticides and complained of headaches, dizziness, skin and eye irritations after spraying of the pesticides ▪ Work not only affected education but also placed children at risk of physical and mental abuse.

Table 2.5: Studies of child labour in developing countries (continued)

Reference	Study design	Sample size	Country	Age range	Findings
Tabassum and Baig (2002)	Cross-sectional	150 working children	Pakistan	12-14 years	▪ Reasons children were working were for family support (89%), parent's pressure (5%), fond of work (4%), learning skills (1%) and self support (1%). ▪ Majority were working < 7hrs a day ▪ 79% stated they did not like to work and wanted to study, play, be born in another family and become doctors, engineers and officers. ▪ Children deprived and trapped b/w work for family and the desire of living the life of a child.
Hawamdeh and Spencer (2001)	Cross-sectional	135 working children	Jordan	10-16 years	▪ Children started working at early age. 76% started work at or before the age of 11. ▪ High prevalence of stunting and anaemia noted in working children ▪ High levels of parental illiteracy and poor education.
Estrella-Gust (2000)	Cross-sectional	30 child workers in footwear industry	Philippines	5-17 years	▪ Subjective complaints included nasal irritation, light/heavy headedness and musculoskeletal problems ▪ Physical exam revealed cervical lymphadenopathy, pale conjunctivae and multiple carious teeth as well as tonsillo-pharyngeal congestion in 3 subjects ▪ Inadequate equipment & lacked basic safeguards
Hadi (2000)	Cross-sectional	4643	Bangladesh	10-15 years	▪ 20% of 4643 children aged 10-15yrs working ▪ Poverty had a sig. positive assoc. with child labour, more boys than girls in the workforce ▪ Working had sig. neg association with schooling ▪ 2.3% of children reported physical assault at work, 2% never received full wages, 1.7% were forced to involve in inappropriate acts & 3% were forced to work long hours beyond their capability. Younger children more vulnerable to physical abuse than older children. ▪ Multivariate analysis controlled for age & sex found the out-of-school children & children of illiterate, landless & unskilled labourers were more likely to be abused.

Table 2.5: Studies of child labour in developing countries (continued)

Reference	Study design	Sample size	Country	Age range	Findings
Nath and Hadi (2000)	Cross-sectional	3809 children	Bangladesh	10-14 years	▪ Inverse relationship b/w working and education. As years of schooling of children & their parents increases, the tendency of children to participate in the labour force decreases ▪ Regression model included age, child's education, mother's education, father's education, land ownership of the household and father's occupation
Ambadekar et al. (1999)	Case control	223 working 223 non-working	India	8-15 years	▪ Weight and height estimates of controls were more than those of child labourers ▪ Malnutrition was prevalent in both groups ▪ Delayed genital development in the child labourers ▪ Child labour has deleterious effect on the growth of a child ▪ Confounding of age and sex controlled for using standard deviation scores
Mitra (1994)	Cross-sectional	40 working 40 non-working	India	7-14 years	▪ 85% of the children worked for more than 10 hours a day and 55% worked for 13-14 hours a day ▪ Significant difference between the education of working children and non-working with 85% of the non-working going to school regularly ▪ Financial reasons main reason for working ▪ Differences in nutritional consumption ▪ 30% of child workers had no aspirations other than to continue in the same work.
Mitra (1993)	Cross-sectional	40 working 40 non-working	India	7-14 years	▪ Working children in small scale leather workshops significantly reported more low back and ankle pain, dizziness and tingling pain in the hands than the non-working children ▪ No sig. differences for height, weight, nutritional state and general morbidity pattern between the two groups ▪ Symptoms may be due to sitting posture & chemical exposure from glues and solvents

The negative consequences of child labour are not limited to health effects but also to deprivation of schooling and psycho- emotional effects on the child. Because working children are easier to manage, they often become objects of extreme exploitation in terms of toiling for long hours for minimal pay (Forastieri, 2002). The nature and severity of the forms of exploitation vary from one region to another and from country to country and the hazards that children face vary according to the occupation and the specific working conditions. However, certain risks are common to most of them, including poor sanitary conditions, inadequate or non-existent personal protective equipment, inappropriate work space and installations, old machinery and inadequate tools, physical strain, long hours of work and low wages (Nkurlu, 2000). Additionally, child labour may impair healthy mental development in many ways as it exposes children to the risks of physical, psychological or sexual abuse (Hadi, 2000). The following sections examine the evidence for the various effects of child labour including the deprivation of schooling, psycho- emotional and health effects.

2.8 Schooling Effects

Illiteracy is a detrimental effect of child labour which carries on to adult life and deprives children of a healthy mental development. Most children in developing countries work for seven days a week and are paid less than the prevailing rates for adults in their localities (Forastieri, 2000; Nuwayhid et al., 2005). Working for such long hours in effect deprives children of their rights of expression and their right to an education. Children who work full-time often never attend school and thereby lose their inherent right to an education. Conley (2000), reports that there are 125 million children of primary school age who have not spent a single day in school and another 150 million drop out before learning to read. She states that one in every three adults in the developing world is illiterate which can be attributed to the overwhelming number of children who are working instead of attending school during their childhood. Venkateswarlu et al. (2003) reported that many children working in India between the ages of 7-14 years of age were deprived of an education because of the long 12 hour days which they worked. Furthermore, a study of 3809 children working in Bangladesh found an inverse relationship between work status and years of schooling of parents with children from illiterate families more likely to be working than those with educated parents (Nath and Hadi, 2000). This in turn may contribute to the vicious cycle mentioned earlier in section 2.1.5, where working children often have illiterate parents or heads of household who may have an influence on their children to work and so the cycle continues.

2.9 Psycho-emotional Effects

A range of negative psychological and emotional effects have been found in working children. Children are deprived of their right to recreation because they have less time to socialise outside of their work which in turn may have both psychological and emotional effects on their development (De Vries et al., 2001). The need to work also has detrimental effects on children's dreams and aspirations preventing children to aspire and think of better futures. A study in India found that the majority of child workers had no aspirations other than to continue in the same work when they were older (Mitra, 1994). In contrast, children working may find themselves deprived and trapped in the desire of living the life of a child with hopes, dreams and aspirations. A study in Pakistan which questioned working children on their hopes and aspirations found that the majority of the children wanted to study, play, be born in another family and become doctors, engineers and officers (Tabassum and Baig, 2002).

Child labour also exposes children to the risks of physical, psychological and sexual abuse (Hadi, 2000). As immature and young workers they are particularly vulnerable to abuse if they fail to perform their duties satisfactorily. A study in Bangladesh reported that the prevalence of child abuse and exploitation of young workers was widespread with 2.3% of all working children physically abused, financially exploited (2%), forced to work for long hours (3%) and forced to be involved in inappropriate activities (1.7%) (Hadi, 2000).

A study by Gharaibeh and Hoeman (2003) of Jordan also showed that working children suffered verbal, physical and sexual abuse. Boys in the study reported being subjected to verbal abuse (including derogatory insults) from the employer and other older boys who supervised the younger workers. Physical abuse commonly described as being hit with the employer's hands about the head and shoulders was reported in about 61% of cases and almost 27% of the boys reported acts of sexual abuse where in all instances except one, the abusers were older boys in the same or nearby workplaces.

2.10 Health effects

Illnesses and injuries associated with child labour appear to pose a significant public health problem (Landrigan and McCammon, 1997) in both developed and developing nations. Whilst the reasons for working may be different between developed and developing countries, workplace injuries still occur in both. However, workplace injuries in developing countries will more likely go unreported than in developed countries. There are a number of published studies on workplace injuries in developed countries which relate mainly to working teenagers and work-related injuries. Most of these studies have been undertaken in North America where there are significantly greater resources available to conduct large studies with larger sample sizes and improved study designs.

The Bureau of Labour Statistics of the US Department of Labour reported that an average of 180 work-related traumatic deaths occurred among working children and adolescents between 1992 and 1995 (Barkume, 2000). Agricultural work and farming has been ranked among the most dangerous occupations in children of developed nations with reports of fatal and serious non-fatal injuries involving heavy farm machinery, animals and the use of other equipment (Lim et al., 2004; Bancej and Arbuckle, 2000). Munshi et al. (2002) report that adolescents employed on both farm and non-farm jobs in rural Minnesota worked longer hours and were at significant risk of work-related injury. A study investigating summer work and injury among middle school students (Zierold et al., 2004) found that children aged 10-14 years who were working in the US were employed in informal job settings, such as working for someone in the home, newspaper delivery, working on family farms or in family businesses. Of these children 18% reported being injured at work and in 26% of these the injury was severe enough to affect their activities for more than three days. A hospital based study of 1361 work-related injuries in adolescent workers in New Zealand (Dufort et al., 1997), found high injury rates (13.8 injuries per 200000 hours worked) among adolescents in Dunedin, the highest rates being in the construction sector. Laceration was the main type of injury, followed by sprain/strain and foreign body. External causes of injury were mainly cutting/piercing objects followed by foreign body and being struck by or against an object. Similarly, Banco et al. (1992) report that teenagers in Connecticut working in restocking operations frequently suffered serious lacerations from box cutters used to open containers. Moreover, in developed countries, many working adolescents are disadvantaged in that their jobs are not covered by workers' compensation and many injuries and poisonings from toxic exposures go unreported (Woolf et al., 2001). The results of a study in Australia (Boufous and Williamson, 2003) suggest that younger workers are less likely to claim compensation for a work-related injury for which they should be entitled to claim. Potential reasons for lack of claiming compensation in this age group may include inexperience, little knowledge of workers' rights, and perhaps perceived fear of reprisal for reporting and concern about possible effects on future employment opportunities.

Workplace injuries in developing countries are an under-researched area and not enough reliable and published data are available on this, especially studies from the Middle East. In a report of a field investigation in Egypt of 78 working children and 104 school children between 10-14 years of age, the identified types of injuries in working children included falls (21%), overexertion (17%), striking against objects (10%), burns (9%), struck by falling objects (7%) and cuts (6%) (Graitcer and Lerer, 2000). Another study in Jordan found occupational hazards for working children included injury from metal parts falling, and causing cuts, eye burnings, and hand injuries as well as older children in the workplace fighting with them using their hands and other means of metal instruments, knives and blades (Gharaibeh and Hoeman, 2003). Nuwayhid et al. (2005) report that working children in Lebanon were almost four times more exposed to injuries in the last 12 months compared to non-working children and that almost half of the injured working children were injured at work. The top causes of injury were sharp objects, falls, and flames or hot objects, cuts and burns. Half of these injuries required days off work. The ILO (1998) has collectively reported on workplace injuries in developing countries and reports that a large number of working children were being exposed to various hazards including punctures, broken or complete loss of body parts, burns and skin disease, eye and hearing impairment, respiratory and gastro-intestinal illnesses, fever, and headaches from excessive heat in the fields or in factories.

It is argued that the reasons why children are more likely to suffer workplace injuries are that children differ biologically from adults in their anatomical, physiological and psychological characteristics because of their growth and development process (WHO, 1987; Forastieri, 2002; O'Donnell, 2002). These differences potentially make them more susceptible to occupational hazards at the workplace as compared to adult workers. It is also argued that the health effects can be more devastating for young children causing irreversible damage to their physical and physiological development including permanent disabilities with serious consequences for their adult lives (Dietert et al., 2000; Etzel, 2004). Most biological systems in the human body do not mature until about the age of 18 (National Research Council, 1993) and compared to adults doing the same type of work, children are more susceptible to various work-related injuries as reported above (Forastieri, 2002; NIOSH, 1997).

It is considered that young workers are at higher risk of injuries because they lack substantial work experience and appreciation of their workplace injury risk and receive inadequate training and supervision (The Centre for Disease Control and Prevention, 2001). This has been attributed to their physical tenderness and incomplete mental maturity and lack of awareness regarding the potential risks involved in their specific occupations or at the workplace itself. There is a major lack of fit between machines and tools designed for adults and the physical dimensions and strength of working children, which may result in an increased risk of fatigue and of work-related injury (Forastieri, 2002; WHO, 1987). Furthermore, adolescence is characterised by a rapid growth rate (National Research Council, 1993), therefore diminished coordination during these periods of rapid growth could increase the risk for work injury.

The health consequences of child labour derive primarily from the belief that work increases the child's exposure to health hazards which threaten to subject the child to illness or injury (O'Donnell, 2002). From a comprehensive study on child labour conducted by the Philippines Institute for Labour Studies in 1994, Aldaba et al., (2002), report that many child labourers were underdeveloped, undernourished, and underweight and were more susceptible to respiratory diseases than children who were not working (Aldaba et al., 2002). The study highlights that various child work, exposed children to health hazards which were not only diseases and illnesses affecting the children's health but also hazards that endangered their limbs and ultimately their lives. Another large scale ILO sponsored survey also undertaken in the Philippines (NSOP, 1998); found that of all child workers, 24% were found to suffer work related illness and/or injury, a prevalence rate much higher than that for adult workers. Most common injuries were cuts, wounds or punctures, accounting for 69% of the total. Body aches and pains (59%) and skin diseases (22%) were the most common work related illness.

A more recent study in Nigeria compared the health status of working and non-working school children. Although the findings of the study showed no differences in the occurrence of diseases between the working and non-working children, more working children were underweight and stunted which was associated with higher malnutrition prevalence among the working children (Omokhodion and Omokhodion, 2004).

Similarly a case-control study in India found that child labour had an effect on the growth of a child where child labourers were shorter and weighed less than their controls and had delayed genital development (Ambadekar et al., 1999).

Whilst many studies have reported on the delayed growth of working children and have attributed this to their work status, it is essential that factors such as poverty and lower socio-economic status be taken into account when considering the slow growth and malnutrition of working children. This study is one of the few which has attempted to eliminate the effects of confounders such as age, sex, environment, lifestyle and dietary habits.

In addition to the detriments of child labour mentioned above, studies have shown that working children are vulnerable to anaemia, fatigue and early initiation of tobacco smoking (Hawamdeh and Spencer, 2001; Forastieri, 2002). A study on children working in the footwear industry in the Philippines found that working children frequently reported problems with nasal irritation, light/heavy headedness and musculoskeletal problems. Furthermore, pale conjunctivae and multiple carious teeth, cervical lymphadenopathy and tonsillo-pharyngeal congestion were among the conditions found on physical examination of these children (Estrella-Gust, 2000).

Children aged 7-14 years working in small scale leather workshops in India significantly reported more low back and ankle pain, dizziness and tingling pain in the hands than the non-working children (Mitra, 1993).

The literature although limited therefore suggests that there are severe health consequences of children working and whilst these are not only prevalent in developing countries but also developed countries; the extent to which these conditions occur and their severity is dependant on the nature of the workplace and the tasks performed.

It is important however to note the limitations of the literature including several methodological issues related to the cross-sectional and descriptive designs used. The absence of comparisons with health status of non-working children in most of these studies is of concern and findings with prevalence rates of illness and injuries do not constitute evidence of a deleterious effect of work on health. Furthermore, it is unclear whether health effects reported are confounded by other pre-existing factors such as lower socio-economic status, lower education and/or other factors. Children working in physically demanding jobs might be working there because of their good health status or other children could have left their jobs because of injury or illness. Moreover, in most cases self-reported health problems are presented and it is not known if interviewers were blinded to reduce the effects of interviewer bias. With these limitations in mind, the studies reviewed had common findings which highlight the negative effects of child labour including lower general health, workplace injuries, schooling effects, and physical and emotional abuse among working children. Of the studies reviewed, there were no studies that showed no effects on working children which raises concerns. Furthermore, a common problem for all working populations is exposure to toxic hazards especially in developing countries where there are not many workplace controls. The following chapter will discuss toxic exposures and the vulnerability of children to toxic exposure.

An eleven year old boy working in an automotive spray painting workshop. Another eleven year old boy can also be seen working in the background

CHAPTER 3: TOXIC EXPOSURE

There are few studies on the effects of specific hazards for specific groups of children, whilst not enough information is available on short-term and long term toxic exposures and their effects on working children. Working children are exposed to toxic and hazardous substances in the workplace including exposure to solvents, lead, mercury, benzene, pesticides, alkaline corrosives, gases and fumes, cleaning agents, bleaches, drugs, acids and hydrocarbons.

The following section will examine children's vulnerability to toxic exposure and the risks associated with exposure. There is very limited research on the type, severity and outcome of the exposure of working children to toxic substances and most data on toxicological effects of hazardous substances to children have been based on environmental exposures. Whilst the magnitude of effects of environmental exposure can be expected to be different and smaller than work-related exposure (Suk et al., 2003a; Stein et al., 2002; Schettler et al., 2001), a review on environmental exposure will look at some evidence for the effects of toxic substances on children. Therefore, an overview of the literature on environmental exposure and the effects of exposure on children and in particular on neurodevelopment will be presented.

3.1 Children's Vulnerability to Toxic Exposures

Many international occupational health specialists warn of children's vulnerability to toxic exposures either in the workplace (Woolf, 2002) or environmental exposures (Landrigan and Garg, 2002). The World Health

Organisation (WHO) has called for improved studies, noting that children may not absorb, metabolize or eliminate toxic chemicals as well as adults and may be more physiologically vulnerable to their harmful effects (WHO, 1987). Furthermore, greater air, food and fluid intakes relative to body weight compared with the adult, increase the child's potential for excessive exposures (Chance and Harmsen, 1998). Children's metabolic pathways, especially earlier in their lives, are immature. Their ability to metabolize, detoxify, and excrete many chemicals differs from that of adults (Etzel, 2004). In many cases, children are less able to deal with chemical toxicants such as lead and organophosphate pesticides because they do not have the enzymes necessary to metabolize these chemicals and thus are more vulnerable to them (Charnley and Putzrath, 2001). Children are also undergoing rapid growth and development, and their developmental processes are easily disrupted thus creating greater vulnerabilities. These developing systems are very delicate and are not able to repair damage that may be caused by particular toxicants. In addition, children have more future years of life than most adults and therefore have more time to develop chronic diseases triggered by early exposures (Suk et al, 2003b). However, it is also important to acknowledge that children and adolescents may in some cases have better recuperative capacities than adults for many toxic agents on a mg/kg or surface area basis, nevertheless if the exposure does result in irreversible effects by exceeding the threshold exposure, then the impact on a developing organism can be more severe than in the adult (Brent et al., 2004).

3.2 Children and Environmental Toxic Exposures

Several studies have addressed children and environmental toxic exposures. Environmental health threats are numerous ranging from the more traditional health hazards such as poor sanitation and unsafe waste disposal to those caused by the introduction of toxic chemicals such as lead and pesticides (Suk et al., 2003). For the purposes of this thesis, it is the introduction of toxic chemicals and the effects which these have on the nervous system which is of interest.

Landrigan and Garg (2002) report that environmental toxicants can exert a range of adverse effects in children. Some of these are clinically evident, while others can be distinguished only through special testing and are not evident on the standard examination which leads to the term "subclinical toxicity". If cells in an infant's brain are destroyed by chemicals such as lead, mercury or solvents, as mentioned earlier, there is a high risk that the resulting dysfunction will be permanent and irreversible (Landrigan and Garg, 2002). Stein et al. (2002) report that exposure to mercury, polychlorinated biphenyls (PCBs) and lead contribute to a wide variety of problems, including impairments in attention, memory, learning, social behaviour and IQ. Some of the few well studied examples of neurodevelopmental toxicity resulting from early environmental exposure are provided by the cases of environmental exposures to methyl mercury PCBs and lead. The literature on environmental exposure to methylmercury, PCBs and lead will be reviewed to demonstrate the neurobehavioural effects associated with these environmental exposures. Table 3.1 provides a summary of the literature available on exposure and the reported neurobehavioural effects associated with the exposure. Of interest to this thesis are also the neurobehavioural and neuropsychological testing methods used for the assessment of these effects in order to establish which testing methods were sensitive to detecting specific neurobehavioural deficits from environmental exposure.

In total, 27 studies on neurobehavioural effects associated with environmental exposures in children were reviewed. These studies investigated the effects of prenatal exposures to methylmercury (7 studies) and PCBs (5 studies) and general environmental exposure to lead (15 studies).

Table 3.1: Neurobehavioural effects associated with environmental exposures in children

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Methylmercury Exposure						
Cordier et al (2002)	Cross-sectional	Children exposed to methylmercury from neighbouring gold mining activities (South America)	156 (104 mothers) high exposure 69 (51 mothers) median exposure 153 (115 mothers) low exposure	▪ Hair mercury samples from children and their mothers.	Neurological evaluation (children 9 mths-6 yrs), neuropsychological testing (children 5-12yrs) including, finger tapping (manual motor), McCarthy leg coordination (locomotor function), Standford-Binet copying (visuospatial), Stanford-Binet bead memory (short-term memory), McCarthy digit span (attention) & Raven Progressive Matrices (Colour) to test mother's reasoning capacity.	▪ Association found between level of exposure to mercury of mother and increased deep tendon reflexes, poorer coordination of legs and deficit in copying test score (visuospatial organisation) ▪ Regression analyses adjusted for age, sex, examiner and Raven maternal score and other potential confounders according to the test performed.
Grandjean et al (2001a)	Prospective cohort	Children prenatally exposed to polychlorinated biphenyls (PCB) from maternal consumption of pilot whale meat (Faroe Islands)	435	▪ Cord blood PCB ▪ Mercury concentration in cord blood ▪ Thyroid stimulating hormone (TSH) ▪ Tetriodothyronine (T4)	NES2 (Finger tapping, Hand-eye coordination, CPT) WISC-R (Digit span, similarities, block designs, bender visual motor gestalt) CVLT, Boston naming test.	▪ Methylmercury neurotoxicity greater hazard than PCB, however possible interaction b/w PCB and methylmercury could augment neurobehavioural deficits at high levels of mercury exposure. ▪ Regression analysis adjusted for age, gender, mother's Raven score, medical risk, parental education, paternal employment day care and acquaintance with computer.

Table 3.1: Neurobehavioural effects associated with environmental exposures in children (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Grandjean et al (2001b)	Prospective cohort	Children prenatally exposed to methylmercury from maternal consumption of whale meat (Faroe Islands)	917	▪ Mercury concentration in cord blood ▪ Hair samples (mother at parturition) and child at 12 months & 7 yrs	Functional Acuity Contrast Test, Visual evoked potentials, NES2 (Finger tapping, hand-eye coordination, CPT) Bender Visual Motor Gestalt, WISCR Block design, WISC-R digit span, WISC-R similarities	▪ Contrast sensitivity found to be associated with performance on the CPT, Bender visual motor and WISC-R block design ▪ Not associated with prenatal mercury exposure ▪ May need to control for contrast sensitivity in future studies .
Grandjean et al (1999)	Cross-sectional	Amazonian Children exposed to methylmercury from consumption of freshwater fish in four different villages (Brazil)	351 (Village A 124, Village B 112, Village C 98 and village D 86)	▪ Hair mercury concentrations of children and their mothers	Finger tapping, Santa Ana, WISC-R digit span, Stanford-Binet Intelligence scale	▪ Neuropsychological tests of motor function, attention and visuospatial performance showed decrements associated with hair-mercury concentration. ▪ Regression analysis adjusted for age, gender, health status, maternal education and maternal marital status in initial analyses but not in final equations
Davidson et al (1998)	Prospective longitudinal	Children prenatally exposed to methylmercury from maternal consumption of a fish diet (Republic of Seychelles)	711 mother-child pairs living in the Seychelles	▪ Maternal hair ▪ Total Hg at 66 months for child's hair ▪ Total Hg in fish ▪ Serum PCBs in 49 children	McCarthy scales of children's abilities (cognitive ability), Preschool language scale (expressive and receptive language ability), Letter & word recognition, Applied problems subtests of the Woodcock Johnson (W-J) tests of achievement (reading and arithmetic achievement), Bender Gestalt 9visual-spatial ability) T score from Child behaviour checklist (social & adaptive), Pure tone hearing thresholds, Raven Progressive Matrices	▪ Mean maternal total mercury level was 6.8ppm. ▪ No adverse outcomes at 66 months were associated with either prenatal or postnatal MeHg exposure. ▪ Regression analysis adjusted for child's birth weight, birth order, gender, history of breastfeeding, hearing status, medical history, maternal age, maternal smoking, maternal alcohol consumption, maternal medical history, intelligence, language spoken and HOME score.

Table 3.1: Neurobehavioural effects associated with environmental exposures in children (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Grandjean et al (1998)	Nested case control in prospective cohort	Children prenatally exposed to methylmercury from maternal consumption of pilot whale meat (Faroe Islands)	112 cases whose mothers had hair mercury conc. b/w 10 - 20µg/g 272 controls with exp> 3µg/g matched by gender, age, year of examination and maternal Raven score	▪ Hair mercury concentration of 10-20 µg/g ▪ PCB concentration in cord tissue	NES2 (Finger tapping, Hand-eye coordination, CPT), WISC-R (Digit span, similarities, block designs) Bender Gestalt, CVLT, Boston Naming Test	▪ Increased mercury exposure associated with deficits in motor coordination in finger tapping, hand-eye coordination, language function and memory in the CVLT. ▪ Subtle effects of on brain function detectable at prenatal methylmercury exposure levels considered to be safe.
Grandjean et al (1997)	Prospective cohort	Children prenatally exposed to methylmercury from maternal consumption of pilot whale meat (Faroe Islands)	917	▪ Mercury concentration in cord blood ▪ Hair samples (mother at parturition) and child at 12 months and 7 yrs	NES (Finger tapping, Hand-eye coordination, CPT), Tactual performance, WISC-R (Digit spans, similarities, block designs), Bender Gestalt, CVLT, Boston Naming, Nonverbal analogue POMS Pattern reversal visual evoked potentials, brain stem auditory evoked potentials, postural sway, child behaviour checklist, Snellen's board (visual acuity) and Functional Acuity Contrast test (contrast sensitivity)	▪ Prenatal methylmercury exposure associated with neuropsychological dysfunctions namely language, attention and memory. ▪ No associations found between methylmercury exposure and visual acuity contrast sensitivity and responses to CBCL ▪ Regression analyses adjusted for age and sex in all analyses. Different confounding variables identified for different tests and included in regression models of these tests.

Table 3.1: Neurobehavioural effects associated with environmental exposures in children (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
PCB Exposure						
Jacobson and Jacobson (2003)	Prospective longitudinal	Children prenatally exposed to PCB from maternal consumption of species of Lake Michigan Fish. (USA)	148 at 11 years of age 154 at 4 years of age	▪ Umbilical cord serum at delivery and shortly after delivery ▪ Maternal milk 4.5 months postpartum	Three forms of CPT (sustained attention), Digit cancellation (focused attention), Wisconsin card sorting test and Stroop colour-word test (executive function), Sternberg memory paradigm (mental rotation), WISC-R arithmetic and digit span (working memory), Corsi (visual-spatial analogue of digit span, Seashore rhythm test	▪ Adverse effects in children not breastfed. Prenatal PCB exposure associated with greater impulsivity, poorer concentration, and poorer verbal, pictorial and auditory working memory. ▪ No association found b/w prenatal PCB exposure and visual-spatial deficit or increased hyperactivity ▪ Regression analysis adjusted for 20 control variables.
Stewart et al (2003)	Prospective longitudinal	Children prenatally exposed to PCB (USA)	194 at 38mths of age 197 at 54mths of age	▪ Umbilical cord blood after delivery ▪ Breast milk 1 and 3 months postnatally ▪ Maternal hair 24hr after birth	McCarthy scales of children's abilities	▪ Significant associations found b/w cord blood PCBs and McCarthy performance at 38 months of age. Significant interaction b/w cord blood PCBs and maternal hair mercury. Negative association between prenatal MeHg exposure and McCarthy performance with reassessment at 44 months. ▪ Regression analysis adjusted for SES, maternal IQ, maternal education, home environment, cigarette smoking and many others (too many to list)

Table 3.1: Neurobehavioural effects associated with environmental exposures in children (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Patandin et al (1999)	Prospective longitudinal	Children enrolled in Dutch PCB/Dioxin study to assess prenatal and postnatal PCB and Dioxin exposure (Netherlands)	202 Groningen 193 Rotterdam	▪ Maternal plasma in last month of pregnancy ▪ Umbilical cord plasma after delivery ▪ Plasma samples at 42months old ▪ Breast milk sample 2wks after delivery	Dutch version of Kaufman Assessment Battery for children (hand movement, number recall, arithmetic, gross and fine motor skills, magic window, face recognition, gestalt closure, vocabulary, faces and places and riddles), Reynell Developmental Language scales (language, verbal comprehension and general mental ability - only in Rotterdam cohort)	▪ In utero 'Background' PCB concentrations associated with poorer performance on cognitive tests. ▪ No associations between lactational exposure to PCBs or Dioxins. Children breastfed performed better on cognitive tests than their formula-fed counterparts ▪ Regression analysis adjusted for maternal age, parity, sex, parental education, verbal IQ, HOME score, maternal alcohol use and smoking during pregnancy, feeding type in infancy, breast-feeding duration and study centre
Winneke et al (1998)	Prospective longitudinal	Children enrolled in European multicentric study to assess neonatal PCB-levels and developmental outcomes	171 mother-infant pairs.	▪ PCB cord blood ▪ Breast milk	Bayley Scales of Infant Development (Mental scale and psychomotor scale) and Fagan Test of Infant Intelligence (visual recognition memory test based on the infant's ability to recognize facial pictures.	▪ Significantly negative association with mental but not motor development or recognition memory in infants at 7 months of age. ▪ Regression analysis adjusted for lead in cord blood, maternal age, APGAR score or HOME (depending on which exhibited significant association with outcome

Table 3.1: Neurobehavioural effects associated with environmental exposures in children (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Jacobson and Jacobson (1996a)	Prospective longitudinal	Children prenatally exposed to PCB from maternal consumption of species of Lake Michigan Fish. (USA)	212 at 11 years of age	▪ Umbilical cord after delivery ▪ Maternal blood postpartum ▪ Maternal milk within 0.2 and 4.5 months post partum ▪ Blood samples from children at 4 and 11 years ▪ Mercury-hair samples	Wechsler Intelligence scales for children IQ test, spelling and arithmetic subtests of wide range achievement test-revised, word and passage comprehension subtests of the woodcock reading mastery tests-revised, word and passage comprehension	▪ In utero exposure to polychlorinated biphenyls is assoc. with ↓ intellectual function in school-age children. ▪ Prenatal exposure to PCB assoc. with lower full-scale and verbal IQ, memory and attention. Highly exp children were 3 times as likely to have avg IQ scores and twice as likely to be at least two yrs behind in reading comprehension. ▪ Regression analysis adjusted for SES, maternal education, vocab, (HOME) inventory, maternal marital status, smoking in pregnancy, no of children as well as many other covariates.
Chiodo et al (2004)	Nested cross-sectional	African-American inner city children participating in a longitudinal study on the effects of prenatal alcohol exposure	237	▪ Blood lead level at 7.5 yrs of age	WISCIII (coding subscale, arithmetic and digit span subscales), CPT, Tall and digit cancellation, Wisconsin Card , Tower of London, (McCarthy Scales of Children's abilities), Seashore rhythm test, Sternberg short-term memory task, mental rotation task, magnitude estimation, colour naming, Wide range assessment of memory learning (WRAML), Grooved pegboard, Corsi test, matching familiar figures test, Beery test of visual-motor integration, CBVL (teacher report) (TRF) & direct observation form (DOF)) &(ADHD)	▪ Low levels of lead exposure associated with consistent neurobehavioural deficits (overall IQ, performance IQ, reaction time, visual-motor integration, fine motor skills, attention including executive function, off-task behaviours and withdrawn behaviours on TRF. Effects on attention identified at levels as low as 3μg/dl. ▪ Regression analysis adjusted for maternal alcohol and drug use plus 19 other variables found to be related to both exposure and outcome.

Table 3.1: Neurobehavioural effects associated with environmental exposures in children (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Lead Exposure						
Ris et al (2004)	Nested cross-sectional in prospective cohort	Children from the prospective Cincinnati Lead Study (USA)	195	▪ Based on 'a priori' to focus on three indices: prenatal maternal PbB, avg childhood PbB (5yrs) and 78 month PbB.	Executive functioning (Wisconsin Card Sorting, Rey-Osterreith Complex figure), Attention (CPT – Conners version), Memory (CVLT), Achievement (Wide Range Achievement Test – 3rd Ed), Verbal (Vocab subtest of WISC-III) Visuoconstructional (WISC-III BD), Fine motor (GP, and FT)	▪ Sig. assoc found b/w 78 month PbB & fine motor function, gender & lead exposure for both attention and visuoconstruction indicating higher risk in males ▪ Regression models adjusted differently for different tests however all were adjusted for maternal IQ, SES, HOME scores & adolescent marijuana consumption.
Canfield et al (2003)	Prospective longitudinal	Children enrolled in dust-control efficacy study born between July 1994 and Jan 1995. (USA)	172	▪ Blood lead measured at 6, 12, 18, 24, 36, 48 and 60 months of age.	Stanford-Binet Intelligence Scale (Vocab, spatial pattern analysis, quantitative ability and memory) administered at 3 and 5 years of age.	▪ Blood lead conc. sig. assoc. with IQ even > 10µg/dl. Linear model shows ↑ in 10µg/dl in lifetime avg blood lead concentration assoc. with 4.6 point decrease in IQ & 7.4 points at concentrations below 10µg/dl. ▪ Regression analysis adjusted for child's gender, birth weight, iron status and mother's IQ, years of education, race, tobacco use during pregnancy, yearly household income and HOME inventory.
Campbell et al (2000)	Nested cross-sectional	Boys enrolled in Pittsburgh Youth prospective study of developmental course of delinquent behaviour. (USA)	156 boys ages 11-14yrs	▪ Tibia lead concentration measured by KXRF	Non-word repetition Task (NRT), Competing Language Processing Task (CLPT), Revised Token Test (RTT)	▪ Boys in highest blood lead quartile yet considered asymptomatic for acute lead toxicity, displayed decreased language processing performance, especially when tasks were demanding. ▪ ANCOVA adjusted for race, mother's IQ, SES and child's age.

Table 3.1: Neurobehavioural effects associated with environmental exposures in children (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Counter et al (1998)	Cross-sectional	Children living in Ecuadorian villages where lead is used in glazing of ceramics (USA)	77 children divided into two groups: 55 Neurological test group) 41 (RCPM group)	▪ Blood lead samples	Group 1: Neurological exam (visual pursuit, saccae velocity, finger to nose, standing balance, tandem walking, FT and deep tendon reflexes, R left discrimination, size discrimination, colour discrimination, DAP and simple math calculation) Group 2: Raven's Coloured Matrices	▪ Children with higher PbB levels had poorer performance on most components of neurological examination namely abnormal tendon reflexes, finger tapping, visual pursuit, size discrimination, DAP & math calculation skills. ▪ Significant correlation b/w RCPM scores and PbB levels for children ages 9 .
Stokes et al (1998)	Cross-sectional	Young adults who were exposed to lead during childhood while living near a lead smelter (USA)	281 exposed 287 controls	▪ Tibia lead concentration – KXRF (long term exposure) ▪ Blood lead	Electrophysiological tests, contrast sensitivity, peripheral vibration, sensitivity, standing steadiness, grooved pegboard, Santa Ana, NES2 (Hand-eye, finger tapping, SRT, symbol-digit substitution, serial digit learning, vocab, mood), Trail making A and B, Raven's progressive Matrices, Swedish Q16.	▪ Regression analysis adjusted for age, gender, height, BMI, skin temperature, education and trying hard, showed significant association b/w exposure and poorer performance on Hand-eye coordination, SRT, Trails B, symbol digit, serial digit learning, Raven progressive matrices and vocab. ▪ Peripheral neurological function also associated with exposure group.
Walkowiak et al (1998)	Nested cross-sectional	Children participating in a study of environmental health aspects in the cities of Leipzig, Gardelegen and Duisburg at 6 yrs of age (Germany)	120 (Duisburg – lead exp.) 191 (Leipzig – some exp.) 73 (Gardelegen – controls)	▪ Blood lead samples ▪ Urine samples for mercury excretion	WISC (German version = HAWIK, vocab, block design), NES2 (finger tapping, pattern comparison, SRT, Pattern memory, CPT). Functional acuity Contrast test (contrast sensitivity) and Titmus II (visual acuity) treated for covariate purposes only.	▪ Significant negative associations found between PbB and performance on the WISC vocab but not WISC Block design, false positive responses and false negative responses in the CPT. ▪ Different regression models used to adjust for different covariates. ▪ Parental education an important confounder for WISC performance however visual contrast sensitivity and computer familiarity proved predictive for performance on NES tests.

Table 3.1: Neurobehavioural effects associated with environmental exposures in children (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Altmann et al (1997)	Nested cross-sectional	Children participating in a study of environmental health aspects in the cities of Leipzig, Gardelegen and Duisburg at 6 yrs of age (Germany)	364 in 1991 382 in 1994	▪ Blood lead samples	Visually evoked potentials (computer controlled, four-channel electrophysiology system), NES (finger tapping, simple visual reaction time, pattern comparison, pattern memory, memory for design, CPT), Titmus II (visual acuity), Functional Acuity Contrast Test (Contrast sensitivity).	▪ Lead related deficits found for tapping and pattern comparison and significant performance deficits in children with blood lead concentrations about 10µg/dl. ▪ Regression analysis adjusted for age, gender, parental education ▪ Field studies showed that all test can be successfully performed even on pre-school-age children.
Tong et al (1996)	Prospective cohort	Children born in or around lead melting town of Port Pirie between 1979 and 1982 (Australia)	375	▪ Blood lead samples at 11-13 yrs of age	WISC-R (12 subtest of performance and verbal IQ)	▪ Sig. assoc. b/w children's IQ and blood lead concentrations at most ages although IQ deficits assoc with blood lead concentrations measured at earlier ages. Assoc. b/w early exp to environmental lead and cognitive development persists into later childhood. ▪ Regression adjusted for 27 covariates
Dietrich et al (1993)	Prospective cohort	Children enrolled in the Cincinnati prospective study (USA)	245	▪ Blood lead ▪ Estimations of prenatal, neonatal and mean PbB levels	Bruininks-Oseretsky Test of Motor Proficiency (Running speed and agility balance, bilateral coordination, strength, upper-limit coordination, response speed, visual motor control, upper-limb speed and dexterity)	▪ Neonatal blood lead levels associated with poorer performance on a measure of upper-limb speed and dexterity and a composite index of fine-motor coordination. ▪ Postnatal blood lead levels significantly associated with poorer scores on measures of bilateral coordination, visual-motor control, upper-limb speed and dexterity and fine-motor composite. ▪ Regression analysis adjusted for HOME, maternal IQ, social class, child gender.

Table 3.1: Neurobehavioural effects associated with environmental exposures in children (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Bellinger et al (1992)	Prospective cohort	Children born between Aug 1979 – April 1981 with umbilical cord blood lead levels > 10th percentile, approx. at 50th percentile or greater than 90th percentile (USA)	148	▪ Blood lead samples at 6, 12, 18, 24 and 57 months and at 10 yrs of age.	WISC-R and Kaufman Test of Educational Achievement (K-TEA) at 6, 12, 18, 24 and 57 months and at 10 yrs of age	▪ Higher levels of blood lead at 24 months were significantly associated with lower scores on WISC-R and K-TEA tests. ▪ Continued presence of an association at 10 years noted at 5 years between child's blood level at 24 months and cognitive function in both intelligence & academic achievement. ▪ Regression analysis for potential confounding
Grandjean et al (1991)	Nested case-control	Children	110 cases 103 controls	▪ Dentin lead ▪ Blood lead	Wechsler Intelligence Scale for Children (WISC) Verbal IQ and Bender gestalt test scored by Göttingen system	▪ Children from high-lead exposure group who had experienced neonatal jaundice showed impaired perform on NB tests compared to other high-lead children. ▪ Bender gestalt scored by the Göttingen system most sensitive to lead exposure.
Needleman et al (1990)	Prospective cohort	Children enrolled in 1st and 2nd grade in Chelsea and Somerville, Massachusetts between 1975 and 1978. (USA)	132 re-examined	▪ Previous dentin lead levels computed into an arithmetic mean lead concentration	Symbol-digit, hand-eye coordination, simple visual-reaction time, finger tapping, pattern memory, pattern comparison, serial-digit learning, vocab, grammatical reasoning, switching attention, mood scales, California Verbal Learning, Boston Naming, Rey-Osterreith Complex Figure, Word-identification, Self-reports of delinquency, review of school reports.	▪ Higher dentin lead levels associated with lower class rank, increased absenteeism, lower scores on vocab, grammatical reasoning, slower finger tapping speed, longer reaction times, poorer hand-eye coordination and lower reading scores. ▪ Regression analysis adjusted for mother's (age at time of birth, educational level, IQ, socioeconomic index (HE) & child's sex, age at time of testing, birth order, alcohol use & neonate hospitalisation. ▪ Authors conclude that exposure to lead in childhood is assoc. with deficits in CNS functioning & persists into young adulthood.

Table 3.1: Neurobehavioural effects associated with environmental exposures in children (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Raab et al (1990)	Cross-sectional	Children enrolled in the Edinburgh lead study (UK)	500	▪ Blood lead levels	Inspection time (IT) and Reaction Time (RT)	▪ Both IT and RT performance worse with higher blood lead levels. ▪ Regression analysis adjusted for school and 33 covariates found that assoc. b/w lead and IT error rates remained significant however lead and RT error rates did not.
Harvey et al (1988)	Cross-sectional	Children living in inner-city dwellings age 5.5years (UK)	201	▪ Blood lead levels	Wechsler Pre-school and primary scale of intelligence, Reitan Indiana Battery, Bender Visual Motor Gestalt Test (BVMG), Klove-Matthews Motor Steadiness Battery, VRT (visual reaction time), vigilance performance (CPT), Behaviour. (school and home), Sattler Rating Scale, Werry-Weiss-Peters Scale	▪ No significant relationship found between overall IQ and blood lead levels ▪ Small significant associations found between blood lead levels and motor skill and attention dysfunctions. ▪ Regression analysis adjusted for confounding variables however unclear as to what these are.

3.2.1 Methylmercury exposure

Methylmercury exposure is a well studied example of how children are affected by environmental exposure. Human exposures to mercury occur in the form of elementary mercury vapour, inorganic mercury with varied oxidation states of the metal and organic mercurial such as methyl mercury (Verity and Sarafian, 2000). The methylated or organic form of mercury is a far more potent CNS poison than mercury in its inorganic state (Weiss, 1979). Elemental and organic mercury cause very different forms of neurotoxicity and evidence of environmental methylmercury poisoning have occurred in Japan and Iraq (Spencer et al., 2000). Dietary fish contaminated with mercury (in the form of methylmercury) is for many people the largest source of exposure (Schettler, 2001). The effects of methylmercury on the developing brain were first recognized in the tragic poisoning epidemic in Minimata Bay, Japan, during the 1950s when residents regularly consumed fish highly contaminated with methylmercury resulting from industrial discharges into the bay (Stien et al., 2002). Infants born to mothers who consumed the fish had a variety of neurological findings, including mental retardation, disturbances of gait, speech, sucking, swallowing and reflexes (Harada, 1978; Watanabe and Satoh, 1996). Prenatal exposure occurs when mercury easily crosses the placenta and enters the foetal brain where it disrupts many processes necessary for normal brain development (Atchison and Hare, 1994). In utero exposure to even low doses results in decreased intelligence and altered behaviour in children (National Research Council 2000; Grandjean et al., 1997).

Mercury-related neuropsychological dysfunction in children environmentally and prenatally exposed to mercury through the environment and contaminated fish consumption have also been identified in the Faroe Islands (Grandjean et al., 1998). This prospective study used different neuropsychological tests, including finger tapping, hand-eye coordination, continuous performance test, Wechsler Intelligence Scale for Children-revised, digit span, similarities, block designs, Bender Visual Motor Gestalt Test, Boston Naming Test, Californian Verbal Learning Test for children and the nonverbal analogue Profile of Mood States (POMS). Neuropsychological dysfunction was most pronounced in the domains of language, attention, motor function and memory at prenatal methylmercury exposure levels previously considered to be safe (Grandjean et al., 1997; Grandjean et al., 1998), although, further research has suggested that these results may have been confounded by exposure to polychlorinated biphenyls (Grandjean et al., 2001a) and may not be a direct effect of methylmercury exposure. Additional analysis on the same study cohort also found that contrast sensitivity was a predictor of performance on the continuous performance test, Bender visual motor and the WISC-R block design, and could be an important determinant of performance on neurobehavioural tests that involve visual stimuli especially when disorders affecting the visual system exist (Grandjean et al., 2001b).

In a cross-sectional study on Amazonian children exposed to methylmercury from consumption of freshwater fish in Brazil, decrements in motor function, attention and visuospatial performance were associated with hair mercury concentrations (Grandjean et al., 1999). Similarly in another cross-sectional study, Cordier et al., (2002) studied neurodevelopmental effects among children prenatally exposed to methylmercury children in French Guiana and found an association between mercury exposure and increased deep tendon reflexes, poorer co-ordination of the legs, and decreased performance in the Stanford-Binet Copying score, which measures visuospatial organisation. The cross-sectional design of these two studies and the retrospective measurement of exposure should be taken into consideration when estimating the true levels of exposure and their effects on neurobehavioural functioning. In addition, the presence of other neurotoxicants (namely lead and PCB) in the environment of the Amazon and French Guiana should also be considered as potential contaminants of exposure.

From the seven papers reviewed (4 from the same longitudinal cohort), on methylmercury exposure and its effects on neurodevelopment, four showed significant associations between levels of exposure and decrements in neuropsychological test performance (Cordier et al., 2002; Grandjean et al., 1999; Grandjean et al., 1998; Grandjean et al., 1997). In contrast to these findings, the study by Davidson and colleagues (1998) in the Seychelles showed no adverse effects associated with both prenatal or postnatal methylmercury and neuropsychological test performance. One study found interaction effects between PCB and methylmercury exposure which the authors of the study suggest may augment the neurobehavioural deficits associated with high levels of mercury exposure (Grandjean et al., 2001a). Moreover, another study concluded that other neurobehavioural effects such as contrast sensitivity may also influence neurobehavioural test performance (Grandjean et al., 2001b).

Overall, four of the papers reviewed (two from the same study) were prospective cohort studies utilizing biological exposure measurements including hair mercury and cord blood samples, two were cross-sectional utilizing hair mercury for the measurement of methylmercury exposure and one nested case control (in a prospective cohort) study, also using hair mercury for measurement of exposure, which suggests relatively quantifiable measurements of exposure in all of the studies reviewed. All of the studies were quite well designed and adjusted for confounding variables including age, sex, and maternal characteristics.

The replication of the findings from these studies strongly suggests that children prenatally exposed to methylmercury exposure showed decrements in memory, motor function, coordination, language dysfunctions and attention deficits. These findings also suggest that the neurobehavioural tests used in children prenatally exposed to methylmercury are sensitive indicators for detecting neurobehavioural effects from this exposure.

3.2.2 Polychlorinated Biphenyls (PCBs) exposure

Another environmental exposure which has been studied in children is exposure to PCBs. Like mercury, PCBs can contaminate fish, but PCBs also end up in many other foods, including beef, dairy products, pork and human breast milk.

PCBs and their metabolites have been found to interfere with thyroid metabolism (Brouwer et al., 1998), thus providing a mechanism for developmental effects on hearing thresholds and other nervous system functions (Goldey and Crofton, 1998). Epidemiological studies have applied various biomarkers to assess prenatal PCB exposure, and neurobehavioural dysfunctions have been determined with a range of neurobehavioural tests (Grandjean et al., 2001). Neurobehavioural and neuropsychological tests have been used in a number of epidemiological studies to assess dysfunctions and prenatal PCB exposure. (Patandin et al., 1999; Winneke et al., 1998). In early childhood, prenatal PCB exposure has been associated with a variety of cognitive impairments including memory and attention, decreased verbal ability and impaired information processing (Jacobson et al., 1985).

There were five papers (two from the same cohort) reviewed on the neurobehavioural effects of PCB exposure and all of these studies employed prospective longitudinal designs with a combination of umbilical cord serum and breast milk for measurement of exposure, and a wide range of neuropsychological tests for measurement of the effects of exposure.

Jacobson and Jacobson (1996a) report on an 11 year study of children who were exposed to PCBs in utero. A variety of neuropsychological tests including the Wechsler Intelligence scales for children IQ tests, spelling and arithmetic subtests of wide range achievement test, word and passage comprehension subtests of the woodcock reading mastery tests, on the children revealed that PCB exposure in utero correlated with decreased IQ in children. In fact, the children exposed to the highest amounts of PCBs had an average IQ that was 6.2 points lower than that of the other children in the study. Furthermore, exposure to PCBs correlated with decreases in children's ability to comprehend words as well as whole bodies of reading material (Jacobson and Jacobson, 1996a). Similarly, Jacobson and Jacobson (2003), in a more recent analysis of data from the same cohort found prenatal PCB exposure was associated with greater impulsivity, poorer concentration and poorer verbal, pictorial and auditory working memory assessed using a selection of 15 neuropsychological tests which measured sustained attention (using a continuous performance test), focused attention (using digit cancellation), executive function (using the Wisconsin card sorting test), working memory (using a Sternberg Memory paradigm) and information processing (using Mental rotation) in children not breastfed whilst no associations were found between prenatal PCB exposure and visual-spatial deficits or increased hyperactivity.

In another study, significant associations were found between cord blood PCBs and McCarthy performance of children prenatally exposed to PCB in the USA at 38 months of age, whilst negative associations between prenatal methylmercury exposure and McCarthy performance were found in children at 44 months with higher levels of prenatal PCB exposure (Stewart et al., 2003). Winneke et al., (1998) in a European study also reported negative associations with mental function but not motor development or recognition memory in infants at 7 months of age measured using Bayleys scales of infant development and the Fagan test of Intelligence.

Other adverse cognitive deficits associated with PCB exposure were found with lower scores on the overall cognitive and sequential and simultaneous processing scales of the Kaufman Assessment Battery for children in a prospective study of children in the Netherlands prenatally exposed to PCB and dioxins (Patandin et al., 1999).

There are number of methodological issues to be considered in the studies of PCB exposure, including issues related to exposure assessment, sample selection and control of potential confounding variables. Children who are environmentally exposed are poorest and usually live in areas that are dirtiest and may have parents with lower education and potentially lower IQ (Schantz, 1996).

All the studies reviewed on PCB exposure were of strong research design which used prospective longitudinal studies and adjusted for potential confounding for a number of covariates including socioeconomic status, maternal IQ, the HOME (Home Observation for Measurement of the environment inventory) assessment score and many other covariates. The overall results from these studies suggest that PCB exposure in children is associated with decrements in cognitive functions more than motor development and that the public health implications from the effects of this exposure could potentially be very significant and should be considered.

3.2.3 Lead exposure

Lead (Pb) is one of the first and perhaps best understood examples of a common chemical that harms brain development (Stein et al., 2002). Humans are exposed to inorganic lead primarily by inhalation or ingestion whereas cutaneous absorption is less significant (Spencer et al., 2000). Winneke et al., 1996, state that "when comparing neurobehavioural observations from occupational lead-exposure of adults on the one hand, and environmental lead exposure of children on the other, it appears that the developing brain relative to the mature brain is more at risk" (Winneke et al., 1996). Although very high lead exposures were recognized to cause encephalopathy, coma and death in children as early as 1900 (Needleman et al.,1990), the enduring effects of lead poisoning on child development became apparent only with the publication of longer follow-up observations in the 1940s, which noted persistent impairment in intellect, behaviour and sensory motor function (WHO, 1995). As such, several studies of lead toxicity have measured clinically asymptomatic children (Altmann et al., 1997; Bellinger et al., 1992; Raab et al., 1990; Walkowiak et al., 1998) where exposure to lead was found to have caused decreases in intelligence and alteration of behaviour, moderate deficits in gross and especially fine-motor developmental status and neurobehavioural effects (Dietrich et al., 1993; Grandjean et al., 1991), even in the absence of clinically visible symptoms of lead toxicity.

Some of the studies on environmental lead exposure in children have been reviewed in Table 3.1. Of the 15 studies reviewed on lead exposure in children, five were prospective cohort studies (Canfield et al., 2003; Tong et al., 1996;

Dietrich et al., 1993; Bellinger et al., 1992; Needleman et al., 1990), using blood lead levels and dentin lead (Needleman et al., 1990) as measurements of lead exposure. The remainder 9 cross-sectional studies and 1 case control study, also utilized blood lead levels while others used dentin lead (Grandjean et al, 1991) and tibia lead (Campbell et al., 2000; Stokes et al., 1998) as measurements of lead exposure. Table 3.1 summarises the associations found between lead exposure and neuropsychological test performance.

An 11 year follow-up study on low level lead exposure in primary school children found that associations previously reported between lead and children's academic progress and cognitive functioning persisted into young adulthood (Needleman et al., 1990). In this study, earlier exposure to lead and its persistent toxicity were found to be significantly associated with diminished academic success, specifically a sevenfold increase in failure to graduate from high school, lower class standing, greater absenteeism and impairment in reading skills. The children's performance on a selection of neurobehavioural tests, namely the Neurobehavioural Evaluation System, California Verbal Learning Test, Boston Naming Test, the Rey-Osterreith Complex Figure and word-identification test also showed deficits in vocabulary, fine motor skills, reaction time and hand-eye co-ordination (Needleman et al., 1990). Similarly, in more recent literature (Dietrich et al., 2001), lead exposure in children has been reported to be associated with cognitive impairment, learning disabilities and behaviours that contribute to the likelihood of dropping out of school. Dietrich et al. (2001), investigated the association of early exposure to lead and juvenile delinquency and found that both prenatal and postnatal exposure to lead were associated with reported antisocial acts and may play a measurable role in the epigenesis of behavioural problems. Moreover, significant adverse central and peripheral neurological effects were reported in a group of young adults 20 years after childhood environmental exposure to lead (Stokes et al., 1998).

Bone lead levels have also been found to be associated with language processing abilities (Campbell et al., 2000). In this study, a group of 11-14 year old boys who were considered asymptomatic for acute lead toxicity but had relatively higher bone lead burdens had decreased language processing performance when assessed on the non-word repetition task, competing language processing task and revised token test, especially when tasks were demanding. The results from this investigation also extend evidence of the negative effect of lead on linguistic function to include the processing of more complex phonological and lexical forms (Campbell et al., 2000).

A cross-sectional study of children living in the Ecuadorian villages where lead was used in the glazing of ceramics divided children exposed to lead into two groups based on test focus. Group one was assessed on a range of clinical neurological tests including visual pursuit, saccade velocity, finger to nose, standing balance and tandem walking, finger tapping, deep tendon reflexes, right/left discrimination, size discrimination (large/small), colour discrimination, draw-a person and simple math calculation. Group two was assessed by using Raven's Coloured Progressive Matrices (RCPM). In group one, children with higher PbB levels had poorer performance on six of the neurological tests: tendon reflexes, finger tapping, visual pursuit, draw-a –person, size discrimination and math calculation skills whilst regression analysis revealed a negative correlation of borderline significance between the RCPM scores and lead levels in group two and statistically inverse correlation between the RCPM score and PbB levels for children over nine years of age (Counter et al., 1998). Given the small sample size in the study and the uncertainty for dividing the children into two groups to receive different neurological examinations, this study suggests that a cumulative lead exposure effect in older children with high PbB levels may be at greater risk for cognitive impairment.

Ris et al. (2004) also report on the significant associations found between lead exposure and performance on a number of neuropsychological measures. The study assessed five functional domains in memory, learning/IQ, attention, visuoconstruction and fine-motor function in male children enrolled in the prospective Cincinnati lead study. They were tested using the Wisconsin Card Sorting, Rey-Osterreith for executive function, the CPT for attention, California Verbal Learning Test for memory and other tests of verbal (WISC III), visuoconstructional (WISC III Block Design) and Fine motor (Grooved Pegboard and finger tapping) functions. Following adjustment for maternal IQ, socioeconomic status, total average HOME scores and adolescent marijuana consumption and a number of other different factors for each specific measure, significant associations were found between lead exposure and fine motor function, attention and visuoconstruction with an indication of a higher risk in male children.

A number of studies have also investigated the specific associations found between lead exposure and performance on IQ tests. Low levels of lead as low as 3µg/dl were found to be associated with neurobehavioural deficits (overall IQ, performance IQ, reaction time, visuomotor integration, fine motor skills, and attention including executive attention, off-task behaviours and withdrawn behaviours) in African American inner city children participating in a longitudinal study on the effects of prenatal alcohol exposure (Chiodo et al., 2004). Tong et al. (1996) also found significant associations between children's IQ and blood lead concentrations at most ages of children born in or around a lead melting town in Australia. Similarly, a significant association was found between blood lead concentrations and IQ measured on the Stanford-Binet Intelligence scale at levels below 10µg/dl in a longitudinal study of children in the USA (Canfield et al., 2003).

In contrast, Harvey et al. (1988) found no significant associations between blood lead levels and overall IQ measured on a number of neurobehavioural tests including the Wechsler pre-school and primary scale of intelligence, Reitan Indiana battery, Bender visual motor gestalt, Klove-Matthews Motor Steadiness Battery, Sattler rating scale, Werry-Weiss Peters scale and measures of reaction time and vigilance performance. However significant associations were found in the measures of motor skills and reaction time.

There is considerable debate in the literature about environmental lead exposure in children and the validity of some of the lead based results, specifically the Needleman studies (Ernhardt et al., 1993). A number of issues need to be considered when interpreting the data presented by these studies particularly for example, the influence of selection bias on the associations found in the Needleman studies (Needleman et al., 1990). The subjects retested in 1988 had more favourable characteristics (lower lead levels, higher socioeconomic status and higher IQ scores and teacher's ratings of classroom behaviour) than those who could not be located or declined to participate in the follow-up part of the study. This raises the questions of whether or not these subjects were representative of the initial group of subjects tested in 1979 (Needleman et al., 1979) and the validity of the prospective outcomes.

Another critical problem identified in these studies is the measurement of lead exposure. Researchers have used either blood lead or dentin lead as a marker of lead exposure. Some studies calculated exposure levels based on a single estimation by formulating indices based on self report or previous blood lead level and dentin concentrations (Ris et al, 2004; Dietrich et al., 1993; Needleman et al., 1990). Whilst blood lead is a useful measure of recent exposure it may also be a poor indicator of previous levels of exposure since lead only remains in the blood for a brief period of time before being excreted or stored in bone. Dentin lead has the advantage of reflecting cumulative lead exposure; however it still cannot be used to assess age of exposure or patterns of previous exposure (Banks et al., 1997). A single estimation may be susceptible to the influence of changing environments and multiple measures across time provide a more reliable index of exposure.

Other methodological issues which need to be observed in the literature include problems with study design and limited control of potential confounding biases. A majority of the studies reviewed were cross-sectional studies which controlled for a number of covariates; however, there seems no agreement to some extent in the selection, measurement and interpretation of covariates. Whilst some studies have associated lead exposure with lower socioeconomic status and parental IQ and education and adjusted for these accordingly (Ris et al, 2004; Canfield et al., 2003; Campbell et al., 2000), other studies have adjusted for other factors (Chiodo et al., 2004).

However regardless of these limitations, it must be emphasized that peak lead exposure typically occurs in children at an age when cognitive processes are rapidly developing, and the child is likely to have limited resources to counteract this exposure. Furthermore, the overall weight of the literature on lead exposure in children reviewed, strongly suggests the continued finding that childhood lead exposure is neurotoxic to the developing child with dose-response effects.

3.2.4 Summary

The consistencies in the literature reviewed, strongly suggest that environmental exposure to methylmercury, PCBs and lead is associated with decreased functional performance on a number of neurobehavioural and neuropsychological tests, with displayed dose-response effects. Prenatal exposure to lower levels of methylmercury showed adverse effects on attention, sensory and motor function, whilst exposure to prenatal PCBs also showed decrements in neurobehavioural and cognitive functioning. Lead was found to be associated with a number of effects including decreases in IQ, poor school performance, and attention deficits. The use of neuropsychological tests for the assessment and measurement of adverse effects from exposure have shown to be effective in the measurement of neurobehavioural deficits in children.

3.3 Children and occupational toxic exposures

Whilst the previous section has reviewed and identified some of the effects of toxic exposures of children in the environment, it also illustrates and to a certain extent confirms the vulnerability and susceptibility of children to neurotoxicants. Nevertheless, there is very limited research available on occupational toxic exposures in working children, despite working children being exposed to a range of toxic substances as illustrated in the discussion on child labour earlier in this chapter. A case study measuring toxicants in working children, found that seven out of ten boys working as shoeblacks had urinary excretion of phenols above the reference value indicating high exposure levels to benzene (Harari et al. ,1997).

Of particular interest and relevance to this thesis are the effects of solvents on working children, specifically neurobehavioural effects. There is a lack of information on solvent exposure in children in the literature and only very limited information on environmental exposure to solvents which clearly identifies the gap in this area of research. The next section of the thesis will introduce solvents and present the concept of solvent neurotoxicity.

3.4 Solvents

In this section, solvents will be defined and the characteristics of solvents will be discussed. The term "organic solvents" refers to a group of volatile compounds or mixtures that are relatively stable chemically and that exist in the liquid state at temperatures of approximately 0° to 250°C (32° to 482°F) (Spencer et al., 2000). Solvents are widely used in industrial societies in a wide range of processes. An estimated 49 million metric tons of solvents are produced per year in the USA alone (Hartman, 1995) and more than 9.8 million workers inhale or come into skin contact with solvents every day (Cincinnati, 1987) either occupationally or through the environment.

3.4.1 Effects of Solvent Exposure

There are many occupations in which workers can be exposed to solvents, including automotive manufacturing and repair, paint and varnish manufacturing, the electronic industry, industrial cleaning, metal-part degreasing and dry-cleaning (White and Proctor, 1997). Clinically, it is especially common to see patients working in dry-cleaning, the paint industry and in occupations involving mechanical or engineering work that requires the use of degreasers. It should be noted also that patients can experience exposure environmentally, through hobbies, and by self-administration of solvents such as ethanol, toluene and gasoline (Hartman, 1995)

Common organic solvents are classified as aliphatic hydrocarbons, cyclic hydrocarbons, aromatic hydrocarbons, halogenated hydrocarbons, ketones, amines, esters, alcohols, aldehydes, and ethers. Many common solvents often exist as mixtures or blends of chemical compounds (e.g., Stoddard solvent and thinners) (WHO, 1985; Parrish, 1983). Solvents are used in paints, adhesives, glues, coatings, and degreasing/cleaning agents, and in the production of dyes, polymers, plastics, textiles, printing inks, agricultural products, and pharmaceuticals (WHO, 1985). Numerous conditions have been reported as a result of contact and exposure to solvents. The toxicological effects common to most solvents are associated with their irritant effects on the mucous membranes, the effect on the skin and the depression of central nervous system function and are dependent to a large extent on the route, chronicity and the severity of exposure (NIOSH, 1997). The differentiation between short-term or acute and long-term or chronic exposures is like distinguishing between hours to days and months to years. Acute effects tend to resolve soon after discontinuation of the exposure, sub-chronic effects are most often reversible within 6 months to one year after discontinuation of the exposure; while chronic effects may not be reversible or only partially so within more than one year of termination of the exposure (NIOSH, 1997).

Even though there are so many different types of solvents, there are many common characteristics. Curtis and Keller (1986) state that all solvents share common characteristics including volatility (significant vapour pressure) and solvency (pass through intact skin). In addition, solvents are lipophilic with an affinity for nerve tissue, are soluble in blood and pass rapidly through lung tissue. Furthermore, solvents seem to have relatively harmless odours which may provoke minor irritation until high concentrations are achieved. Exposure to solvents has also been reported to cause chemical dependency (Hartman, 1995).

Table 3.2 provides a summary of studies on symptoms including neurobehavioural symptoms associated with occupational solvent exposure in adults. The table highlights the different study designs, study subjects (occupations), exposure measurements, tests used for the measurement of different symptoms and the findings from the research.

In total, 33 studies were reviewed. Three of these were prospective longitudinal studies; two were controlled exposure studies, three case studies, three case control studies and 22 cross-sectional studies. The majority of the studies involved adults occupationally exposed to solvents except the controlled exposure and case studies (Mackie et al., 2004; Ozgenal et al., 2004; Jones et al., 2003; Van Thriel et al., 2003). In the majority of the studies, solvent exposure was assessed by calculating exposure indices based on self-reports, work history, duration of work, walk-through studies and in some studies ambient air and biological monitoring. Only about half of these studies adjusted for confounding variables such as age, gender, education and social habits. However, there was no consistency or agreement between the studies on the different variables which were identified as potential covariates.

The majority of the studies reviewed, showed adverse symptoms associated with solvent exposure with a number of these showing dose-response relationships (Van Thriel et al, 2003; Issever et al, 2002; Chen et al, 2001a;

Chen et al, 2001b; Campagna et al, 2001; Castillo et al, 2001; LoSasso et al, 2001; Cavalleri et al, 2000; Julien et al, 2000; Eller et al, 1999; Chen et al, 1999b; Hooisma et al, 1994; Wang and Chen, 1993). The common findings reported from these studies suggest that workers exposed to solvents suffer decrements in memory and cognitive functioning as well as report higher number of neurotoxic symptoms.

Table 3.2: Common Symptoms associated with solvent exposure in adults

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Symptoms	Comments
Mucous membrane irritant effects							
Van Thriel et al (2003)	Exposure chamber study	Male students (Germany)	24 participants	▪ Organic solvents	SPES Acute symptoms (extended version), AAR, nasal lavage	Specific psychological reactions, self-reported nasal irritations	▪ Psychological indicators of olfactory stimulation and sensory irritation showed does-response relationships.
Bråtveit and Moen (2001)	Cross-sectional	Car finishing workers exposed to organic solvents from 32 shops (Norway)	36 exposed 17 controls	▪ Personal air	Symptoms questionnaire (headaches, vertigo, nausea, euphoria, sore eyes, soreness or itching in the nose and throat, discomfort in breathing and skin rashes) use of personal protective equipment.	Acute health symptoms	▪ Highest levels of exposure during degreasing of new cars. ▪ Washing of second hand cars associated with low levels of exposure ▪ NO evidence of pronounced acute effects of exposure, however car-finishing workers can be exposed to high levels of organic solvents.
Chen et al (2001b)	Cross-sectional	Dockyard painters (from a previous study, Chen et al 1999) (China and UK)	260 painters, 539 controls (UK) 109 painters 255 controls (China)	▪ Measured as number of years worked	Questionnaire as stated in (Chen et al 2001a)	Nasal, eye and skin irritation	▪ Nasal, eye and skin irritation significantly related to exposure to paint which resolved after stopping exposure ▪ Regression model adjusted for age, education, smoking, alcohol and social conformity

Table 3.2: Common Symptoms associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Symptoms	Comments
Lee et al (1997)	Cross-sectional	Newspaper Workers (USA)	215 exposed 34 non-exp.	▪ Mixed organic solvents ▪ Walk-through ▪ Air monitoring ▪ Personal monitoring	Comprehensive health questionnaire, Spiro metric testing	Pulmonary & upper respiratory tract.	▪ ↑ prevalence of pulmonary and URT mucous membrane symptoms in exposed printers ▪ Regression analysis adjusted for age, height, smoking, number of years in printing
Skin Effects							
Mackie et al (2004)	Case report	52 yr old male (suicide attempt) (UK)	1 case	▪ Drank and poured white spirit (turpentine) on himself	None	Extensive dermal burns	▪ Deep dermal burns associated paint thinner contact.
Ozgenal et al (2004)	Descriptive review	Burns patients (Turkey)	32 cases	▪ Paint thinner	None	Thermal burns	▪ Paint thinner a cause of thermal injury ▪
Jones et al (2003)	Controlled exposure	Volunteers (UK)	2 male 2 female	▪ 9 exposure sessions, 50 ppm. of 2 butox-ethanol for 2 hours	None	Dermal absorption	▪ Protective clothing had no effect ▪ Increased temperature and humidity increased dermal absorption

Table 3.2: Common symptoms associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Symptoms	Comments
Neuropsychological Symptoms							
Zupanic et al (2002)	Cross-sectional	Workers in rotogravure printing plants exposed to toluene (Germany)	154 exposed 124 low exposure	▪ Ambient air monitoring ▪ Mean lifetime weighted avg exposure (LWAE) calculated from exposure levels and self report	Subjective symptoms and Psychomotor performance (steadiness, line tracing, aiming, tapping, pegboard)	Psychomotor effects	▪ ANOVA found no association b/w 2 exposure groups. ▪ Regression analysis adjusted for age showed no association with LWAE and psychomotor performance.
Prince and Spengler (2001)	Case-study	33 year old woman (USA)	1 case	▪ Airborne lubricating fluid with Stoddard solvent	None	Headaches	▪ Symptom resolved when non-Stoddard solvent used
Chen et al (2001a)	Cross-sectional	Dockyard painters (from a previous study, Chen et al 1999) (China and UK)	260 painters, 539 controls (UK) 109 painters 255 controls (China)	▪ Measured as number of years worked	Questionnaire including neuropsychological symptoms, 12 statements of the neuroticism (N) scale and 12 statements of dissimulation and social conformity scale of the Eysenck personality questionnaire short scale (EPI)	Neuroticism and personality	▪ Association between duration of exposure and an increase in symptoms indicating neuroticism but no association for social conformity and dissimulation. ▪ Regression model adjusted for age, education, smoking and alcohol.

Table 3.2: Common symptoms associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Symptoms	Comments
LoSasso et al (2001)	Cross-sectional	Nail technicians (USA)	150 exposed 148 controls	▪ Workplace assessment (ventilation, hours worked)	Neuropsychological impairment scale (self report)	Neuropsychological symptoms	▪ Exposure to low level solvents associated with self-reported cognitive and neurological symptoms (cognitive efficiency, memory and learning) ▪ Regression analysis showed association between level of exposure and severity of symptoms
Aaserud et al (2000)	Case-control	Workers with 10+ years exposure	36/36	▪ Organic solvents	Cerebral MRI	Nervous system impairment e.g. brain atrophy	▪ No association between exposure and nervous system impairment
Challenor and Wright (2000)	Cross-sectional	Boat builders (UK)	213 exposed 144 controls	▪ Air monitoring ▪ Biological urine concentrations of 23 employees (styrene)	Mood (POMS)	Altered mood states	▪ Weak association between styrene exposure and aggression/hostility
Moen and Hollund (2000)	Descriptive cross-sectional	Car painters (Norway)/ admin staff of garages	28/18	▪ Air/ personal monitoring	Non-standard questionnaire	Acute CNS symptoms	▪ Exposure lower than limits. No difference in symptom reports found b/w exposed and non exposed

Table 3.2: Common symptoms associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Symptoms	Comments
Julien et al (2000)	Cross-sectional	Blue-collar workers from 41 plants exposed to neurotoxic substances	55 couples	▪ Self report ▪ Exposure levels categorized into high, medium, low and trace based on work history and job activities	Symptom-checklist-90-R, French version of POMS, Social interaction stress (SIS)	Psychological symptoms and marital stress	▪ Higher degrees of exposure associated with higher levels of workers' psychological stress, psychological symptoms and marital problems/conflicts
Chen et al (1999a)	Nested cross-sectional and case-control	Dockyard painters (Scotland)/ Male non-painters	953 painters 953 controls	▪ Heavy and prolonged exposure to paint solvents ▪ Measured as number of years worked and time since left work	Questionnaire including Q16 and other neurological questions.	Death and Neuro-psychological symptoms	▪ No association with mortality ▪ Association found with high symptoms scores and exposure. ▪ Multivariate Analyses adjusted for age, education , smoking, alcohol, social conformity and years of exp.
Chen et al (1999b)	Cross-sectional	Dockyard painters (China & UK)/ non painters	116 painters 263 non-painters	▪ Not measured group divided based on occupation	Questionnaire including Q16 and other neurological questions.	Neuropsychological symptoms	▪ Higher relative number of symptoms for painters compared to non-painters ▪ Multivariate analysis controlled for age, gender, education, smoking, alcohol intake and social conformity.

Table 3.2: Common symptoms associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Symptoms	Comments
Eller et al (1999)	Cross-sectional	Workers in rotogravure plant exposed to toluene (Denmark)	98 exposed	▪ Self report ▪ Three groups, group 0= no exposure, group 1 = TWA < 20 ppm of toluene ≤ 13 yrs, group 2 = TWA > 100 ppm more than 12 yrs.	Symptoms questionnaire, Cognitive function scanner, co-ordination ability, tremor and position stability	CNS effects	▪ Higher exposure associated with higher score on symptom index (concentration, reduced memory and fatigue) and worse performance on visuospatial function, number learning and word recognition ▪ Long-term exposure of toluene associated with impaired neuropsychological function
Welp et al (1996)	Prospective cohort	Workers employed in 660 plants manufacturing reinforced plastics between 1945-1991 and exposed to Styrene (Europe)	32802 exposed	▪ Personal exposure measurements b/w 1955-1990. ▪ Calculation of cumulative exposure and average exposure.	Calculation of Standardised Mortality Ratio.	Mortality from nervous system diseases, mental disorders and suicide.	▪ Styrene may contribute to chronic disease of the CNS. ▪ Mortality from diseases of the CNS increased with time since first exp, duration of exp, avg level of exp and cumulative exposure to styrene ▪ Mortality from epilepsy increased monotonically with all styrene exposure while associations for degenerative diseases of CNS were weaker

Table 3.2: Common symptoms associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Symptoms	Comments
Hakkola (1994)	Cross-sectional	Road tanker drivers exposed to solvents (Finland)	61 exposed 56 occasional and limited exp 31 control	▪ Personal air (20)	Symptoms questionnaire (sleep disturbances, fatigue, memory and concentration, emotional distress, somatic complaints and sensory and motor symptoms + POMS (Finish modification)	Neuropsychological symptoms	▪ Drivers had more solvent related acute symptoms compared to the control group with no exposure. Remarkable differences with fatigue, depression, hostility, listlessness and uncertainty however differences not significant.
Hooisma et al (1994)	Cross-sectional	House, industry and construction painters randomly selected from SFS database (Netherlands)	Young painters 120 exposed 169 controls Older painters 127 exposed 157 controls	▪ None	Questionnaire	Psycho-organic syndrome (i.e./specific symptoms of fatigability, poor memory, concentration etc)	▪ Frequency of complaints higher in both young and older painters exposed than non-exposed ▪ Significant relationship between frequency of periods of heavy exposure and severity of symptom categories.
Nelson et al (1994)	Case control	Automobile assembly workers (USA)	299 cases	▪ Exposure indices based on work history, current and historical exposures	None	Chronic neuropsychiatric disease	▪ Chronic neurological disease, multiple sclerosis associated with exposure ▪ Univariate analysis adjusted for solvent exposure, lead and alcohol consumption.

Table 3.2: Common symptoms associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Symptoms	Comments
Wang and Chen (1993)	Cross-sectional	Paint manufacturers - low, medium, high exposure (China)	196	▪ Personal / air monitoring ▪ Walk-throughs	Symptoms (Q16) questionnaire. Physical function. Liver function	Acute and chronic neurological symptoms	▪ Exposure positively associated with acute symptoms (headaches, chest tightness, dizziness, fatigue, depressed mood, palpitations) ▪ Higher exposure associated with increased risk to develop ≥3 chronic CNS symptoms. ▪ Logistic regression controlled for age, duration of employment and smoking
Colour vision dysfunction							
Boeckelmann and Pfister (2003)	Cross-sectional	Workers from silk screen printing exposed to solvents > 3 years (Germany)	42 printers 28 age-stratified controls	▪ Self report ▪ Exposure indices stratified into low, middle, high based on interview	Vistech Chart VCTS 6500 (Vision contrast test system)	Contrast sensitivity, visual defects	▪ Exposure to solvents associated with more abnormalities in contrast sensitivity in printers ▪ Regression model adjusted for age, alcohol, nicotine, consumption
Ihrig et al (2003)	Cross-sectional	Painters with long-term exposure to organic solvents (Germany)	140 painters	▪ Personal air sampling ▪ Two indices EI and CEI	Colour vision (Lanthony D15d) and Q18 (Modified German version of the Q16).	Colour vision dysfunction	▪ No significant correlation found between CCI, responses to Q18 and chronic solvent exposure ▪ Regression analysis adjusted for exposure indices, age, alcohol and smoking

Table 3.2: Common symptoms associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Symptoms	Comments
Issever et al (2002)	Cross-sectional	Workers in leather industry diagnosed with polyneuropathy	26 exposed 50 controls	▪ Biological monitoring (Urinary Phenol and trichloroacetic acid ▪ Hospital records	FM-100 Hue test, EMG, EEG, Questionnaire	Colour vision	▪ Significant relationship found between n-hexane exposure and development of defects in colour vision.
Campagna et al (2001)	Longitudinal	Male workers exposed to toluene in a photogravure plant (France)	72 exposed 34 ambient exposure 19 non-exposed	▪ Personal air monitoring ▪ Job-exposure matrix based on work history and self report	Visual acuity (National Optical Visual Chart), Colour vision (Lanthony D15d	Colour vision	▪ Positive relationship between colour vision loss and airborne toluene, past cumulative toluene and past total cumulative hydrocarbon exposure. ▪ Regression analysis adjusted for age, alcohol and duration of employment.
Castillo et al (2001)	Longitudinal	Workers in reinforced plastic plants (Canada)	18 styrene exposed	▪ Cumulative Exposure Index (CEI) with correction for respirator use ▪ Urinary Mandelic acid (MA)	Lanthony D15d, Vistech 6000 card system	Colour vision and visual acuity	▪ Significant association b/w cumulative exposure and near visual contrast sensitivity loss (chronic damage to neuro-optic pathways) ▪ No significant difference in colour vision. ▪ Co-variance analysis adjusted for age.

Table 3.2: Common symptoms associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Symptoms	Comments
Cavalleri et al (2000)	Cross-sectional	Rubber workers exposed to Toluene (Italy)	33 exposed 16 controls	▪ Biological monitoring (urine) ▪ Walk-through	Lanthony D15d	Colour vision	▪ Significant association between lower colour discrimination and toluene exposure ▪ Regression analysis adjusted for age, seniority, alcohol and smoking
Dick et al (2000)	Descriptive case reports	Painters from a previous study (Chen et al 1999) with similar findings on neuropsycho-logical examination (UK)	5 cases	▪ Exposure estimates based on work history ▪ Cumulative lifetime solvent exposure	Psychometric tests (Trailmaking A & B, Benton visual retention, National adult reading test, WAIS Vocab, NES2 CPT, symbol digit without paired associate, Associate learning and Delayed associate recall. Tests of visual acuity (3 m Snellan chart), colour vision (Lanthony D15d) grip strength.	Colour vision, cognitive defects, tremor and loss of vibration	▪ All cases showed neurological deficits including blue-yellow colour vision deficits, coarse tremor, impaired vibration sensation in the legs and cognitive impairment
Semple et al (2000)	Nested Cross-sectional	Dockyard workers selected on the basis of their responses to Orebro Q16 in previous study (UK)	68 exposed 42 controls	▪ Exposure indices (CEI, OEL based on self report, work history, lifetime exposure	Lanthony D15d, Keeler Snellen half size chart	Colour vision and visual acuity	▪ Exp to mixed solvents assoc. with impairment in colour vision ▪ Impairment of colour vision not associated with neuropsychological symptoms. ▪ Regression analysis adjusted for age and alcohol intake.

Table 3.2: Common symptoms associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Symptoms	Comments
Muttray et al (1999)	Cross-sectional	Printshop workers exposed to Toluene (Germany)	8 exposed 8 unexposed	▪ Personal air ▪ Blood samples	Farnsworth panel D-15 test, Lanthony desaturated D-15, Standard Pseudoisochromatic plates part 2 (SPP2-test)	Colour vision	▪ Measured acute & chronic effects ▪ Acute exp not associated with impairment in colour vision
Gonzalez et al (1998)	Cross-sectional	Workers exposed to solvents > 3 years (France)	129 exposed 120 controls	▪ Exposure indices based on work history, work practices ▪ Personal and air monitoring ▪ Hygienic effect index calculated	Lanthony D15d	Acquired dyschromato-psia	▪ Higher proportion of acquired dyschromatopsia found in exposed group ▪ Complex defect dyschromatopsia associated with higher cumulative exposure index than those with blue-yellow defect ▪ Regression model adjusted for age, tobacco and alcohol

3.4.2 Mucous membrane irritant effects

Solvents vary in their potential for irritability of mucous membranes and irritant effects seem to occur with most solvents. They appear to occur at levels considerably below current hygienic standards. In most cases the irritability disappears within a short period of time as a result of adaptation to the effects of the solvent (Fajardo,2002). Most solvents irritate the mucous membranes of the eyes, nose and throat with the eyes being the most sensitive. The initial manifestation is typically a burning sensation, resulting from stimulation of the trigeminal nerve endings of the nose and eyes, although a cough may also be apparent as a result of stimulation of the laryngeal nerve endings in the throat. Aspiration of solvent into the lung can result in rapid and sever pulmonary damage (NIOSH,1997). Heavy exposures are commonly manifested by cough, chest tightness and loss of breath. Strong irritant solvents such as toluene can induce symptoms at low exposure levels, which at high concentrations even common solvents like toluene, xylene and methylene chloride can induce pulmonary oedema (Baker and Fine, 1986). One study compared the pulmonary and upper respiratory tract mucous membrane symptoms in newspaper pressroom workers who were occupationally exposed to organic solvent and lubricant mixtures, and compositors who were not occupationally exposed to solvents or lubricants (Lee et al., 1997). Compared with the compositors, press workers were more likely to experience pulmonary and upper respiratory tract mucous membrane symptoms (including chronic cough, phlegm, wheezing, dyspnoea, haemoptysis, chest tightness, nose or throat irritation, eye irritation or sinus trouble). Furthermore, different frequency of use to different solvents caused different significant associations. The frequency of use of isopropanol and solvent type 1 (Naphtha and mineral spirits blend) were significantly correlated with the prevalence of chest tightness, the frequency of use of isopropanol and plate cleaner were significantly associated with the prevalence of wheezing, the frequency of use of kerosene (C_9-C_{16} hydrocarbons), solvent type 1 and all-purpose cleaner (Glycol ethers) were significantly associated with the prevalence of eye irritation and the frequency use of Mobil Oil (oils), kerosene, all purpose cleaner and isopropanol were significantly associated with prevalence of nose and throat irritation (Lee et al, 1997), even though the degree of exposure was within the current permissible exposure limits. Van Thriel et al. (2003) conducted an exposure chamber study of male students in Germany to assess self reported nasal irritations from exposure to organic solvents. No associations were found between subjective and objective methods assessing chemosensory effects, however, psychological indicators of olfactory stimulation and sensory irritation showed dose-response relationships.

Chen et al. (2001b) also found nasal, eye and skin irritations significantly associated with exposure to paint in dockyard painters in China and the UK. However, the effects of this exposure were acute and resolved after exposure stopped.

In contrast, Bråtveit and Moen (2001) found no evidence of acute symptom health effects associated with solvent exposure in car-finishing workers exposed to organic solvents from 32 shops in Norway. Nevertheless the authors state that based on measurements of solvents by personal air monitoring from three representative workshops, car-finishing workers were exposed to high levels of organic solvents in their work. Care should be taken in the interpretation of these results because the sample size used in this study is small and it would be difficult to generalise from these numbers.

However, the findings from the other three studies reviewed strongly suggest that exposure to solvents in adults is associated with mucous membrane irritant effects including nose, throat and eye irritations, wheezing and other mucous membrane symptoms. Although most studies reported acute effects which resolved when exposure stopped, these effects do exist and the implications which they may have on children with increased susceptibility should be considered.

3.4.3 Skin Effects

Organic solvents account for approximately 20% of occupationally induced dermatitis with this condition being most commonly localized to the hands (Fajardo, 2002). The hands are commonly affected while cleaning with solvents, by accidents, or by not using proper protective equipment. The main effects of solvents result from the dissolving of fats from the skin, which with repeated exposures will result in a red, dry, itchy skin. This is illustrated in Kishi et al, 1993 (displayed in Table 3.3), where reported symptoms of dry and scaly skin were significantly higher in organic solvent-exposed workers than non-exposed workers amongst other neurobehavioural effects. Moreover, paint thinner, a chemical containing aromatic hydrocarbons such as xylene, toluene and n-hexane, is a cause of thermal injury in many workplaces across Turkey (Ozgenel et al., 2004) due to inappropriate use and handling. All patients in the study sustained burn injury on the face, arms and hands and five patients among those studied had extended burn areas on the trunk and/or lower extremities. This suggests that paint thinner may be the cause of catastrophic thermal injury (Ozgenel et al., 2004). Similarly, Mackie et al. (2004), reported on a case report which found extensive dermal burns associated with paint thinner contact. Jones et al. (2003), however reported that the dermal absorption of solvent vapours can be significantly affected by the environmental conditions of the workplace. Specifically this controlled exposure study found that increased temperature and humidity increased dermal absorption. The authors also found that some types of protective clothing may not always be suitable to reduce absorption.

Whilst most of the studies on skin effects were descriptive in nature, the consistency of results addresses specific effects of solvents on the skin. Overall the results of the studies suggest that solvents have an effect on the skin. The implications these may have on working children should be considered as working children are more likely to be washing workplace equipment in solvents and are more prone to workplace accidents and injuries (Nuwayhid et al., 2005). Furthermore, the working environment the children work in, in so far as inadequate ventilation, increased temperatures and high humidity, may significantly impact the levels of solvent absorbed into a child's body system.

3.4.4 Neuropsychological symptoms and nervous system effects of solvents

The effects of solvents on the nervous system (also known as solvent neurotoxicity) have been well recognised since the 19th century, especially their effects of depression of CNS activity via anaesthetic action. Solvent-exposed individuals are rendered progressively less sensitive to stimuli as a function of solvent concentration and/or exposure duration until unconsciousness; coma or death occurs (NIOSH, 1997). The acute, transient neurotoxic effects of organic solvent exposure in humans result from the pharmacologic action of the solvent within the CNS and tend to resolve soon after discontinuation of the exposure. These effects include CNS depression, psychomotor impairment and narcosis. With a spectrum of intermediate symptoms that include drowsiness, headache, dizziness, dyspepsia and nausea (NIOSH, 1997; Xiao and Levin, 2000). The early signs of acute exposure consist of feelings of euphoria and disinhibition. Higher intensity exposure may result in prenarcotic symptoms such as dizziness, light-headedness, impaired judgment, nausea and vomiting, incoordination, paresthesia and increased salivation (Spencer et al., 2000; Chen et al., 1999a; Hooisma, 1994). A case study by Prince and Spengler (2001) found that headaches were associated with occupational exposure to Stoddard solvent and that symptoms resolved when the lubricating fluid was changed to a non-Stoddard solvent.

Neuropsychological and neurological impairments have been found in workers exposed to organic solvents. Neuropsychological symptoms were associated with heavy exposure to painting work in China where neuropsychological symptoms were assessed using a symptoms questionnaire including the (Q16) and other neurological questions in active and retired painters (both men and women) who had worked for at least 1 year and non-painters who had not been exposed to organic solvents (Chen et al., 1999b). There was a significant excess of symptoms overall among painters over non-painters of both sexes. After adjustment for confounders this study identified, the highest relative risks (RRs) of symptoms for women were from having problems with buttoning and unbuttoning and hands trembling, and for men were from bumping into people or things when moving around and also problems buttoning and unbuttoning. Summarised scores also showed that painters had more neuropsychological symptoms than had the controls (Chen et al., 1999b).

Wang and Chen (1993) also found solvent exposure in paint manufactures in China was positively associated with acute symptoms measured on the symptoms (Q16) questionnaire, including headaches, chest tightness, dizziness, fatigue, depressed mood and increased palpitations. Furthermore, the authors found that higher exposure levels were associated with increased risk to developing more than 3 chronic CNS symptoms. Another study by LoSasso et al. (2001) in nail technicians exposed to solvents also found that low levels of solvent exposure were associated with neuropsychological symptoms (memory, verbal learning, academic skills) including self reported neurological symptoms. Similarly, Eller et al. (1999) found higher exposure in workers in a rotogravure plant exposed to toluene in Denmark, associated with higher scores on the symptom index (including concentration, reduced memory and fatigue) and worse performance on visuospatial function, number learning and word recognition. The authors concluded that long term exposure of toluene was associated with impaired neuropsychological function.

Altered mood states have also been reported to be associated with solvent exposure. A prospective cohort study of workers exposed to styrene and employed in 660 plastic manufacturing plants, found that styrene may contribute to chronic diseases of the central nervous system as well as increase suicide and mortality with increased time and duration of exposure (Welp et al, 1996). Julien et al. (2000) also found higher degrees of exposure to neurotoxic substances associated with higher levels of psychological stress, psychological symptoms and marital problems, whilst Chen et al. (2001a) reported on the association found between duration of exposure and an increase in symptoms indicating neuroticism and altered mood states but no association for social conformity and dissimulation. Hakkola, (1994) also reported a higher percentage of general symptoms and fatigue, depression and hostility in tank drivers exposed to solvents.

However, in contrast, another study of boat builders in the UK found weak associations between styrene exposure and aggression and hostility which were assessed using the Profile of Mood States (POMS) for measurement of mood (Challenor and Wright, 2000).

It is important to note that not all studies report significant findings and some research has found no effects associated with solvent exposure. Aaserud et al. (2000) found no association between solvent exposure and nervous system impairment in a case control study of workers with more than ten years solvent exposure. The sample size of this study however was small and measurement of nervous system impairment is unclear using Cerebral MRI. Likewise, in a descriptive cross-sectional study of car painters in Norway, no difference in symptom reports were found between workers exposed to solvents and non-exposed workers (Moen and Hollund, 2000), however the design of this study and the small sample size also raises questions in the interpretation of the results. Zupanic et al. (2002) also found no dose-response relationships between toluene exposure and subjective symptoms or psychomotor effects in workers from rotogravure printing plants in Germany.

Dick et al., (2000), investigated neurological deficits in five individuals who had worked between 16 – 45 years as industrial painters. Structured neurological examination, colour vision testing and detailed psychometric testing showed neurological deficits including mild cognitive impairment, tremor, mild peripheral neuropathy and some had overt neurological disease such as grand mal epilepsy. The most striking features, sufficient to constitute a syndrome, were acquired blue-yellow colour vision deficits, coarse tremor, impaired vibration sensation in the legs and cognitive impairment (Dick et al., 2000). Although this study has shortcomings in that the sample size is too small, the findings are consistent with other studies of solvent exposure and give an indication of the concentrations of solvents likely to lead to serious neurological disease in humans.

Other neurological effects of solvent exposure have ranged from chronic toxic encephalopathy (Baker et al., 1986), chronic neurological disease (Nelson et al 1994) to impaired colour vision (Mergler et al., 1990) and acquired dyschromatopsia (Gonzalez et al., 1998). Many studies of workers exposed to solvents have identified an excess of deficits in colour vision (Iregren, 2002; Issever et al., 2002; Mergler et al., 1996; Campagna et al., 2001; Dick et al., 2000; Semple et al., 2000). Most acquired loss of colour vision is subclinical although some studies do report altered blue yellow perception. Acquired deficits usually affect blue-yellow but may progress to affect red-green vision. Semple et al., (2000), report on a study conducted on 68 male dockyard workers and 42 male community controls with and without neuropsychological symptoms. Indices of cumulative and intensity based exposure to solvents were calculated for all subjects, alcohol, drug and smoking histories were obtained and colour vision was tested by Lanthony D15d colour vision test. Results of the study indicated that annual exposure to mixed solvents was significantly associated with reduced colour vision and impairment of colour vision was not associated with neuropsychological symptoms as measured by the Q16 solvent symptoms questionnaire (Semple et al., 2000). Similarly, Issever et al., 2002, report on a relationship found between n-hexane exposure in patients diagnosed with polyneuropathy and development of defects in colour vision using the Farnsworth 100-hue test in workers in the leather industry. Another study of rubber workers exposed to toluene in Italy (Cavalleri et al., 2000) found significant associations between lower colour discrimination and toluene exposure however, Castillo et al. (2001), found no significant associations in colour vision and styrene exposure in plastic plant workers, but significant associations between cumulative exposure and near visual contrast sensitivity. These results are consistent with another study measuring exposure to solvents and the association with abnormalities in contrast sensitivity in printers (Bockelmann and Pfister, 2003).

Ihrig et al. (2003) reported that no significant correlations were found between colour vision dysfunction, responses to Q16 and chronic solvent exposure in painters with long term exposure to organic solvents in Germany. Similarly, Muttray et al. (1999) in Germany also found no association between acute exposure to toluene in print shop workers and impairment in colour vision.

Almost all of the studies reviewed on the effects of solvent exposure on neuropsychological symptoms and colour vision dysfunction were cross-sectional study designs. Only three of the studies were longitudinal (Welp et al, 1996; Campagna et al, 2001; Castillo et al, 2001). Solvent exposure was measured using a combination of exposure measurements including self-report (Julien et al, 2000; Eller et al, 1999), workplace assessment (LoSasso et al, 2001) and indices based on duration of work and work history (Chen et al., 1999a; Chen et al., 1999b). Other studies calculated exposure indices based on a combination of the above and in some cases biological and air monitoring (Ihrig et al., 2003; Zupanic et al., 2002; al., 2001; Challenor and Wright, 2000; Castillo et Gonzalez et al., 1998).

There are many factors to consider in the interpretation of the results from these studies. Many of the studies were cross-sectional, utilizing self report for the recall of symptoms and parameters used in the assessment of solvent exposure levels. In addition, of the 26 studies reviewed, only 14 adjusted for confounding variables such as age, height, education and smoking. However, the consistency in the findings on colour vision especially from those studies considered to be methodologically sound (Campagna et al., 2001; Castillo et al., 2001) demonstrate that solvent exposure is associated with colour vision dysfunction. Furthermore, most of the positive findings related to measures developed specifically for the assessment of neurotoxicity showed significant associations between solvent exposure and neuropsychological symptoms. The positive findings of most studies that used the Q16 are the most persuasive particularly where exposure-effect relationships have been demonstrated.

3.4.5 Neurobehavioural testing in the evaluation of neurobehavioural effects of solvents

Neurobehavioural performance testing has been shown to be helpful in defining intellectual and affective deficits that may be associated with exposure to solvents . Many studies conducted have shown clear dose-effect relations between the degree of exposure and the magnitude of the associated neurobehavioural deficits (Ng et al., 1990; Kishi et al., 1993), whereas other studies did not suggest persistent patterns of effect on neurobehavioural function (Muijser et al., 1996; Chouaniere et al., 2002). Table 3.3 provides a summary of the literature available on the neurobehavioural effects evaluated in occupationally solvent exposed adults using neurobehavioural and neuropsychological performance tests. The table reports on the study design, study subjects, exposure measurement, neurobehavioural tests used and the findings of these studies.

In total, there were 33 studies reviewed on neurobehavioural performance effects associated with adult solvent exposure. Almost all the studies were cross-sectional and compared two groups of workers, (exposed and non-exposed). Many of the studies also carried out analyses of exposure-effect relationships using either duration or a cumulative index as a measure of exposure. There were 5 prospective longitudinal studies (Mergler et al., 1996; Williamson, 1996b; White et al., 1995; Williamson and Winder, 1993;). All of these also measured exposure-effect relationships. Almost all of the studies investigated active workers exposed to solvents with the exception of one study which investigated retired painters and aerospace workers (Daniell et al., 1999). Three studies investigated environmental exposure to solvents (Reif et al., 2003; Kilburn 2002; Altmann et al., 1995) and have been included in the review for comparison of results between environmental and occupational solvent exposure.

Table 3.3: Neurobehavioural performance effects associated with solvent exposure in adults

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Dick et al (2004)	Nested cross-sectional	Dockyard painters who were survivors from a previous study (Semple et al 2000) (UK)	82 painters 38 controls	▪ Exposure indices (CEI, OEL based on self report, work history, lifetime exposure	Cognitive: Benton visual retention (visuomotor, visuospatial perception, visual and verbal conceptualisation, immediate memory span), Trail making A and B (visuomotor tracking and visual conceptualisation), Premorbid IQ (NART) Colour vision: based on previous methods (Semple et al 2000)	▪ Acquired colour vision associated with cognitive impairment in solvent exposed workers. ▪ Regression analysis adjusted for IQ, alcohol and smoking.
Reif et al (2003)	Cross-sectional	Residents of a community exposed to water supply contaminated by TCE and other chemicals (USA)	143 exposed	▪ Exposure to TCE estimated using hydraulic simulation model with a geographic info system	NCTB (Santa Ana, aiming, SRT, Digit symbol, Benton Visual Retention, Digit span and POMS) contrast sensitivity C and D	▪ Long-term exposure to low concentrations of TCE associated with neurobehavioural deficits in humans. ▪ Strong interaction b/w exposure to TCE and alcohol consumption, ▪ Multivariate analysis adjusted for seafood ingestion, education, smoking and alcohol.
Bockelmann et al (2002)	Cross-sectional	Car painters (Germany)	84 painters 85 controls	▪ Self-report ▪ Air monitoring	Psychological & neurological questionnaire P&P tests, vocabulary, block design, cerebral insufficiency, attention, SRT, digit span	▪ Exposed differentiated from controls by more neurological symptoms and slower SRT ▪ Multivariate analyses accounting for age, alcohol consumption, schooling and vocabulary scores (MWT-B)

Table 3.3: Neurobehavioural performance effects associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Chouaniere et al (2002)	Cross-sectional	Workers in 2 printing plants exposed to toluene	128 blue collar workers (39 from Plant A, 89 from Plant B)	▪ Personal and ambient air monitoring ▪ Exposure indices (CEI) based on job and exposure history,	EURONEST, NES, (Simple reaction time, simple digit, digit span, pattern memory, associate learning and associate recall.	▪ No significant relationship found between CEI and neurotoxic effects ▪ Low toluene concentrations associated with decrements of memory test performance. ▪ Regression analysis adjusted for gender, age, synonym score, history of CNS disease, alcohol, psychoactive drug consumption, concentration, computer experience, lead exposure.
Dick et al (2002)	Retrospective Case-control	Occupational Painters (UK)	78 exposed 42 controls	▪ Work history ▪ Estimated exposure ▪ Organic solvents	NES2(CPT, paired-assoc, SDT, Assoc Recall trails A/B, Benton); Premorbid IQ-(NART) Neurological exam; (grip strength, nystagmus, tremor, 2 point discrimination, finger nose, vibration percept, muscle wasting)	▪ Regression analyses skewed significance assoc with solvent exposure and cognitive impairment ▪ Regression analyses adjusted for smoking, alcohol consumption in all cases (age in neurological tests and trail making, IQ for all other cognitive tests).
Kilburn (2002)	Cross-sectional	Residents in exposure zone of electronic manufacturing plants (USA)	236 exposed 161 regional referents 67 unexposed	▪ Exposure estimates on analysis of well water (Halogenated volatile organic chemicals (HVOCs), Trichloroethylene (TCE), TCA, PCE and VC)	SRT, 2 CRT, body balance, blink reflex latency, Lanthony D15d, Culture fair battery 2 A (nonverbal, non arithmetic intelligence test) WAIS block design, slotted pegboard, trail making A & B, Immediate verbal recall memory, POMS with subsets from American Rheumatism Association's lupus erythematosus questions, standard respiratory questions & pulmonary function (vital capacity & expiratory flow)	▪ Neurobehavioural functions (delayed simple and choice reaction times, attention, perceptual motor speed and recall) significantly impaired in residents who lived in exposure zones. Reduced pulmonary functions, elevated POMS scores, excessive symptom frequencies and abnormal colour discrimination also found. ▪ Regression analysis adjusted for age, gender, education, height, weight, family income, social class

Table 3.3: Neurobehavioural performance effects associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Nordling Nilson et al (2002)	Prospective over 18 years	Carpet layers (Sweden)	41 floor layers (exp) 40 carpenters (non-exp)	▪ Exposure indices calculated from self-report	(TUFF) Test battery for investigating functional disorder (verbal understanding, reasoning, visuospatial skill, perceptual speed accuracy, attention, motor function and visual memory).	▪ Greater deterioration in visual memory, sustained attention, perceptual speed & visuospatial skill associated with higher exposure. ▪ Regression model included previous test results, age and CEI.
Daniell et al (1999)	Cross-sectional	Retired painters (USA)	89 exposed painters 126 carpenter controls. Exposed included 22 aerospace painters high exp 67 painter med exp	▪ Self-report ▪ Exposure indices based on work and exposure history	Verbal fluency, WAIS-R (vocabulary, simulations, block design, digit span, digit symbol), Wisconsin card sort, verbal aphasia screen, trails A/B, finger tapping, Wechsler memory tests (logical and visual memory), Rey auditory verbal learning, Benton visual retention, attention, Stroop test, grooved pegboard, SRT, Beck depression inventory, symptoms:Q-16	▪ Exposed painters had poorer motor and reasoning functions and memory plus more neurological and depressive symptoms compared to painters. ▪ Exposed aerospace workers (with highest exposure) also showed poorer motor and visuomotor speed and attention and memory. ▪ Logistic regression controlling for age, years of education, vocabulary score and alcohol use.
Feldman et al (1999)	Case study	Occupational painter (USA)	N=1, 4 years after long term exposure	▪ Exposure history ▪ Work history ▪ Biological Monitoring	Neurological exam including neuroimaging (EEG + MRI), neuropsychological testing (CVLT, Rey-Osterreith complex figure, Trails A & B, Wisconsin Card, Grooved pegboard, mood, Boston naming	▪ Persistent cognitive deficits

Table 3.3: Neurobehavioural performance effects associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Nasterlack et al (1999)	Cross-sectional	Painters (Germany)	401 painters 209 construction controls	▪ Expert rating based on occupational history, recent solvent exposure (EI) and lifelong cumulative exposure (CEI)	Q16 symptoms, Neurotoxic symptom score (NTSS), psychiatric exam, physical exam, EEG, EMG, NCV, verbal and fluid IQ, Benton visual retention, concentration (d2), reaction time	▪ Main finding was increase in mood and behavioural symptoms in painters and those with highest exposure were more likely to report symptoms ▪ ANCOVA adjusted for IQ and age
Lee et al (1998)	Cross-sectional	Female workers in shoe manufacturing industry (Korea)	22 adhesive process = high exp. 18 in frame-making process = low exposure 28 controls	▪ Personal air (4 workers) ▪ Exposure indices: current department, exposure duration, CEE	NCTB (POMS, SRT, digit span, Santa Ana, digit symbol, Benton visual retention, Pursuit aiming) – POMS excluded from analysis due to cultural background (difficulties)	▪ Significant differences found between higher exposure and poorer performance between groups on Santa Ana Dexterity only in CEE analysis. ▪ Multivariate analysis adjusted for educational level
Smargassi et al (1998)	Predictive validity study of symptom screen (Q16)	Styrene-exposed (Italy)	74 exposed and non-exposed	▪ None	WAIS tests (logical memory, verbal learning)	▪ Weak relationship found between symptom (Q16 answers) and performance on neurobehavioural measures
Mitran et al (1997)	Cross-sectional	workers exposed to acetone, MEK, cyclohexanon from coin printing , cable and furniture factories respectively (Romania)	Acetone 71 exposed 86 controls MEK 41 exposed 63 controls Cyclohexano n 75 exposed 85 controls	▪ Air monitoring - 8hr shifts ▪ Exposure indices for acetone and cyclohexanon ▪ Cyclohexanon and acetone urine levels	Subjective symptoms, motor nerve conduction velocity test, ulnar and peroneal nerves, reaction time to auditory and visual stimuli, the Praga test for distributive attention, Woodworth-matthews personality question for psychoneurotic tendencies, labyrinth test to identify attention	▪ Workers exposed to acetone were most affected in terms of human performance and evidence of neurotoxicity, followed by workers exposed to MEK and workers exposed to cyclohexanon. ▪ Mood disorders most frequent in workers exposed to cyclohexanon and MEK. Irritability most frequent in acetone and MEK. Memory more frequent in MEK.

Table 3.3: Neurobehavioural performance effects associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Tsai et al (1997)	Cross-sectional	Paint manufacturers (Taiwan)	298 participants categorised into low and high exposure	▪ Personal sampling (EI) ▪ Hygienic Effect	NES2 Chinese Version (Finger Tapping, CPT, Associate learning, symbol digit, pattern comparison, pattern memory, digit span, attention, Assoc. delayed recognition, mood) Vibration and thermal threshold tests.	▪ Regression analyses controlling for age, gender, education and alcohol intake showed high exposure associated with larger response latency in CPT, pattern comparison and pattern memory
Bolle et al (1996)	prospective cohort study performance compared 2X over 3 years	Painters (Switzerland)	57 apprentice painters 62 non-exposed apprentices	▪ None	NES2 French Translation (Pattern comparison, symbol digit, digit span, vocabulary)	▪ Exposed & n-exposed differed only on verbal ability test (lower ability for exposed) but this was also affected by socioeconomic background ▪ Regression analysis adjusted for schooling, mother tongue and social background
Grosch et al (1996)	Cross-sectional	Painters (USA)	133 exposed 51 controls	▪ Exposure indices based on self report	NES2 (SRT, Visual digit span, symbol-digit, pattern memory, vocabulary, mood)	▪ Exposed poorer than controls on symbol-digit, pattern memory and vocabulary tests. These functions also showed association with increasing exposure ▪ Multivariate analyses adjusted for age, alcohol consumption and smoking
Mergler et al (1996)	Longitudinal	Reinforced plastics manufacturers (Canada)	118 workers studied over 2 years	▪ Personal sampling ▪ Biological monitoring (styrene)	NBCT and field assessment sensory tests	▪ Styrene exposure associated with poorer colour vision, SRT, digit span, tension, fatigue and some symptoms

Table 3.3: Neurobehavioural performance effects associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Muijser et al (1996)	Cross-sectional	Carpet layers (Netherlands)	89 exposed 85 controls	▪ Air monitoring (personal samples)	NES2 (SRT, symbol-digit, hand-eye coordination, digit span)	▪ Exposure over the day showed effects in digit span test performance ▪ No evidence of persistent deficits in NB functioning ▪ ANCOVA adjusting for age, education, alcohol and smoking
Seeber et al (1996)	Comparison of exposure indices for predicting neurobehavioural effect in 5 studies	Paint manufacturers in all 5 studies	vary	▪ Hygienic effect ▪ Litres solvent used/day years ▪ Cumulative lifetime exp. ▪ Lifetime weighted exp.	5 studies all used different tests. Tests included NES, EURONEST, P&P tests including digit symbol and trail making, Q16, PNF, POMS	▪ Symbol digit test showed most significant dose-response relationship in the studies.
Tsai et al (1996)	Cross-sectional	Fibreglass manufacturing (Taiwan)	41 exposed 45 non-exposed	▪ Air monitoring ▪ personal sampling ▪ controlled for acute exposure	Symptoms (Q16), NES2 Chinese Version (FT, CPT, Assoc. learning, symbol digit, pattern comparison, pattern memory, digit span, attention, Assoc. delayed recognition, mood) Vocab, Vibration and thermal threshold tests.	▪ Styrene exposed showed poorer CPT and vibration threshold controlling for variables in regression analysis (age, gender, education and alcohol)
Williamson (1996b)	Prospective cohort	Occupational car painters (Australia)	n=189 exposed f/u for 4 years	▪ Self-estimated ▪ Personal / air monitoring	CFF, hand-steadiness, SRT, visual pursuit, Sternberg memory, paired associates	▪ Decrease in hand steadiness with increase in solvent exposure ▪ Regression analyses adjusted for drinks per week, education, test year, and workplace exposure.

Table 3.3: Neurobehavioural performance effects associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Altmann et al (1995)	Cross-sectional	Residents living in neighbourhood of dry cleaning shops exposed to tetrachloro-ethene (Germany)	14 exposed 23 controls	▪ Blood samples twice (in own home and immediately before testing) ▪ Passive air samples	NES (CPT, Hand-eye coordination, finger tapping, simple reaction time, visual memory), VEP, vibration perception and visual acuity (Titmus II)	▪ Long term TCE exposure may affect NB outcomes. Exposure associated with reduced vigilance, RT and visual memory compared to matched controls ▪ Regression analysis adjusted for age, gender and education
Bolla et al (1995)	Retrospective cohort	Workers from an organo-lead manufacturing plant and employees at 2 different paint manufacturing plants (USA)	Lead 226 exposed 320 controls Solvents 187 exposed 247 controls Negative control 62	▪ Exposure indices based on personnel records, work histories, zone exposure matrices ▪ Cumulative exposure to inorganic and organic lead ▪ Mean cumulative hydrocarbon exposure for solvents	WAIS-R (Vocab - premorbid verbal intelligence, block design) Rey Auditory Verbal Learning Test, Serial digit learning, symbol digit paired associate learning, visual retention, digit symbol substitution, simple visual reaction time, Trails A and B, Purdue pegboard, finger tapping, Olfaction, Q16.	▪ Both lead and solvents associated with diminished neurobehavioural performance with same magnitude of adverse effects on tests of manual dexterity. ▪ Lead exposure associated with greater effects on memory and learning but less adverse effects on executive/motor tests and on test of olfaction. ▪ Regression analysis adjusted for premorbid intellectual ability, age, race.
Escalona et al (1995)	Cross-sectional	Adhesive (glues) factory Workers (Venezuela)	82 exposed 67 controls	▪ Air monitoring ▪ Walk-through survey	NCTB	▪ Regression analyses showed POMS symptoms, digit symbol and SRT were poorer for exposed and showed significant association with exposure ▪ Regression analyses adjusted for age, sex and education

Table 3.3: Neurobehavioural performance effects associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
White et al (1995)	Prospective cohort	Workers in screen printing (USA)	30	▪ Air samples (12 from individual workers and 8 from different work areas) ▪ Additive model (worst case estimate and best case estimate)	WAIS-R (vocab, similarities, block design, digit span, digit symbol), CPT, WMS (visual reproductions), WMS-R (Paired associate learning), Santa Ana, POMS, year 1 (controlled oral word association, trail making test), year 2 (Wisconsin sorting test)	▪ Higher acute exposure associated with poorer performance on visual short-term memory and manual motor dexterity (digit symbol, Santa Ana, no dominant hand and on mood changes (depression and confusion subscales of the POMS). ANCOVA Analysis adjusted for age, education, but only Santa Ana remained significant when adjustment for gender made ▪ Anger and confusion of POMS significantly associated with chronic exposure after adjusting for age and education but no significance after adjusting for gender.
Colvin et al (1993)	Cross-sectional	Paint manufacturers (South Africa)	43 exposed 24 controls	▪ Air monitoring ▪ Work history	NCTB (excluding POMS),NES2, 4 word memory, paragraph memory (immediate and delayed) Geometric shape drawing.	▪ Lifetime exposure to solvents predicted power performance on CPT, switching attention, SRT, pattern memory ▪ Linear regression adjusted for age, alcohol consumption and schooling.
Daniell et al (1993)	Cross-sectional	Car body repairers (USA)	39 painters – high exp 32 painters-medium exp 29 painters low past exp 24 painter low exp no past exp	▪ Personal sampling. ▪ Self report	NES (verbal, affect, motor speed, hand-eye coordination, CPT, symbol-digit, memory	▪ High current exposure performed worse with visual perception and memory especially those aged 35+ years ▪ High and medium current exposure reported significantly more acute and chronic neurological symptoms. ▪ ANCOVA adjusted for relations between test scores, solvent exposure categories, age, years of education , vocabulary score and alcohol use.

Table 3.3: Neurobehavioural performance effects associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Hooisma et al (1993)	Cross-sectional	House, industry and construction painters randomly selected from SFS database (Netherlands)	Young painters 47 exposed 53 controls Older painters 45 exposed 43 controls	▪ Lifetime exposure indices based on self-report, work history, work practices etc	NCTB (POMS, SRT, digit span, Santa Ana, digit symbol, Benton recognition, pursuit aiming) , block design, NES (POMS, digit span, vocab, symbol-digit substitution, pattern comparison, pattern memory, FT, Hand-eye, associate recognition, serial digit, colour word vigilance)	▪ No strong evidence for solvent-related changes in psychometric performance of painters compared to controls. ▪ Significant diff found b/w painters and controls on SRT, Pattern memory (inferior performance of exposed) and CPT false, CWV false and mean (superior performance) ▪ ANCOVA analysis adjusted for vocab.
Kishi et al (1993)	Cross-sectional	Industrial painters (Japan)	81 painters 154 non-exp.	▪ Air and biological monitoring	Acute and chronic symptom questionnaire, SRT, digit symbol, Santa Ana, Benton visual retention, vocabulary, block design, digit span, mood (POMS) (From NCTB and NES)	▪ Regression analyses showed higher solvent exposure associated with poorer block design and digit span. Toluene exposure linked with poorer Santa Ana and Benton visual retention results ▪ Pairwise comparison showed dry and scaly skin, depression, cold hands and legs, irritation, loss of appetite, dizziness and unsteadiness sig. more among exposed ▪ Regression model adjusted for age, education and alcohol intake.
Lee and Lee (1993)	Cross-sectional	Car painters & printers (Korea)	113 exposed 81 controls	▪ Air monitoring (HE)	NCTB (SRT, Santa Ana, digit symbol, Benton visual retention)	▪ Benton visual retention poorer in highest solvent exposure group ▪ Factorial ANOVA controlling for education, age, duration of exposure and alcohol consumption.

Table 3.3: Neurobehavioural performance effects associated with solvent exposure in adults (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Williamson & Winder (1993)	Prospective cohort f/u over 3 yrs	Apprentice spray painters (Australia)	50 spray painters 50 electricians	▪ Personal sampling ▪ Exposure index based on self report.	Symptoms (Q16), Visual perception (Critical flicker), Visual motor (Hand steadiness), perceptual speed (Simple Reaction), psychomotor (Visual pursuit), short-term memory (Sternberg memory, paired associates).	▪ No significant changes in NB performance associated with solvent exposure.
Ng et al (1990)	Cross-sectional	Workers in screen printing, spray painting & paint-manufacturing factories (Singapore)	78 exposed 145 controls	▪ Additive severity factor ▪ Blood lead concentrations for a small number	Q16 (modified), Choice reaction time, WAIS-R (digit symbol, block design, digit span), WMS (visual reproduction, assoc. learning, logical memory) Benton Visual Retention	▪ Significantly worse performance of exp. on tests of psycho-motor function (CRT & digit symbol) and auditory memory (digit span & assoc. learning) adjusted for age and education. ▪ ↑ Symptoms. of fatigue, irritability, depression, poor memory and sleep disturbances in exposed group .
Fidler et al (1987)	Cross-sectional	Construction painters (USA)	101 painters 31 controls	▪ Exposure index based on self report	Neurotoxic Symptoms (Q16), NES (CPT, symbol-digit, hand-eye coordination, pattern memory, digit span, Sternberg memory, vocabulary, mood)	▪ Exposure associated with increased symptoms and poorer performance on symbol-digit and digit span tests ▪ Regression analysis adjusted for age, schooling, alcohol, Hollingshead index.

A large number of studies have examined the effects of solvent exposure on neurobehavioural test performance in adults and more recently in adults occupationally exposed to low concentrations of solvents (Xiao and Levin, 2000; Tsai et al., 1997). The results of these studies, despite the inconsistencies relating to the findings of particular tests, strongly suggest that solvents have an effect on the central nervous system and influence poorer neurobehavioural test performance. Functional modalities found to be affected by solvent exposure have included loss of dexterity, delayed reaction time, lack of concentration and loss of memory (Mitran et al, 1997; Tsai and Chen 1996; Bolla et al., 1995; Colvin et al, 1993).

Neurobehavioural studies have used a wide range of tests which assess many different aspects of cognitive functioning as shown in Table 3.3. In one study (Tsai et al., 1997) used a wide range of tests including vibration threshold test, thermal threshold test, and a range of subtests from the Neurobehavioural Evaluation System 2 (NES) including finger tapping, continuous performance test, associate learning, symbol-digit, pattern comparison, pattern memory, visual digit span, attention switching, associate delayed recognition, mood scales, and a vocabulary test). A Chinese version of the NES2 was used as well as translations of the five-dimensional mood profile and vocabulary test. The authors of this study found that visual attention and perceptual function (speed and memory) on the continuous performance test, pattern comparison (latencies) and pattern memory tests, might be the neurobehavioural functions affected first by low level occupational exposure to solvents in adult paint manufacturing workers. Exposure assessment using personal passive samplers showed that the workers were exposed to benzene, toluene, xylene, n-hexane, methyl iso-butyl ketone, n-butyl acetate and acetone and showed dose-response effects. As with most neurobehavioural studies, the cross-sectional design of this study is a limitation in reaching strong conclusions from the results reported.

Another study (White et al., 1995), examined the neurobehavioural effects of acute and chronic exposure to mixed solvents in screen printers over a 12 month period. Screen printers categorised as having higher acute exposure demonstrated significantly impaired neurobehavioural test performance on tasks involving manual motor dexterity, visual short-term memory (digit symbol test, WAIS-R; Santa Ana, nondominant hand) and mood (specifically on depression and confusion subscales of the Profile of Mood States POMS). Those with higher chronic exposure which was measured using an additive model demonstrated significantly poorer performance on visual memory tasks and mood (anger and confusion). The results from this study suggest that the mixed solvents used in the screen printing industry have an effect on central nervous system functioning in the absence of obvious clinical disease. (White et al., 1995).

In a cross-sectional study, Lee and Lee (1993) studied a group of high and low level solvent exposed workers who had worked an average of 7.8 years, and compared them with non exposed controls. The high and low exposure levels were determined by calculating the hygienic effect levels of a mixture of solvents found on the air samples collected form the working stations which included toluene, xylene, methyl ethyl ketone, trichloroethylene, perchloroethylene, gasoline, and n-hexane. Solvent workers performed significantly more poorly than controls on the Benton Visual Retention (BVR) test, digit symbol, and the Santa Ana Dexterity Test (left hand) but when age, education, alcohol consumption, and smoking were accounted for, only the BVR remained significant, while digit symbol became marginally significant. The control group in this study comprised volunteers not matched on confounding factors specifically educational level which was significantly higher in the control group.

A mixed group of Chinese spray painters, printers and paint manufacturing workers exposed to solvents for an average of 9.4 years were investigated by Ng et al., (1990) in a cross-sectional study. Significant differences between workers and matched controls showed that workers performed significantly worse on psychomotor function (WAIS-R digit Symbol Test, test of choice reaction time), auditory memory, (Digit Span and Wechsler Memory Scale (WMS) - Associate Learning). Performance on WAIS-R Block Design and Logical Memory scores were marginally significant. Exposed workers also reported higher frequencies of affective symptoms such as fatigue, irritability, depression and poor memory, sleep disturbances and autonomic symptoms. It is plausible to state however that exposed subjects, had one year less education than controls which was accounted for statistically. The choice of controls for this study imposes selection bias, such that they were volunteers and may have represented a self-selected group of healthy persons.

In another cross-sectional study, Escalona et al. (1995) also found a significant association between exposure to solvents and performance on the digit symbol, simple reaction time and POMS symptoms scores and all subtests from the NCTB (Neurobehavioural Core Test Battery) in a group of adhesive factory workers in Venezuela. Regression analyses in this study adjusted for age, gender and education. A key component of the findings of this study is the dose-exposure effect of the deficits, when dose was expressed as years of exposure in the current job. Similarly, Lee et al. (1998) found significant differences in workers with high solvent exposure and low solvent exposure, working in the shoe manufacturing industry. Higher cumulative exposure estimate was associated with poorer performance on the Santa Ana Dexterity test whilst current exposure and duration exposure estimates showed no effects.

Even in concentrations below German threshold limit values, Bockelmann et al., (2002), reported adverse psychological effects of exposure to mixed organic solvents on car painters. The study investigated 84 car painters and 85 controls using a test battery including paper-pencil tests (vocabulary, block design, C.i [to detect signs of cerebral insufficiency], D2 attention stress test to detect attention deficits), computer-based tests (digit span, simple-choice reaction time test) and a questionnaire to assess the participants' mental state. Deficits in cognitive performance capacities were found in memory and ability to concentrate as well as negative effects on the painters' subjective state of well-being. Car painters with long-term exposure to solvents showed psychological deviations such as deficits in concentration, memory and reaction time compared to non-exposed subjects (Bockelmann et al., 2002).

Daniell et al., (1993) evaluated neuropsychological test performance and symptom reporting in a cohort of car body repair workers exposed to solvents. A selection of tests from the neurobehavioural evaluation system (NES) and incorporating tests of verbal ability, affect, motor speed, visuomotor performance, visual perception and visual memory was used, Subjects with higher current exposure performed significantly less well on selected tests of visual perception and memory but there were no significant exposure-related differences in mood state, motor speed, or visuomotor performance. Subjects with high and medium current exposure to solvents and paints, and subjects with low exposures but had formerly painted, reported significantly more acute and chronic neurological symptoms than did low exposure subjects with no history of painting. Exposure-related effects were most noticeable among subjects 35 years or older (Daniell et al., 1993). Therefore it is plausible that neurodegenerative processes of aging might have a contributing role in the development of chronic effects of exposure to solvents, such that a neurotoxic injury related to solvents that remains subclinical during the years of exposure could manifest itself clinically in later years of life (Daniell et al., 1999).

To further investigate the possible relation between the effects of solvents and aging, Daniell et al., (1999), evaluated the risk for functioning in retired male workers 62-74 years of age and compared men who had previous long term occupational exposure to solvents (retired painters and aerospace manufacturing workers) with people who had relatively minimal histories or previous exposure to organic solvents (retired carpenters). Questionnaires collecting information on personal background, medical history, medication, alcohol use, neurological symptoms, employment and exposure history were used. Blood cell counts, thyroid function and blood lead were also measured to detect possible unrelated exposure and causes of CNS dysfunction. A standard battery of neuropsychological tests including: verbal fluency test, vocabulary, similarities, block design, digit span and digit symbol subtests of the Wechsler adult intelligence scale, Wisconsin card sorting test, verbal aphasia screening, trails A and B and finger tapping tests from the Halstead-Reitan battery; logical and visual subtests of the Wechsler memory scale-revised; Rey auditory verbal learning test, Benton visual retention test; d2 test; Stroop test; grooved pegboard test and simpler reaction time was selected. Affective status was assessed by the Beck depression inventory and the interviewer administered, computer assisted diagnostic interview schedule. Indices of exposure to solvents were calculated with a semi quantitative model incorporating duration and intensity of exposure and frequency of protective factors.

The results showed that the painters on average reported greater cumulative alcohol consumption and had lower scores on the WAIS-R vocabulary subtest, usually presumed to reflect premorbid intellectual functioning. After controlling for age, education, vocabulary score and alcohol use, the painters had lower mean scores on test measures of motor (grooved pegboard), memory (WMS-immediate visual memory) and reasoning ability (WAIS-R block design); and a subgroup of aerospace workers with moderate to high cumulative exposure to solvents had lower mean scores on measures of visuomotor speed, and motor (grooved pegboard), attention, memory (immediate verbal memory) and reasoning ability. Increased number of relatively abnormal test scores was more likely among both the painter group and the subgroup of aerospace workers with higher cumulative exposure. The painters but not the aerospace workers reported significantly more neurological and depressive symptoms thus making the findings consistent with residual central nervous system dysfunction from long term exposure to organic solvents persisting years after the end of exposure (Daniell et al., 1999).

Long term exposure to solvents has also been reported to lead to chronic, irreversible brain damage, with intellectual impairment and decrements in performance. Feldman et al. (1999), report on a case-study findings in a 57-year old painter who had been working as a painter at 16 years of age and exposed to various solvents for over 30 years, frequently working in poorly ventilated areas; using solvents to remove paint from the skin of his arms and hands at the end of work shift. Impaired short-term memory function and changes in affect were noticed by the patient and his family in his early forties which progressed until after he stopped working and was thus no longer exposed to paints and solvents. After exposure had ended, serial neuropsychological testing revealed impaired performance on tests of verbal (California Verbal Learning test) and nonverbal memory (delayed reproduction of Rey-Osterreith complex figure), attention and executive function (Trails A and B and Wisconsin Card Sort Test) and visuomotor coordination (Grooved Pegboard Test). Tests of mood and affect also revealed anxiety and depression. The authors of this study concluded that these cognitive deficits and findings were consistent with chronic toxic encephalopathy (Feldman et al., 1999).

In contrast, some studies have found no associations between solvent exposure and neurobehavioural performance. Williamson and Winder, (1993), in a longitudinal study, found no significant changes in neurobehavioural function in the first 2 years of exposure to solvents in apprentice car spray painters. Nasterlack et al. (1999), found no significant differences in cognitive functions assessed by a range of neuropsychological tests between painters exposed to solvents and their controls but found differences in respect to the frequency of symptoms in mood and behaviour in these groups.

Hooisma et al. (1993), also reported no strong evidence for solvent-related changes in psychometric performance measured by traditional tests from the WHO Core Test Battery and computerised tests from the NES. Both of these batteries include tests for response speed, attention, perceptual motor speed, visual perception, memory and affective behaviour. Using lifetime exposure indices as measures of exposure, this study failed to identify any differences in neurobehavioural performance between the painters and two age-matched control groups or to identify any dose-response relationships. More recently, Chouaniere et al. (2002) also found no significant relationship between cumulative exposure indices and neurotoxic effects but reported that low toluene concentrations were found to be associated with decrements of memory test performance.

In another study (Dick et al., 2002), failed to identify any significant neuropsychological differences between symptomatic and asymptomatic painters. The investigators used a battery of psychometric tests, (continuous performance, paired associate learning, symbol digit substitution and associate recall from the computerised neurobehavioural evaluation system (NES) together with the trail making A and B tests and the Benton Visual Retention Test. Pre-morbid ability was also assessed using a hold test, the National Adult Reading test (NART). Neurological examination included grip strength dynamometry, nystagmus, tremor, two-point discrimination, vibration perception, finger-nose approximation and muscle wasting. There were no differences in neurological function found between painter cases and painter controls; however there was evidence of an association between increasing intensity of solvent exposure and poorer performance on a range of cognitive tests, including those measuring visual memory, verbal memory and planning. The negative association between intensity of solvent exposure and mean grip strength, after adjusting for smoking, alcohol and age, was statistically significant (Dick et al., 2002).

There are many reasons which might have contributed to the negative findings of these studies including a lack of test sensitivity or differences in testing technique. Insensitive measures of exposure estimates, inadequate study design, biases in the selection of the control and exposed groups, and other confounding factors such as age, education and socioeconomic background could also contribute to these findings.

3.4.6 SUMMARY

A very large number of different neurobehavioural tests have been used in the measurement of neurobehavioural deficits which presents a number of problems in terms of comparing the results of different studies and therefore reaching conclusions as a whole. Most obviously it is also difficult to define exactly what is being measured in each case. Clearly, different tests measure different aspects of cognitive function and it is often difficult to group together different tests which claim to measure a particular function, due to the substantial overlap between the different tests in terms of what they measure. However these tests have been successful in identifying neurobehavioural performance deficits associated with solvent and other toxic exposures.

The majority of the studies reviewed were cross-sectional which highlight considerable methodological issues associated with the study designs including self-reported exposure assessment and inappropriate selection of matched control groups. Two of these studies used no exposure measurements and compared between exposed and non-exposed groups (Smargassi et al., 1998; Bolle et al., 1996). Both studies reported no differences between exposed and non-exposed groups on neurobehavioural test performance.

Duration of exposure estimates for the measurement of solvent exposure have also been used in the literature and showed dose-response relationships in one study (Escalona et al., 1995) but not others (Kishi et al., 1993; Lee et al., 1993). The basis of these measurements however are self-reported which may be influenced by factors such as recall and interviewer bias. Other studies have used more sophisticated cumulative exposure indices using a combination of self-report, work history, and biological and/or air monitoring estimates and have reported dose-response relationships between exposure and neurobehavioural test performance (Nordling Nilson et al., 2002; Lo Sasso et al., 2001; Daniell et al., 1999; Grosch et al., 1996; Bolla et al., 1995; Colvin et al, 1993; Daniell et al., 1993).

A limitation of cross-sectional study designs is the selection of well matched control groups. In a number of the studies reviewed, the control group was selected on a volunteer basis rather than matched on potential confounding variables such as age, education and other exposures (Hooisma et al., 1993; Lee and Lee, 1993). Whilst in other studies, the subject selection method was not stated (Escalona et al., 1995; Ng et al., 1990).

Regardless of the limitations mentioned above, the overall findings of the studies reviewed are reasonably consistent in their attribution of neuropsychological and neurobehavioural effects from occupational solvent exposure in adults. The consistency of the results from these studies suggest adverse effects on neurobehavioural functions especially reports in deficits in the functional domains of memory, motor dexterity, concentration and attention which have been shown to be associated with solvent exposure in adults. These findings are plausible and bring on concerns which cannot be ignored, especially when these findings are consistent with studies regarded as being methodologically strong (Nordling Nilson et al., 2002; Dick et al., 2002; Mergler et al., 1996; White et al., 1995).

Specifically, this raises concerns for children especially in the absence of research on the effects of solvent exposure in working children and significant efforts must be made to fulfil the information gap in this area of solvent neurotoxicity.

The next section of this review will identify a very limited number of studies which have investigated neurobehavioural effects of solvents in children.

3.5 Neurodevelopmental effects of solvents.

As reiterated throughout this review, there is a lack of studies examining the effects of solvents on children who are also at risk of exposure to solvents through their work. As discussed in an earlier section of this thesis, previous studies have investigated the magnitude of developmental neurotoxicity and the effects of environmental exposure of children to various pollutants including methylmercury, lead, PCB and other toxins but no study has investigated the association between neurotoxicity and solvent exposure of children in the workplace. Studies on solvent exposure to children have been limited to prenatal exposure. The results of the studies of prenatal exposure to solvents show that occupational exposure in mothers to organic solvents during pregnancy is associated with an increased risk of colour vision and visual acuity impairment (Till et al., 2003; Till et al., 2001a), poorer cognitive and neuromotor functioning (Till et al., 2001b), increased risk of major foetal malformations (Khattak et al., 1999) and lower scores on subtests of intellectual, language, motor and neurobehavioural functioning (Laslo-Baker et al., 2004) in offspring.

Table 3.4 provides a summary of the literature available on neurobehavioural and other effects associated with solvent exposure in children. Similar to the previous table on neurobehavioural effects associated with solvent exposure in adults, the following table presents information on the study design, study subjects, measurements of exposure, neurobehavioural tests used and the findings of the studies.

Table 3.4: Neurobehavioural and other effects associated with solvent exposure in children

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Laslo-Baker et al (2004)	Prospective controlled	Children born to mothers (counselled through the Motherisk program b/w 1989-1998) who were occupationally exposed to organic solvents during pregnancy (3- 9 yrs) (Canada)	32 exposed mother-child pairs 32 matched control pairs	▪ Self report exposure recorded prenatally and twice postnatally	Wechsler preschool and primary scale of intelligence (3-5.11yrs), Wechsler Intelligence Scale for children (6-8.11), Preschool language scale (3-5.11), Clinical evaluation of language fundamentals (6-8.11), Beery-Buktenica developmental test of visual motor integration, grooved pegboard, CBCL, Conner's Rating Scale-R, Behavioural style questionnaire. Wechsler Abbreviated scale of intelligence (Maternal cognitive functioning)	▪ In utero exposure to organic solvents associated with poorer performance on specific subtle measures of neurocognitive and neurobehavioural function (subtests of intellectual, language, motor functioning and behaviour). ▪ Regression analyses adjusted for maternal education and IQ
Till et al (2003)	Case study from a Prospective longitudinal cohort	Child exposed prenatally to PCE from mothers work. Exposure (Canada)	1 exposed 3 non-exposed controls	▪ Self report	Retinoscopy, Ophthalmoscopy, Sweep and transient VEP (visual evoked potential) system, Minimalist test (colour vision)	▪ Reduced visual contrast and abnormal chromatic responses found in 30 month old boy prenatally exposed to PCE compared to controls.
Till et al (2001a)	Prospective cohort	Children born to mothers (counselled through the Motherisk program b/w 1992-1996) occupationally exposed to solvents during pregnancy (3-7 yrs) (Canada)	32 exposed mother-child pairs 27 matched control pairs	▪ Estimated exposure index based on self/employer report of workplace exposure. Exposure parameters assigned weighted scores, added to derive EI.	Minimalist test (colour vision), Cardiff cards (visual acuity)	▪ In utero exposure to organic solvents associated with an increased risk of colour vision and visual acuity impairment in offspring. ▪ No dose-response relationship found

Table 3.4: Neurobehavioural and other effects associated with solvent exposure in children (continued)

Reference	Study design	Study Subjects	Sample Size	Exposure	Tests	Comments
Till et al (2001b)	Prospective controlled	Children born to mothers (counselled through the Motherisk program b/w 1992-1996) occupationally exposed to solvents during pregnancy (3-7 yrs) (Canada)	33 cohort 28 controls	▪ Estimated exposure index based on self / employer report, workplace exposure, ▪ Exposure parameters assigned weighted scores added to derive EI categorized as high &low.	Developmental Neuropsychological Assessment (NEPSY) (Body part naming, speeded naming, verbal fluency, visual attention, tower, statue, block construction, hand positions, arrows, visuo-motor precision, design copying, Peabody picture Vocab, Expressive one-word picture vocab test, pegboard, matching, child behaviour checklist (CBCL) and CPT (Birdie in the tree)	▪ Maternal exposure to organic solvents during pregnancy is associated with poorer outcome in cognitive and neuromotor function (receptive and expressive language, and graphomotor ability) in offspring. ▪ Regression analyses adjusted for gender, mother's age, education, smoking during pregnancy gestational age, breastfeeding and SES based on Hollingshead Index.
Khattak et al (1999)	Prospective observational controlled	Pregnant women occupationally exposed to solvents counselled by Motherisk program b/w 1987 -1996) (Canada)	125 exposed to solvents 125 matched controls exposed to non-teratogenic agents	▪ Self report of work history, work practices, adverse effects known to be caused by solvents	Interviews, assessments, developmental milestones recorded using Denver scale.	▪ Women occupationally exposed to solvents during pregnancy had a 13 fold risk of major foetal malformations as well as increased risk for miscarriages in previous pregnancies. ▪ Women reporting symptoms associated with organic solvents had a significantly higher risk of major foetal malformations

Exposure to organic solvents in utero was found in a prospective cohort study to adversely affect subsequent colour vision and visual acuity in children (Till et al., 2001a). In total, 32 solvent exposed mother-child pairs were matched with a control group of 27 mother-child pairs on age of child, gender, ethnicity, maternal education and socioeconomic status and recruited from a database of women who had been exposed to a nonteratogenic agent during pregnancy. The solvent exposed group showed mild to severe impairment on the tritan and protan colour axes, unlike the matched non-exposed children whose visual functions were normal. However, no dose-response relationships were found and exposure index was not significantly related to colour discrimination or visual acuity scores (Till et al., 2001a)

Further analysis of the same study, (Till et al., 2001b) examined prospectively the cognitive and behavioural functioning of 3 to 7 year –old children whose mothers worked with organic solvents during pregnancy in comparison with a group of matched, unexposed children. The two groups of children were compared on a variety of tasks, including subtests from the NEPSY, a visual CPT as well as on parent-rated measures of children's behaviour. On tests of cognitive functioning, the solvent-exposed group performed generally in the normal range, however in comparison to children in the matched, normal control group, the solvent exposed group showed deficits in selective cognitive abilities. Dose-response deficits were most pronounced on tasks of Graphomotor ability, namely the NEPSY Design Copy and Visuo-motor Precision tasks, therefore suggesting poorer cognitive and neuromotor functioning in children of mother's occupationally exposed to organic solvents during pregnancy (Till et al., 2001b).

More recently, Till et al. (2003) reported on the reduced visual contrast and abnormal chromatic responses found in a case study from a prospective cohort subject (30 month old boy prenatally exposed to Perchloroethylene) compared to controls.

Similarly in a more recent study, children of women occupationally exposed to solvents during pregnancy were assessed on a range of neurodevelopmental and cognitive functioning tests (Laslo-Baker et al., 2004). In this prospective study, pregnant women occupationally exposed to organic solvents were recruited during pregnancy and followed up. Exposed mothers were matched to control mothers identified from those counselled by the Motherisk Program with exposure to a nonteratogenic substance on maternal age, child age, child sex, socioeconomic status and reported cigarette use. The results of this study suggested adverse foetal effects of occupational exposure to organic solvents during pregnancy as measured by neurocognitive, behavioural and motor coordination measures. Exposed children performed at a lower level than control children in subtests that measured short-term auditory memory, general verbal information and attention, motor and behavioural functioning. Furthermore, children who were exposed to organic solvents in utero showed reduced ability in recalling sentences, even when their global scores were within the normal range even when the effects of maternal IQ were accounted for (Laslo-Baker et al., 2004).

The above studies are well controlled prospective studies measuring prenatal effects of solvent exposure in children and highlight the potential vulnerability of children to harmful exposure. Prenatal exposure in these studies has demonstrated significantly adverse effects on children and therefore it would be essential to investigate children who have direct exposure as the results of these studies strongly suggest that these children will also show adverse neuropsychological effects. Further research is necessary to fulfil the gap in knowledge on the effects of solvents on working children to prevent serious health effects and preclude further deterioration in performance.

3.6 OVERALL SUMMARY OF THIS CHAPTER

An investigation into the literature on toxic exposure brings on alarming results. Even though toxic exposure in children has only been investigated in environmental settings, the potential vulnerability and susceptibility in children and the harmful effects to the body system and specifically the central nervous system have been demonstrated and are disturbing. Specifically, children have shown adverse neurobehavioural effects of exposure to other neurotoxins including methylmercury, PCB and lead which have been studied widely.

Whilst solvents are a common toxic exposure in working children, there are limited studies to investigate the size of this effect. The literature has reported consistently significant neurobehavioural effects on the central nervous system especially in specific functional domains of memory, motor dexterity, concentration and attention in adults occupationally exposed to solvents.

Given the lack of information on the dynamics of solvent toxicity on children, the adult literature on solvent effects on the central nervous system was reviewed. A wide range of studies suggest significant associations between solvent exposure and neurobehavioural deficits.

Whilst some of the studies were seriously flawed by a range of confounding, biases and limitations, other studies which were of sound methodological design showed remarkable consistencies in reports of neurobehavioural deficits and should be considered. The overall results of the studies on environmental and prenatal exposure of children to solvents shows clear effects of neurobehavioural deficits which need to be addressed.

Perhaps the greatest problem confronting all neurobehavioural research regardless of study design is true exposure estimation and the establishment of true dose-response relationships not reliant solely on self report. Furthermore, batteries of neurobehavioural tests need to be specific and sensitive to the particular modalities they are testing with adequate control for external influences. Therefore research investigating neurobehavioural effects of working children exposed to solvents with sound methodological approaches need to be addressed. The next chapter will address some of these methodological issues.

CHAPTER 4: METHODOLOGICAL ISSUES

This chapter will outline the methodological issues and considerations which are important for the development of a well designed study on neurobehavioural performance in working solvent exposed children. Issues in the selection of neurobehavioural tests, research study design, confounding variables, motivational effects and the measurement of exposure will be discussed.

4.1 Selection of neurobehavioural tests

There are a number of issues associated with the selection of neurobehavioural tests for studies of the effects of chemicals with potential neurobehavioural effects, including the reliability, validity, sensitivity and specificity of the tests. Reliability is a fundamental prerequisite of any good test and attributes to the consistency of measurement (Gregory, 2000), hence a reliable test must consistently assign to each individual tested, the same score that best reflects their level of performance (Rohlman et al., 2003). A valid test is one that measures what the user of the tests expects it to measure whilst sensitivity is the degree to which the tests discriminate between exposed and non-exposed populations (Rohlman et al., 2003). Williamson (1995), states that, "Tests need to be sufficiently sensitive to detect neurotoxic effects where they exist", and tests with high reliability and good validity will help reduce the error variance to reveal effects due to exposure. Another desirable attribute of a test battery is its specificity and how well the battery discriminates between the effects of different toxic substances (Williamson, 1990). It is essential that when considering the choice of tests specifically for this study, the tests are standard measures with demonstrated reliability and validity and sensitive to detect early central nervous system functional domains likely to be affected in children occupationally exposed to solvents

Because of the dearth of literature on exposure to solvents in working children, it is difficult to devise a study design by building on previously used batteries of tests, specifically to understand which tests are sensitive to detecting specific neurobehavioural deficits. Nevertheless, in the absence of studies on working children, it is important to consult the published literature on the different neurobehavioural test batteries used in the assessment of occupational solvent exposure in adults and environmental exposure in children, in order to recognize which neurobehavioural measures are sensitive indicators of effects of exposure on central nervous system function (Letz et al., 1996).

When selecting neurobehavioural tests to assess potential neurotoxicity in an exposed population, the primary factor to consider is the chemical to which the target population is exposed (Anger, 2003), and the population to which this battery of tests is being selected for. The nature of the study population including their age, cultural background, educational level and socioeconomic status also need to be considered. Specifically for the purposes of this study, a battery of tests applicable to children who come from a non-English speaking background with lower or no educational level represents a far more challenging problem than most other populations. Not only because children are the most sensitive end point for some chemical exposures, but also because of the many developmental stages through which they progress (Anger, 2003). A selection of non-verbal performance rather than verbal tests is also necessary to account for the illiteracy and non-English speaking background of the children in the study population.

There are several batteries which have been designed specifically for neuropsychological assessment of environmental or occupational exposure to neurotoxic substances and there have been a number of batteries developed to study childhood exposure to individual toxicants, most notably lead, methylmercury and PCBs. Winneke et al. (1988) recommend that a children's neurotoxicology battery include tests of intelligence, language, memory, perception, attention and motor functions. Most of the studies on environmental exposures in children (see Table 3.1) have employed neuropsychological tests to identify cognitive dysfunction rather than clinical and neurological examinations. However, White and Feldman (1987), state that a much richer picture of neurotoxic effects is provided by thorough neuropsychological testing with attendant clinical judgement in the evaluation of the results than with the small sample of information provided by the time-limited test batteries developed to assess such effects. Furthermore, (Lezak, 1983), states that it is also essential that in a study of neurobehavioural effects any battery of neuropsychological tests is carefully selected to reveal clinical patterns and to employ established neuropsychological principles in the analysis of such tests

In the lead literature as outlined in Table 3.1, the most commonly used measures of neuropsychological effects in children included subtests of the WISC-R, McCarthy's' Scales of Children's abilities, NES2, Bender Visual Motor

Gestalt, Bruininks Oseretsky Test of Motor Proficiency, Stanford Binet Intelligence Scale, Rey-Osterreith Complex Figure and the Wide Range Assessment of memory and learning. Also consistent among the studies on the effects of lead exposure were measures of intelligence (IQ) functioning (Stokes et al., 1998; Walkowiak et al., 1998; Altmann et al., 1997; Tong et al., 1996 Dietrich et al., 1993; Bellinger et al., 1992; Needleman et al., 1990). Of the studies reviewed on lead effects, only three employed clinical assessment (neurological examinations and electrophysiological tests) as well as neuropsychological testing (Counter et al., 1998; Stokes et al., 1998; Altmann et al., 1997).

In the methylmercury literature, more common neuropsychological tests of motor function (Finger tapping, Hand-eye coordination, Bender visual motor gestalt), attention (Continuous Performance Test), visuospatial function (Stanford Binet copying) and memory (WISC-R block design, digit span) tests were found to be accurate measures of neurobehavioural deficits in prenatally methylmercury exposed children. (Grandjean et al, 1997; Grandjean et al., 1998; Grandjean et al., 1999; Grandjean et al., 2001a; 2001b; Cordier et al., 2002). Only one of these studies employed electrophysiological testing (Grandjean et al., 1997). The feasibility and validity of three computer-assisted neurobehavioural tests from the NES2 that were designed for adults, namely the Continuous Performance Test (CPT), Finger Tapping and Hand-eye coordination were tested on the same cohort of Faroe Island children from the methylmercury literature (Grandjean et al., 1996). These tests were found to be feasible and valid for the measurement of neurobehavioural deficits in children after slight modifications which included changing the sequence of letters in the CPT to a sequence of animal silhouettes which were more easily recognisable in children.

In the PCB literature, the choice of neuropsychological tests is less consistent than the choice of tests in measuring the effects of lead and mercury and only included neuropsychological testing on measures of sustained attention (CPT), focused attention (digit cancellation), executive function (Wisconsin Card sorting and Stroop colour-word tests), memory (digit span, WISC-R arithmetic, Sternberg memory) and more common batteries designed specifically for children including the Kaufman Assessment Battery for children, McCarthy scales of Children's abilities, Wechsler Intelligence scales for children IQ tests and Reynell Developmental Language scales (Jacobson and Jacobson, 2003; Stewart et al., 2003; Patandin et al., 1999; Jacobson and Jacobson, 1996a).

The selection of tests in the above studies suggests a pragmatic representation of what functions might be affected based on previous research (Williamson, 1995). The replication of results in the different studies reviewed in Chapter Three, of the same effect associated with the same chemical exposure helps establish a neurotoxic effect at least in the lead, mercury and solvent literature where substantial replication of findings in the studies from different countries using similar tests are found. Previous research on solvent exposure in adults has been reported to affect neurobehavioural performance such as loss of dexterity, delayed reaction time, lack of concentration and loss of memory and therefore the selection of tests for children occupationally exposed to solvents should address these specific functions and modalities. To this effect, a selection of tests which give a reasonably comprehensive coverage of the major areas of known neurobehavioural function likely to be affected by solvent exposure were chosen for this study. A flexible battery will be compiled from a set of existing neuropsychological tests whose diagnostic utility and validity have already been demonstrated in the literature will be used. The aim of selecting these tests however is not only to answer the question of whether a particular neurotoxicant affects the nervous system but also to determine which function(s) or behaviour in particular is affected by that exposure (Williamson, 1990). The tests were chosen from three core test batteries, including the WHO Neurobehavioural Core Test Battery (NCTB), the Neurobehavioural Evaluation System 2 (NES2) and the Performance and Information Processing System (PIPS) and include both computerised and non-computerised tests.

The WHO recommended Neurobehavioural Core Test Battery (NCTB) is a compendium of tests of the seven most widely used tests in human behavioural neurotoxicology. The WHO NCTB was developed in the early 1980's in an attempt to provide a 'screening' or core battery approach to neurobehavioural investigations (Anger, 2003), and was selected based on encompassing a selection of tests sampling the wide range of functions likely to detect any adverse affects from neurotoxic exposure. The tests selected were considered to be easy to administer paper and pencil tests and which were culture-fair (Hartman, 1995). These tests include the digit symbol, digit span, Benton visual retention, pursuits aiming II, simple reaction time, Santa Ana and profile of mood states.

The Neurobehavioural Evaluation System 2 (NES2) is a computer based testing system which was developed in the mid 1980's in line with the NCTB. The NES2 is a widely used computer based neurobehavioural testing system that incorporates the cognitive tests from the NCTB and a number of other tests used in clinical neuropsychology (Anger, 2003).

The Performance and Information Processing system (PIPS) is a computer based battery of tests based on 'diagnostic' and theoretical interpretation (Spurgeon, 1995). The tests in the Performance and Information Processing battery system are based on an information processing model of human performance generation. The information processing approach is useful for organizing information about the human system and also for guiding human factor designs which portray human information processing as a flow of information between various information stores and transformational processes (Wickens and Carswell, 1997). Williamson (1990) argues that tests of behaviours like manual dexterity and memory are an amalgamation of a number of fundamental processes which can be traced to particular nervous processes and, in order to produce either behaviour, a critical level of attention is required. To this effect, if the required level of attention is not achieved, performance on these tests will be reduced. The battery of tests from the Performance and Information Processing System (PIPS) has been included in an attempt to overcome such problems in the interpretation of complex and integrated measures. The concept underlying this battery of tests is that behaviour is the result of combining a number of simple but inter-related processes and in order to understand why and how a behaviour is produced in a particular way, it is necessary to test these simpler processes. This improves the ability to assess the effects of a wide range of influences on behaviour due to the tests' focus on converging evidence or changes in specific functions. The Performance and Information Processing system was developed on a model of human information processing which concentrates on eight inter-related functions: sensory store, perception, response selection, decision making, short-term memory, long-term memory, attention and response generation (Williamson et al., 1988)

The nine non-verbal performance tests selected for the study of neurobehavioural effects of children occupationally exposed to solvents include: *measures of attention*; the NES2 Continuous Performance Test which will measure the child's ability to sustain attention and the PIPS Dual Tracking Task, an adaptive task which will measure the child's ability to divide attention between more than one task including reaction time, and hand-eye coordination. *Measures of memory*; both working auditory memory (WISC-R digit span) and spatial memory (PIPS spatial memory search), *measures of motor coordination*; (grooved pegboard) and *measures of reaction time*; (PIPS choice reaction time) which also measures perception and elements of motor coordination. Reaction time is also an important component of a number of the other tests (Symbol-digit, Dual Tracking task, CPT and grooved pegboard) in which reaction speed is a measure. The PIPS symbol digit has also been included as a *measure of complex decoding* and has been cited as being among the most sensitive tests of neurotoxic chemicals (Anger, 1990). The

Draw a Person test has been incorporated as an integrated test of complex and motor functions but also as an estimation of pre-morbid intelligence. The Profile of Mood States will contribute as a measure of mood symptoms. A more detailed description on each of these tests will be discussed in Chapter Five.

Pre-morbid intelligence has been used in the literature of exposure effects as a measure of pre-exposure intellectual capabilities and has been considered to be a better predictor of premorbid neurobehavioural performance than education (Gregory, 2000). The comparison of an individual's current neuropsychological performance with his/her premorbid level of intellectual functioning is fundamental in detecting and quantifying cognitive impairment (Lezak, 1983) which in this case may be associated with solvent exposure. Many of the studies reviewed on the effects of solvent exposure have incorporated tests of "vocabulary" and "verbal intelligence" into neurobehavioural test batteries as measures of pre-morbid intelligence or "hold-no hold" tests, not seen to be directly influenced by solvent exposure. Bolla et al., (1995), included the WAIS-R vocabulary subtest as an estimate of premorbid verbal intelligence, and found significant decrements in neurobehavioural functioning with solvent and lead exposures after controlling for pre-morbid intellectual ability, age and race. Grosch et al., (1996) however, found that vocabulary (also used for measuring pre-morbid functioning) to have significant dose-effect relationships with solvent exposure.

In this study, the Draw a Person test which is a non-verbal measure of pre-morbid intelligence with inherent appeal to children (Dykens, 1996), will be used as a dependent variable of the effects of solvent exposure on motor functions, as well as a potential confounder and predictor of neurobehavioural test performance.

4.2 Research Study Design

To design a study in neurobehavioural research, a proper source population and a feasible sampling frame must be chosen with a suitable comparison group identified. The prospective longitudinal cohort study is often recommended as the most reliable source of information in neurobehavioural research to help overcome some of these serious bias problems (Grandjean et al., 1996). Prospective longitudinal studies have several advantages over cross-sectional studies, including more accurate assessment of degree and timing of exposure and of relevant control variables (Jacobson and Jacobson, 1996b). However despite the advantages of longitudinal studies, the majority of the studies reviewed in Chapter Three on neurobehavioural effects of solvent exposure were cross-sectional in nature. Whilst data from longitudinal studies are generally preferred, only 4 out of the 33 studies reviewed on neurobehavioural performance effects associated with solvent exposure in adults used longitudinal study designs (Table 3.3) (Nordling Nilson et al., 2002; Mergler et al., 1996; Williamson, 1996; White et al., 1995; Williamson and Winder, 1993). Of these studies, the Nordling Nilson and colleagues study constitutes an 18 year follow-up of workers and represents the most useful longitudinal study in the current context (Spurgeon, 2002). The other longitudinal studies reviewed other than Williamson and Winder (1993), had shorter periods of follow-up which may be explained by loss to follow-up and significant rates of drop-outs thus making longitudinal studies less practical. Also, in longitudinal studies involving children, it may be difficult to attribute changes because of developmental changes over time.

There are limitations associated with using cross-sectional studies most notably the measurement of exposure for a short period of time and the potential for bias and confounding effects. Furthermore, cross-sectional studies provide a "snap-shot", comparing performance of subjects divided into categories based on concurrently measured parameters of exposure (Rice, 1998). However, compared to longitudinal studies, cross-sectional study designs appear practical, convenient and inexpensive and can help in providing some baseline evidence of neurobehavioural effects before a full-scale prospective investigation is undertaken.

A well-controlled cross-sectional study with quantifiable exposure measures and a carefully selected battery of reliable and valid neurobehavioural tests will attempt to reduce the limitations and bias problems of cross-sectional studies. Moreover, the selection of a matched control group will help eliminate the effects of bias and confounding variables on neurobehavioural performance and the interpretation of these results.

4.3 Effects of Confounding Variables

A major problem in neurobehavioural research is determining which inherent factors are true effects of exposure and which factors can be accounted for by other variables. The impact of potential confounding factors (commonly age, education and gender) should be considered and accounted for in the analysis of neurobehavioural effects. Almost all of the studies reviewed in Chapter Three accounted for covariates likely to have had an effect on outcome. Williamson (1996), studied the role of confounding variables in the assessment of neurobehavioural effects of chronic solvent exposure and concluded that confounding variables (age, educational level, and alcohol use) showed greater influences on performance, however, education level played the greatest role in explaining each test performance in this study population of young apprentices. This finding therefore suggests that education and literacy levels will be factors to consider in the analysis of neurobehavioural performance results, especially with young participants.

Therefore, in developing a well designed research study, careful selection of the control group is required to control for these confounding factors. Furthermore, potential confounding from different medical and lifestyle conditions specific to the population selected should be identified and distinguished early in the research from those diseases that may be caused by the exposure. Such information may be collected in the questionnaire. (Anger et al., 1994).

4.4 Motivational Effects

Another issue to consider in neurobehavioural research is motivation of the study population to participate in the study and the effects this may have on neurobehavioural performance. This is especially true in studies where "volunteers" or "healthy worker" controls are used in a study. Williamson, (1995) states that "Motivational effects can take two opposite forms, subjects trying to do well (faking good) and trying to do poorly (faking bad) and that all behaviour requires a certain level of motivation or incentive to generate it".

Subjects may show a lack of interest in being tested at all whilst others are bored by the tests or testing situation (Letz, 2003). In order for neurobehavioural test results to be valid, a subject needs to exert maximal effort in performing the task on that test and it is therefore important to encourage the subject's motivation and to use tests that maximise motivation, in order to eliminate the effects of such behaviour. Letz, (2003), recommends a list of partial remedies to the problem of motivational difficulties in neuropsychological testing which are listed in Table 4.1 below.

Table 4.1: Suggestions for decreasing the impact of motivational variables on test performance*

- Emphasize power, not speed in the tests
- Use intrinsically interesting tasks
- Make tests shorter
- Target the difficulty of items to the subject's ability level
- Identify individuals with suspicious performance in real-time
- Include specific measures of anxiety, depression and malingering in test battery
- Implement Item-Response Theory (IRT) and Computerised-Adaptive Testing (CAT) methods

***(Adapted from Letz, 2003)**

Motivational influences are just as important in testing children as adults and it is essential that these recommendations are used in studies of children and considered when designing neurobehavioural test batteries for children. Specifically, to win child acceptance, the ideal component tests of a basic test battery must be engaging, user-friendly and reinforcing with pleasant feedback (Amler et al., 1996). The neurobehavioural tests which have been selected for this study, are engaging, simple to understand and user-friendly. The choice of both computerised and non-computerised tests will enable the child to experience the use of a computer (which will be a novelty for most of these children) as well as experiment with non-computerised tests. The break-up between the two settings will enhance motivation in the children and ensure the above mentioned recommendations are met.

4.5 Measurement of Exposure

The determination of exposure-response relationships is important for confirmation of the causality of a toxic effect and poor exposure assessment can be an important limitation to the finding of such a relationship in neurobehavioural research (Jang et al., 1999). Exposures in cross-sectional studies are generally quantified only using very crude estimates of the dose of exposure like painter years or simply a classification into categories like high/low (Iregren, 1996); however exposure assessment for neurobehavioural research studies in recent years is becoming more refined. In the majority of the studies reviewed on the effects of solvent exposure in Chapter Three, two groups of workers (exposed and non-exposed) were compared. Sixty three of the seventy two studies reviewed included an analysis of solvent exposure effects as well as group comparisons. However the measurement of exposure was different between these studies. Most studies developed at least one cumulative exposure index based on a combination of duration of work and of exposure (Chen et al., 2001a; Chen et al., 2001b; Chen et al., 1999b) and some estimation of exposure levels as an analysis of historical monitoring data and lifetime exposures (Semple et a.l, 2000; Dick et al., 2000; Daniell et al., 1999; Nelson et al., 1994), and job type including work practices (Julien et al., 2000; Hooisma et al., 1993) or hygienist assessment by walk through surveys (LoSasso et al., 2001). Whilst many of these studies have reported dose-response effects, the limitation in using such measures of exposure is the inaccurate exposure classification based on self-report and the likelihood of potential biases. To estimate exposure, many of these studies relied on retrospective assessments of workers regarding occupational history, work environment, job duties and so forth and have relied heavily on subjective recall to measure each individual's exposure. This has problems in that study subjects may recall exposure to solvents in greater concentrations than was the case to be consistent with beliefs that exposures to solvents cause present symptoms (Lees-Haley and Williams, 1997) and hence length of exposure may be overestimated and the use of protective equipment underestimated.

Biological and air monitoring have been used in the literature to provide a more accurate and current measurement of exposure and have identified solvent exposure effects (Challenor and Wright, 2000; Mitran et al., 1997; Tsai et al., 1997; Mergler et al., 1996; Muijser et al., 1996; Tsai et al., 1996; Altmann et al, 1995; Escalona et al, 1995; Muttray et al., 1995; Hakkola, 1994; Kishi et al., 1993; Lee and Lee, 1993; Wang and Chen, 1993) .

Other studies have used more elaborate measures of solvent exposure including a calculation of cumulative exposure comprising of exposure indices and measurements of ambient, personal air or biological monitoring and have reported dose-response relationships (Bockelmann et al 2002; Castillo et al., 2001; Campagna et al., 2001; Feldman et al 1999; Seeber et al, 1996; Welp et al., 1996; Colvin et al., 1993; Daniell et al., 1993). Of these studies, no significant dose-response associations were found in four studies (Ihrig et al., 2003; Chouaniere et al., 2002; Zupanic et al., 2002; Williamson and Winder, 1993)

In an attempt to establish an accurate measure of solvent exposure in working children in Lebanon, a combination of self-report (questionnaire) and personal air monitoring will be used. Biological monitoring as well as these measures would be the best approach to measure body state and air monitoring. However, for a study population in Lebanon, biological monitoring would be seen as intrusive and would be difficult to be accepted by working children and their parents. In a country that is still recovering from many years of war, the element of trust is not easily established. Therefore air monitoring and self-reported measures will be used.

4.6 Overall summary of this chapter

There are a number of methodological issues which need to be addressed in the design of a study on occupationally solvent exposed children and neurobehavioural performance effects. Specifically, a selection of tests which are valid, reliable, specific and sensitive to the core modalities known to be affected by solvent exposure and the population to which it is being administered needs to be considered. Other factors to be taken into consideration include issues such as motivational effects, the identification and control of confounding variables which may influence the outcome of performance on tests, the selection of a well controlled and matched comparison group especially in cross-sectional studies, and the selection of an accurate and quantifiable measure for the estimation of solvent exposure. The following chapter will outline the specific methods and materials selected for this study keeping in mind and particularly addressing the above mentioned methodological issues.

CHAPTER 5: METHODS AND MATERIALS

5.1 Overview of the Chapter

This chapter presents the research methods used to achieve the aims and objectives of this study. This study aims at an in depth understanding of the hazards and work conditions that working children in Lebanon are being exposed to, specifically the association between solvent exposure and neurobehavioural deficits. The factors which need to be examined to achieve these aims include the general work environment, the level of exposure to neurotoxicants among working children in Lebanon and the neurotoxic effects associated with this exposure. The research methods and materials selected for this study will help to examine these effects.

5.2 Research Design

A convenience sampling cross-sectional study design, which used an interviewer administered questionnaire, neurobehavioural testing and ambient air exposure assessment as measurement tools was selected for this study. Each of these measurement tools was specifically selected in order to achieve the objectives and purposes of the study. Convenience sampling is a form of non-probability sampling where subjects are selected because of their convenient accessibility to the researcher (Lunsford and Lunsford, 1995). The disadvantage of convenience sampling is that some of the population have no chance of being selected and there is no way of knowing whether the sample represents the whole population. However, this sampling method is easy, fast and usually the least expensive and troublesome (Lunsford and Lunsford, 1995) and with a cross-sectional study design would provide baseline data required for further cohort studies in future.

5.3 Ethics Approval

Ethics approval was granted by the University of NSW Human Ethics Research Committee in October 1999. Time duration was five years allowing time for the study to be conducted as part of a PhD research thesis. The Institutional Review Board (IRB) and research committees at AUB also granted ethics approval in May 1999. The Lebanese National Committee on Child Labour and IPEC approved the study before partial funding of the study.

5.4 Subject Selection

The source population for this study were working children between the ages of 10 and 17 years. It was estimated that 92 children would be required for the study. This was calculated by estimating the population proportion of working children at 6% in Lebanon within 5 percentage points and assuming with absolute precision at 0.08 and 90% confidence interval. Based on this calculation, a total of 300 children aged 10-17 years were recruited to the study. The study sample consisted of;

a) 100 working children exposed to organics solvents at work (the subject group)
b) 100 working children not exposed to organic solvents at work (the positive control group) and,

c) 100 non-working, non-exposed school children (the negative control group).

There are no child labour registries in Lebanon, therefore working children were sought for the study by means of walk-through surveys within the cluster of industrial areas of the city of Tripoli and its environs in North Lebanon. These areas are known for their small industrial establishments and the relatively high rates of working children.

Children working in places with potentially high exposures to solvents (automotive spray painting, mechanical repair and furniture painting workshops) were identified during the walkthroughs and approached at work. A total of 207 establishments (furniture painting, mechanical repair and spray painting workshops) were approached in order to recruit the working exposed children. The objectives of the study were explained to each child and to the child's employer on initial contact. For the facilitation of this study it was of extreme importance to secure the employer's cooperation. The child was approached at least three times at work to arrange appointments for collection of data and for exposure assessment and the lack of cooperation from the employer would have made this difficult. The initial visit to the workplace was followed by a second visit in order to arrange a visit to the child's home to introduce the study to the child's guardians (parents, etc) and to obtain their consent. The consent of the guardian, the child and the child's employer were all required for participation in this study.

The working non-exposed children (positive control group) were also selected by means of walk-through surveys in the vicinity of where the exposed group was recruited. However, the 110 workplaces approached for this group, were those known to have no or low potential for solvent exposure. These included barber shops, butcheries and retail convenience stores. The non-exposed non-working school children were residential neighbours of the working children who attended school and were approached to participate in the study in their homes. The subjects and positive and negative controls were frequency-matched on age and area of residence. Because of the nature of the workplaces, all working children in the study were male. As gender-matching was required, all the school children controls were also male.

5.5 Eligibility Criteria

5.5.1 Working children

Children aged 17 years and under who had worked in any of the above mentioned establishments on a full-time basis for at least 12 consecutive months were eligible for inclusion in the working exposed group. No lower age limit was set. However, the youngest working child identified was 9 years of age. If the child was a seasonal worker (i.e. only worked during summer), or had been in the workforce for less than 12 months, they were excluded from the study.

5.5.2 Non-working school children

Children aged 17 years and under, who were attending an educational institution on a full-time basis and had never been engaged in any type of employment, either paid or unpaid, were eligible for inclusion in the non-working school group.

5.5.3 Exclusion Criteria

Children were excluded from the study if there was a previous history of: head injury with loss of consciousness (LOC) for more than half an hour; had a history of epilepsy; or other known peripheral (neurological) and central nervous system disorder. Only two children (both working children) were excluded from the study on these health grounds.

5.5.4 Refusal rates

Definite refusals were received from 37 (18%) of the 207 workplaces which had high potential for exposure to solvents. Refusals were predominantly from the employers who refused to have the child participate in the study. The parents of 18 exposed working children refused consent.

The refusal rate for the working non-exposed group was less than the working exposed group. Definite refusals were received from 6 (5%) of the 110 workplaces with no risk of exposure to solvents. The parents of one child refused consent.

There were no refusals received from the 100 non-working school children who were approached in their homes for recruitment in the study.

5.5.5 Withdrawals

A total of 30 children had changed their place of employment between the first and second visits to the workplace (there is a high turnover rate, with children changing jobs frequently). If the child's new workplace was known, the new employer was approached and his consent was sought. If consent was not given, or potential for exposure to solvents in the new workplace were unknown, the child was withdrawn from the study and a replacement child recruited. Children were also withdrawn from the study if during the study period type of work was changed leading to a change in exposure level. In total, 18 children were withdrawn from the study because their working conditions had changed.

5.6 Data collection

5.6.1 Questionnaire

A standard questionnaire was developed using open and closed ended questions with the objective of collecting information on the child and the child's sociodemographics, work history, social habits, general health and any neurological manifestation of exposure to neurotoxic organic solvents. *(See Appendix C).*

Sociodemographic data included information on the child's age, date of birth, address, educational history, the highest level of education attained by siblings, parent's occupation and the parents' level of education. Work history information included the number of years a working child had worked, all previous workplaces (if any), their work start and finish times, number of breaks and the use of protective equipment. Data on general health included history of any illness, injuries, or medications and social habits such as smoking and alcohol ingestion.

The questions on neurotoxic symptoms were derived from the Swedish Q16 Neurotoxic questionnaire (Högstedt et al., 1984) developed to monitor effects on the central nervous system among workers exposed to solvents. The Q16 questionnaire contains 16 short questions with yes or no response alternatives on symptoms commonly described by workers exposed to solvents (Lundberg et al., 1997). For the purposes of this study, these questions were modified to make them more applicable and comprehensible to children. Specifically, the questions on changes in sex life were deleted and questions, which were pertinent to an illiterate population, were included to make a total of 17 questions. These included questions such as "do you understand the meanings of things you watch on TV". The questionnaire was translated into Arabic and administered in colloquial Arabic by the researcher. Because the questionnaire was interviewer-administered, the child was especially prompted regarding the type of work he did, actual tasks he performed and any other information which would help determine his level's of exposure to solvents. A neurotoxicity score was calculated for each child by adding up the number of positive responses to all 17 symptoms (range 0 to 17).

5.6.2 Neurobehavioural Tests

The neurobehavioural tests for this study were selected from a number of different test batteries used in previous studies. These included the PIPS (The Performance and Information Processing Systems Test Battery) (Williamson, 1990), the NES2 (Neurobehavioural Evaluation System 2) (Letz, 1991) and the NCTB (Neurobehavioural Core Test Battery) (WHO, 1986). In selecting the tests for this study, particular emphasis was placed on non-verbal performance tests rather than verbal tests, which were specifically selected and tailored to a non-English speaking and illiterate population. It was also important to ensure that cultural implications such as offensive language, pictures or notations associated with the selected tests were minimized and that these tests assessed the specific domains and modalities known to be affected by neurotoxic solvents (See Table 5.1).

Table 5.1: Neurobehavioural tests selected and the domains they assess

Test	Domain
Non-Computerised tests	
Profile of Mood Scale (Non-Verbal Analogue)	Affect/Measure of mood
Grooved Pegboard	Motor coordination
Digit Span (WISC-R)	Attention/ Memory
Draw a Person Test	Pre-morbid intelligence
Computerised tests	
Continuous Performance Test (NES2)	Attention/vigilance
Choice Reaction Time (PIPS)	Cognitive/ Motor
Spatial Memory Search (PIPS)	Cognitive / short term memory
Dual Tracking Test (PIPS)	Attention (divided)
Symbol Digit Coding (PIPS)	Cognitive/ coding

The selected tests as displayed above were as follows:

- Non-computerised tests of mood (POMS), motor coordination (Grooved Pegboard), memory (WISC-R digit span) and the Draw a Person (DAP) test which was used in an attempt to estimate complex cognitive function or intelligence and to attempt to obtain an indicator of premorbid intellectual abilities.

- Computerised tests of attention (NES2-Continuous Performance Test (CPT), PIPS Choice Reaction Time), spatial memory (PIPS Spatial Memory Search), divided attention (PIPS Dual Tracking Test) and perceptual-motor and cognitive skills (PIPS Digit Symbol coding)

The computerised tests were administered on a Pentium II 233 MHz Laptop computer. The tests used in the study are briefly described below. A more elaborate discussion on the selection of the tests is described in Chapter 3.

5.6.2.1 The Profile of Mood States (POMS) test

This is a non-verbal analogue profile of mood test used to determine the mood of the child. This test has been previously used by Grandjean et al., (1997) on children to assess mood states. Cartoon pictures of faces portraying various mood states (happy, tired, afraid, angry, energetic, sad, confused and tense) were presented with a non-verbal response scale consisting of a horizontal 10cm line between the neutral face and the one portraying a mood state. The child was asked to indicate on the scale how they felt mood-wise and was presented with a total of 8 stimuli.

5.6.2.2 Grooved Pegboard

In this test, the child was presented with small pegs with a groove on one side and a board with holes. The child was asked to fill the holes in the board with the pegs as quickly as possible using only one hand to pick up, rotate and fill the holes in a structured manner, left to right or right to left depending on the hand used. The dominant hand was used first and then the non-dominant hand. A total of 25 pegs filled the board and the child's time for each hand was recorded.

5.6.2.3 Wechsler Intelligence Scale for Children – Revised (WISC-R) Digit Span.

The digit span is a simple test of attention and auditory memory in which a series of numbers between 1 and 9 are read in Arabic to the child. The task of the child is to repeat the sequences, in the same order as they are given in the digit forward test and in the reverse order in the digits backward test. The trial is discontinued when the child fails both sequences of the same length. The overall score is the sum of digits forward and digits backward. The WISC-R Digit Span standard scoring system was used for this test.

5.6.2.4 Draw a Person (DAP) Test

The Draw a Person test was used in this study as it is a nonverbal, non-intrusive and easy to administer estimate of intelligence with inherent appeal to most children (Dykens, 1996; Naglieri, 1988). The children were asked to draw pictures of a man, a woman and then themselves. They were given 5 mins to draw each picture, or less if they felt that they had nothing else to add to the picture. A separate page was used for each picture drawn. To test inter-rater reliability each picture was evaluated by three scorers for content and complexity and scored using Naglieri's (1988) cognitive criteria. In this system, 14 features (arms, attachment, clothing, ears, eyes, feet, fingers, hair, head, legs, mouth, neck, nose and trunk) are rated on scales that range from 0 up to a maximum of 3, 4, 5 or 7 points. Raw scores were converted to standard scores and age-equivalent scores using tables for individual drawings supplied in the Naglieri (1988) manual. Draw a Person standard scores from only one scorer were used in the data analyses as no significant differences were found between the three scorers using Kruskal-Wallis testing (man score p=0.993, woman score p=0.730, self score p=0.879 and total score p=0.926).

5.6.2.5 NES2 Continuous Performance Test (CPT) – Animal Version

This is a sustained attention test derived from the NES2 battery (Letz, 1991). The children were shown a series of animal silhouettes flashed onto the computer screen over a 3-minute interval. The children were required to press a button on a keypad as quickly as they could every time the cat silhouette appeared.

5.6.2.6 PIPS Choice Reaction Time Test.

This is a simple visual-motor response speed test involving a rectangle, which changed colour (red and green) on the computer screen irregularly. The child was instructed to press the button on a keypad corresponding to the colour of the rectangle displayed on the screen as soon as it appeared. The child was required to do this 25 times.

5.6.2.7 PIPS Sequential Spatial Memory (SSM)

This is a test of memory for spatial location. In this test, squares in a 3x3 grid are presented on the computer screen and flashed for 250 milliseconds one at a time in a random sequence. At the end of the sequence the child attempted to reproduce the sequence from memory by moving and clicking the mouse cursor to each of the relevant squares in turn. If the sequence was reproduced correctly, it was then repeated with an additional square added to the end of the sequence. The sequence continued to grow in this way until the child was unable to reproduce it correctly, at which the trial terminated and a new sequence began. The child completed a total of 8 sequences

5.6.2.8 PIPS Dual Tracking Task

This dual task test is a computerised divided attention test involving hand eye coordination and tests of simple reaction time. The child was presented with a moving yellow circle on the computer screen and the task involved attempting to keep a small green dot inside the circle. This is an adaptive task run over a 3 minute period where the movement of the circle increased as the child became more accurate at keeping the dot in the circle. The circle decreased if tracking accuracy declined. The irregularity (or wander) of the circle's movement is a measure of task difficulty attained. At the same time, as it increased/decreased, the circle changed colour and as a secondary task, the child was asked to respond to the colour change by pressing any button on the keypad with his other hand.

5.6.2.9 PIPS Symbol Digit coding

This is a test of perceptual-motor skills and attention. In this task, a key containing symbols paired with digits between zero and nine appeared at the top of the screen. At the bottom of the screen individual symbols were presented one at a time in a random sequence. The children responded to each symbol by pressing the associated number on the keypad as quickly as possible. After each response, the next symbol was presented. The duration of this test was 90 seconds.

5.6.3 Walk-through Surveys

During the initial walk-through survey which was conducted to identify the working children, the researcher also subjectively observed and assessed the general conditions within the workplace. Of particular importance was the overall physical environment and the presence and use of control measures and personal protective equipment. The researcher also inquired about the chemicals used and the history of work-related incidents.

5.6.4 Exposure Assessment

Personal indirect passive samplers (3M brand Organic Vapour Monitor) were used to assess ambient air levels of solvents in the workplace. These samplers were selected and used in accordance with the Australian Standard 2986 – 1987. These monitors are non-invasive and user-friendly. They clip onto the subject's clothing within the breathing zone and are used to record the exposure level to solvents in a working day of 8 hours. The 3520 Organic Vapour monitor with backup section, uses the principle of diffusion, which is the gradual mixing of molecules of two or more substances. It has a primary and secondary back-up charcoal sorbent pad for easy collection of organic vapours and is used for sampling in demanding environments. This monitor is suited for compounds for which activated carbon shows limited capacity and is at least 75% accurate (95% confidence limits +/-25%) in the case of many workplace contaminants. During the piloting of these samplers, a number of employers complained about the length of the child's work time used and the interruptions they felt it caused their workplace. It was also found during the piloting phase of the study that in the smash repair and furniture painting workshops, too much dust was accumulating on the top layer of the sampler, thus preventing the appropriate adsorption of solvents onto the charcoal pads within the sampler. It was thus decided that the samplers would be clipped onto the child's clothes for half a workday, (4 hours) and the results doubled to represent sampling for a full work day. All the 100 working exposed children, 10% of the working non-exposed children and 10% of the school children were assessed using the samplers. The samplers were analysed by means of conventional gas chromatography at the American University of Beirut (AUB) Environmental Core Laboratory. 3M standardised calculation data were used in the analysis.

5.7 Pilot Testing

A number of pilot studies were conducted to assess the validity and feasibility of the research instruments mentioned above.

The neurobehavioural tests were piloted on a group of 20 Australian schoolchildren with Arabic speaking backgrounds before the study was conducted in Lebanon. This was done to ensure ease of administration of these tests, and to help identify any discrepancies or difficulties in the management of these tests.

Two of the tests were modified as a result of the pilot study conducted. Slight variation was made to the administration of the Draw a Person test and the profile of mood states. The Profile of Mood States originally used a vertical line with one face depicting a mood at the top and a neutral face at the bottom of this line (Grandjean et al., 1997). Children in the pilot study complained that they did not understand how they could measure their mood on the vertical line and always drew a cross on the bottom of the line regardless of their mood. The line was therefore changed to a horizontal position with the faces on the left and right hand side of the line. This change ensured that the children performed the task appropriately and in keeping with instructions.

The Draw a Person test was also slightly modified. The change here referred to the time taken to do the task. The original test instructions allow the child a maximum time of 5 minutes to complete the test. All the children in the pilot study completed their drawing in well under 5 minutes so it was decided that the time taken would be recorded, with a maximum of 5 minutes allowed.

The order of administration of the tests was also changed as a result of the pilot study. It was found that administration of the manual tests followed by the computerised tests was more manageable and helped reassure the child in a testing environment.

The questionnaire was piloted on a group of university students in Lebanon to review factors such as questionnaire appropriateness and time requirements to conduct the interviews. The questionnaire was found to be sufficient to address the purposes of the study and no modifications were made to the questionnaire.

The 3M 3520 samplers were piloted on a group of adults randomly selected from the furniture painting, automotive spray painting and mechanical workshops used as the study sites. In 10 cases, two samplers were attached to the same person, (one on each side of their collar). One sampler was sent for analysis at the Workcover laboratory in Australia and the other was analysed in the environmental core laboratory at the American University of Beirut (AUB) in Lebanon. It was the first time that the 3520 monitors were analysed at the AUB core laboratory and therefore in order to ensure that the analysis was correct, it was measured against the Australian analysis. The Australian analysis was regarded as the 'gold' standard as it is standardised though the National Association of Testing Authorities, Australia (NATA). This process continued for a period of 4 months until the results returned from both laboratories were the same and quality control was assured. It was necessary to keep the samplers at low temperatures (below 4 degrees Celsius) following sampling and hence for this and for cost and convenience reasons, analysis at the AUB laboratories was preferred over sending the samplers to Australia from Lebanon.

5.8 Testing Procedure

5.8.1 Questionnaire

The interviewing and testing components of the study were carried out on separate days. Parental consent was obtained at the first interview. The questionnaire was administered in the child's home, often in the presence of the parents; if the parent's preferred this. The child was asked and answered most of the sociodemographic questions except for those relating to the parents' education and occupational history. Parents were also asked to comment on any history of injury that the child may have had and to make comments on specific relevant questions in the neurotoxic section of the questionnaire.

The interview helped to provide a relaxed environment and to reassure the parents about participation in the study. The interview also assured the parents that the study was non-invasive and that data collected was confidential.

5.8.2 Neurobehavioural Testing

All the children were tested at home. This had the advantage of allowing parents to see what tests were administered. In most cases the parents were present during the testing of the child. Testing was carried out during the weekend in the working-exposed group on a day the child had off from work (usually on a Sunday). This ensured that as far as possible the study was gauging chronic rather than acute effects of solvent exposure on test performance. The working non-exposed and school children were tested on days that were convenient both to the interviewer and the children under study.

An adequate testing room was created in the child's home for testing as far as was permissible. The testing room needed adequate lighting and to be free of distracting noise and intrusions. It was set up with a table and two chairs. In cases where these criteria were unattainable due to the size of the home or other factors, an environment as close as possible to the standard was created. On 5 accounts, a testing session was rescheduled because of inadequate lighting caused by power-failure.

A thorough and standard verbal introduction using clear and distinct wording in Arabic was given at the beginning of the testing. The children were introduced to the manual (non-computerised) tests followed by the computerised tests. The Profile of Mood States test was administered first followed by the Draw a Person test, the grooved pegboard test and the WISC-R verbal digit span.

Following these tests, the children were given a practice test on the 4 computerised PIPS tests used in the following order (choice reaction time, symbol digit, spatial memory and dual tracking). The practice run was a shorter and slower version of the original test to help familiarize the children with the computer, the use of the "mouse" and the general feel of the testing procedure. The instructions were verbally translated to the children in colloquial Arabic in a standard manner. Following the practice run, the children performed the NES2 CPT followed by the full versions of the PIPS tests in the same order mentioned above. This sequence of testing was the same for all children in the study exposed and non-exposed alike. The testing session lasted approximately 40-45 minutes in total per child.

5.8.3 Exposure Assessment

The 3M 3520 samplers were attached to the child on a day within the week following administration of the tests. The workplace was approached on any random day for exposure assessment. This was either a morning or afternoon session. The importance of maintaining their usual day's work for the purposes of the study were explained to the child and the employer and it was stressed that they not alter any of their usual work practices. The sampler remained clipped onto the child's collar for a period of 4 hours and the child was asked not to remove it. Following its collection, the sampler was kept in a mobile cooler at a temperature below 4 degrees Celsius before being taken to the laboratory for analysis.

5.9 Data Analysis

Data on sociodemographic characteristics, personal habits, occupation, reported health problems, neurotoxicity symptoms and neurobehavioural performance were compared among the three groups of children.

Test scores were manually calculated for each of the non-computerised tests, Profile of Mood States, Draw a Person, Grooved Pegboard and Digit Span using the standard scoring methods as specified for each test. The scores for the Draw a Person test were compared and validated using three different scorers. The computerised test scores were automatically scored and collected by each specific test's software parameters and transferred for statistical analysis. All the data, computerised and non-computerised, were analysed using SPSS for windows V11.0 (Statistical Package for the Social Sciences – Version 11). One-way analysis of variance (ANOVA) using Bonferroni post-hoc contrasts, t-tests, Kruskal-Wallis, Mann-Whitney and Chi-square analysis were used to test for statistical significance, set α at 0.05, for both continuous and categorical variables. Where multiple tests were done, a Bonferroni adjustment was used. For example, if 8 comparisons were made, the level of significance, set α was reduced to 0.006 for each test. For the neurobehavioural tests, one-way analysis of covariance was used when demographic characteristics such as age and education were shown to affect performance on the neurobehavioural tests. These effects were determined by correlating potential confounders (i.e. age and education) with each neurobehavioural test using Spearman correlation.

Multiple linear regression analysis was used to measure the relationship between exposure to individual solvents and performance on the neurobehavioural tests.

5.9.1 Exposure Analysis

Analysis of exposure to organic solvents was carried out at the AUB environmental core laboratory using Gas Chromatography – Flame Ionisation Detector (GC-FID) and according to 3M sampling and analysis specifications (3M, 1998). Organic contaminants in air trapped on the 3M 3520 organic vapour monitor were desorbed in the laboratory with carbon disulfide (CS_2) and an aliquot of the desorbant was analysed by capillary gas chromatography with FID detection using two capillary columns of different polarity and two FID detectors. The information needed to calculate the contaminant concentration included the sampling time in minutes (t), the calculation constant A or B supplied from 3M, the contaminant weight in micrograms (W_p) which is the weight collected on the primary pad corrected for blank and (W_s) weight collected on the secondary pad corrected for blank , the recovery coefficient(r) and temperature effects. The time-weighted average concentration of contaminant, in milligrams per cubic metre was calculated using the expression:

$$C\ (mg/m^{3)} = (W_p + 2.2 \times W_s) \times A\ /\ (r \times t\ (minutes))$$

and the time-weighted average concentration of contaminant in parts per million (ppm) was calculated from the following expression:

$$C\ (ppm) = (W_p + 2.2 \times W_s) \times B\ /\ (r \times t\ (minutes)).$$

Hygienic effects were calculated for each sample. This is a relative measure assuming an additive effect of the solvents. The 'hygienic effect' (HE) is a summarized index for threshold limit value-weighted concentrations of the compounds of the mixture (Seeber et al., 1996). The concentrations for each of the compounds are standardized by the occupational standard values for the individual solvents of the mixture. In the absence of occupational health standards in Lebanon, the Australian National Occupational Health and Safety

Commission (NOHSC) standards were used for this study. The occupational standard values for each solvent were as follows: Toluene=100ppm, Styrene=50ppm, Xylene=80ppm, Benzene=5ppm, MEK=150ppm, Hexane=50ppm). For example, if the concentration of toluene found on a sampler is 46 ppm this is divided by the occupational standard of toluene (i.e. 46/100). This is done for each compound in the mixture and the ratio for each is added together. For example, one spray painter had the following concentrations found on his sampler for a period of 4 hours. (Hexane 2.63 ppm, MEK 41.17 ppm, Benzene 1.95 ppm, Toluene 25.06 ppm, Xylene 0.55 ppm and Styrene 8.93 ppm). In order to calculate the HE for this sampler these concentrations are divided by their respective NOHSC threshold limit values and the sum of these ratios is the HE.

(E.g. 2.63/50 +41.17/150 + 1.95/5 + 25.06/100 +0.55/80 + 8.93/50) =1.15

Therefore the HE for this child over a period of 4 hours is 1.15 or 2.30 over a period of 8 hours. An HE of 1.0 or less in an eight hour period should protect against adverse effects. (National Occupational Health and Safety Commission 2002).

Of the samplers analysed, 37% were excluded from the data analysis because they were found to be faulty (i.e. had a leak). However, when 3M were consulted, this percentage was still found to be within the approved ratio set to allow for errors and misclassification and did not affect the analysis. This will be discussed in more detail in the following chapter.

5.10 Overall Summary of this Chapter

This chapter has outlined the research design and methods which were used to effectively collect the data required to test the hypothesis of this research. The methodologically issues which were discussed in Chapter Four, were considered and applied to in selecting the suitable methods for this study. The following chapter will display and report the findings of the data which were collected using the above mentioned methods.

A fourteen year old working in a mechanical workshop

CHAPTER 6: RESULTS

6.1 Overview of Chapter

This chapter is composed of three sections and reports the findings of the analyses of data collected from several different sources including self-report surveys, neurobehavioural tests and 'exposure measures'. The first section presents the sociodemographic characteristics of the study population. These factors include social habits, self-reported health problems, work characteristics and self-reported neurotoxic symptoms. Specific covariates identified from these data will also be investigated in this section. The second section will present the neurobehavioural performance test results and demonstrate the differences found between working exposed, working non-exposed and school children taking into account the covariates identified. In the third section, results on the measurement and analysis of solvent exposure will be presented and the associations and effects this exposure has on neurobehavioural test performance will be explored.

Section One: Sociodemographic and Descriptive Findings

6.2 Sociodemographic Characteristics

The sociodemographic and work characteristics of the children are presented in Table 6.1. One way ANOVA with Bonferroni post-hoc contrasts showed that the mean age of school children was significantly younger than the working non-exposed children although, this was a very small overall difference between the two groups ($F_{(2, 297)}$=3.91, p=0.021). There was no significant difference in mean age between the working exposed children and the non-exposed groups. The working exposed children, their parents and siblings had significantly lower mean education levels than the working non-exposed and school children ($F_{(2,297)}$=78.61, p<0.001), and their parents and siblings The working exposed children came from larger families with significantly more siblings than children in the working non-exposed and school groups ($F_{(2,297)}$=45.93, p<0.001). The majority of the fathers of the working exposed children were labourers with none of the children's fathers in this group employed in professional occupations ($\chi^2_{(8)}$=61.52, p<0.001). Even though most fathers in the three groups indicated they were currently employed, it was significantly more common for fathers in the working exposed group to report that they were not in current employment ($\chi^2_{(6)}$=34.40, p<0.001).

Table 6.1: Sociodemographic characteristics of working exposed, working non- exposed and school children

	Working Exposed N=100	Working Non-Exposed N=100	School Children N=100	P value *
Age of child (years) **				
9 – 14	50	39	52	
15 – 17	50	61	48	
Mean (SD)	14.5 (1.6)	14.7 (1.6)	14.0 (2.0)	**0.021**
Education of Child				
Mean years (SD)	3.8 (1.9)	6.3 (1.9)	7.6 (2.5)	**<0.001**
Number of Siblings				
2 – 5	31	48	49	
6 – 9	52	45	38	**0.002**
10 – 16	17	7	13	
Education of Siblings				
Mean years (SD)	6.8 (2.9)	9.6 (2.3)	10.3 (2.7)	**<0.001**
Education of father				
Mean years (SD)	3.4 (2.8)	5.3 (3.4)	5.7 (4.0)	**<0.001**
Father's occupation				
Labourer	40	18	8	
Self-employed	38	35	50	
Tradesman	18	28	15	**<0.001**
Associate professionals	-	10	24	
Deceased	4	9	3	
Father currently working				
Yes	74	86	90	**<0.001**
Education of mother				
Mean years (SD)	2.8 (2.9)	5.2 (3.8)	6.2 (4.0)	**<0.001**
Mother's occupation				
Housewife	96	94	92	
Employed	4	6	8	**NS**

** Using ANOVA for continuous variables and chi-square analysis for categorical variables. Significant at P<0.05*
*** Bonferroni post-hoc tests show significant difference between working non-exposed and school children.*

Table 6.2 illustrates the child's self-reported literacy levels. Working exposed children were significantly more likely to have lower literacy than children in the other two groups ($\chi^2_{(4)}$=130.11, p<0.001). They were also significantly more likely to report having difficulty dealing with everyday demands of literacy such as understanding things read, understanding things watched on TV and the ability to follow Arabic subtitles on TV.

Table 6.2: **Self – reported literacy between working exposed, working non- exposed and school children**

	Working Exposed N=100	Working Non-Exposed N=100	School Children N=100	P value*
Illiterate / Gets by (%)	77	36	5	<0.001
Understands things read (%)	30	82	92	<0.001
Understands things on TV (%)	70	100	100	<0.001
Follows Arabic subtitles on TV (%)	26	72	90	<0.001

* *Using chi-square analysis and significant at P<0.05*

Table 6.3: **Correlation between children's level of education and parental education.**

	Correlation Value	P value**
Father's Level of education	0.369	<0.001
Mother's Level of education	0.282	<0.001

** *Using bivariate Spearman's correlations and significant at p<0.05*

The children's levels of education in the three groups were found to be significantly correlated with their mothers' and fathers' levels of education. This indicated that the children were more likely to have higher levels of education if their parents had attained higher levels of education (Table 6.3).

6.2.1 Reported Social Habits

Due to the small number of children who reported social habits of smoking, coffee drinking and substance sniffing, no tests of significance were attempted on each individual social habit. None of the children reported drinking alcohol but the working children reported a higher frequency of smoking, coffee drinking, and substance sniffing than the school children as shown in Table 6.4.

Reported substance sniffing however, tended to be a one-off experience rather than be engaged in on an addictive basis and children tended to state they enjoyed the smell of these fumes rather than admitting to an urge to sniff them on a regular basis.

However, the three variables, smoking, coffee-drinking and substance sniffing were categorised into one variable on the basis of reported use of one or more substance. This variable will now be referred to as 'social habits'. Further analysis showed that children in the working exposed group were significantly more likely to have reported ever trying any one or more of these social habits ($\chi^2_{(2)}$ =21.04, p<0.001).

Table 6.4: Self - reported social habits

	Working Exposed N=100	Working Non-Exposed N=100	School Children N=100
Current smoker (%)	10	6	1
No. of cigs per day			
1 – 10	5	3	0
11 – 20	4	2	1
Nargileh *(one-off experience)*	1	1	1
Intake of alcohol	0	0	0
Intake of coffee	13	8	1
Substance sniffing	7	1	0
Types of substances			
Exhaust fumes	2		
Petrol	2	1	N/A
Thinner	3		
Reported use of social habit*			
Yes	22	9	2
No	78	91	98

6.2.2 Reported Health Problems

The children's self-reported health problems are shown in Table 6.5. Overall the groups did not differ in reporting of health problems and there were no reports of many of the specified health problems. The only borderline significant finding was a higher proportion of eye irritation in the working exposed group compared to the working non-exposed and school children. In most cases, except for injuries and self-reported visual problems, tests of significance were not possible due to the small number of cases in each group. No other significant differences in self-reported health problems were found.

Table 6.5: Self – reported health problems

	Working Exposed N=100	Working Non-Exposed N=100	School Children N=100	P value *
Eye irritation (%)	29	18	16	**0.052**
Diabetes mellitus (%)	0	0	0	**N/A**
Peripheral Vascular Disease (%)	0	0	1	**N/A**
CNS disorder (%)	0	0	0	**N/A**
Psychiatric illness (%)	0	0	0	**N/A**
Head injury with LOC <15 mins (%)	5	1	7	**N/A**
Intake of medication (%)	1	1	2	**N/A**
Injuries (%)				
Limb	29	20	18	
Eye	1	0	0	**0.183**
Other	0	3	1	
Wears prescription glasses (%)	2	9	7	**N/A**
Self–reported visual problems (%)	2	9	5	**0.087**

* *Using chi-square analysis and significant at P<0.05*

6.2.3 Work Characteristics

Comparison of the work characteristics of the two working groups showed a number of statistically significant differences. Working exposed children reported on average that they had worked, 1.3 years longer than the working non-exposed children (Table 6.6). The working exposed children also reported being a younger age when starting work than the working non-exposed. One child in the working exposed group indicated starting work at the age of five. However, the working exposed reported slightly shorter hours of work a day, working just over 1 hour less per day on average. Up to 70% of working children indicated that they were working for financial reasons and most of these were in the working exposed group, while a similar percentage of working children indicated they were working because they had found a good employer to teach them the trade. Most of these were from the working non-exposed group. In both groups, a similar percentage of working children had changed employers recently (within the 6 months in which they were interviewed). Reasons for changing employers included no pay (13%) in the working exposed group. Other reasons in both the exposed and non-exposed working groups included employer problems and bad work conditions. Personal protective equipment was hardly reported as being used by either group, even those in the solvent exposed group.

Nevertheless, all the children in the working exposed group indicated that they had special everyday clothes, which they only wore to work. These clothes were changed at home everyday and were washed by the mother, but; clothes were less often washed in the working exposed group compared to the non-exposed group. Nearly all of the mothers in the working exposed group stated that they could smell the chemicals on their child's clothes.

Table 6.6: Work characteristics of working children using t-Test and Chi-square analysis

	Working Exposed N=100	Working Non-Exposed N=100	P value
Type of work			
Spray painter	45	---	
Mechanic	32	---	N/A
Furniture Painter	23	---	
Barber	---	90	
Butcher/Baker/Other	---	10	
Reasons for working			
Financial reasons	47	23	
Working with relative	16	11	0.001*
Good employer/learn the trade	29	48	
Other	8	18	
Years at work			
Mean (SD)	3.7 (2.0)	2.4 (1.5)	<0.001**
Age started work (years)			
Mean (SD)	10.8 (2.2)	12.3 (1.7)	<0.001**
Hours at work per day			
7 – 9	37	8	
10 – 16	63	92	<0.001**
Mean (SD)	10.4 (1.7)	11.9 (1.7)	
Break at work			
Yes	97	95	NS
No	3	5	
Time for breaks			
None	3	5	
Less than 1 hour	39	11	0.001*
1 hour and over	58	84	
Changed workplace recently			
Yes	23	21	NS
No	77	79	
Reasons for changing workplace			
Employer problems	3	6	
No pay	13	5	NS
Bad work conditions	4	2	
Closer to home	3	8	
Protective equipment worn			
None	95	100	
Overalls	2	0	
Masks	2	0	NS
Gloves	1	0	
Respirators	0	0	
Eye protection	0	0	
Summer work before starting FT work			
Yes	43	41	NS
Age began summer work			
7 – 10	17	1	
10 – 12	19	29	0.001*
13 – 16	7	11	
How often work clothes washed			
Everyday	19	43	
Twice a week	51	39	0.001*
Once a week	30	18	
Mother smells chemicals on clothes			
Yes	88	0	
No	12	100	<0.001*

* *Using Chi-square and significant at p<0.05*
** *Using t-Tests and significant at p<0.05*

6.2.4 Neurotoxic Symptoms

Table 6.7 shows statistically significant differences in the reporting of neurotoxic symptoms across the three groups. Light-headedness, difficulty concentrating, confusion, difficulty remembering, irritation, difficulty sleeping, headaches, feeling high and depression were more commonly reported in the working exposed children than in the working non-exposed or the school children. The only symptoms that did not show this pattern were, 'making notes to remember' and 'a reported seizure where there was no difference found between working non-exposed and school children. A neurotoxic symptom score based on the total number of symptoms reported by each study participant was analysed and showed a significant difference in the number of neurotoxic symptoms reported per person within the three groups. The working exposed children significantly reported around 6 times the mean number of symptoms as the working non-exposed and school children ($F_{(2,297)} = 148.79$, $p<0.001$) (Table 6.7). Because of the 19 measures used in this analysis and adjustment for multiple comparisons, the level of significance for neurotoxic symptoms was set at $p< 0.003$ based on Bonferroni corrections.

Table 6.7: Reported neurotoxic symptoms in the working exposed, working non-exposed and school children.

	Working Exposed **N=100**	Working Non-Exposed **N=100**	School Children **N=100**	P-value*
Light-headedness	51	5	2	<0.001
Tires easily	57	7	3	<0.001
Difficulty concentrating	41	8	8	<0.001
Confusion	42	11	16	<0.001
Trouble remembering	45	12	17	<0.001
Relatives note trouble remembering	36	9	12	<0.001
Makes notes to remember	3	0	0	NS
Easily irritated	72	24	26	<0.001
Reported seizure	0	0	0	NS
Sleeps more often	28	5	9	<0.001
Difficulty sleeping	41	10	7	<0.001
Incoordination/loss of balance	16	2	1	<0.001
Loss of muscle strength	28	7	7	<0.001
Difficulty moving fingers	22	1	1	<0.001
Numbness in toes	31	3	3	<0.001
Headaches	54	4	3	<0.001
Feels high	48	0	0	<0.001
Hands tremble	30	5	3	<0.001
Depression	34	16	5	<0.001
Total Neurotoxic symptoms ** Mean (SD)	6.8 (3.6)	1.3 (2.0)	1.2 (1.8)	<0.001

* *Using chi-square analysis and significant at P<0.003 adjusted for multiple comparisons*
** *Using ANOVA and significant at P<0.05*

6.2.5 Neurobehavioural Test Performance

The subject (working exposed) and control groups (working non-exposed and school children) mean performance on each of the neurobehavioural tests were assessed taking into account a range of variables as potential covariates. Those variables which were identified as potentially having a significant effect on test performance included the child's age, his level of education, his mother's level of education and his father's level of education Due to the significant correlation found between the child's level of education and his parents level of education, it was important that these variables be accounted for as potential covariates. The new variable, "reported use of social habit" as mentioned earlier in section 6.2.1 was also considered to be a potential covariate given the significant differences found in reported use between the three groups. The Draw a Person (DAP) total score was included as a potential covariate in this analysis to investigate the possible effect of pre-morbid intelligence on test performance.

Therefore, in order to detect whether any of these covariates had a significant influence on test performance, analysis using bivariate Spearman's correlation was conducted to assess associations between the performance on the tests and the potential covariates including, child's age, the child's, mother's and father's levels of education, the reported use of social habit and the DAP total score.

6.3 Effects of Potential Confounders on Neurobehavioural Test Performance

Table 6.8 presents the correlations found between each of these potential covariates. The child's age was significantly correlated with the child's level of education indicating that older children had significantly higher levels of education. Older children were also significantly more likely to report the use of one or more social habit. As previously discussed, the child's level of education was significantly correlated with the mother's and fathers levels of education. Furthermore, the child's level of education was also significantly correlated with the DAP total score, indicating higher levels of education to be associated with a higher DAP total score. Similarly, higher maternal levels of education were significantly associated with a higher DAP total score. Children whose mothers' had a lower level of education were significantly more likely to report use of one or more social habit.

Although correlations in most of the analysis in this section were found to be statistically significant, this did not always indicate a strong correlation. The significant correlation values ranged between (0.114 - 0.492).

Table 6.8: Spearman's correlations on potential confounders

	Child's age	Child's education	Mother's education	Father's education	Social habit	DAP score
Child's age						
Correlation Value	1.000	0.294*	-0.109	0.074	0.172*	0.012
P value	-	<0.001	0.060	0.213	0.003	0.830
Child's Education						
Correlation Value	0.294*	1.000	0.282*	0.369*	-0.069	0.292*
P value	<0.001	-	<0.001	<0.001	0.236	<0.001
Mother's Education						
Correlation Value	-0.109	0.282*	1.000	0.300*	0.163*	0.178*
P value	0.060	<0.001	-	<0.001	0.005	0.002
Father's Education						
Correlation Value	0.074	0.369*	0.300*	1.000	-0.095	0.097
P value	0.213	<0.001	<0.001	-	0.109	0.105
Social habit						
Correlation Value	0.172*	-0.069	-0.163*	-0.095	1.000	-0.075
P value	0.003	0.236	0.005	0.109	-	0.194
DAP Score						
Correlation Value	0.012	0.292*	0.178*	0.097	-0.075	
P value	0.830	<0.001	0.002	0.105	0.194	1.000

* *Correlation is significant at p<0.05*

6.3.1 PIPS Choice Reaction Time

Table 6.9 demonstrates the correlation found between the child's performance on the PIPS choice reaction time and their age, education, mother's education, father's education, reports of engaging in one or more social habit and the DAP total score using bivariate Spearman correlations.

Table 6.9: Correlation between performance on PIPS Choice Reaction Time and potential confounders using Spearman's correlation

	Child's age	Child's education	Mother's education	Father's education	Social habit	DAP score
PIPS Choice RT						
Reaction speed						
Correlation Value	-0.187*	-0.329*	-0.140*	-0.158*	0.125*	-0.013
P value	0.001	<0.001	0.016	0.008	0.030	0.823
No. Correct						
Correlation Value	-0.016	0.089	0.012	0.021	-0.024	0.084
P value	0.780	0.124	0.838	0.730	0.675	0.149

* *Correlation is significant at p<0.05*

There were a number of statistically significant negative associations found between the potential confounders and performance on the Choice Reaction Time (see Table 6.9). Age was significantly negatively correlated with performance on this test. This indicated that older children had quicker reaction times than younger children. There was a significant negative association also found between the child's level of education and their overall mean reaction speed, in which children with lower educational level were slower in their mean response speed compared to those with higher levels of education. The child's reaction time was also significantly slower with decreasing levels of maternal and paternal education. Children who reported the use of one or more social habits also had significantly slower reaction time on this test. However, the number of correct responses in this test did not correlate with any of the potential confounders.

6.3.2 PIPS Spatial Memory Search

A statistically significant correlation was found between the child's performance on the PIPS Spatial Memory Search (SMS) and their age as shown in Table 6.10. Older children showed better performance on this test.

Table 6.10: Correlation between performance on PIPS Spatial Memory Search and potential confounders using Spearman's correlation

	Child's age	Child's education	Mother's education	Father's education	Social habit	DAP score
PIPS SMS						
Avg. length of sequence						
Correlation Value	0.159*	0 .334*	0.068	0.160*	-0.089	0.276*
P value	0.006	<0.001	0.244	0.007	0.123	<0.001

**Correlation is significant at p<0.05*

The child's level of education and the average length of sequence in the PIPS SMS were correlated in that the average length of sequence increased with higher levels of education. Similarly, the child's average length of sequence significantly increased with increasing levels in the father's education. A higher total score on the Draw a Person test was also significantly correlated with increasing average length of sequence in this test.

6.3.3 PIPS Dual Tracking Task

No correlation was found between the child's accuracy of performance on the PIPS dual tracking task and any of the potential confounders. However, significant correlations were found between reaction time on this test and the child's age, education and parental education but not for reported use of social habit or DAP total score (Table 6.11).

Younger children had significantly slower reaction time on this test. Furthermore, the children who had lower levels of education and lower levels in maternal and paternal education also showed significantly slower reaction time on the PIPS dual tracking task.

Table 6.11: Correlation between performance on PIPS Dual Tracking Task and potential confounders using Spearman's correlation

	Child's age	Child's education	Mother's education	Father's education	Social habit	DAP score
<u>PIPS Dual Tracking Task</u>						
Wander – accuracy						
Correlation Value	0.077	0.076	0.078	0.105	-0.007	0.011
P value	0.183	0.189	0.180	0.078	0.906	0.845
Reaction time (ms)						
Correlation Value	-0.181*	-0.270*	-0.132*	-0.155*	0.058	-0.013
P value	0.002	<0.001	0.023	0.009	0.315	0.826

**Correlation is significant at $p<0.05$*

6.3.4 PIPS Symbol Digit

Significant correlations were found between the child's performance on the PIPS symbol digit test and their age as shown in Table 6.12. Older children performed better with higher numbers of correct responses and quicker reaction times than younger children. However, percentage correct in this test was not influenced by age which suggests that older children saw more symbols than younger children as this is a self paced test. There was a significant correlation found between the child's level of education and the number and percentage of symbols correct. The number and percentage correct increased, with increasing levels of education.

Mean reaction time in the symbol digit was also significantly correlated with level of education and children with a lower level of education had slower reaction time. Both the mother's and the father's levels of education correlated with the child's performance on this test. Children who had higher parental levels of education had significantly more correct responses and quicker reaction time than children who had less-literate mothers and fathers.

The DAP total score was also significantly correlated with performance on the symbol digit test. Children with a higher DAP total score had a significantly higher number and percentage of symbols correct. Children with higher DAP total scores also had significantly quicker reaction time in this test than children with lower DAP scores.

Table 6.12: Correlation between performance on PIPS Symbol Digit test and potential confounders using Spearman's correlation

	Child's age	Child's education	Mother's education	Father's education	Social habit	DAP score
PIPS Symbol Digit						
Number Correct						
Correlation Value	0.206*	0.492*	0.171*	0 .192*	-0.082	0.292*
P value	<0.001	<0.001	0.003	0.001	0.159	<0.001
Percentage Correct						
Correlation Value	-0.039	0.175*	0.077	0.042	-0.098	0.201*
P value	0.502	0.002	0.186	0.483	0.091	<0.001
Reaction time (msec)						
Correlation Value	-0.219*	-0.490*	-0.176*	-0.191*	0.064	-0.256*
P value	<0.001	<0.001	0.002	0.001	0.271	<0.001

* *Correlation is significant at p<0.05*

6.3.5 NES2 Continuous Performance Task (CPT)

Statistically significant but small negative correlations were found between all measures of the child's performance on the NES2 CPT and their age as shown in Table 6.13. These correlations indicate that older children had quicker mean response latencies, less variability in performance and less non-responses and false-positives than younger children.

Children with a higher level of education had quicker response latency than those with lower levels of education. Similarly, significant associations were found between the child's level of education and the standard deviation of response latencies. Children with lower levels of education had larger standard deviations on mean response latencies indicating more variable performance. The standard deviation decreased with higher levels of education. Significant associations were also found between the child's level of education and the number of non-responses in the NES2 CPT. Children with a higher level of education had fewer non-responses than those with a lower level of education. The number of false positives in the NES2 CPT was also found to be significantly associated with the levels of education. Children with lower levels of education had a significantly greater mean number of false positives than those with higher levels of education.

There were no significant associations found between the mother's or father's level of education and the child's mean response latency in the NES2 CPT. However, children with parents who had a lower level of education significantly had the highest number of non-responses and false positives.

Table 6.13: Correlation between performance on NES2 CPT and potential confounders using Spearman's correlation

	Child's age	Child's education	Mother's education	Father's education	Social habit	DAP score
<u>NES2 CPT</u>						
Mean response latencies						
Correlation Value	-0.220*	-0.413*	-0.090	-0.111	0.046	-0.235*
P value	<0.001	<0.001	0.120	0.061	0.427	<0.001
SD of response latencies						
Correlation Value	-0.149*	-0.373*	-0.110	-0.085	0.121*	-0.011
P value	0.010	<0.001	0.057	0.155	0.037	0.856
No. of non-responses						
Correlation Value	-0.183*	-0.286*	-0.128*	-0.238*	0.064	-0.032
P value	0.001	<0.001	0.027	<0.001	0.269	0.581
No. of false-positives						
Correlation Value	-0.167*	-0.369*	-0.129*	-0.157*	0.058	-0.029
P value	0.004	<0.001	0.026	0.008	0.317	0.622

* *Correlation is significant at p<0.05*

6.3.6 (WISC-R) Digit Span

No significant correlations were found between age and performance on any of the components of the WISC-R digit span as shown below in Table 6.14.

Table 6.14: Correlation between performance on WISC-R Digit Span and potential confounders using Spearman's correlation

	Child's age	Child's education	Mother's education	Father's education	Social habit	DAP score
Digit Span – (WISC-R)						
Forward (No. correct)						
Correlation Value	0.072	0.417*	0.160*	0.187*	-0.118*	0.423*
P value	0.212	<0.001	0.006	0.002	0.041	<0.001
Backward (No. correct)						
Correlation Value	-0.036	0.378*	0.184*	0.137*	-0.088	0.409*
P value	0.540	<0.001	0.001	0.021	0.131	<0.001
Total (No. correct)						
Correlation Value	0.020	0.466*	0.205*	0.182*	-0.126*	0.486*
P value	0.728	<0.001	<0.001	0.002	0.030	<0.001

** Correlation is significant at p<0.05*

There was a significant association; however, found between the child's level of education and the number of digits recalled in the digit span forward, digit span backward and digit span total tests. The number of digits recalled in both the digit span forward and backward tests significantly increased with higher levels of education for the child. The total number of digits recalled in this test also significantly increased with increasing levels of the child's education.

Similarly, a significant correlation was found between the mother's and father's level of education and the child's performance on the digit span forward, backward and total in the WISC-R digit span test. Children with less literate parents recalled significantly fewer digits in all components of this test.

A significantly negative correlation was found between performance on the WISC-R digit span forward and digit span total and reported use of social habit. Children, who indicated they had engaged in one or more social habit, significantly recalled fewer digits in the digit span forward and total tests.

A significant correlation was found between performance on the WISC-R Digit span and the DAP total score. Children who recalled more digits in the digit span forward, digit span backward and digit span total tests, had significantly higher DAP total scores.

6.3.7 Grooved Pegboard

Table 6.15 demonstrates significantly negative correlations between the child's performance on the grooved pegboard and their age, their level of education, their mother's level of education and their DAP total score. Older children and children with higher levels of education had significantly faster completion times on the grooved pegboard dominant and non-dominant hand trials.

There were significant associations found between performance on the grooved pegboard and the child's level of education. Children with a higher level of education completed the grooved pegboard in less time than those with lower levels of education in both the dominant and on-dominant hand trials.

A significant but low association was also found between the mother's level of education and the child's performance on the grooved pegboard in the dominant hand trial. Children whose mother's had a lower level of education had slower completion times on the grooved pegboard dominant hand trial. However, no association was found between the child's completion time on the grooved pegboard dominant hand trial and the father's level of education or child's reported use of social habits. Similarly, the child's performance on the non-dominant grooved pegboard trial was not significantly correlated with either parent's level of education or reported use of social habit and no significant correlations were found.

Performance on the grooved pegboard was significantly correlated with the DAP total score. Children who had faster completion times on both the dominant and non-dominant hand trials had significantly higher DAP total scores.

Table 6.15: Correlation between performance on Grooved Pegboard and potential confounders using Spearman's correlation

	Child's age	Child's education	Mother's education	Father's education	Social habit	DAP score
Grooved Pegboard						
Dominant hand						
Correlation Value	-0.233*	-0.423*	-0.131*	-0.096	-0.049	-0.167*
P value	<0.001	<0.001	0.024	0.105	0.395	0.004
Non-Dominant hand						
Correlation Value	-0.253*	-0.393*	-0.095	-0.048	-0.036	-0.224*
P value	<0.001	<0.001	0.101	0.423	0.537	<0.001

** *Correlation is significant at p<0.05*

6.3.8 Profile of Mood States (POMS)

Table 6.16 demonstrates the correlations found between the child's responses on the Profile of Mood States and the child's age, education, parental education, reporting of any use of social habit and the child's DAP score.

Very small but statistically significant negative correlations were found between the child's age and responses in the POMS for the moods 'not tired' and 'not confused'. Older children significantly rated themselves as being more tired and more confused than younger children. Similarly, small but significantly significant correlations were found between the child's level of education and responses to the Profile of Mood States for the moods 'not sad', 'not tired', 'not angry' and 'not confused' (Table 6.16). Children with higher levels of education rated themselves as being significantly less sad, less tired, less angry and less confused than children with lower levels of education. The other moods states did not appear to be associated with the child's level of education

Significant correlations were also found between the mother's level of education and the child's self-rated responses on the 'not tired' and 'not confused' mood scales. Children with mothers who were less literate reported to be the most tired and most confused than children whose mother had higher levels of literacy. The other mood scales did not appear to be correlated with the mother's level of education and no significant associations were found.

The father's level of education was associated with the 'not angry' and 'not confused' mood scale and significant associations were found between different levels of the father's level of education. Again, children whose fathers were less literate reported to be angrier and more confused than those children with higher literacy. There were no further significant correlations found between the different levels of the father's education and the other mood scales in this test.

Children who reported not using any of the social habits (cigarettes, coffee, sniffing drugs) were significantly happier, less sad, less tired, less angry, less confused and less tense than those children who did report engaging in a social substance.

A number of responses on the POMS were also significantly correlated with the child's DAP total score. Children with a higher DAP score significantly rated themselves as being happier, less tired, less angry, less confused and less tense than children with a lower DAP total score.

Table 6.16: Correlation between POMS and potential confounders using Spearman's correlation

	Child's age	Child's education	Mother's education	Father's education	Social habit	DAP score
<u>POMS</u>						
Happy						
Correlation Value	-0.024	0.065	0.112	0.073	-0.188*	0.135*
P value	0.681	0.264	0.054	0.223	0.001	0.020
Not Sad						
Correlation Value	0.019	0.125*	-0.026	0.088	-0.140*	0.015
P value	0.748	0.031	0.655	0.140	0.016	0.800
Energetic						
Correlation Value	-0.044	0.073	0.046	0.077	-0.071	0.022
P value	0.448	0.209	0.428	0.197	0.220	0.701
Not Tired						
Correlation Value	-0.131*	0.114*	0.128*	0.037	-0.167*	0.144*
P value	0.023	0.050	0.028	0.533	0.004	0.013
Not Angry						
Correlation Value	-0.040	0.151*	0.108	0.152*	-0.221*	0.139*
P value	0.490	0.009	0.062	0.011	<0.001	0.016
Not Confused						
Correlation Value	-0.124*	0.254*	0.222*	0.180**	-0.204*	0.145*
P value	0.033	<0.001	<0.001	0.002	<0.001	0.012
Not Afraid						
Correlation Value	-0.072	0.024	0.035	0.009	-0.092	0.034
P value	0.212	0.683	0.547	0.881	0.114	0.564
Not Tense						
Correlation Value	-0.073	0.019	0.050	0.029	-0.114*	0.150*
P value	0.207	0.741	0.391	0.625	0.050	0.009

**Correlation is significant at p<0.05*

6.3.9 Draw a Person Test (DAP)

Table 6.17 illustrates the correlations found between the child's performance on the Draw a Person test and the child's age, child's education, mother's education, father's education, reported use of social habits and the DAP total score.

Table 6.17: Correlation between performance on Draw a Person Test and potential confounders using Spearman's correlation

	Child's age	Child's education	Mother's education	Father's education	Social habit	DAP score
Draw a Person Test						
Man						
Correlation Value	0.048	0.300*	0.136*	0.069	-0.085	0.933*
P value	0.412	<0.001	0.018	0.245	0.143	<0.001
Women						
Correlation Value	-0.013	0.277*	0.190*	0.099	-0.003	0.920*
P value	0.818	<0.001	0.001	0.097	0.958	<0.001
Self						
Correlation Value	0.036	0.284*	0.195*	0.128*	-0.050	0.937*
P value	0.530	<0.001	0.001	0.031	0.389	<0.001
Total						
Correlation Value	0.012	0.292*	0.178*	0.097	-0.075	1.000
P value	0.830	<0.001	0.002	0.105	0.194	-

* *Correlation is significant at p<0.05*

There were no significant correlations found between the child's age and the child's performance on the Draw a Person test. Statistically significant correlations however were found between the child's performance on the Draw a Person Test and their education level. Children with higher levels of education achieved higher scores on each of the three drawings, draw a man, draw a woman and draw self trials.

Similarly, a significant correlation was found between the mother's level of education and the child's performance on each of the three drawings in the Draw a Person test. Children, whose mothers had higher literacy levels also achieved higher scores on the draw a man, draw a woman and 'draw self' trials. However, in the father's level of education, only the 'draw self' trial was found to be significantly correlated with the father's level of education. Children whose fathers had higher levels of literacy achieved better scores on this test than those whose fathers had lower levels of literacy. No significant correlations were found between reports of engaging in one or more social habit and performance on the Draw a Person Test.

6.3.10 Summary of the Relationship Between Confounding Variables and Performance Measures

The previous analysis has identified the covariates that are likely to influence the child's performance on the neurobehavioural tests. Based on this analysis, Table 6.18 presents an overall summary of each measured variable and the association found with each neurobehavioural test. The child's level of education had an influence on performance on almost all of the neurobehavioural tests both computerised and non-computerised, whereas the child's age appeared to mainly influence performance on the computerised neurobehavioural tests. Parental education also appeared to affect performance on a number of neurobehavioural tests. Maternal education appeared to influence performance on reaction time, digit span and the Draw a Person test, whereas paternal education appeared to influence performance on reaction time tests, spatial memory and digit span. The reported use of social habits showed an effect on the children's reaction time test and responses to the Profile of Mood States.

The number correct in the Choice Reaction Time, wander in the Dual Tracking Task and the moods, energetic and afraid in the Profile of Mood States have not been included in (Table 6.18) because none of the selected variables were found to be associated with performance or responses to these tests. The choice reaction time number correct and the dual tracking wander results both had very little range so this is probably why they showed no associations with covariates.

Subsequent statistical analysis in this chapter will adjust for the covariates found to influence performance on each neurobehavioural test.

Table 6.18: Confounding variables which influenced performance on neurobehavioural tests

	Test	Child's Age	Child's Education	Mother's Education	Father's Education	Social Habit	DAP score
Computerised Tests	Choice Reaction Time (overall RT)	*	*	*	*	*	
	Spatial Memory Search	*	*		*		*
	Dual-Tracking (RT)	*	*	*	*		
	Symbol Digit (No. correct)	*	*	*	*		*
	Symbol -Digit (% correct)		*				*
	Symbol Digit (RT)	*	*	*	*		*
	CPT-Mean response	*	*				*
	CPT- SD of response	*	*			*	
	CPT (non-response)	*	*	*	*		
	CPT (False-positives)	*	*	*	*		
Non-computerised Tests	Digit Span (Forward)		*	*	*	*	*
	Digit Span (Backward)		*	*	*		*
	Digit Span (Total)		*	*	*	*	*
	Grooved Pegboard (DOM)	*	*	*			*
	Grooved-Pegboard (ND)	*	*				*
	POMS (Happy)					*	*
	POMS (Not Sad)		*			*	
	POMS (Not Tired)	*	*	*		*	*
	POMS (Not Angry)		*		*	*	*
	POMS (Not Confused)	*	*	*	*	*	*
	POMS (Not Tense)					*	*
	DAP (Man)		*	*			N/A
	DAP (Woman)		*	*			N/A
	DAP (Self)		*	*	*		N/A
	DAP (Total)		*	*			N/A

Social habit= reported use of one or more social habit, DAP Draw a Person. CPT=Continuous Performance Test .Grooved Pegboard (DOM) =Dominant hand, Grooved Pegboard (ND) =Non dominant hand. The Choice Reaction Time (no. correct), Dual Tracking Task (wander) and POMS (energetic and afraid) not included in table as not found to be affected by any of the selected variables.

Section 2: Neurobehavioural Test Performance

6.4 Neurobehavioural Performance Comparisons

Performance on the neurobehavioural tests was compared between the three groups of children; working exposed, working non-exposed and school children. Table 6.19, illustrates the differences in performance on each of the computerised neurobehavioural tests (PIPS choice reaction time, PIPS spatial memory search, PIPS dual tracking task, PIPS symbol digit and the NES2 Continuous performance test) across the three groups of children.

As discussed earlier, possible confounders for performance on the neurobehavioural tests were the child's educational level, child's age, parental education, reports of social habits and the DAP total score. Analysis using general linear models (one-way ANOVA and one-way ANCOVA with Bonferroni post hoc contrasts) was undertaken first only with group as a fixed factor, then again with the covariates listed above and which were found to affect performance on these tests.

Significant differences were found in performance on the five computerised neurobehavioural tests analysed in the first analysis using ANOVA and with no covariates controlled. Only wander (accuracy) in the PIPS Dual Tracking Task was not significantly different between the three groups. Working exposed children had significantly slower mean reaction time on the PIPS Choice Reaction Time, PIPS Dual Tracking Task, PIPS Symbol Digit and the NES2 CPT, than children in the working non-exposed and school groups. The average length of sequence in the PIPS Spatial Memory Search was significantly shorter for children in the working exposed group than the other two groups.

Analysis with covariates controlled using ANCOVA, remained significant for the same five computerised neurobehavioural tests. In the choice reaction time, after controlling for age, educational level, parental education and reports of social habits, exposed children still showed poorer performance in that they were significantly slower than the working non-exposed and school children and made significantly lower mean number of correct responses than the other two groups. The results of the spatial memory test also showed poorer responding by the working exposed children with children in this group recalling significantly shorter average sequences than working non-exposed or nonworking children. The results remained significant after controlling for age, child's educational level, father's educational level and DAP total score. For the dual tracking task, which comprised simple reaction time and tracking or hand eye coordination tests, there was no significant effect on the accuracy of tracking, but mean reaction time was again statistically significantly slower for working exposed children even after controlling for age, child's education and parental education.

Similarly, for the Symbol Digit test, the covariate adjusted results indicated significant differences in performance between the three groups with the working exposed children having overall slower mean reaction time and consequently fewer digits correct as this is a timed test. However, the significant differences in percentage correct disappeared after controlling for child's education and DAP total score.

In the NES2 Continuous Performance Test (CPT), the mean response latencies were significantly slower in the working exposed group than the working non-exposed and school children even after controlling for age, child's education and the DAP total score. The mean standard deviation of response latencies was significantly larger in the working exposed group and the working exposed also had significantly higher mean number of non-responses and false-positives to the stimuli presented than the working non-exposed and school children. All of these differences remained significant after controlling for age, child's education, mother's education and father's education.

Table 6.19: Neurobehavioural test performance on computerised tests in the three groups of children

	Working Exposed Mean (SD)	Working Non Exposed Mean (SD)	School Children Mean (SD)	*Unadjusted Analysis ANOVA#*		*Analysis adjusted for potential confounding variables ANCOVA ##*	
				F#	*P Value#*	*F##*	*P Value##*
PIPS Choice Reaction Time							
Overall Reaction Time (msec)[a]	33483 (1300)**	23706 (8132)	22570 (4840)	41.77	<0.001	26.22	<0.001
No. Correct	22.0(4.0)**	23.9(1.7)	23.4(2.9)	11.55	<0.001	N/A	N/A
PIPS Spatial Memory Search							
Average length of sequence .[b]	2.33 (0.82)**	3.26 (1.10)	3.02 (0.96)	25.51	<0.001	8.398	<0.001
PIPS Dual Tracking Task							
Wander – accuracy	18.1 (29.3)	17.2 (19.9)	19.5 (20.8)	0.23	0.796	N/A	N/A
Reaction Time (msec)[c]	1227.4 (400.74)**	947.9 (318.22)	999.70 (351.19)	15.87	<0.001	8.38	<0.001
PIPS Symbol Digit							
No. Correct[b]	21.5 (6.3)**	31.0 (8.8)	29.9 (9.7)	38.08	<0.001	10.28	<0.001
% Correct[d]	92.4 (9.4)	94.7 (6.1)	95.3 (6.3)	4.18	0.016	0.58	0.560
Reaction Time (msec)[b]	4132.4 (1417.0)**	2885.1 (872.8)	3034.2 (977.0)	37.39	<0.001	11.06	<0.001
NES2 CPT							
Mean Response Latencies (msec)[e]	675.7 (111.5)**	537.7 (66.9)	578.24 (85.9)	62.13	<0.001	38.74	<0.001
SD of Response latencies[f]	149.26 (37.56)**	119.82 (36.69)	109.40 (38.60)	28.65	<0.001	12.14	<0.001
No. of non-response[g]	3.43 (2.6)**	1.7 (1.9)	2.3 (2.0)	15.15	<0.001	7.16	0.001
No. of false-positive[g]	5.29 (4.9)**	1.07 (2.2)	1.32 (2.3)	49.21	<0.001	30.33	<0.001

#Using ANOVA ##Using ANCOVA N/A=Not applicable, performance not affected by selected variables.
***Bonferroni post-hoc test concludes statistically significant difference between mean of working exposed group and working non- exposed and between working exposed group and school children at p<0.05 value*
[a]Controlling for age, child's education, mother's education, father's education, social habits and DAP score [b]Controlling for age, child's education, fathers education and total DAP score [c]Controlling for age, child's education, and parental education [d]Controlling for child's education and DAP score [e]Controlling for age, child's education and DAP score [f]Controlling for age, child's education and social habits [g]Controlling for age, child's education, mother's education and father's education.

Table 6.20 displays the differences in performance between the working exposed, working non-exposed and school children on the non-computerised tests (WISC-R Digit Span, Grooved Pegboard, Profile of Mood States and the Draw a Person tests).

In the WISC-R Digit Span test, the working exposed group recalled a significantly lower mean number of digits in the digit span forward and backward tests compared to the other two groups as shown in Table 6.20. The digit span forward and digit span total tests remained significant after adjusting for child's education, parental education, reports of social habits and DAP total score. The difference in digit span backward also remained significant when child's education, parental education and DAP total score were accounted for,

There was a significant difference in performance on the grooved pegboard between the working exposed, working non-exposed and school children. The working exposed children showed significantly slower mean reaction and completion time on this task for both the dominant and non-dominant hand trials. After adjusting for child's age, child's education, mother's education and DAP total score for the dominant hand trial and adjusting for child's age, child's education and DAP total score for the non-dominant hand trial, the differences in performance between the three groups remained significant.

In the Profile of Mood States, significant differences were found between the working exposed, working non-exposed and school children. Significant differences were also found between the working (exposed and non-exposed) and non-working children. Working exposed children reported being less happy than the working non-exposed and school children. Bonferroni post-hoc contrasts showed that school children were significantly happier than working children (exposed and non-exposed); however, when this was adjusted for social habits and the DAP total score; the differences did not remain significant. Similarly, working exposed and working non-exposed children were significantly less energetic and more tired than the school children. These differences remained significant when further analysis controlled for the child's age, education, mother's education, social habits and DAP total score for the tired mood state. No further analysis was undertaken on the energetic mood state as no covariates were found to affect this mood in the earlier analysis. Working exposed children significantly reported being angrier and more confused than working non-exposed and school children. These differences remained significant even after controlling for the child's education, father's education, social habits and the DAP total score for the angry mood state and controlling for the child's age, education, parental education, social habit and DAP total score for the confused mood state.

In the Draw a Person (DAP) test, working exposed children had lower scores in the man, woman, self and overall total trials. This test showed significant differences between working exposed, working non-exposed and school children initially, but these differences disappeared when further analysis with covariates controlled for child's education and mother's education in the DAP man, woman and total trials and for child's education, mother's education and father's education in the DAP self trial.

Table 6.20: Neurobehavioural test performance on non-computerised tests in the three groups of children

	Working Exposed Mean (SD)	Working Non Exposed Mean (SD)	School Children Mean (SD)	*Unadjusted Analysis ANOVA*[*]		*Analysis adjusted for potential confounding variables ANCOVA*[#]	
				F[*]	*P Value*[*]	*F*[#]	*P Value*[#]
WISC-R Digit Span							
Forward [a]	6.48 (1.5)**	7.96 (1.4)	8.18 (1.7)	36.19	<0.001	9.93	<0.001
Backward [b]	3.42 (1.2)**	4.41 (1.4)	4.73 (1.6)	22.34	<0.001	3.04	0.049
Total [a]	9.91 (2.03)**	12.36 (2.4)	12.9 (2.9)	41.08	<0.001	8.70	<0.001
Grooved Pegboard							
Dominant hand [c]	85.86 (17.0)**	70.58 (11.7)	71.31 (10.6)	41.19	<0.001	22.45	<0.001
Non-Dominant hand [d]	93.82 (22.7)**	76.01 (11.9)	78.60 (14.2)	31.99	<0.001	14.43	<0.001
Profile of Mood States							
Happy*** [e]	68.60 (31.0)	75.90 (24.5)	79.40 (25.9)	4.00	0.019	0.79	0.454
Not Sad [f]	80.05 (25.7)	78.80 (25.9)	86.61 (24.8)	2.72	0.068	2.01	0.136
Energetic***	79.44 (25.2)	79.73 (21.9)	90.65 (19.8)	8.10	<0.001	N/A	N/A
Not Tired*** [g]	74.38 (29.2)	76.68 (26.3)	90.38 (20.7)	11.34	<0.001	4.99	0.007
Not Angry** [h]	74.55 (22.2)	84.42 (22.6)	88.58 (22.3)	10.22	<0.001	5.46	0.005
Not Confused** [i]	76.93 (20.9)	88.18 (20.3)	91.29 (18.0)	14.38	<0.001	6.51	0.002
Not Afraid	90.46 (17.9)	90.75 (16.2)	92.22 (18.6)	0.28	0.753	N/A	N/A
Not Tense [e]	84.99 (26.7)	85.07 (23.3)	86.09 (26.4)	0.06	0.944	0.67	0.514
Draw A Person							
Man [j]	84.82 (17.8)**	94.41 (15.7)	94.50 (15.3)	11.38	<0.001	2.50	0.084
Woman [j]	85.01 (16.8)**	93.22 (15.9)	92.82 (14.5)	8.47	<0.001	1.53	0.219
Self [k]	87.24 (18.2)**	95.94 (15.8)	96.86 (15.2)	10.24	<0.001	1.49	0.227
Total [j]	82.60 (19.6)**	92.54 (16.8)	93.33 (16.7)	11.17	<0.001	2.07	0.127

*[*]Using ANOVA [#]Using ANCOVA **Bonferroni post-hoc test concludes statistically significant difference between mean of working exposed group and working non- exposed and between working exposed group and school children at **p<0.05** ***Bonferroni post-hoc test concludes statistically significant difference between the means of school children and working children (exposed and non exposed) at **p<0.05** value [a]Controlling for child's education, parental education, reported use of social habits and DAP score [b]Controlling for child's education, parental education and DAP score [c]Controlling for age, child's education, mother's education and DAP score [d]Controlling for age, child's education and DAP score [e]Controlling for social habits and DAP score [f]Controlling for child's education and social habits [g]Controlling for age, child's education, mother's education, social habits and DAP score [h]Controlling for child's education, father's education social habits and DAP score [i]Controlling for age, child's education, mother's education, father's education, social habits and DAP score [j]Controlling for child's education and mother's education [k]Controlling for child's education, mother's education and father's education.*

Section 3: Exposure Analysis

6.5 Overview of This Section

The results from the analysis of the workplace exposure measures used in the study will be presented in this section. Individual and cumulative levels of exposure will be reviewed and the relationship between these exposures and performance on the neurobehavioural tests will be explored.

6.6 Sampler Leakage

As mentioned earlier in the Methods chapter (Chapter 5), 37% (N=44) of the samplers were found to have leaks and were therefore regarded as faulty and the results were consequently unreliable. The measurements from these samplers were excluded from the analysis, however, this did not affect any specific group and no significant difference was found between sampler leakage and groups studied (Table 6.21) or sampler leakage and type of industry (Table 6.22).

Table 6.21: Representation of sampler leakage site by study group

Leakage site	Working Exposed N=100	Working Non-Exposed N=10	School Children N=10	P Value*
None	60	6	10	0.280
Front leak	26	2	0	
Back leak	3	0	0	
Front and back leak	11	2	0	

* *Using Chi-Square analysis*

Table 6.22: Representation of sampler leakage by type of industry in working exposed group

Leakage	FP N (%)	Mech. N (%)	SP N (%)	Working NE N (%)	School Children N (%)	P Value
None	15 (65%)	20 (65%)	25 (54%)	6 (60%)	10 (100%)	0.292*
Front leak	5 (22%)	8 (26%)	13 (28%)	2 (20%)	0	
Back leak	2 (9%)	0	1 (2.2%)	0	0	
Front and back leak	1 (4%)	3 (9.7%)	7 (15%)	2 (20%)	0	

FP : Furniture Painters; Mech: Mechanics; SP: Spray painters; Working NE: Working non-exposed

Using Chi-Square analysis and significance at P<0.05

6.7 Hygienic Effect Levels

Of the samplers analysed, more than two thirds in the working exposed group were found to be over the hygienic effect threshold level of one (HE>1.0) as shown in Table 6.23. When the samplers in the working exposed group were categorised by type of industry, a hygienic effect level of more than one was found most frequently in samplers from mechanical workshops, followed by furniture painting and spray painting workshops. Not surprisingly, none of the working non-exposed or school children had detectable solvent levels above 1.0.

Table 6.23: Percentage of cases with Hygienic Effect (HE > 1.0) for each study group and type of industry

	Working Exposed N (%)			Working NE N (%)	School N (%)	*P Value*[*]
HE >1.0						
Yes	40 (67%)			0	0	<0.001
No	20 (33%)			6 (100%)	10 (100%)	
	FP	Mech.	SP			
HE >1.0	60%	85%	56%	0	0	<0.001

FP : Furniture Painters; Mech: Mechanics; SP: Spray painters; Working NE: Working non-exposed

[*] *Using Chi-square analysis and significant at p<0.05*

The Mean hygienic effect levels for the working exposed, working non-exposed and school children are displayed in Table 6.24. Non Parametric Kruskal-Wallis tests were used because the data were not Normally distributed. Significant differences were found in mean rank hygienic effect levels between the working exposed, working non-exposed and school children.

Table 6.24: Mean hygienic effect (HE) levels by study group

	Mean (SD)	Mean Rank	P Value[*]
Working Exposed (n=60)	1.76 (1.32)	46.48	<0.001
Working Non-Exposed (n=6)	0.06 (0.05)	7.17	
School Children (n=10)	0.11 (0.07)	9.40	

[*] *Using Kruskal-Wallis test and significant at P<0.05*

Table 6.25 illustrates the mean rank of hygienic effect levels for each industry in the working exposed group. Similarly, Kruskal-Wallis testing was used because the data were not Normally distributed. Significant differences were found between mean rank hygienic effect levels in the different industries, furniture painting, spray painting and mechanical workshops. Children working in mechanical workshops had the highest mean rank hygienic effects levels than children working in furniture painting and spray painting workshops.

Table 6.25: Mean Hygienic Effect (HE) levels by industry in the working exposed group

	Mean (SD)	Mean Rank	P Value*
Furniture painters (n=15)	2.19 (1.62)	34.70	0.011
Mechanics (n=20)	2.07 (1.21)	37.28	
Spray painters (n=25)	1.24 (1.05)	22.56	

** Using Kruskal-Wallis test and significant at $P<0.05$*

6.7.1 Hygienic Effect Levels and Neurobehavioural Test Performance

In order to understand dose-response relationship between solvent exposure and neurobehavioural test performance, initial analysis investigated the association between hygienic effect levels and neurobehavioural test performance.

Performance on each neurobehavioural test was analysed using t-test analysis for Normally distributed data and Mann-Whitney analysis for ordinal data. In this analysis, because multiple tests were done, a Bonferroni adjustment was used.

For the analysis of the computerised tests (Table 6.26) the alpha level was reduced to 0.004 because comparisons on 12 measures were made. In the non-computerised tests analysis (Table 6.27) the alpha level was reduced to 0.003 because 17 comparisons were made.

Working children with a Hygienic Effect (HE) of more than one, showed poorer mean performance on the choice reaction time test in that they were significantly slower than children with a HE of less than or equal to one as displayed in Table 6.26. Slower mean reaction time in the PIPS symbol digit test was also significantly associated with hygienic effect levels indicating slower mean performance with higher exposure levels; however, following adjustment for multiple comparisons, this did not remain significant. The standard deviation on mean response latencies was significantly larger in the NES2 CPT test indicating that children who were exposed to higher levels of solvents had more variable mean performance than those exposed to lower levels. Following adjustment for multiple comparisons, the number of non-responses and false positives in this test were not significantly associated with hygienic effect levels

Table 6.26: Performance scores for computerised neurobehavioural tests by hygienic effect level in working children

	HE≤1.0 Mean (SD) N=36	HE>1.0 Mean (SD) N=40	*t-Test Value (df=74)*	*Mann-Whitney U (df=74)*	*P value[*]*
PIPS Choice Reaction Time					
Overall (msec)	26049.31 (9561.23)	34613.75 (13695.73)	N/A	397.00	0.001
No. Correct	22.72 (2.84)	21.08 (4.92)	N/A	580.00	0.139
PIPS Spatial Memory Search					
Avg. length of sequence	2.62 (0.96)	2.30 (0.75)	1.638	N/A	0.106
PIPS Dual Tracking Task					
Wander – Accuracy	18.86 (27.91)	14.93 (16.39)	N/A	712.00	0.934
Reaction time (msec)	1104.00 (281.83)	1217.85 (458.58)	N/A	621.00	0.303
PIPS Symbol digit					
No. Correct	24.47 (6.89)	22.40 (7.41)	1.259	N/A	0.212
% Correct[**]	93.53 (6.09)	93.42 (6.95)	N/A	N/A	0.766
Reaction time (msec)	3604.17 (1027.40)	4259.40 (1773.40)	N/A	588.00	0.017
NES2 CPT					
Mean response latency (msec)	636.94 (114.03)	665.23 (109.41)	-1.103	N/A	0.274
SD of response latencies (msec)	129.72 (39.11)	156.85 (40.08)	-2.980	N/A	0.004
No. of non-responses	2.58 (2.08)	3.80 (2.22)	N/A	486.50	0.014
No. of false positives	3.39 (4.36)	5.63 (4.57)	N/A	474.50	0.010

[*] *Using T-test or Mann-Whitney analysis and significant at p<0.004*
[**] *Using Chi-square analysis and significant at p<0.004*

In the non-computerised tests, working exposed children with HE levels of greater than one, significantly recalled less numbers on the digit span forward and total than the children with HE levels less than one. Digit span backward did not remain significant following adjustment for multiple comparisons. Similarly, children with higher hygienic effect levels had slower mean completion time on the grooved pegboard dominant hand and non-dominant hand trials as shown in Table 6.27. However, only performance on the dominant hand trial remained significant following multiple comparison adjustments. The Draw a Person test and Profile of Mood States did not appear to be associated with hygienic effect level.

Table 6.27: Performance scores for non-computerised neurobehavioural tests by hygienic effect level

	HE≤1.0 N=36 Mean (SD)	HE>1.0 N=40 Mean (SD)	*T-test Value (df=74)*	*Mann-Whitney U (df=74)*	*P value**
Digit span – (WISC-R)					
Forward (No. correct)	7.49 (1.96)	6.30 (1.34)	3.012	N/A	0.004
Backward (No. correct)	3.77 (1.09)	3.18 (1.22)	2.225	N/A	0.029
Total (No. correct)	11.26 (2.64)	9.48 (1.89)	3.317	N/A	0.002
Grooved Pegboard					
Dominant hand trial (secs)	75.53 (15.68)	85.35 (14.01)	N/A	392.00	0.001
Non-dominant hand trial (secs)	85.54 (17.68)	93.92 (21.02)	N/A	485.00	0.022
Profile of Mood States					
Happy	67.74 (31.12)	70.25 (32.92)	N/A	658.50	0.657
Not Sad	79.43 (28.95)	81.55 (25.91)	N/A	670.00	0.744
Energetic	87.14 (18.95)	80.68 (25.28)	N/A	660.00	0.663
Not Tired	72.94 (33.30)	79.03 (24.85)	N/A	630.00	0.451
Not Angry	83.89 (24.69)	76.72 (19.64)	N/A	473.50	0.016
Not Confused	75.09 (28.61)	75.13 (23.36)	N/A	654.00	0.624
Not Afraid	90.49 (19.21)	92.03 (14.28)	N/A	657.50	0.623
Not Tense	82.26 (29.25)	88.00 (25.91)	N/A	603.00	0.281
Draw a Person Test					
Man	83.29 (15.51)	84.38 (19.27)	-0.267	N/A	0.790
Women	83.49 (14.70)	85.90 (18.61)	-0.617	N/A	0.539
Self	85.83 (16.91)	88.30 (19.51)	-0.582	N/A	0.562
Total	80.91 (17.92)	82.80 (22.00)	-0.403	N/A	0.688

**Using t-Test and Mann-Whitney analysis and significant at p<0.003*

Table 6.28: Neurotoxic symptoms by hygienic effect levels

Individual symptoms	HE ≤ 1.0 **N=36** **N (%)**	HE > 1.0 **N=40** **N (%)**	P-value*
Feels light-headedness	10 (31.3%)	22 (68.8%)	0.016
Tires easily	14 (41.2%)	20 (58.8%)	0.331
Difficulty concentrating	11 (39.3%)	17 (60.7%)	0.281
Confusion	8 (34.8%)	15 (65.2%)	0.148
Trouble remembering	11 (37.9%)	18 (62.1%)	0.196
Easily irritated	18 (39.1%)	28 (60.9%)	0.075
Difficulty sleeping	14 (56%)	11 (44%)	0.291
Sleeps more often	14 (45.2%)	17 (54.8%)	0.983
Incoordination/loss of balance	2 (25%)	6 (75%)	0.180
Loss of muscle strength	5 (33.3%)	10 (66.7%)	0.224
Difficulty moving fingers	5 (33.3%)	10 (66.7%)	0.224
Numbness in toes	5 (29.4%)	12 (70.6%)	0.092
Headaches	11 (30.6%)	25 (69.4%)	0.005
Feels of being "high"	11 (36.7%)	19 (63.3%)	0.131
Hands tremble	6 (28.6%)	15 (71.4%)	0.043
Depression	9 (42.9%)	12 (57.1%)	0.626
Total Neurotoxic symptoms ** **Average number per child** Mean (SD)	4.42 (4.25)	6.63 (3.66)	0.017

* *Using Chi-square analysis and significant at P<0.003*
** *Using t-test and significant at P<0.05*

Table 6.28 presents reported neurotoxic symptoms by hygienic effect level. The neurotoxic score which has been used previously to calculate the number of symptoms reported by each study participant also showed a significantly higher reporting of symptoms in children with hygienic effect levels of more than one. The mean number of symptoms was greater in those with HE level >1.0. Individual reports of light-headedness, headaches and hands trembling in children who had hygienic effect levels higher than one, did not remain significant after adjusting the alpha level for multiple comparisons.

6.8 Individual Solvent Exposure Levels

Table 6.29 displays the individual solvent exposure levels measured for the working exposed, working non-exposed and school children. It is clear from the previous analysis that mean hygienic effect levels in working exposed children are much higher than those seen for the working non-exposed and school children. The following analysis will assist in understanding the types and levels of solvents that the working exposed children experience in their workplace. Table 6.29 presents details on the different levels of individual solvents found in each of these groups. Because the data were not Normally distributed, non parametric Kruskal Wallis testing was used. Significant differences were found in the mean rank of hexane, MEK, benzene, toluene, xylene and styrene between the three groups. The working exposed children had consistently higher mean parts per million (ppm) values than the working non-exposed and school children.

Table 6.29: Levels of exposure among working exposed, working non-exposed and school children by solvent

	Working Exposed N=60	Working NE N=6	School Children N=10	*P Value*[*]
Hexane ppm				
Mean (SD)	4.28 (4.38)	0.57 (0.67)	0.38 (0.39)	
Range	23.56	1.46	0.94	<0.001
Skewness	2.09	0.47	0.27	
Mean Rank	44.29	16.58	16.90	
MEK ppm				
Mean (SD)	19.30 (43.04)	0.14 (0.19)	0.37 (0.29)	
Range	272.65	0.44	0.88	<0.001
Skewness	4.60	1.00	0.39	
Mean Rank	45.80	8.17	12.90	
Benzene ppm				
Mean (SD)	2.75 (3.23)	0.03 (0.07)	0.02 (0.04)	
Range	13.69	0.20	0.14	<0.001
Skewness	1.58	2.38	2.09	
Mean Rank	44.30	16.67	16.80	
Toluene ppm				
Mean (SD)	10.61 (11.66)	0.80 (1.00)	0.38 (0.45)	
Range	53.13	2.46	1.36	<0.001
Skewness	2.38	0.94	1.22	
Mean Rank	46.17	10.83	9.10	
Xylene ppm				
Mean (SD)	4.30 (4.75)	0.02 (0.03)	0.02 (0.07)	
Range	17.61	0.08	0.23	<0.001
Skewness	1.43	1.05	2.90	
Mean Rank	45.47	13.17	11.90	
Styrene ppm				
Mean (SD)	4.38 (6.80)	0.00	0.00	
Range	32.39	0.00	0.00	<0.001
Skewness	2.10	0.00	0.00	
Mean Rank	43.97	18.00	18.00	

[*] *Using Kruskal Wallis test and significant at P<0.008*

The working exposed children were further disaggregated by type of industry (furniture painting, mechanical repairs and spray painting) to investigate the individual types and levels of solvents they were being exposed to within their area of work. It was also necessary to examine whether or not there were differences in distribution of solvents between the different work environments as type of work could become a potential confounder of levels of exposure and performance on the neurobehavioural tests

Figures 6.1 to 6.5, illustrate the percentage of samplers that showed an exposure to each of the individual solvents within the three work environments; furniture painting, mechanical repairs and spray painting. All of the figures showed high levels of solvent exposure across the three groups with some variation between groups. The specific individual mean levels of these exposures and the associations they may have on the children's neurobehavioural test performance will be examined in more detail later in this chapter.

Figure 6.1: Percentage of hexane exposure within type of work

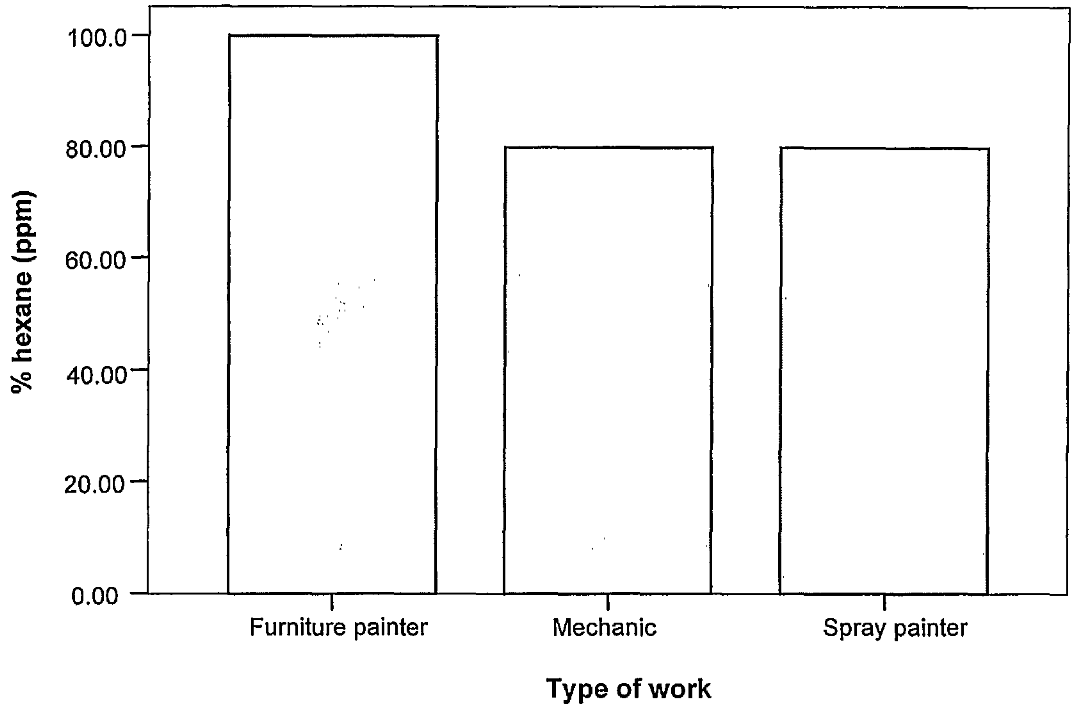
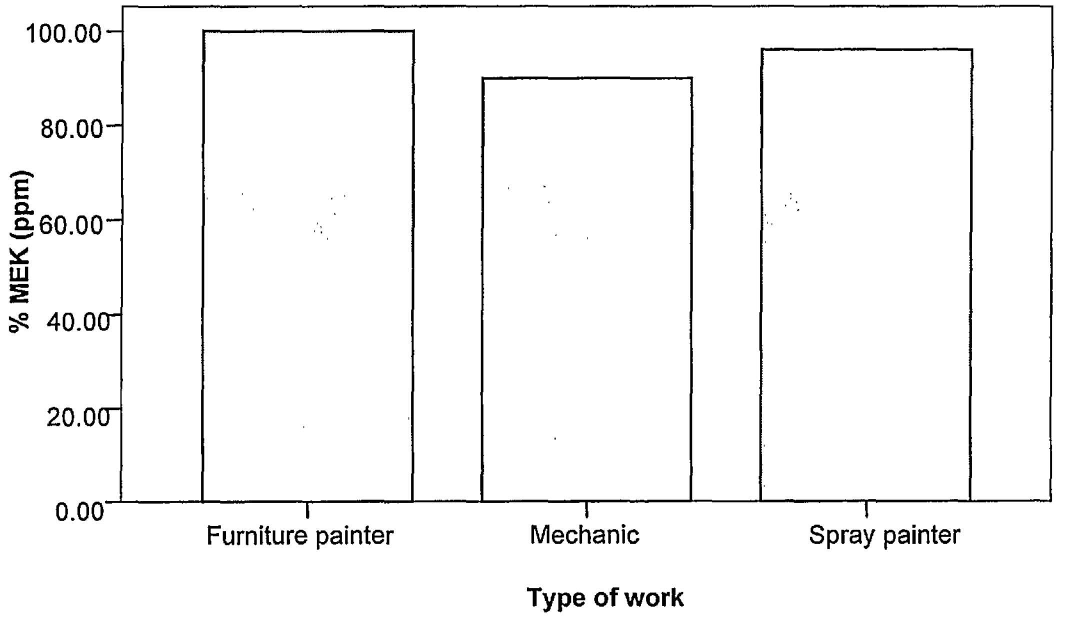


Figure 6.1 illustrates that at least 8 in 10 of the working exposed children were exposed to some level of hexane irrespective of their workplace. All of the furniture painters registered a level of hexane exposure on the air samplers.

Figure 6.2: Percentage of MEK exposure within type of work



Similarly, Figure 6.2 shows that at least 9 in 10 of the working exposed children were exposed to some level of MEK regardless of their workplace. Again, all of the furniture painters registered a level of MEK exposure on the air samplers.

Figure 6.3: Percentage of benzene exposure within type of work

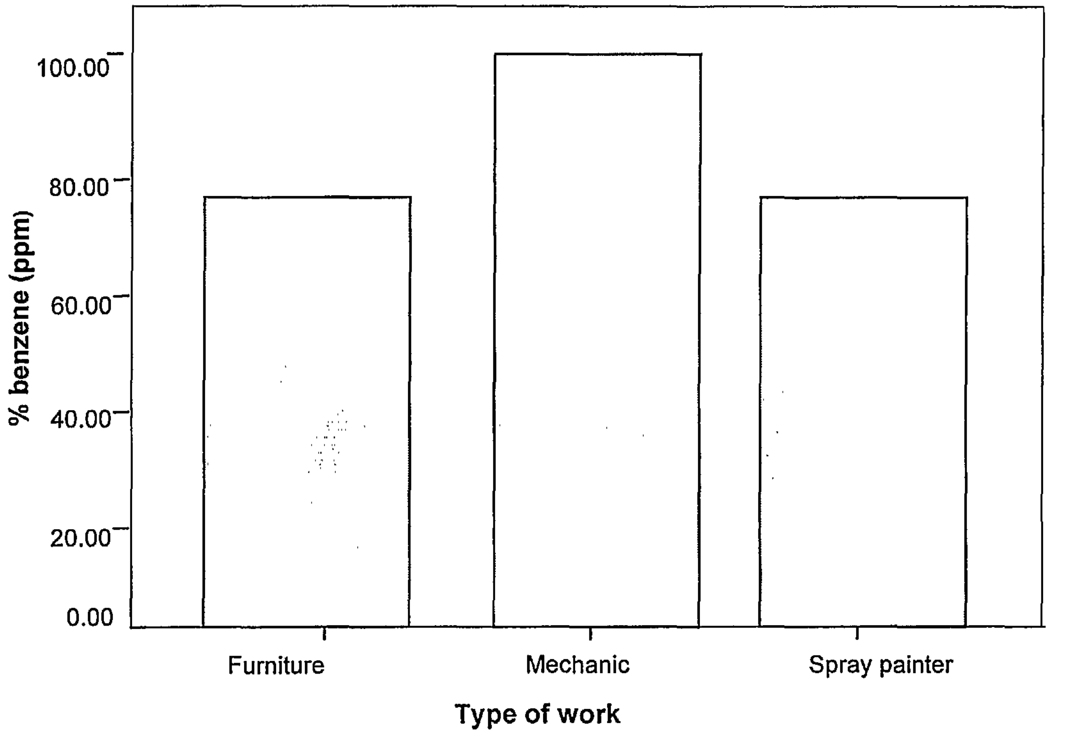
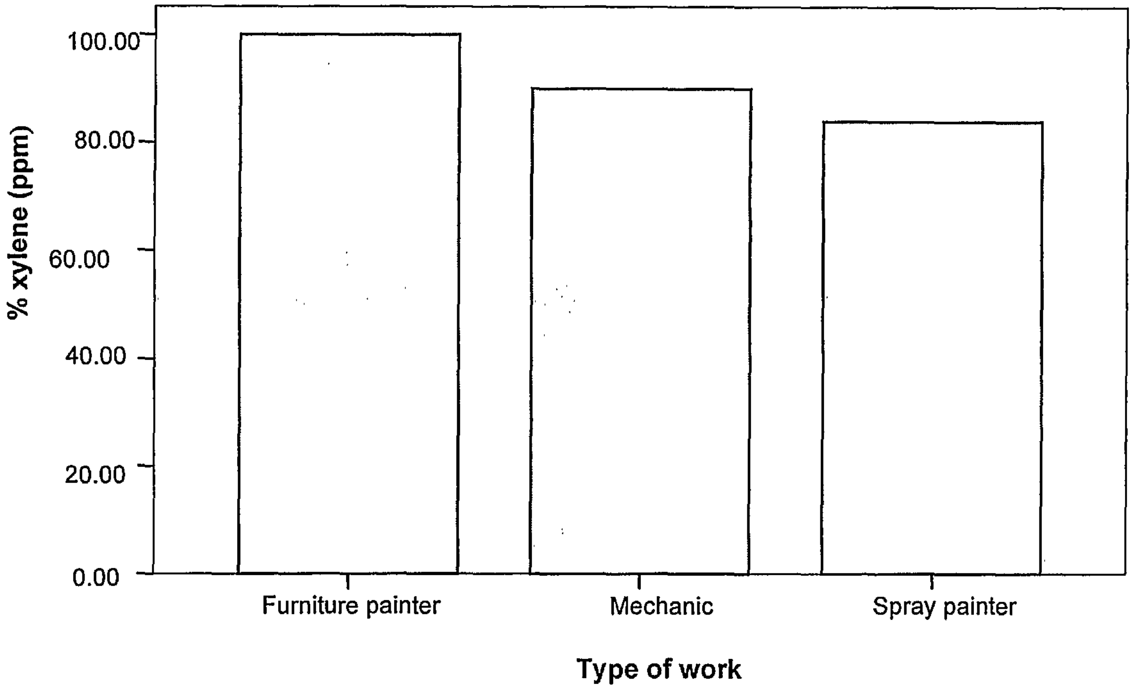


Figure 6.3 reveals that exposure to benzene was found in the air samplers of all the children working in mechanical workshops and at least 8 in 10 of the working children working in furniture and spray painting workshops

Exposure to toluene registered equally (100%) on all the air samplers of the working exposed children regardless of the type of work they were working in (Figure not shown).

Figure 6.4: Percentage of xylene exposure by type of work



At least 80% of the spray painters and 90% of the mechanics registered exposure to levels of xylene on their air samplers. All of the furniture painters registered a level of xylene on their samplers (Figure 6.4).

Figure 6.5: Percentage of styrene exposure within type of work

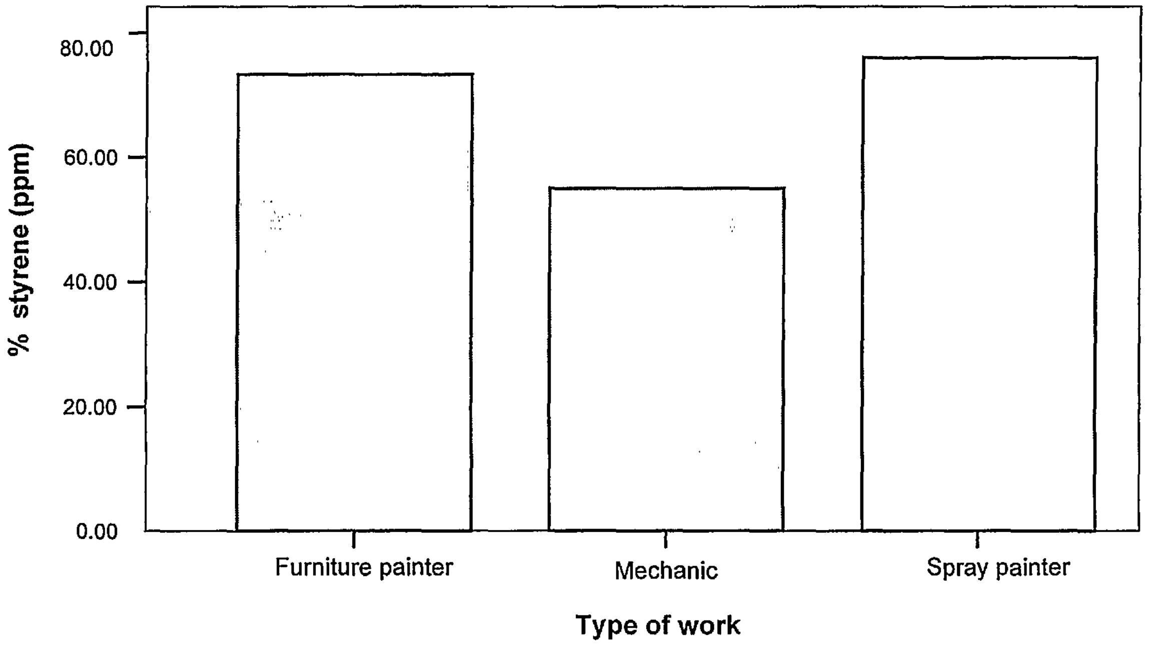


Figure 6.5, illustrates the distribution of styrene exposure within the three groups. At least 7 in 10 of the furniture painters and 8 in 10 of the spray painters registered styrene on their air samplers. Only about half of the samplers from the children working in mechanical workshops recorded styrene exposure

Whilst the above figures have presented an illustration as to the percentage of distribution and occurrence of each solvent within the three different industries, it is important to investigate and compare the actual mean levels of these exposures within each group. Table 6.30, displays the mean exposure level for each solvent within each of these groups. Using Kruskal Wallis testing, the median exposure level for Benzene exposure was found to be significantly higher in mechanics than in furniture and spray painters, while toluene exposure was found to be significantly higher in furniture painters than in mechanics and spray painters. The levels of hexane, MEK, xylene and styrene were not found to be significantly different between the three industries.

Table 6.30: Levels of exposure of working exposed children in each industry

	Furniture Painters N=15	Mechanics N=20	Spray Painters N=25	*P Value**
Hexane ppm				
Mean (SD)	4.70 (3.46)	4.76 (5.91)	3.65 (3.42)	
Range	12.58	23.56	12.56	0.522
Skewness	1.15	2.22	1.09	
Mean Rank	34.73	30.10	28.28	
MEK ppm				
Mean	42.67 (78.94)	10.47 (13.01)	12.34 (18.10)	
Range	270.94	41.17	89.50	0.094
Skewness	2.41	1.26	3.55	
Mean Rank	37.83	24.88	30.60	
Benzene ppm				
Mean (SD)	2.43 (4.17)	4.50 (3.14)	1.56 (1.90)	
Range	13.69	11.75	7.98	0.001
Skewness	1.80	1.30	1.78	
Mean Rank	24.20	42.70	24.52	
Toluene ppm				
Mean (SD)	15.55 (15.80)	7.19 (6.90)	10.39 (11.21)	
Range	51.16	24.68	44.66	0.037
Skewness	2.09	1.47	2.11	
Mean Rank	39.63	24.38	29.92	
Xylene ppm				
Mean (SD)	5.29 (4.88)	3.95 (4.40)	3.98 (5.03)	
Range	15.91	17.32	17.61	0.570
Skewness	0.96	1.69	1.71	
Mean Rank	34.57	29.73	28.68	
Styrene ppm				
Mean (SD)	5.40 (5.50)	2.96 (4.16)	5.99 (8.81)	
Range	13.82	13.39	32.39	0.292
Skewness	0.66	1.26	1.95	
Mean Rank	33.87	25.65	32.36	

*Using Kruskal Wallis test and significant at $P<0.05$

Table 6.31: Levels of individual solvent exposure by neurotoxic effects.

	Hexane (ppm) Mean (SD)	MEK (ppm) Mean (SD)	Benzene (ppm) Mean (SD)	Toluene (ppm) Mean (SD)	Xylene (ppm) Mean (SD)	Styrene (ppm) Mean (SD)
Feels light-headed						
Yes	3.90 (3.86)	29.09 (56.86)*	2.76 (3.47)	14.16 (14.41)**	4.85 (5.28)*	5.41 (8.00)
No	3.17 (4.44)	5.26 (8.50)	1.76 (2.72)	4.37 (5.03)	2.34 (3.66)	2.66 (4.55)
Tiredness						
Yes	4.20 (4.72)	18.14 (47.19)	2.40 (3.13)	10.83 (11.31)	4.59 (5.21)*	5.72 (8.02)*
No	2.89 (3.67)	12.99 (31.18)	1.91 (3.04)	6.60 (10.76)	2.43 (3.75)	2.28 (4.05)
Concentration						
Yes	3.97 (3.78)	23.36 (51.58)	2.63 (3.07)	11.72 (12.28)*	4.13 (5.44)	4.68 (8.24)
No	3.18 (4.43)	10.59 (28.85)	1.92 (3.08)	6.60 (10.07)	2.97 (3.96)	3.31(4.95)
Confusion						
Yes	4.01 (4.62)	22.81 (41.64)	2.49 (2.88)	12.15 (6.90)*	4.65 (5.42)	4.03 (6.06)
No	3.24 (4.02)	12.03 (41.64)	2.05 (3.18)	6.90 (9.99)	2.85 (4.07)	3.31 (7.06)
Remembering						
Yes	4.04 (4.92)	8.70 (15.78)	2.46 (2.17)	10.00 (13.18)	3.46 (4.09)	4.87 (7.32)*
No	2.56 (2.46)	19.37 (47.74)	2.01 (3.54)	6.04 (6.08)	3.36 (4.87)	2.10 (3.85)
Irritation						
Yes	3.55 (3.39)	21.23 (48.71)*	2.27 (2.93)	10.13 (11.90)	3.49 (4.21)	4.38 (7.32)
No	3.36 (5.26)	6.20 (10.13)	2.05 (3.33)	5.98 (9.50)	3.26 (5.12)	2.96 (4.44)
Difficulty sleep						
Yes	3.66 (3.77)	12.79 (16.70)	2.08 (2.99)	7.87 (7.57)	3.88 (5.25)	4.69 (5.82)
No	3.38 (4.42)	16.52 (46.24)	2.23 (3.15)	8.80 (12.58)	3.16 (4.22)	3.38 (4.99)
Sleeps more						
Yes	3.57 (4.26)	9.13 (9.96)	2.60 (3.32)	6.95 (6.66)	2.97 (4.67)	2.64 (5.90)
No	3.45 (4.21)	17.07 (43.83)	2.06 (3.02)	8.93 (12.14)	3.52 (4.56)	4.16 (5.90)
Incoordination						
Yes	3.29 (4.03)	16.23 (26.10)	1.67 (1.31)	11.31 (8.37)	5.22 (6.56)	4.09 (5.38)
No	3.50 (4.24)	15.19 (40.35)	2.24 (3.22)	8.16 (11.42)	3.18 (4.28)	3.78 (6.48)
Loss of muscle						
Yes	4.21 (4.40)	30.88 (69.57)	2.75 (3.13)	13.17 (13.16)	5.18 (5.94)	3.43 (4.79)
No	3.29 (4.16)	11.46 (26.31)	2.04 (3.07)	7.34 (10.38)	2.96 (4.09)	3.91 (6.70)
Moving fingers						
Yes	3.57 (3.28)	18.74 (27.97)	1.91 (1.71)	9.79 (10.08)	3.43 (4.58)	2.62 (3.53)
No	3.45 (4.41)	14.45 (41.37)	2.25 (3.34)	8.17 (11.44)	3.39 (4.49)	4.11 (6.85)
Numbness						
Yes	3.74 (2.70)	21.89 (45.18)	1.93 (2.65)	10.59 11.84)	3.15 (3.90)	3.86 (5.36)
No	3.40 (4.55)	13.40 (37.20)	2.25 (3.21)	7.89 (10.96)	3.47 (4.76)	3.80 (6.64)
Headaches						
Yes	4.19 (4.01)	18.90 (34.04)	2.39 (3.11)	10.72 (10.94)*	4.45 (5.27)*	4.88 (7.07)
No	2.82 (4.30)	12.05 (43.09)	1.99 (3.07)	6.48 (11.07)	2.45 (3.62)	2.86 (5.53)
Feels "high"						
Yes	4.59 (4.49)	15.43 (20.65)	2.84 (3.50)	10.74 (7.97)	4.55 (5.34)	5.41 (7.54)
No	2.74 (3.86)	15.21 (47.49)	1.75 (2.72)	7.03 (12.66)	2.64 (3.85)	2.78 (5.26)
Hand Tremble						
Yes	4.57 (5.06)	11.49 (17.94)	3.81 (3.69)**	8.41 (7.14)	5.25 (5.63)*	2.26 (4.11)
No	3.06 (3.78)	16.75 (44.51)	1.56 (2.58)	8.52 (12.39)	2.69 (3.91)	4.41 (6.95)
Depression						
Yes	5.00 (4.05)*	23.93 (59.43)	2.24 (2.96)	11.10 (11.57)	4.08 (5.41)	3.59 (5.55)
No	2.89 (4.14)	11.99 (27.57)	2.16 (3.15)	7.49 (10.91)	3.14 (4.22)	3.90 (6.67)
Eye Irritation						
Yes	3.64 (4.47)	17.25 (43.22)	2.23 (3.25)	9.10 (12.12)	3.38 (4.72)	4.33(6.74)*
No	2.79 (2.80)	7.36 (6.61)	1.98 (2.34)	6.03 (5.23)	3.47 (4.01)	1.74 (3.87)

**Using t-test analysis and significant at $p<0.05$*

***Using t-test analysis and significant at $p<0.003$ following Bonferroni correction for multiple comparisons.*

Table 6.31 illustrates the mean levels of individual solvent exposure by reported symptoms and neurotoxic effects. Children who had significantly higher mean levels of exposure to MEK, reported feeling light-headedness and were easily irritated. A significantly higher mean level of toluene was associated with reported feelings of light-headedness, loss of concentration, confusion, and headaches. Xylene had significant effects on reported feelings of light-headedness, tiredness, headaches and hand trembling. Higher exposure to styrene also appeared to be associated with tiredness, difficulty remembering and eye irritation. Because of the borderline significance found in earlier analysis (section 6.2) for eye irritation found in solvent exposed working children, it was included into the analysis of individual solvent effects. Further analysis now showed a significant association between reports of eye irritation and exposure to higher mean levels of styrene. Higher mean levels of benzene exposure only appeared to be associated with hand trembling while higher exposure to hexane was associated with reports of feeling depressed.

However following Bonferroni correction for multiple comparisons and reducing alpha level to $p<0.003$, higher levels of toluene were associated with light-headedness and significantly higher levels of benzene were associated with hands trembling.

6.9 Multiple Linear Regression Analysis on Solvent Exposure and Neurobehavioural Test Performance.

To measure collinearity between levels of exposure and performance on the neurobehavioural tests, multiple regression analysis was conducted with each neurobehavioural test as the dependent variable and cumulative exposure as an independent variable. Cumulative exposure is the total hygienic effect level of exposure calculated earlier in this chapter, but in this analysis will be used in its continuous value rather than a value of equal or higher or less than one. Other variables that were included into the regression model were the specific covariates found to affect performance on each individual neurobehavioural test in the ANCOVA analysis conducted earlier. These included child's age, child's education, mother's education, father's education, reported use of one or more social habit and the DAP total score. Those variables that did not show an effect on neurobehavioural test performance were not included in the regression analysis.

If a significant correlation was found between cumulative exposure and test performance, further analysis was conducted by adding each of the individual solvents (hexane, MEK, benzene, toluene, xylene and styrene) into the regression model as independent variables. This would allow the examination of specific effects of solvents on test performance as well as predict specific dose-response relationships. In all the cases presented in the multiple regression analysis, the proportion of variance explained by the variables in the model were relatively small (R^2 = 0.01-0.32).

Table 6.32, presents statistically significant collinearity found between cumulative exposure and performance on the PIPS choice reaction time test. A statistically significant linear relationship was found between cumulative exposure and reaction time and between cumulative exposure and number correct in this test. No covariates were added to the regression model as no covariates were found to affect performance on this test.

Table 6.32: **Multiple linear regression analysis of cumulative solvent exposure and PIPS Choice Reaction Time**

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
PIPS Choice Reaction				
Overall (msec)*	Constant	25734.96 (1956.83)	<0.001	P= 0.001
	Cumulative exposure	3429.647 (1005.83)	0.001	R^2 = 0.20
No. Correct	Constant	23.21 (0.66)	<0.001	P= 0.006
	Cumulative exposure	-0.962 (0.34)	0.006	R^2 = 0.09

Since a significant relationship was found between cumulative exposure and performance on the Choice Reaction Time, further regression analysis adding each of the individual solvents into the regression model was undertaken. There was a significant association found between exposure to benzene and slower reaction time in this test. Exposure to styrene also showed a borderline significant association with performance on this test. In the number correct on the Choice Reaction Time, although benzene showed a significant effect on the number correct, no significant linear relationship could be concluded because the overall model fit was not significant (Table 6.33).

Table 6.33: Multiple linear regression analysis of individual solvent exposure and PIPS Choice Reaction Time

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
PIPS Choice Reaction				
Overall (msec)	Constant	26581.69 (2032.87)	<0.001	
	Hexane (ppm)	-506.45 (427.41)	0.240	
	MEK (ppm)	90.84 (61.11)	0.142	
	Benzene (ppm)	1511.11 (550.68)	0 .008	P= 0.020
	Toluene (ppm)	-290.30 (243.86)	0.240	$R^2 = 0.20$
	Xylene (ppm)	528.77 (388.05)	0.177	
	Styrene (ppm)	460.34 (250.37)	0.059	
No. Correct	Constant	22.49 (0.69)	<0.001	
	Hexane (ppm)	0.22 (0.15)	0.143	
	MEK (ppm)	-0.01 (0.02)	0.522	P= 0.14
	Benzene (ppm)	-0.38 (0.19)	0 .048	$R^2 = 0.13$
	Toluene (ppm)	-0.03 (0.08)	0.693	
	Xylene (ppm)	0.13 (0.13)	0.337	
	Styrene (ppm)	-0.13 (0.09)	0.126	

There was no significant relationship found between cumulative exposure and performance on the PIPS Spatial Memory Search. The average length of sequence in this test was not affected by exposure (Table 6.34)

Table 6.34: Multiple linear regression analysis of cumulative solvent exposure and PIPS Spatial Memory Search

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
PIPS Spatial Memory				
Avg. length of sequence	Constant	2.48 (0.39)	<0.001	P= 0.092
	Cumulative exposure	-0.11 (0.10)	0.092	$R^2 = 0.04$

Similarly, there was no significant correlation found between cumulative exposure and performance on the PIPS Dual Tracking Task. Neither measure of this test (wander or reaction time) showed a relationship with exposure level.

These findings suggest that the differences in performance found earlier on this test between the working exposed, working non-exposed and school children may not be due to exposure.

Table 6.35: Multiple linear regression analysis of cumulative solvent exposure and PIPS Dual Tracking Task

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
PIPS Dual Tracking				
Wander - Accuracy	Constant	16.13 (3.76)	0.764	P= 0.809
	Cumulative exposure	0.469 (1.93)	0.809	R^2 = 0.01
Reaction Time (msec)	Constant	1099.95 (63.82)	<0.001	P= 0.170
	Cumulative exposure	45.50 (32.80)	0.170	R^2 = 0.03

In contrast, significant linear relationships were found between overall solvent exposure and two measures of the PIPS Symbol Digit test. The child's number of correct responses and mean reaction time were significantly associated with cumulative solvent exposure (Table 6.36). Children who were exposed to a number of solvents had slower reaction time and less correct answers on this test. The percentage correct in this test did not appear to be affected by solvent exposure levels, however, it showed a significant association with the DAP total score. Nevertheless, the overall model was not significant. The DAP total score was included in the regression model since it was found in the earlier ANCOVA analysis to affect performance on this component of the test. .

Table 6.36: Multiple linear regression analysis of cumulative solvent exposure and PIPS Symbol Digit Test

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
PIPS Symbol digit				
No. Correct	Constant	25.92 (2.98)	<0.001	P= 0.016
	Cumulative exposure	-0.987 (0.61)	0.016	R^2 = 0.14
Percentage Correct	Constant	88.45 (3.65)	<0.001	
	Education level	-0.16 (0.87)	0.855	P= 0.134
	DAP total score	0.07 (0.04)	0.048	R^2 = 0.07
	Cumulative exposure	-0.64 (0.55)	0.251	
Reaction Time (msec)	Constant	3489.30 (239.35)	<0.001	P= 0.021
	Cumulative exposure	289.55 (123.03)	0.021	R^2 = 0.18

When further regression analysis was undertaken on the PIPS Symbol Digit with individual solvents added to the regression model, each of the solvents benzene, xylene and styrene showed a significant effect on symbol digit reaction time. The significant effect of solvent exposure on the number of correct responses in the symbol digit test as seen earlier with cumulative exposure, no longer remained when individual solvents were included in the regression model (Table 6.37).

Table 6.37: Multiple linear regression analysis of individual solvent exposure and PIPS Symbol Digit Test

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
PIPS Symbol digit				
No. Correct	Constant	21.46 (2.92)	<0.001	
	Hexane (ppm)	0.20 (0.25)	0.445	
	MEK (ppm)	0.03 (0.04)	0.410	P= 0.158
	Benzene (ppm)	-0.23 (0.34)	0.509	R^2 = 0.14
	Toluene (ppm)	-0.24 (0.14)	0.099	
	Xylene (ppm)	0.59 (0.23)	0.013	
	Styrene (ppm)	-0.14 (0.15)	0.334	
Reaction Time (msec)	Constant	4349.03 (301.09)	<0.001	
	Hexane (ppm)	-26.10 (32.19)	0.418	
	MEK (ppm)	-5.55 (5.28)	0.295	P= <0.001
	Benzene (ppm)	91.30 (40.85)	0.026	R^2 = 0.32
	Toluene (ppm)	26.86 (19.75)	0.175	
	Xylene (ppm)	-100.31 (31.95)	0.002	
	Styrene (ppm)	72.61 (21.47)	0.001	

Table 6.38 displays multiple linear regression analysis undertaken with solvent exposure and the NES2 Continuous Performance Test. No significant associations were found between cumulative exposure and mean response latency, or cumulative exposure and number of non-responses. Significant associations however were found between cumulative exposure and standard deviation of response latencies indicating larger variability in performance in solvent exposed children. A significant association was also found between cumulative exposure and the number of false positives in the NES2 CPT .

Table 6.38: Multiple linear regression analysis of cumulative solvent exposure and NES2 CPT

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
NES2 CPT				
Mean Response Latency (msec)	Constant Cumulative exposure	647.80 (47.68) 8.14 (12.64)	<0.001 0.524	P= 0.524 R^2 = 0.05
SD of response latencies (msec)	Constant Cumulative exposure	131.42 (6.66) 8.94 (3.42)	<0.001 0.011	P= 0.011 R^2 = 0.08
No. of non-responses	Constant Cumulative exposure	2.74 (0.36) 0.34 (0.19)	<0.001 0.071	P= 0.071 R^2 = 0.04
No. of false positives	Constant Cumulative exposure	3.39 (0.74) 0.84 (0.38)	<0.001 0.032	P= 0.032 R^2 = 0.06

Significant collinearity was found between styrene and the standard deviation of response latencies. Borderline statistical significance was found on the overall model fit. There also appeared to be a significant association between benzene and the number of false positives; however similar to the previous measure a significant linear relationship could not be concluded as the overall model fit was not significant (6.39).

Table 6.39: Multiple linear regression analysis of individual solvent exposure and NES2 CPT

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
NES2 CPT				
SD of response latencies (msec)	Constant	136.92 (6.93)	<0.001	
	Hexane (ppm)	-0.60 (1.46)	0.680	
	MEK (ppm)	0.19 (0.21)	0.355	P= 0.058
	Benzene (ppm)	3.53 (1.88)	0.065	R^2 = 0.14
	Toluene (ppm)	-1.19 (0.83)	0.155	
	Xylene (ppm)	0.41 (1.29)	0.749	
	Styrene (ppm)	1.89 (0.85)	0.029	
No. of false positives	Constant	3.89 (0.78)	<0.001	
	Hexane (ppm)	-0.15 (0.16)	0.352	P= 0.218
	MEK (ppm)	0.02 (0.02)	0.367	R^2 = 0.11
	Benzene (ppm)	0.47 (0.21)	0.028	
	Toluene (ppm)	-0.12 (0.09)	0.203	
	Xylene (ppm)	0.16 (0.14)	0.266	
	Styrene (ppm)	0.08 (0.10)	0.390	

Table 6.40, presents the significant linear relationship found between performance on the WISC-R digit span and cumulative exposure. Performance on the digit span forward and the digit span total were significantly associated with cumulative solvent exposure which indicates that cumulative exposure is a predictor on the number of digits recalled in this test. There was no significant relationship found between the digit span backward and cumulative exposure whereas DAP results again show effects. A significant association was found between the DAP total score and the child's performance on this test. The child's education also appeared to be a significant predictor of performance on

this test. The child's education, mother's education, father's education and DAP total score were included in the regression model as these covariates were found to affect performance in the earlier ANCOVA analysis conducted.

Table 6.40: Multiple linear regression analysis of solvent exposure and WISC-R Digit Span

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
Digit Span				
Forward (No. Correct)	Constant	7.36 (0.28)	<0.001	P= 0.013
	Cumulative exposure	-0.36 (0.14)	0.013	R^2 = 0.17
Backward (No. Correct)	Constant	1.40 (0.64)	0.031	
	Child's education	0.33 (0.15)	0.032	P= 0.003
	Mother's education	-0.15 (0.09)	0.116	R^2 = 0.22
	Fåther's education	0.15 (0.09)	0.107	
	DAP score	0.01 (0.01)	0.038	
	Cumulative exposure	-0.05 (0.09)	0.627	
Total (No. Correct)	Constant	10.98 (0.39)	<0.001	P= <0.019
	Cumulative exposure	-0.49 (0.20)	0.019	R^2 = 0.17

Further regression analysis on the WISC-R digit span with individual solvent exposures included into the regression model as independent variables showed no significant linear relationships (Table 6.41). None of the separate solvents exerted any specific influence.

Table 6.41: Multiple linear regression analysis of individual solvent exposure and WISC-R Digit Span

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
Digit Span				
Forward (No. Correct)	Constant	7.45 (0.29)	<0.001	
	Hexane (ppm)	-0.36 (0.06)	0.604	
	MEK (ppm)	0.03 (0.06)	0.695	P= 0.160
	Benzene (ppm)	-0.08 (0.08)	0.293	R^2 = 0.12
	Toluene (ppm)	-0.04 (0.03)	0.243	
	Xylene (ppm)	-0.02 (0.05)	0.611	
	Styrene (ppm)	-0.03 (0.04)	0.346	
Total (No. Correct)	Constant	10.92 (0.41)	<0.001	
	Hexane (ppm)	0.05 (0.09)	0.545	
	MEK (ppm)	0.09 (0.01)	0.476	P= 0.331
	Benzene (ppm)	-0.14 (0.11)	0.347	R^2 = 0.09
	Toluene (ppm)	-0.07 (0.05)	0.139	
	Xylene (ppm)	-0.02 (0.08)	0.766	
	Styrene (ppm)	-0.04 (0.05)	0.405	

Table 6.42 outlines the significant association found between cumulative exposure and performance on the grooved pegboard. Only the dominant hand trial in this test appeared to be associated with exposure. When further analysis with hexane, MEK, benzene, toluene, xylene and styrene were included in the regression model as independent variables, exposure to hexane and styrene were found to be significant predictors of performance on the grooved pegboard, dominant hand trial, however exposure to hexane appeared to be negatively associated with performance on this test. Children who had higher levels of exposure to hexane had significantly quicker completion times on the grooved pegboard dominant hand trial than those children who had lower

exposure levels. Exposure to benzene also showed a borderline significant association with performance on this test (Table 6.43)

Table 6.42: Multiple linear regression analysis of cumulative solvent exposure and Grooved Pegboard

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
Grooved Pegboard				
Dominant hand time (sec)	Constant	76.91 (2.50)	<0.001	P= 0.036
	Cumulative exposure	2.74 (1.29)	0.036	R^2 = 0.11
Non-Dominant hand time (sec)	Constant	84.82 (8.76)	<0.001	P= 0.091
	Cumulative exposure	2.87 (1.68)	0.091	R^2 = 0.04

Table 6.43: Multiple linear regression analysis of individual solvent exposure and Grooved Pegboard

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
Grooved Pegboard				
Dominant hand time (sec)	Constant	80.18 (2.54)	<0.001	
	Hexane (ppm)	-1.40 (0.54)	0.011	P= 0.033
	MEK (ppm)	0.07 (0.07)	0.377	R^2 = 0.19
	Benzene (ppm)	1.17 (0.70)	0.053	
	Toluene (ppm)	-0.22 (0.30)	0. 469	
	Xylene (ppm)	0.23 (0.47)	0.629	
	Styrene (ppm)	0.77 (0.31)	0.015	

Table 6.44, demonstrates that solvent levels of exposure did not predict the children's responses on the profile of mood states. When social habits and the

DAP total score were included in the regression model as potential covariates on responses to this mood state, the DAP total score showed a significant association with reports of feeling "happy". Notwithstanding this finding, a linear relationship cannot be concluded as the overall model fit was not significant.

Table 6.44: Multiple linear regression analysis of cumulative solvent exposure and POMS

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
Profile Of Mood States				
Happy	Constant	48.84 (15.73)	0.003	
	Social habits	-20.25 (2.64)	0.264	P= 0.063
	DAP total score	0.24 (0.18)	0.030	$R^2 = 0.10$
	Cumulative exposure	2.97 (2.64)	0.180	
Not Sad	Constant	78.64 (4.50)	<0.001	P= 0.556
	Cumulative exposure	1.37 (2.32)	0.556	$R^2 = 0.05$
Energetic	Constant	86.92 (3.72)	<0.001	P= 0.234
	Cumulative exposure	-2.30 (1.91)	0.234	$R^2 = 0.02$
Not Tired	Constant	72.57 (4.79)	<0.001	P= 0.299
	Cumulative exposure	2.58 (2.46)	0.299	$R^2 = 0.02$
Not Angry	Constant	82.56 (3.68)	<0.001	P= 0.351
	Cumulative exposure	-1.77 (1.89)	0.351	$R^2 = 0.01$
Not Confused	Constant	73.14 (4.27)	<0.001	P= 0.739
	Cumulative exposure	-0.73 (2.20)	0.739	$R^2 = 0.02$
Not Afraid	Constant	89.88 (2.76)	<0.001	P= 0.476
	Cumulative exposure	1.01 (1.42)	0.476	$R^2 = 0.02$
Not Tense	Constant	81.00 (4.51)	<0.001	P= 0.189
	Cumulative exposure	3.07 (2.32)	0.189	$R^2 = 0.02$

In the draw a person test, the child's level of education and the mothers level of education were included in the regression model for the man, woman and total trials, in addition to the father's level of education in the self trial as these covariates appeared to affect the child's performance on this test even after controlling for them in earlier analysis. In all of the components of this test, exposure did not appear to be significantly associated with the child's performance. The child's level of education consistently appeared to be a significant predictor of performance on this test for all measures except the draw a person self trial (Table 6.45).

Table 6.45: Multiple linear regression analysis of cumulative solvent exposure and Draw a Person Test

Dependent Variable	Independent variable	β coefficient (SE)	P	Model fitting
Draw a Person Test				
Man Score	Constant	66.17 (7.55)	<0.001	
	Child's education	6.03 (2.19)	0.008	P= 0.046
	Mother's education	0.447 (1.43)	0.756	R^2 = 0.11
	Cumulative exposure	-0.463 (1.45)	0.751	
Woman Score	Constant	61.01 (7.04)	<0.001	
	Child's education	6.81 (2.05)	0.001	P= 0.007
	Mother's education	1.50 (1.34)	0.278	R^2 = 0.16
	Cumulative exposure	0.49 (1.36)	0.716	
Self Score	Constant	70.45 (8.38)	<0.001	
	Child's education	3.58 (2.38)	0.138	P= 0.282
	Mother's education	2.12 (1.60)	0.191	R^2 = 0.07
	Father's education	0.38 (1.57)	0.805	
	Cumulative exposure	0.27 (11.10)	0.864	
Total Score	Constant	60.20 (8.67)	<0.001	
	Child's education	6.28 (6.28)	0.015	P= 0.051
	Mother's education	1.71 (1.65)	0.302	R^2 = 0.10
	Cumulative exposure	-0.25 (1.67)	0.883	

6.10 Overall Summary of Chapter

This study has identified that there is an association between exposure to solvents and lower neurobehavioural performance with significant neurobehavioural deficits among children exposed to solvents in comparison to working children not exposed to solvents and non-working school children.

Analysis of the computerised neurobehavioural tests showed that, working exposed children had significantly slower mean reaction time on the PIPS Choice Reaction Time, PIPS Dual Tracking Task, PIPS Symbol Digit and the NES2 Continuous Performance Test than children in the working exposed and school-groups. The average length of sequence in the PIPS Spatial Memory Search was also significantly shorter for children in the working exposed group than the other two groups indicating poorer memory performance. Analysis of the non-computerised tests demonstrated that working exposed children performed significantly worse than the two non-exposed groups (working and non-working) on the motor dexterity (grooved pegboard) and memory (WISC-R digit span) tests. These differences between working exposed children and the other two groups remained when the analysis controlled for potential confounding variables such as age and education.

Analysis of workplace exposure measures showed that working exposed children had significantly higher levels of hexane, MEK, benzene, toluene, xylene and styrene, than the working non-exposed and school children. In the working exposed children, almost two thirds (67%) were found to have a cumulative hygienic effect level of more than 1.0. Analysis of the relationship between workplace exposure and performance on the neurobehavioural tests showed that children with exposure levels above the hygienic effect threshold performed significantly worse on a number of tests, specifically those which assessed functional domains in reaction time and memory functions. Working children with higher solvent exposure showed significantly higher reporting of neurotoxic symptoms with specific solvents of MEK, toluene, xylene and styrene found to be associated with more symptoms. Furthermore, multiple regression models revealed significant dose-response relationships, with poorer performance on the neurobehavioural tests with increasing cumulative exposure for the PIPS Choice Reaction Test, PIPS Symbol Digit, NES2 CPT, WISC-R Digit Span, and the Grooved Pegboard. Specifically, benzene, xylene and styrene exposure significantly predicted slower reaction time and lower accuracy in a number of measures of these tests.

The following chapter will present a synthesis and more detailed discussion of these results. The implications these results have on working exposed children will also be addressed.

CHAPTER 7: DISCUSSION

7.1 Neurobehavioural Effects and Solvent Exposure

This study provides evidence of a positive association between exposure to solvents and significant neurobehavioural deficits in working children. Children working in mechanical, spray painting and furniture painting workshops were found to be exposed to a number of solvents and had significantly poorer neurobehavioural functions compared to non-working children and more importantly compared to non-exposed working children. These findings highlight a situation of considerable concern for the health and safety of these children. This chapter will discuss the results of this study including the associations found between solvent exposure and neurobehavioural deficits and a description of the work conditions of exposed working children.

The consistent pattern of symptoms and functional effects found in this study support the conclusion that solvent exposure is responsible for these effects. In the initial comparisons between working exposed, working non-exposed and school children, the largest differences were seen for reported neurotoxic symptoms that might be expected due to solvent exposure such as feeling light headed or high, and reports of headaches. Around half of the working exposed reported all of these symptoms compared to very small proportions in the two control groups. Furthermore, while working exposed children were more likely to report most symptoms, the effect was not found for all symptoms, for example, no children from any group reported seizures and very few reported making notes to remember. These patterns indicate that the results for the working exposed children were not due to simply a higher tendency to report all symptoms. In the same vein, there were symptoms that were also commonly reported by the other two control groups, in particular, being easily irritated, depression, having trouble remembering and difficulty concentrating. For all of these symptoms, however, much higher reporting was found for the working exposed group. In total, the working exposed group reported around six times the number of neurotoxic symptoms compared to both the working non-exposed and school children. Previous studies on the effects of solvent exposure have also shown higher reporting of subjective neurotoxic symptoms. Wang and Chen (1993) reported on the positive association found between solvent exposure and reports of acute neurotoxic symptoms including headaches, chest tightness, dizziness, fatigue, depressed mood and palpitations. Bockelmann et al. (2002) also reported on the tendency for solvent exposed car painters to report more neurological symptoms of concentration and memory than their controls.

Although there are few studies of solvent toxicity in children assessed by neurobehavioural tests, previous studies have reported and assessed occupational solvent exposure in adults and have shown effects on memory, attention, motor dexterity and reaction speed (Nordling Nilson et al., 2002; Daniell et al., 1999). These functions were also clearly affected in this study when comparisons between the working exposed, working non-exposed and school children were made. Furthermore, the nature and magnitude of the effects on performance in the working exposed children were of statistical and practical significance even after controlling for some of the common potential confounders of performance on neurobehavioural tests. This was demonstrated in the performance of the working children on the PIPS choice reaction time, PIPS dual tracking task, PIPS symbol digit and the NES2 CPT where statistically significantly poorer performance was shown for working exposed children compared to the non-exposed controls. The effects of slower response in these children have implications for safe responding in situations when they are at risk. The deficits in memory found in the performance tasks, PIPS spatial memory search and WISC-R digit span, were also supported by higher frequency of reports of memory-related symptoms, such as self-reported trouble remembering and of more reports from relatives of the child's memory problems. This study found very little effect on accuracy of performance for the working exposed group specifically on the number and percentage correct in the symbol-digit task and the choice reaction time and wander in the dual tracking task, suggesting that solvent exposure resulted only in general slowing of performance.

The performance of working exposed children on neurobehavioural tests in this study is consistent with other studies on solvent exposure and neurobehavioural performance between exposed and non-exposed groups. Escalona et al. (1995), reported significantly poorer performance in the solvent exposed group in digit-symbol and simple reaction time. White et al., (1995), also found significantly impaired neurobehavioural test performance on tasks involving manual dexterity, visual memory and mood disorders on workers exposed to mixed solvents.

In the current study, solvent exposed children showed roughly a twenty percent slowing in hand-eye coordination and manual dexterity (Grooved pegboard) and in the capacity to remember new information (WISC-R Digit Span Forward and total) compared to non-exposed children in both groups. These effects are likely to have implications for the capacity of the exposed children to respond to new demands and to learn new information.

In addition, the findings of this study on mood effects further suggest a role for solvent exposure in this effect, particularly when more reports of anger and confusion in working exposed children are consistent with other studies on mood states and solvent exposure (Ng et al., 1990; Julien et al., 2000)

When exposure-performance relationships were explored in this study, children with solvent exposure levels above the hygienic effect threshold of one performed worse on a number of tests specifically those which assessed functional domains in reaction time and memory functions. Furthermore, the pattern of effects of solvent exposure on neurobehavioural performance showed that solvent exposure was associated with significant deficits in neurobehavioural performance where increasing solvent exposure was associated with higher performance decrements on tests. Higher exposure levels showed significant effects on specific domains that depend on reaction speed, such as in the choice reaction time, symbol-digit reaction time, NES2 CPT, and grooved pegboard, and those that depend on memory such as digit span.

Reaction time in the choice reaction time and symbol digit tests indicated slower performance with Hygienic effect levels greater than one, thus suggesting an associated effect of cumulative solvent exposure. The variability in performance on the NES2 CPT (SD of response latencies) was also larger with hygienic effect levels greater than one. Other domains of auditory memory (WISC-R digit span) hand-eye coordination and manual dexterity (Grooved Pegboard) were also affected by higher levels of solvent exposure.

This study also identified the individual types of solvents working children are potentially exposed to and allowed comparison of the specific effects these solvents may have on the central nervous system. As expected, higher mean levels of benzene were found in mechanical workshops. This was probably due to the presence of benzene in petrol. Similarly, higher mean levels of toluene were found in furniture painting workshops. Again this is not unusual due to the presence of toluene in paints, varnish and its use as a cleaner and degreaser.

The consistency of the results with patterns found in previous studies of solvent exposure suggests quite strongly that these neurobehavioural deficits may be due to solvent exposure with dose-response relationships. There was a significant reporting of neurotoxic symptoms with exposure to these solvents. Higher levels of individual solvents indicated different effects on the central nervous system and performance on the neurobehavioural tests with toluene, xylene and styrene significantly associated with the most reported neurotoxic effects. However, following the conservative Bonferroni correction for multiple comparisons, only toluene and benzene were associated with neurotoxic effects of feeling light-headed and hands trembling respectively. Chen et al., (1999b) also reported on the association found between hand trembling and solvent exposure in female dockyard painters. The effects of toluene of the nervous system have been reported in the literature. Eller et al., (1999) found long term toluene exposure associated with impaired neuropsychological function and higher scores on symptom indexes in a group of workers in a rotogravure plant exposed to toluene.

Additional analysis using multiple regression models revealed significant dose-response relationships with poorer performance on the neurobehavioural tests with increasing cumulative exposure for the choice reaction time, symbol digit, CPT, digit span and grooved pegboard. Analysis for the individual solvents showed that benzene, xylene and styrene exposure significantly predicted slower reaction time, hand-eye motor coordination and lower accuracy in a number of measures of these tests. Benzene showed a consistent affect on reaction time in choice reaction time, symbol digit and motor coordination in the grooved pegboard tests, whilst xylene showed an affect on the number correct and reaction time in the symbol digit test. Styrene had an effect on reaction time in the choice reaction time (with borderline significance), symbol digit, CPT and motor coordination/reaction time on the grooved pegboard. Even with the relatively small amount of variance explained by the independent variables in most of the regression models, these exposures remained significant predictors on performance on these tests.

The dose-response findings in this study are consistent with other studies on adult workers occupationally exposed to xylene and styrene. The effects of benzene on neurobehavioural performance have not been well documented in the literature. Tsai et al. (1997) reported significant associations between exposure to solvent mixtures which included xylene and slower reaction time in the CPT.

It is evident from the literature that slower reaction times seem to be the most prominent neuropsychological effect of styrene exposure. The results of this study are consistent with these reported effects. Tsai et al (1996), reported adverse affects of exposure to styrene and prolonged response latencies in the NES CPT. Viaene et al. (2001) and Letz et al. (1990) reported a significant relationship between styrene exposure and impaired performance on the symbol digit test in boat builders. Mergler et al. (1996) also reported on neurobehavioural deficits found in styrene exposed workers in reinforced plastics manufacturing plants and found that lower exposure was associated with better performance on reaction time and digit span forward tests.

In the Draw a Person test, exposed working children showed significantly poorer performance than working non-exposed and school children, but these effects disappeared when other covariates were accounted for (child's and parental education). This indicates that the lower performance for working exposed children on this test was due to factors other than exposure.

The DAP test was used in this study as a premorbid measure of intelligence for its non-verbal characteristics in addition to the fact that it was a potentially "hold–no hold" or "best performance" test. However, the use of this test as a measure of pre-morbid ability did not show any effects on the outcome measures of this study. Premorbid measures of intelligence should not be affected by education or other factors that are likely to change as the child ages (Laak J, 2005), however, the DAP in this study did not fulfil the suggested criteria for a premorbid intelligence measure which should not be affected by factors like the child's education or parental education which also showed to be significantly correlated to DAP performance. This suggests that the neurobehavioural performance effects for working exposed children found in this study were probably not due to inherent differences in basic IQ levels, (i.e.: working exposed children did not necessarily have lower levels of intelligence than the working non-exposed and school children) but to specific adverse effects of solvent exposure.

Many studies have reported the use of vocabulary (and related measures of verbal intelligence) as indicators of pre-morbid ability, not directly influenced by solvent exposure (Dick et al., 2002; Grosch et al., 1996; Bolla et al., 1995). Measures of premorbid intelligence rely on performance levels which should not be affected by neurologic insult or demographic variables (Griffin et al., 2002). However, Grosch et al. (1996) and Kishi et al. (1993) found that measures of vocabulary showed significant differences between exposed and non-exposed workers suggesting that vocabulary, used often as a measure of premorbid functioning may be adversely affected by solvent exposure and therefore caution is warranted in the interpretation of the results.

In the current study, DAP was not affected by solvent exposure unlike most of the other measures and it may be that it has some strengths as a premorbid measure of intelligence which needs further research.

7.2 Sociodemographic, Health and Work Characteristics

This study has also identified the lifestyle disadvantages of working exposed children. Working exposed children were less educated, had less literate parents and siblings and generally lower socioeconomic status than the other two groups. These factors impact on the reasons children work and influence the decisions in choosing the type of work. The reality of poorer families, more siblings, the fathers' occupation and the complexity of the family comprising a single bread winner and the difficulty parents face with meeting the basic requirements of their children is probably the reason why these children work and do not attend school. The lower levels of education and literacy in the working exposed also impacted on the children's ability to function on a daily basis and to carry out basic everyday demands of literacy such as reading newspapers and watching TV. Many studies have reported on education and parental education as a confounder of effects on neurobehavioural performance, specifically maternal education in environmental studies on children (Stewart et al., 2003; Patandin et al., 1999; Jacobson & Jacobson, 1996). However in this study, when these factors were accounted for statistically the adverse effects on neurobehavioural performance remained.

The working exposed children also reported the highest frequencies of smoking, coffee drinking and substance sniffing. However, both working groups reported higher frequencies in comparison to the school children. Given that working children join the 'adult' world earlier these effects are not unexpected. Of those children who admitted to sniffing substances, most of them reported that they were not addicted to these substances and only enjoyed the smell whenever it was around as a result of their work. Social habits have also been reported in the literature to affect performance on neurobehavioural tests (Ihrig et al., 2003; Chen et al., 2001a; Chen et al., 2001b) however, when further analysis accounted for these confounders in the present study, the effects of exposure between the three groups remained significant.

This study did not identify any significant health effects of working children exposed to solvents. The only differences found were that working children reported more limb injuries which were not necessarily directly linked to their work. Self reporting by the child and his mother revealed that that these were mainly injuries the children had experienced when they were younger and were not necessarily an effect of work. An earlier study on the physical and mental health of working children in Lebanon (Nuwayhid et al., 1998) revealed that working children were disadvantaged in that they reported a higher number of injuries and other health complaints compared to non-working children. However the authors of this study reported that the differences between the two groups were not striking because in most cases working children had not been working for a long time and consequently health effects might not have been clinically detected which in the present study could also be the case.

Notwithstanding these findings, the working conditions presented in this study highlight a situation of considerable concern for the health and safety of these working children and especially for working exposed children.

A previous report submitted to IPEC (Nuwayhid et al., 2001) identified and described the conditions of the workplaces where the children from this same study cohort worked, and observed in some detail what children did on a regular workday. The workplaces lacked basic hygienic principles where toilets, washing basins or eating facilities were not present. The report also identified that workers, children and adults, used available chemicals to "wash" their hands. This was a common practice found in all three exposed groups, spray painters, furniture painters and mechanics. Workplaces also lacked basic safety measures where control measures and protective guards or personal equipment were missing from the majority of the shops with no safety or precautionary instructions. Furthermore, ventilation in almost all of these establishments depended solely on the natural airflow through doors and windows. Workers attempted to reduce their risk of exposure by occasionally working outside the shop in the open air and no spray booths or respirators were provided. These working conditions and characteristics lead to one outcome that is indicative of increased exposure through skin contact, ingestion and inhalation. In a country with limited occupational health and safety regulations, it is no surprise that none of the children in this study reported an adequate use of protective equipment. Of the two children that reported wearing overalls and masks in the working exposed group, it was unclear as to whether these were specifically designed for children or they were adult sizes. In any case the results reflected a lack of use of protective equipment.

The initial walkthrough surveys of workplaces for both exposed and non-exposed children found that work in the non-exposed group was less demanding than that in mechanics, furniture painting and spray painting workshops. Children's responsibilities and tasks increased with age and younger children assisted their employer or older workers with preparing, cleaning and organising tools. Nevertheless, work in exposed environments was ergonomically stressful for most of the child's work shift. Children used tools that were manufactured for "average adult men", worked in awkward positions and performed tasks (twisting, pulling and pushing) that are known to stress the musculoskeletal system (back, shoulder, joints) (Nuwayhid et al., 2001). Gallagher (2005) highlights the importance of limiting unusual and restricted postures in adults in the workplaces and states that workers who adopt unusual or restricted postures in their work often experience higher musculoskeletal injury rates.

The reasons for children working in Lebanon are similar to those discussed in other studies with the main reason being financial reasons (Venkateswarlu et al., 2003; Mitra 1994). In the present study, most of the working exposed children reported that the reasons they were working were financial reasons, which again emphasizes the socioeconomic backgrounds of these children. The working children in this study are similar to those in other studies (Tabassum and Baig, 2002; Mitra 1994), in that they worked for long hours sometimes without a break, therefore keeping them outside their home environment all day with no time for school or other social activities. Furthermore, many of the children remained at work during their break and decided to eat in the workplace. As reported by Nuwayhid et al., (2001), "their food was most probably being contaminated with their hands or from the surrounding environment itself". Nevertheless, the hours which these children both exposed and non-exposed were working, are beyond the average adult workday which may have detrimental effects for these children.

A considerable number of children who had changed employers had done so because they were not being paid suggesting child exploitation in the workplace with children toiling for long hours at work with no pay. Hadi (2000) also highlights this exploitation of working children in Bangladesh with children being forced to work longer hours with minimal pay.

Possible secondary exposure to solvents extending to the mother and the child's home cannot be underestimated. The majority of the working exposed children reported their mother washed their work clothes at home. Almost all of the mothers of the solvent exposed working children, reported being able to smell the chemicals on her son's clothes highlighting the concern of secondary exposure extending to the mother and the child's home. A study of indirect lead exposure (Aguilar-Garduño et al., 2003) found that children of radiator repair workers were at increased risk of lead exposure from higher dust lead levels found in the home from contact with clothes, shoes, automobiles, and other articles that were contaminated in the workplace and then taken into their homes.

7.3 Methodology

There have been relatively few studies of neurobehavioural toxicity effect in children, especially from developing countries. As a result, the choice of methodology and especially of the most appropriate tests was crucial to overcome potential problems of literacy, understanding of the requirements of the test and cultural differences. The tests were chosen to be sensitive to the effects of solvents on children and to be as far as possible nonverbal and culturally appropriate. This study has shown that the test battery used was a sensitive indicator of neurobehavioural deficits of solvents without the effects of socioeconomic, sociodemographic and cultural factors. While there were no problems with the computer-based tests, after a pilot study conducted on Arabic-speaking children in Australia, changes were made to the symptoms questionnaire and to the Profile of Mood states to make them more appropriate for the children and in this setting. The results of this study indicate that there were few problems with understanding of the requirements of the tests analysed as the test accuracy was not affected for almost all tests.

Whilst there are criticisms in the literature of the use of cross-sectional study designs in research, this study has attempted to overcome some of the common problems found in cross-sectional studies. The methodological strengths of this cross-sectional study include: the inclusion of positive and negative control groups in the study which were frequency matched by age and geographic location; a rigorous neurobehavioural assessment with a selection of tests from different neurobehavioural batteries and specifically tailored at assessing precise modalities known to be affected by solvents, the inclusion of the Draw a Person test as a measure of pre-morbid functioning, the use of personal air monitoring for an accurate estimation of exposure levels, the calculation of hygienic effect levels for a cumulative exposure of effects, and the ascertainment of a dose-response relationship between solvent exposure and neurobehavioural deficits. Furthermore, this study has examined the role of and controlled for confounding variables and adjusted for multiple comparisons using Bonferroni correction to eliminate the possibility of any significant associations with exposure by chance (Type I error). There are criticisms in the literature (Jacobson and Jacobson, 2005) which suggest that the adjustment of results by Bonferroni correction may increase Type II error and hence important effects may be missed. This is important in a study such as this, which is breaking new ground investigating solvent exposure effects in working children. Where there is near significance in the results which is compatible with the research hypotheses, the comparison should be at least regarded a trend and worthy of comment and not necessarily dismissed as not significant. Nevertheless, statistically significant associations between solvent exposure and neurobehavioural deficits in working children remained in many of the tests even after the conservative Bonferroni corrections.

7.4 Limitations of the study

A limitation of this study is the cross-sectional nature of the research design. However, the limited time and resources of this study, made it difficult to adopt a longitudinal prospective study design to address the research question. Moreover, in a developing country with limited child labour registries the establishment of this study population has the advantage of creating a baseline population for future longitudinal studies. The inclusion of a positive control and the dose-response nature of the study are also attempts to diminish the limitations of a cross-sectional study.

Another limitation is the characteristics of the employers and the workplaces that agreed to participate in the study. It is possible that those who agreed to participate differed from those who did not regarding the working conditions or work tasks expected from working children. It may be that those employers that felt comfortable with their workplace practices agreed to participate in comparison to those that were not comfortable.

Whilst every attempt was made to measure accurate reports of exposure, self reports of neurotoxic symptoms and health effects are inevitable. The 3M organic vapour monitor does not take into account respiratory volume measures and biological monitoring might have revealed differences in effects of exposure on the different types of work performed. Since biological monitoring was not possible in this baseline study it should be considered in future studies. However, the measurement of a dose-response relationship and the consistency of these effects on a number of tests continued to show the association between reported neurotoxic symptoms and solvent exposure.

The presence of the parents in the room whilst the child was undergoing testing may have also been a possible limitation of this study as the presence of the child's parents may have influenced his test performance. Whilst all attempts were made to administer the tests in a standardised manner during the neurobehavioural examination, this was not always possible especially in cases where there was only one room in the house. Furthermore, another limitation may have been the order effect of the administered tests. Tests done later may have been affected by fatigue while tests done earlier may have been affected by nervousness or work-up effects. The pilot study attempted to eliminate these effects and hence the order of tests selected was based on the children's overall preferences. The pilot test indicated a preference for the non-computerised tests to be administered before the computerised tests.

Several studies have reported the effects of solvents on colour vision, contrast sensitivity and visual acuity (Issever et al., 2002; Castillo et al., 2001; Semple et al., 2000; Mergler et al., 1996) and the inclusion of a measure to assess these effects might have introduced some revealing results to this thesis especially with the consistent findings of styrene exposure. However, the inclusion of another test to the selected battery of neurobehavioural tests would have made the test session too long for the children. The chosen test battery provided an appropriate balance between the children's attention span and the test selection. However, further studies should measure and assess the effects of solvent exposure on colour vision and visual acuity on performance on neurobehavioural tests.

7.5 Overall Summary of chapter

Overall, the results of this study have demonstrated that solvent exposure in working exposed children has an effect on neurobehavioural performance. Working exposed children have slower reaction time on a number of neurobehavioural tests as well as decrements in memory and motor dexterity. This chapter has discussed the implications of solvent exposure on working children and demonstrated the detrimental effects these may have on their everyday functioning. The working conditions these children are working in are also disconcerting and urgent action needs to be taken to address the effect of exposure in this group to prevent further deterioration in performance. The following chapter will present the conclusions of this study as well as propose some recommendations.

A thirteen year old boy spray painting without any personal protective equipment in an automotive spray painting workshop

CHAPTER 8: CONCLUSIONS AND RECOMMENDATIONS

8.1 Conclusions

In conclusion, this study has demonstrated a significant association between exposure to solvents and lower neurobehavioural performance in 10-17 year old working children in comparison to working non-exposed and school children in Lebanon. The major types of solvents working children are being exposed to have been identified and measured and most importantly, dose-response relationships between solvent exposure and neurobehavioural performance were found.

A range of neurobehavioural tests including PIPS choice reaction time, PIPS spatial memory search, PIPS dual tracking, PIPS symbol digit, NES2 continuous performance test, digit span, grooved pegboard, profile of mood states (POMS) and Draw a Person (DAP) were used to assess the differences in neurobehavioural performance between children exposed to solvents and non exposed groups. The tests were found to be sensitive for detecting neurobehavioural deficits and for identifying the differences in effects between neurobehavioural functions. Significant neurobehavioural effects and demonstrated neurotoxicity from solvent exposure were established in this study. Specifically, measures of functional domains in reaction time, memory and motor coordination were found to be effected by solvent exposure levels. Furthermore, benzene, xylene and styrene exposure significantly predicted slower reaction time, number correct and hand eye coordination/ motor dexterity in a number of measures of these tests.

The implications of the adverse effects found in solvent exposed children are many and will interfere with the child's undertaking of everyday demands. The effects of slower response in these children will affect their safe and quick responding in situations when they are at risk and they are more likely to be injured it they are too slow to react. Slower reaction time may also indicate that they are slower in their jobs and therefore may not prosper and progress as well as other children who are working in non-exposed areas. Lower memory will also affect the solvent exposed children's capacity to respond to new demands and to learn new information. Pre-existing lower levels of education and literacy in the working exposed children will also impact on the children's ability to function on a daily basis and to carry out basic everyday demands of literacy such as reading newspapers and watching TV.

Overall the results of this study indicate serious health and social problems in children working in areas exposed to solvents in Lebanon. These are greater than the effects of simply working and need to be addressed especially since some of these effects are sub-clinical and only found on investigation. Furthermore, the conditions of work for working children have been investigated and the findings are alarming. Work standards regulating permissible exposure limits at work to different physical, chemical, and ergonomic hazards do not exist in Lebanon. However, it is clear that the assessed workplaces will not meet standards set by the ILO, the USA, or European countries and possible interventions must be made.

This study suggests that urgent action needs to be taken to address the effects of exposure in this group of children before further deterioration in performance; and that specific measures be undertaken to improve working conditions for these children. The results also suggest that longitudinal studies also need to be conducted to assess the long term neurobehavioural effects of solvent exposures in children and adults working in these occupations and in these conditions

8.2 Recommendations for Possible Interventions

The potential for intervention remains the most elusive and difficult issue to address. Curbing poverty, which is hurting the least advantaged social groups in Lebanon, remains the only long-lasting successful intervention. This is far-fetched, now more than ever, with the current economic recession and the limited options for social and occupational mobility in Lebanon. Hence, short- and medium-term interventions should be planned with the aim of reducing the risk of exposure to work hazards and monitoring their health status. Employers and owners of small workshops cannot provide such protection on individual basis. Action should be directed towards a community-based approach to which employers can contribute.

Reducing the risk of exposure requires the following:

- Educating the employers and all workers (including the working children) about the potential hazards of the workplace
- Coordinating with employers and workers the possibility of introducing low-cost technologies that might reduce exposures
- Borrowing from the experience of other developing countries (and ILO's own program in this regard) in introducing low-cost ergonomic changes and control measures
- Training working children on new basic work practices that reduce the potential for ingesting chemicals or absorbing them through skin. A clear example is to stop the practice of gasoline siphoning.
- Ensuring an acceptable level of housekeeping and organization with all containers covered and the like
- Providing working children with work and social skills in after-work sessions to help them deal with work pressures and hazards and defend themselves from potential risky personal behavioural lifestyles (smoking, sniffing, etc.)
- Providing a shared accessible facility where working children can wash themselves, eat in clean environment, and use a decent toilet. Special soaps and a place to change clothes could be provided.
- Preparing and posting safety signs, which are prepared by the working children themselves

Monitoring the health of working children:

- A standing or mobile health unit could be established to assess on a periodic basis (once every six months or a year) their overall physical and mental health. Specific tests should be offered based on children's exposures.
- Some kind of basic accident and medical insurance should be provided
- Priority could be given to working children 13-14 years of age and younger.

The above recommendations do not absolve us from the long-term objective of eliminating child labour. This requires an ongoing pressure to modify the laws and regulations and a vigilant effort to ensure their application. The ILO, through IPEC, has been driving governments towards political commitment to eliminate child labour. Non Government Organisations (NGO)s could conduct campaigns to support such actions and to pressurize the government to achieve the following:

- Addressing the social and economic situations that lead to child labour within the context of a national policy.
- Conducting awareness campaigns targeting communities, social partners, and government leaders and other decision-making bodies.
- Providing economic support to families whose children are potential workers;
- Funding a public system of basic education that ensures quality schooling, physically and economically accessible to children of even the poorest families

- Identifying and removing children working in hazardous conditions and then trying to reintegrate them into schools in order to provide them with skills that will allow them an alternative productive employment.

LIST OF REFERENCES

Aaserud O., Nakstad P.H., Bakke S.J., Reinvang I., Borchgrevink H.M., Lie V., Malt U.F., Gjerstad L. (2000) Failure to confirm neurotoxic impairment using cerebral magnetic resonance imaging on solvent-exposed workers **Scandinavian Journal of Work, Environment and Health** Vol. 26(3); pp. 346-352.

Aguilar-Garduño C., Lazasaña M., Tellez-Rojo M.M., Auilar-Madrid G., Sanin-Aguirre L.H., Romieu I., Hernandez-Avila M. (2003) Indirect lead exposure among children of radiator repair workers **American Journal of Industrial Medicine** Vol.43; pp. 662-667.

Aldaba F.T, Lanzona L., Tamangan R. (2002) **A Review of the Literature on Child Labour in the Philippines**. Ateneo de Manila University – Economics Department. [Online] Available: http://dirp3.pids.gov.ph/dnet/documents/review%20of%20related%20literature.pdf [28/04/2003]

Alonzo R.P, Edillion R.G. (2002). **Eliminating Child Labour in the Philippines.** Report submitted to International Labour Organisation – International Programme for the Elimination of Child Labour - Phillippines

Altmann L., Neuhann H.F., Kramer U., Witten J., Jermann E. (1995) Neurobehavioural and Neurophysiological outcome of chronic low-level Tetrachloroethene exposure measured in neighbourhoods of dry cleaning shops. **Environmental Research** Vol. 69; pp. 83-89.

Altmann L., Sveinsson K., Kramer U., Winneke G., Wiegnand H. (1997) Assessment of Neurophysiologic and Neurobehavioural Effects of Environmental Pollutants in 5 and 6 year old children. **Environmental Research** Vol. 73; pp: 125-131.

Ambadekar N.N., Wahab S.N., Zodpey S.P., Khandait D.W. (1999). Effect of child labour on growth of children. **Public Health** Vol. 113; pp. 303-306.

Amler R.W., Gibertini M., Lybarger JA., Hall A., Kakolewski K., Phifer BL. Olsen KL. (1996) Selective approaches to basic neurobehavioural testing of children in environmental health studies **Neurotoxicology & Teratology** Vol.18(4); pp.429-34.

Anger W.K. (1990) Worksite behavioural research: Results, sensitive methods, test batteries and the transition from laboratory data to human health **Neurotoxicology** Vol. 11; pp. 629-720.

Anger W.K. (1994) Neurobehavioural test methods for environmental health studies of adults **Neurotoxicology and Teratology** Vol. 16(5); pp. 489-497.

Anger W.K. (1997) Human neurobehavioural research methods: Impact of subject variables **Environmental Research** Vol. 73; pp. 18-41.

Anger W.K. (2003) Neurobehavioural tests and systems to assess neurotoxic exposures in the workplace and community **Occupational and Environmental Medicine** Vol. 60; pp.531-538.

Australian Standard (1987) **AS 2986-1987 : Workplace atmospheres - Organic vapours - Sampling by solid adsorption techniques** Australian Standards Association

Atchison W.D., Hare M.F. (1994) Mechanisms of methylmercury-induced neurotoxicity **The FASEB Journal** Vol. 8; pp.622-629.

Baker E.L., Fine L.J. (1986) Solvent neurotoxicity: The current evidence **Journal of Occupational Medicine** Vol. 28; pp. 126-129.

Bancej C., Arbuckle T (2000). Injuries in Ontario Farm Children: A population based study. **Injury Prevention** Vol. 6; pp. 135-140.

Banco L., Lapidus G., Braddock M. (1992) Work-related injury among Connecticut minors. **Pediatrics** Vol 89 (5 part 1); pp. 957-960.

Banks E.C., Ferretti L.E., Schucard D.W. (1997) Effects of low level lead exposure on cognitive function in children: A review of behavioural, neuropsychological and biological evidence. **Neurotoxicology** Vol. 18(1); pp. 237-282.

Barkume A. (2000) Occupational injuries, illnesses and fatalities. **Report on the Youth Labor Force** US Department of Labor. [Online] Available: http://www.bls.gov/opub/rylf/rylfhome.htm [18/03/2004]

Bellinger D.C., Stiles K.M., Needleman H.L (1992) Low-level lead exposure, intelligence and academic achievement: a long-term follow-up study **Pediatrics** Vol. 90(6); pp. 855-61.

Bellinger D., Leviton A., Waternauz C., Needleman H., Rabinowitz M. (1987). Longitudinal Analysis of Prenatal and Postnatal Lead Exposure and Early Cognitive Development. **New England Journal of Medicine** Vol: 316; pp. 1037 -1043.

Bockelmann I., Darius S., McGauran N., Robra B.P., Peter B., Pfister E.A. (2002). The psychological effects of exposure to mixed organic solvents on car painters. **Disability & Rehabilitation** Vol. 24; pp. 455-61.

Bockelmann I., Pfister E.A. (2003) Influence of occupational exposure to organic solvent mixtures on contrast sensitivity in printers. **Journal of Occupational and Environmental Medicine** Vol. 45(1); pp. 25-33.

Bolle L., Herrera H., Loretan E., Boillat M-A. (1996) Neurobehavioural test performance among apprentice painters: Baseline data **American Journal of Industrial Medicine** Vol. 29; pp. 539-546.

Bolla K. I., Schwartz B.S, Stewart W., Rignani W., Agnew J., Ford D. P. (1995). Comparison of neurobehavioural function in workers exposed to a mixture of organic and inorganic lead and in workers exposed to solvents. **American Journal of Industrial Medicine** Vol 27(2); pp. 231-46.

Boufous S., Williamson A. (2003). Work-related injury in NSW hospitalisation and workers' compensation datasets: a comparative analysis. **Australian and New Zealand Journal of Public Health** Vol 27(3); pp.352-357.

Boyden J, Ling B, Myers W. (1999). **What works for working children?** Save the children and UNICEF: Stockholm – Sweden

Bråtveit M., Moen B.E. (2001) Exposure to organic solvents during cosmetic finishing of cars **Occupational medicine** Vol. 51; pp. 396-400

Brent R.L., Tanski S., Weitzman M. (2004) A pediatric perspective on the unique vulnerability and resilience of the embryo and the child to environmental toxicants: the importance of rigorous research concerning age and agent. **Pediatrics** Vol. 113(4 Suppl); pp.935-44

Brouwer A., Morse D.C., Lans M.C., Schuur A.G., Murk A.J., Klasson-Wehler E., Bergman A., Visser T.J (1998) Interactions of persistent environmental organohalogens with the thyroid hormone system: Mechanisms and possible consequences for animal and human health. **Toxicology and Industrial Health** Vol: 14(1-2) pp: 59-84.

Campagna D., Stengel B., Mergler D., Limasset J.C., Diebold F., Michard D., Huel G. (2001) Color vision and occupational toluene exposure. **Neurotoxicology and Teratology** Vol. 23; pp. 473-480.

Campbell T.F., Needleman H.L., Riess J.A., Tobin M.J. (2000) Bone lead levels and language processing performance **Developmental neuropsychology** Vol. 18(2); pp. 171-186.

Canfield R.L., Henderson C.R., Cory-Slechta D.A., Cox C., Jusko T.A., Lanphear B.P. (2003) Intellectual impairment in children with blood lead concentrations below 10 microg per deciliter **The New England Journal of Medicine** Vol. 348(16); pp. 1517-1526.

Castillo L., Baldwin m., Sassine M., Mergler D. (2001) Cumulative exposure to Styrene and visual functions. **American Journal of Industrial Medicine** Vol. 39; pp. 351-360.

Cavalleri A., Gobba F., Nicale E., Fiocchi V. (2000) Dose-related color vision impairment in Toluene-exposed workers **Archives of Environmental Health** Vol. 55(6); pp. 399-404.

Central Administration of Statistics (CAS) (1997). **Living conditions in 1997**. Lebanese Republic – Lebanon

Central Administration of Statistics (CAS) and UNICEF (2002). **Status of children in Lebanon 2000.** CAS and UNICEF: Beirut

Challenor J., Wright D. (2000) Aggression in boat builders: a search for altered mood states in boat builders exposed to styrene **Occupational Medicine** Vol. 50(3); pp. 185-192.

Chance G.W., Harmsen E. (1998) Children are different: environmental contaminants and children's health. **Canadian Journal of Public Health**. Vol. 89 (Suppl 1); pp.S9-13, S10-5.

Charnley G., Putzrath R.M. (2001) Children's health, susceptibility, and regulatory approaches to reducing risks from chemical carcinogens. **Environmental Health Perspectives** Vol. 109(2); pp. 187-192.

Chen R., Dick F., Seaton A. (1999a) Health effects of solvent exposure among dockyard painters: mortality and neuropsychological symptoms **Occupational and Environmental Medicine** Vol. 56; pp. 383-387.

Chen R., Wei L., Seaton A. (1999b) Neuropsychological symptoms in Chinese male and female painters: an epidemiological study in dockyard workers. **Occupational and Environmental Medicine** Vol. 56; pp. 388-390.

Chen R., Dick F., Semple S., Seaton A., Walker L.G. (2001a) Exposure to organic solvents and personality **Occupational and Environmental Medicine** Vol. 58; pp.14-18.

Chen R., Semple S., Seaton A. (2001b) Nasal, eye and skin irritation in dockyard painters **Occupational and Environmental Medicine** Vol.58; pp. 542-543.

Chiodo L.M., Jacobson S.W., Jacobson J.L. (2004) Neurodevelopmental effects of postnatal lead exposure at very low levels **Neurotoxicology and Teratology** Vol. 26; pp. 359-371.

Chouanière D., Wild P., Fontana J., Hèry., Fournier M., Baudin V., Subra I., Rousselle D., Toamain J-P., Saurin S., Ardiot M-R. (2002) Neurobehavioural disturbances arising from occupational toluene exposure **American Journal of Industrial Medicine** Vol. 41; pp. 77-88.

Cincinnati (1987) **Organic solvent neurotoxicity** Occupational Health: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health.

Colvin M, Myers J, Nell V, Rees D, Cronje R. (1993). A cross-sectional survey of neurobehavioural effects of chronic solvent exposure on workers in a paint manufacturing plant. **Environmental Research** Vol. 63; pp. 122-32.

Conley J. (2000) Child Labor – Robbing Children of Their Youth. **Pediatric Nursing** Vol. 26(6); pp. 637-639

Cordier S., Garel M. Mandereau L., Morcel H., Doineau P., Gosme-Seguret S., Josse D., White R., Amiel-Tison C. (2002) Neurodevelopmental investigations among methylmercury-exposed children in French Guiana **Environmental Research** Section A. Vol: 89 pp. 1-11.

Counter S.A., Buchanan L.H., Rosas H.D., Ortega F. (1998) Neurocognitive effects of chronic lead intoxication in Andean children **Journal of Neurological Sciences** Vol. 160; pp. 47-53.

Curtis M.F., Keller L.W (1986) Exposure issues in the evaluation of solvent effects **Neurotoxicology** Vol. 7; pp.524.

Dancescu P., Inungu J., Tuffuor E. (1999). An indicator of the participation of children in manual labour. **Tropical Doctor** Vol. 29; pp 121-122.

Daniell W., Stebbins A., O'Donnell J., Horstman S.W., Rosenstock L. (1993) Neuropsychological performance and solvent exposure among car body repair shop workers **British Journal of Industrial Medicine** Vol. 50; pp. 368-377.

Daniell W.E., Claypoole K.H., Checkoway H., Smith-Weller T., Dager S.R., Twones B.D., Rosenstock L. (1999) Neuropsychological function in retired workers with previous long term occupational exposure to solvents. **Occupational and Environmental Medicine** Vol. 56; pp. 93-105.

Davidson P.W., Myers G.J., Cox C., Axtell C., Shamlaye C., Solane-Reeves J., Cernichiari E., Needham L., Choi A., Wang Y., Berline M., Clarkson T.W. (1998) Effects of prenatal and postnatal methylmercury exposure from fish consumption on neurodevelopment – Outcomes at 66 months of age in the Seychelles child development study. **Journal of the American Medical Association** Vol. 280; pp. 701-707.

De Souza e Silva J., Urani A. (2002) **Children in drug trafficking: A rapid assessment** A report prepared for the ILO/IPEC: Geneva.

Del Rosario R., Bonga M. (2000). **Child Labour in the Philippines**. Manila: University of the Philippines Diliman and the United Nations Children's Fund.

De Vries S.T, Agbuya M.C, Rubia D., Fogas J. (2001) **The local trafficking of Filipino Girls for Employment: The Case of Girl-Children trafficked for Entertainment Work, Domestic Services and Factory Work**. The Institute for Labor Studies and UNICEF: Philippines.

Diab S. (2001) Child Labour in South Lebanon. **An-Nahar daily newspaper.** 9th July 2001 (in Arabic) – Lebanon.

Dick F., Semple S., Chen R., Seaton A. (2000) Neurological deficits in solvent-exposed painters: a syndrome including impaired colour vision, cognitive defects, tremor and loss of vibration sensation. **QJM: An international Journal of Medicine** Vol. 93(10); pp. 655-661.

Dick F., Semple S., Osborne A., Soutar A., Seaton A., Cherrie J.W., Wlaker L.G., Haites N. (2002) Organic solvent exposure, genes and risk of neuropsychological impairment **QJM: An International Journal of Medicine** Vol. 95(6); pp. 379-387.

Dick F., Semple S., Soutar A., Osborne A., Cherrie J.W., Seaton A. (2004) Is colour vision impairment associated with cognitive impairment in solvent exposed workers? **Occupational and Environmental Medicine** Vol. 61; pp.76-78.

Dietert R.R., Etzel R.A, Chen D., Halonen M., Holladay S.D., Jarabek A.M., Landreth K., Peden D.B., Pinkerton K., Smialowicz R.J., Zoetis T. (2000) Workshop to identify critical windows of exposure for children's health: immune and respiratory systems work group summary. **Environmental Health Perspectives** Vol. 108 (Suppl 3); pp. 483-490.

Dietrich K. N., Berger O.G., Succop P.A. (1993). Lead exposure and the motor developmental status of urban six-year-old children in the Cincinnati Prospective Study. **Pediatrics**. Vol: 91(2); pp. 301-307.

Dietrich K. N., Ris M. D., Succop P.A., Berger O.G., Bornschein R.L. (2001). Early exposure to lead and juvenile delinquency. **Neurotoxicology & Teratology.** Vol. 23(6); pp. 511-518.

Dufort V.M., Kotch J.B., Marshall S.W., Waller A.E, Langley J.D. (1997). Occupational injuries among adolescents in Dunedin, New Zealand, 1990-1993. **Annals of Emergency Medicine** Vol. 30; pp. 266-273.

Dykens E. (1996) The draw-a-person task in persons with mental retardation: What does it measure? **Research in Developmental Disabilities** Vol. 17; pp. 1-13.

Edralin D. (2002) **In depth study on the situation of Children in Pyrotechnics.** International Labour Organisation – International Programme for the Elimination of Child Labour.

Eller N., Netterstrom B., Laursen P. (1999) Risk of chronic effects on the central nervous system at low toluene exposure. **Occupational Medicine** Vol. 49(6); pp. 389-395.

Ernhardt C.B. (1995) Inconsistencies in the lead-effects literature exist and cannot be explained by "effect modification". **Neurotoxicology and Teratology** Vol. 17(3); pp. 227-233.

Escalona E., Yanes L., Feo O., Maizlish N. (1995) Neurobehavioural evaluation of Venezuelan workers exposed to organic solvent mixtures. **American Journal of Industrial Medicine** Vol. 27; pp. 15-27.

Estrella-Gust D.P. (2000) A case study of child labour in the Philippine footwear industry: Health, safety and the work environment. **Asian-Pacific Newsletter on Occupational Health and Safety** Vol. 7(2)

Etzel R.A. (2004) Environmental risks in childhood. **Pediatric Annals** Vol. 33(7); pp. 431-436.

Fajardo M.E (2002) **Organic solvent toxicity** Occupational Medicine Module (lecture 14) Agency for Toxic Substances and Disease Registry (ATSDR)

Fattore T. (2005) **Children at work** – A report researched and written for the NSW Commission for children and young people. NSW Commision for Children and Young People, Sydney.

Feldman R.G., Ratner M.H., Ptak T. (1999) Chronic toxic encephalopathy in a painter exposed to mixed solvents **Environmental Health Perspectives** Vol. 105(5); pp. 417-422.

Fidler A.T, Baker E.L, Letz R.E. (1987) Neurobehavioural effects of occupational exposure to organic solvents among construction painters. **British Journal of Industrial Medicine** Vol. 44; pp. 292-308.

Fiedler N. (1996) Neuropsychological approaches for the detection and evaluation of toxic symptoms **Environmental Health Perspectives** Vol. 104(S2); pp.239-245

Fischbach M.R. (1998) Spotlight: Lebanon. **Population Today** 7/8: pp. 7.

Forastieri V. (2000) Challenges in combating child labour from an occupational health perspective. **African Newsletter on Occupational Health and Safety** Vol. 10 (2); pp. 32-35.

Forastieri V. (2002) **Children at work: Health and safety risks (2nd Edition).** Geneva – International Labour Office.

Gallagher S. (2005) Physical limitations and musculoskeletal complaints associated with work in unusual or restricted postures: A literature review **Journal of Safety Research** Vol. 36; pp.51-61.

Gharaibeh M, Hoeman S. (2003) Health hazards and risks for abuse among child labour in Jordan. **Journal of Paediatric Nursing** Vol. 18 (2); pp. 140-147.

Goldey E.S., Crofton K.M. (1998). Thyroxine replacement attenuates hypothyroxinemia, hearing loss, and motor deficits following developmental exposure to Aroclor 1254 in rats. **Toxicological Sciences** Vol. 45(1); pp. 94-105.

Gonzalez M., Velten M., Cantineau A. (1998) Increased acquired dyschromatopsia among solvent-exposed workers: an epidemiology study on 249 employees of an aluminum-foil printing factory. **International Archives of Occupational and Environmental Health** Vol. 71; pp. 317-324.

Graitcer P.L, Lerer L.B. (2000). **The impact of child labour on health**: Report of a field investigation in Egypt. Early Child Development Series, World Bank.

Grandjean P., Lyngbye T., Hansen O.N. (1991). Lessons from a Danish study on neuropsychological impairment related to lead exposure. **Environmental Health Perspectives** Vol. 94; pp. 111-115.

Grandjean P., White R.F., Weihe P. (1996) Neurobehavioural Epidemiology: Application in risk assessment **Environmental Health Perspectives** Vol. 104(S2); pp. 397-400.

Grandjean P., Weihe P., White R.F., Debes F., Araki S., Yokoyama K., Murata K., Sørensen N., Dahl R., Jørgensen P.J. (1997). Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. **Neurotoxicology Teratology** Vol. 19; pp. 417-28.

Grandjean P., Weihe P., White R.F., Debes F. (1998). Cognitive performance of children prenatally exposed to "safe" levels of methylmercury. **Environmental Research.** Vol. 77(2); pp. 165-172.

Grandjean P., White R.F., Nielsen A., Cleary D., De Oliveira Santos E.S. (1999) Methylmercury neurotoxicity in Amazonian children downstream from gold mining **Environmental Health Perspectives** Vol. 107(7); pp. 587-597.

Grandjean P., Weihe P., Burse V.W., Needham L.L., Storr-Hansen E., Heinzow B., Debes F., Murata K., Simonsen H., Ellefsen P., Budtz-Jørgensen E., Keiding N., White R.F (2001a) Neurobehavioural deficits associated with PCB in 7-year-old children prenatally exposed to seafood neurotoxicants **Neurotoxicology and Teratology** Vol. 23; pp. 305-317.

Grandjean P., White R.F., Sullivan K., Debes F., Murata K., Otto D.A., Weihe P. (2001b) Impact of contrast sensitivity performance on visually presented neurobehavioural tests in mercury-exposed children **Neurotoxicology and Teratology** Vol. 23; pp.141-146.

Gregory R.J. (2000) **Psychological Testing: History, principles and applications (3rd Ed).** Allyn and Bacon: Boston

Griffin S.L., Mindt M.R., Rankin E.J., Ritchie A.J., Scott J.G.(2002) Estimating premorbid intelligence. Comparison of traditional and contemporary methods across the intelligence continuum **Archives of Clinical Neuropsychology** Vol. 17; pp. 497-507.

Grosch J. W., Neale A.V., Demers R. (1996). Neurobehavioural and health-related deficits in solvent-exposed painters. **American Journal of Industrial Medicine**. Vol. 30(5); pp. 623-32.

Hadi A. (2000). Child abuse among working children in rural Bangladesh: prevalence and determinants. **Public Health** Vol. 114; pp.380-384.

Hakkola M. (1994) Neuropsychological symptoms among tanker drivers with exposure to solvents **Occupational Medicine** Vol. 44; pp. 243-246.

Hamdan H. (1997). **National report on child labour in Lebanon**. A report prepared for the International Labour Organisation and Ministry of Labour – Lebanon.

Harada H., (1978) Congenital Minimata Disease: Intrauterine methylmercury poisoning **Teratology** Vol. 18; pp. 285-288.

Hartman D.E. (1995) **Neuropsychological toxicology – Identification and assessment of human neurotoxic syndromes (2nd Edition).** Plenum press – New York.

Harari R., Forastiere F., Axelson O. (1997) Unacceptable "Occupational" exposure to toxic agents among children in Ecuador **American Journal of Industrial Medicine** Vol. 32; pp. 185-189.

Harvey P.G., Hamlin M.W., Kumar R., Morgan K.G., Spurgeon A., Delves H.T. (1988) Relationships between blood lead, behaviour, psychometric and neuropsychological test performance in young children **British Journal of Developmental Psychology** Vol. 6; pp. 145-156.

Hawamdeh H., Spencer N. (2001) Work, family socioeconomic status, and growth among working boys in Jordan. **Archives of Disability Child** Vol. 84; pp 311 – 314.

Heptinstall E., Jewitt K., Sherrif C. (1997). **Young Workers and Their Accidents.** Child Accident Prevention Trust, London.

Högstedt C., Andersson K., Hane M. (1984). A questionnaire approach to the monitoring of early disturbances in central nervous function. In: **Biological Monitoring and Surveillance of Workers Exposed to Chemicals**, Aitio A, Riihimäki A, Vainio H., editors. Washington, Hemisphere Printing Co., pp. 275-87

Hooisma J., Hänninen H., Emmen H.H., Kulig B. (1993) Behavioral effects of exposure to organic solvents in Dutch painters **Neurotoxicology and Teratology** Vol. 15; pp. 397-406.

Hooisma J., Hänninen H., Emmen H.H., Kulig B (1994) Symptoms indicative of the effects of organic solvent exposure in Dutch painters **Neurotoxicology and Teratology** Vol. 16; pp. 613-622.

Ihrig A., Nasterlack M., Dietz M.C., Hoffman J., Triebig G. (2003) Pilot study on prevalence of color vision dysfunction in long-term solvent-exposed painters. **Industrial Health** Vol. 41; pp. 39-42.

ILO (1997) **Action against Child labour: Lessons& strategies priorities for the future.** Geneva: International Labour Office.

ILO (1998). **Statistics on working children and hazardous child labour in brief**. Geneva : International Labour Office.

ILO (2002). **A Future without Child Labour – Global Report.** A report of the Director-General under the follow-up to the ILO Declaration on Fundamental Principles and Rights at work. International Labour Conference – 90th Session. Geneva - International Labour Office.

Images of child labour (date unknown) **Child labour and the global village: Photography for social change** [Online]. Available: http://www.childlaborphotoproject.org/links.html [14/03/2004]

International Labour Organisation (ILO) and International Programme on the Elimination of Child Labour (IPEC) (2002). **Lebanon: Child Labour on Tobacco Plantations: A Rapid Assessment**. Consultation and Research Institute . Geneva: International Labour Office.

International Programme on the Elimination of Child Labour (IPEC) and Statistical Information and Monitoring Programme on Child Labour (SIMPOC) (2002). **Every Child Counts – New Global Estimates on Child Labour.** Geneva: International Labour Office. [Online]. Available: http://www.ilo.org/public/english/standards/ipec/simpoc/others/globalest.pdf [15/06/2003].

Iregren A. (1996) Behavioral methods and organic solvents: Questions and consequences **Environmental Health Perspectives** Vol. 104(S2); pp. 361-366.

Iregren A., Andersson M., Nylen P. (2002) Color vision and occupational chemical exposures. II. Visual functions in non-exposed subjects. **Neurotoxicology**. Vol.23(6); pp.735-45.

Issa N, Houry M. (1997). **Characteristics of child labour in Lebanon**. A report prepared for the Ministry of Social Affairs and UNICEF – Lebanon.

Issever H., Malat G., Sbuncu H.H., Yuksel N. (2002) Impairment of colour vision in patients with n-hexane exposure-dependent toxic polyneuropathy **Occupational Medicine** Vol.52; pp.183-186.

Jacobson S.W., Fein G.G., Jacobson J.L., Schwartz P.M., Dowler J.K. (1985). The effect of intrauterine PCB exposure on visual recognition memory. **Child Development.** Vol. 56(4); pp.853-860

Jacobson J.L., Jacobson S.W. (1996a) Intellectual impairment in children exposed to polychlorinated biphenyls in utero. **New England Journal of Medicine** Vol. 335; pp. 783-789.

Jacobson J.L., Jacobson S.W. (1996b) Prospective, longitudinal assessment of developmental neurotoxicity **Environmental Health Perspectives** Vol. 104(S2); pp. 275-283.

Jacobson J.L., Jacobson S.W. (2003) Prenatal exposure to polychlorinated biphenyls and attention at school age **Journal of Pediatrics** Vol. 143; pp.780-8.

Jacobson J.L., Jacobson, S.W. (2005) Methodological issues in research on developmental exposure to neurotoxic agents **Neurotoxicology and Teratology** Vol. 27(3);pp. 395-406.

Jang J-Y., Lee, S.Y., Kim J.III., Park J.B., Lee, K.J., Chung H.K. (1999) Application of biological monitoring to the quantitative exposure assessment for neuropsychological effect by chronic exposure to organic solvents **International Archives of Occupational and Environmental Health** Vol. 72; pp.107-114.

Jones K., Cocker J., Dodd L.J., Fraser I. (2003) Factors affecting the extent of dermal absorption of solvent vapours: A human volunteer study **Annals of Occupational Hygiene** Vol. 47(2); pp. 145-150.

Julien D., Mergler D., Baldwin M., Sassine M.P., Cormier N., Chartrand E., Bèlanger S. (2000) Beyond the workplace: An exploratory study of the impact of neurotoxic workplace exposure on marital relations. **American Journal of Industrial Medicine** Vol. 37; pp. 316-323.

Kapinga T. (2000) Action against child labour in Tanzania. **African Newsletter on Occupational Health and Safety** Vol. 10 (2); pp. 48-51.

Khattak S., Moghtader G.K., McMartin K., Barrera M., Kennedy D., Koren G. (1999) Pregnancy outcome following gestational exposure to organic solvents: A prospective controlled study. **Journal of the American Medical Association** Vol. 281; pp. 1106-1109.

Kilburn K.H. (2002) Is neurotoxicity associated with environmental trichloroethylene (TCE)? **Archives of Environmental Health** Vol. 57(2); pp. 113-120.

Kishi R., Harabuchi I., Katakura Y., Ikeda T., Miyake H. (1993) Neurobehavioural effects of chronic occupational exposure to organic solvents among Japanese industrial painters **Environmental Research** Vol. 62; pp. 303-313.

Koopman-Esseboom C., Weisglas-Kuperus N., de Ridder M.A., Van der Paauw C.G., Tuinstra L.G,. Sauer P.J. (1996). Effects of polychlorinated biphenyl/dioxin exposure and feeding type on infants' mental and psychomotor development. **Pediatrics** Vol. 97(5); pp.700-706

Laak J., Goede M., Rijswijk P. (2005) The Draw-a-Person Test: An indicator of children's cognitive and socioemotional adaptation **The Journal of Genetic Psychology** Vol.166 (1); pp.77-93.

Landrigan P.J., Garg A. (2002) **Chronic effects of toxic environmental exposures on children's health**. Clinical Toxicology Vol. 40(4); pp. 449-456.
Landrigan P.J., McCammon J.B. (1997) Child labour – Still with us. **Public Health Reports** Vol. 112(6); pp. 466-473.

Lansky M. (1997) Child labour: How the challenge is being met **International Labour Review** Vol. 16(1);pp. 21-28

Laslo-Baker D., Barrera M., Knittel-Keren D., Kozer E., Wolpin J., Khattak S., Hackman R., Rovet J., Koren G. (2004) Child neurodevelopmental outcome and maternal occupational exposure to solvents **Archives of Pediatrics and Adolescent Medicine** Vol. 158(10); pp.956-961.

Lee B.W., Kelsey K., Hashimoto D., Yakes B., Seitz T., Christiani D. (1997) The prevalence of pulmonary and upper respiratory tract symptoms and spirometric test findings among newspaper pressroom workers exposed to solvents **The Journal of Occupational and Environmental Medicine** Vol. 39(10); pp. 960-969.

Lee D.H., Park I.G., Kim J.H., Lee Y.H., Kim D., Kang S. (1998) Neurobehavioural changes in shoe manufacturing workers. **Neurotoxicology and Teratology** Vol. 20(3); pp. 259-263.

Lee S., Lee Seung. (1993) A study on the neurobehavioural effects of occupational exposure to organic solvents in Korean workers **Environmental Research** Vol. 60; pp. 227-32.

Lees-Haley P.R., Williams C.W. (1997) Neurotoxicity of chronic low-dose exposure to organic solvents: A sceptical review **Journal of Clinical Psychology** Vol. 53; pp. 699-712

Letz R., Mahoney F.C., Hershman D.L., Woskie S., Smith T.J. (1990) Neurobehavioural effects of acute styrene exposure in fibreglass boat builders **Neurotoxicology and Teratology** Vol. 60; pp. 665-668

Letz R. (1991). **NES2 user's manual (version 4.4)** Winchester, MA: Neurobehavioural Systems, Inc.

Letz R., Green R.C., Woodard J.L. (1996) Development of a computer-based battery designed to screen adults for neuropsychological impairment **Neurotoxicology and Teratology** Vol. 18(4); pp. 365-370.

Letz R. (2003) Continuing challenges for computer-based neuropsychological tests **Neurotoxicology** Vol. 24; pp. 479-489.

Lezak M.D. (1983) **Neuropsychological Assessment 2nd Ed.** Oxford University Press; New York.

Lim G.W., Belton K.L., Pickett W., Schopflocher D.P., Voaklander D.C. (2004) Fatal and Non-Fatal Machine Related Injuries suffered by children in Alberta Canada, 1990-1997. **American Journal of Industrial Medicine** Vol. 45; pp. 177-185

Lim J.A. (2002) **Strengthening the Role of International Labour Standards in Selected DMCs.** Integrative paper for child labour component of ILO/ADB project. International Labour Organisation and ADB.

LoSasso G.L., Rapport L.J., Axelrod B.N. (2001) Neuropsychological symptoms associated with low-level exposure to solvents and (meth)acrylates among nail technicians. **Neuropsychiatry, Neuropsychology and Behavioral Neurology** Vol.14(3); pp. 183-189.

Lundberg I., Högberg M., Michèlsen H., Nise G., Högstedt C. (1997) Evaluation of the Q16 questionnaire on neurotoxic symptoms and a review of its use **Occupational and Environmental Medicine** Vol. 54(5); pp. 343-350.

Lunsford T.R., Lunsford B.R. (1995) The Research Sample, Part 1: Sampling **Journal of Prosthetics and Orthotics** Vol. 7(3); pp. 105 -111.

Mackie I.P., Rubin P., Wilson D.I. (2004) White spirit-paint thinner, skin stripper **Burns** Vol. 30; pp. 86-87.

Mergler D., Bowler R., Cone J. (1990) Colour vision loss among disabled workers with neuropsychological impairment. **Neurotoxicology & Teratology**. Vol. 12(6); pp. 669-72.

Mergler D., Huel G., Belanger S., Bowler R., Truchon G., Drolet D., Ostiguy C. (1996) Surveillance of early neurotoxic dysfunction **Neurotoxicology** Vol. 17(3-4); pp. 803-812.

Mitra S. (1993) A study of the health conditions of child workers in a small scale leather industry in Calcutta. **British Journal of Industrial Medicine**. Vol. 50(10); pp. 938-940

Mitra S. (1994) Factors in the sociocultural environment of child labourers: A study in a small scale leather goods industry in Calcutta. **Occupational and Environmental Medicine**. Vol 51(12); pp. 822-825.

Mitran E., Callender T., Orha B., Dragnea P., Botezatu G. (1997) Neurotoxicity associated with occupational exposure to Acetone, methyl ethyl ketone and cyclohexanone. **Environmental Research** Vol. 73; pp. 181-188.

Moen B.E., Hollund B.E. (2000) Exposure to organic solvents among car painters in Bergen, Norway **Annals of Occupational Hygiene** Vol. 44(3); pp. 185-189.

Muijser H., Geuskens R.B.M., Hooisma J., Emmen H.H., Kulig B.M. (1996) Behavioral effects of exposure to organic solvents in carpet layers **Neurotoxicology and Teratology** Vol. 18(4); pp. 455-462.

Munshi K., Parker D.L., Bannerman-Thompson H., Merchant D. (2002). Causes, nature and outcomes of work-related injuries to adolescents working at farm and non-farm jobs in rural Minnesota. **American Journal of Industrial Medicine** Vol. 42; pp. 142-149.

Muttray A., Wolters V., Jung D., Konietzko J. (1999) Effects of high does of toluene on color vision **Neurotoxicology and Teratology** Vol. 21(1); pp. 41-45.

Naglieri J.A. (1988) **Draw-a- Person: A quantitative scoring system**. San Antonia, TX; New York: The Psychological Corporation, 1988.

Nasterlack M, Dietz M. C, Frank K.H, Hacke W, Scherg H, Schmittner H, Stelzer O, Zimber A, Triebig G. (1999). A multidisciplinary cross-sectional study on solvent-related health effects in painters compared with construction workers. **International Archives of Occupational Environmental Health** Vol. 72; pp. 205-14.

Nath S.R., Hadi A. (2000) Role of Education in reducing child labour: Evidence from rural Bangladesh. **Journal of Biosocial Science** Vol. 32; pp. 301-313.

National Occupational Health and Safety Commission (2002). **OHS Information – additive effects.** Commonwealth of Australia [Online]. Available: http://www.nohsc.gov.au/OHSInformation/NOHSCPublications/fulltext/docs/h5/892.htm. [23/09/2002]

National Research Council (2000). **Toxicological effects of Methylmercury**. National Academic Press – Washington DC.

National Research Council (1993) **Pesticides in the Diets of Infants and Children.** National Research Council. Committee on Pesticides in the Diets of Infants and Children. Washington, DC: National Academy Press.

National Statistical Office of the Philippines (NSOP) (1998). **1995 Survey on Children 5-17 years old** (SCL), Manila, Philippines [Online]. Available: http://www.ilo.org/public/english/standards/ipec/simpoc/phillipines/report/philip1995/index.htm. [15/10/2001]

Needleman H.L., Gunnoe C., Leviton A., Reed R., Peresie H., Maher C., Barrett P. (1979) Deficits in psychologic and classroom performance of children with elevated dentine lead levels **New England Journal of Medicine** Vol. 300(13); pp.689-695.

Needleman H.L., Schell A., Bellinger D., Leviton A., Allred E.N. (1990). The Long-Term Effects of Exposure to Low Doses of Lead in Childhood. An 11 year follow-up report. **New England Journal of Medicine** Vol. 322(2); pp. 83-88.

Nelson N.A., Robins T.G., White R.F., Garrison R.P. (1994) A case-control study of chronic neuropsychiatric disease and organic solvent exposure in automobile assembly plant workers **Occupational and Environmental Medicine** Vol. 51; pp. 302-307.

Ng T.P., Ong S.G., Lam W.K., Jones G.M. (1990) Neurobehavioural effects of industrial mixed solvent exposure in Chinese printing and paint workers. **Neurotoxicology and Teratology** Vol. 12; pp. 661-664.

NIOSH (National Institute for Occupational Safety and Health) (1997). In Special hazard review: **Child labour research needs, recommendations from the NIOSH Child Labour Team.** US Department of Health and Human Services, Public Health Services, Centers for Disease, Control and Prevention [Online]. Available:http://www.cdc.gov/niosh/97-143b.html. [21/06/2001]

NIOSH (National Institute for Occupational Safety and Health) (1997) **Organic Solvent Neurotoxicity –Current intelligence Bulletin # 48.** US Department of Health and Human Services, Public Health Services, Centers for Disease, Control and Prevention

Nkurlu J.I (2000). Child Labour: A background paper. **African Newsletter on Occupational Health and Safety** Vol. 10(2); pp. 36-39.

Nordling Nilson L., Sällsten G., Hagberg S., Bäckman L., Barregård L. (2002) Influence of solvent exposure and aging on cognitive functioning: an 18 year follow up of formerly exposed floor layers and their controls **Occupational and Environmental Medicine** Vol. 59(1); pp. 49-57.

Nuwayhid I., El-Zein A, Khodr A., Usta J., Makarem M., Kouzi S., Sabbah M., Terre des Hommes (1998). **Physical and mental health of male children (10-17 years old) working in small industrial workshops in urban settings in Lebanon**. A study prepared for the Ministry of Social Affairs and UNICEF – Lebanon.

Nuwayhid I., Saddik B., Quba'a R. (2001) **Working children in small industrial establishments in Tripoli & Akkar- Lebanon: Their work environment and work activities**. Submitted to the International Programme for the Elimination of Child Labour (IPEC) at the International Labour Organization, Geneva, November 2001.

Nuwayhid I.A., Usta J., Makarem M., Khudr A., El-Zein A. (2005). Health of children working in small urban industrial shops. **Occupational and Environmental Medicine** Vol 62; pp. 86-94.

O'Donnell O., Doorslaer E.V., Rosati F. (2002) **Child labour and health: Evidence and research issues** A report written for The International Labour Organisation; UNICEF and the World Bank: Geneva, January 2002

Office of the United Nations High Commission for Human Rights (OHCHR) (2003) **Committee on the Rights of the Child** [Online]. Available: http://www.ohchr.org/english/bodies/crc/ [19/10/2004]

Omokhodion F.O., Omokhodion S.I. (2004) Health status of working and non-working school children in Ibadan, Nigeria. **Annals of Tropical Paediatrics**. Vol. 24(2); pp. 175-178.

Özgenel G.Y., Akin S., Özbek S., Kahveci R., Özcan M. (2004) Thermal injuries due to paint thinner **Burns** Vol. 30; pp. 154-155.

Parrish C.F. (1983) Solvents, industrial. In: Grayson M, Eckroth D, Mark HF Othmer DF, Overberger CG, and Seaborg GT, eds. **Kirk-Othmer encyclopedia of chemical technology.** Volume 21. New York, NY: John Wiley & Sons, Inc., pp. 377-401

Patandin S., Lanting C.I., Mulder P.G., Boersma R.E., Sauer P.J., Weisglad-Kuperus N. (1999) Effects of environmental exposure to polychlorinated biphenyls and dioxins on cognitive abilities in Dutch children at 42 months of age **The Journal of Pediatrics** Vol. 134(1); pp. 33-41.

Prince T.S., Spengler S.E. (2001) Severe headache associated with occupational exposure to Stoddard solvent **Occupational Medicine** Vol. 51(2); pp. 136-138.

Raab G.M., Thomson G.O., Boyd L., Fulton M., Laxen D.P. (1990) Blood lead levels, reaction time, inspection ability in Edinburgh children. **British Journal of Developmental Psychology** Vol. 8; pp.101-118

Reif J.S., Burch J., Nuckols J.R., Metzger L., Ellington D., Anger W.K. (2003) Neurobehavioural effects of exposure to trichloroethylene through a municipal water supply **Environmental Research** Vol. 93; pp. 248-258.

Rice D.C. (1998) Issues in developmental neurotoxicology: Interpretation and implications of the data **Canadian Journal of Public Health** Vol. 89(S1); pp.S31-S36.

Ris M.D, Dietrich K.N., Succop P.A, Berger O.G., Bornschein R.L. (2004). Early exposure to lead and neuropsychological outcome in adolescence. **Journal of the International neuropsychological Society** Vol. 10; pp. 261-270.

Rohlman D.S, Gimenes L.S., Eckerman D.A., Kang S.K., Farahat F.M., Anger W.K. (2003) Development of the behavioural assessment and research system (BARS) to detect and characterise neurotoxicity in humans **Neurotoxicology** Vol. 24; pp. 523-531.

Saddik B., Nuwayhid I. (2003) **Assessing neurotoxicity of working children in Lebanon between the ages of 10-17 in Lebanon.** A report submitted to the International Programme for the Elimination of Child Labour (IPEC) at the International Labour Organization – Geneva.

Saddik B., Nuwayhid I., Williamson A., Black D. (2003) Evidence of neurotoxicity in working children in Lebanon. **Neurotoxicology** Vol. 24 (4-5); pp. 733 – 739

Schantz S.L. (1996) Developmental neurotoxicity of PCBs in Humans: What do we know and where do we go from here? **Neurotoxicology and Teratology** Vol. 18(3); pp. 217-227

Schettler T., (2001) Toxic threats to neurologic development of children **Environmental Health Perspectives** Vol. 109(S6); pp.813-816

Seeber A., Sietmann B., Zupanic M. (1996) In search of dose-response relationships of solvent mixtures to neurobehavioural effects in paint manufacturing and painters. **Food and Chemical Toxicology**. Vol. 34; pp. 1113 – 1120.

Semple S., Dick F., Osborne A., Cherrie J.W., Soutar A., Seaton A., Haites N. (2000) Impairment of colour vision in workers exposed to organic solvents **Occupational and Environmental Medicine** Vol. 57(9); pp. 582-587.

Siddiqi F., Patrinos H. (1996) **Child labour: Issues, causes and intervention.** Working paper presented for the Human Capital Development and Operations Policy. HCOWP. 56. [Online]. Available: www.worldbank.org/html [14/05/2002].

Slikker W., Beck B.D., Cory-Slechta D.A., Paule M., Anger W.K., Bellinger D. (2000) Cognitive tests: Interpretation for neurotoxicity? (Workshop summary) **Toxicological Sciences** Vol. 58; pp. 222-234.

Smargiassi A., Bergamaschi E., Muttti A., Cella T. (1998) Predictive validity of the Q16 questionnaire: A comparison between reported symptoms and neurobehavioural tests **Neurotoxicology** Vol. 19(4-5); pp. 703-708.

Spencer P.S., Schaumburg H.H., Ludolph A.C (Eds) (2000) **Experimental and clinical neurotoxicology 2nd Edition Oxford** University Press: New York

SPSS Inc. (2001) **Statistical Package for the Social Sciences** Version 11.0 Chicago: SPSS, Inc.

Spurgeon A. (1995) The use of neurobehavioural test batteries for research, diagnosis and screening: methodological aspects **Toxicology Letters** Vol.82/83; pp.191-195.

Spurgeon A. (2002) **A review of the literature relating to the chronic neurobehavioural effects of occupational exposure to organic solvents.** Institute of Occupational Health, University of Birmingham – UK.

Stein J., Schettler T., Wallinga D., Valenti M. (2002) In Harms Way: Toxic Threats to Child Development **Journal of Developmental and Behavioral Pediatrics** Vol. 23(1S); pp. S13- S22.

Stewart P.W., Reihman J., Lonky E.I., Darvill T.J., Pagano J. (2003) Cognitive development in preschool children prenatally exposed to PCBs and MeHg **Neurotoxicology and Teratology** Vol. 25; pp. 11-22.

Stokes L., R. Letz R., Gerr F., Kolczak M., McNeill F.E., Chettle D.R., Kaye W.E. (1998). Neurotoxicity in young adults 20 years after childhood exposure to lead: the Bunker Hill experience. **Occupational & Environmental Medicine.** Vol. 55(8); pp. 507-516.

Stollery B.T. (1996) Cognitive neurotoxicology: A luxury or necessity? **Neurotoxicology and Teratology** Vol. 18(4); pp. 359-364.

Suk WA., Murray K. Avakian M.D. (2003a) Environmental hazards to children's health in the modern world. **Mutation Research** Vol. 544(2-3); pp. 235-242

Suk W.A., Mathuros R., Balakrishnan K., Berger M., Carpenter D., Damstra T., Pronczuk de Garbino J., Koh D., Landrigan P.J., Maklinao I., Sly P.D., Xu Y., Zheng B.S. (2003b) Environmental threats to children's health in Southeast Asia and the Western Pacific **Environmental Health Perspectives** Vol. 111(10); pp. 1340-1347.

Syed K., Mirza R., Sulta R. (1991) Child labour-socioeconomic consequences. **Pakistan and Gulf Economist.** Vol. 10; pp 36-39.

Tabassum F., Baig L.A. Child labour a reality: results from a study of a squatter settlement of Karachi. **Journal of the Pakistan Medical Association**. Vol 52 (11); pp 507-510.

The Center for Disease Control and Prevention (2001). Nonfatal occupational injuries and illnesses treated in hospital emergency departments – United States - 1998. **Journal of the American Medical Association**. Vol. 285(19); pp. 2443-2444.

3M (1998) **Organic Vapor Monitor Sampling and Analysis Guide**. 3M Occupational Health and Environmental Safety Division. MN; USA

Till C., Westall C.A., Rovet J.F., Koren G. (2001a) Effects of maternal occupational exposure to organic solvents on offspring visual functioning: A prospective controlled study. **Teratology** Vol. 64; pp. 134-141.

Till C., Koren G., Rovet J.F. (2001b) Prenatal exposure to organic solvent and child neurobehavioural performance. **Neurotoxicology and Teratology** Vol. 23; pp. 235-245.

Till C., Rovet J.F., Koren G., Westall C.A. (2003) Assessment of visual functions following prenatal exposure to organic solvents. **Neurotoxicology** Vol. 194; pp. 1-7.

Tong S., Baghurst P., McMichael A., Sawyer M., Mudge J. (1996) Lifetime exposure to environmental lead and children's intelligence at 11-13 years: the Port Pirie cohort study **British Medical Journal** Vol. 312(7046); pp. 1569-1575.

Tsai S.Y., Chen J.D. (1996) Neurobehavioural effects of occupational exposure to low-level styrene **Neurotoxicology and Teratology** Vol. 18(4); pp.463-469.

Tsai S. Y., Chen J. D., Chao W. Y., Wang J. D. (1997) Neurobehavioural effects of occupational exposure to low-level organic solvents among Taiwanese workers in paint factories. **Environmental Research** Vol. 73; pp. 146-155

UNICEF (1995). **Preliminary study on the state of working children in Lebanon.** UNICEF, Lebanon Office.

UNICEF (1997), **The State of the World's Children Report** [Online] Available: http://www.unicef.org/sowc97/ [16/10/1999].

UNICEF (2003) **The State of the World's Children Report.** The United Nations Children's Fund, UNICEF House: New York

United Nations (UN) (2003) **Convention on the rights of the child** The United Nations: New York

US Department of Labour (2003) Bureau of International Labor Affairs – Lebanon. [Online] Available: www.dol.gov/ilab/media/reports/iclp/tda2003/Lebanon.htm [19/05/2005]

Viaene M.K., Pauwels W., Roels H.A., Masschelein R. (2001) Neurobehavioural changes and persistence of complaints in workers exposed to styrene in polyester boat building plant: influence of exposure characteristics and microsomal epoxide hydrolase phenotype **Occupational and Environmental Medicine** Vol. 58; pp.103-112.

Van Thriel C., Seeber A., Kiesswetter E., Blaszkewicz M., Golka K., Wiesmüller G.A. (2003) Physiological and psychological approaches to chemosensory effects of solvents **Toxicology Letters** Vol.140-141; pp. 261-271.

Venkateswarlu D., Kasper J., Mathews R., Reis C., Lacopina V., Wise P. (2003). Child Labour in India: a health and human rights perspective. **The Lancet** Vol: 362; pp. s32.

Verity M.A., Sarafian T.A. (2000) Mercury and mercury compounds. In: Spencer P.S., Schaumburg H.H., Ludolph A.C (Eds) **Experimental and clinical neurotoxicology 2nd Edition** Oxford University Press: New York pp. 763-770.

Wang J.D, Chen J.D. (1993). Acute and chronic neurological symptoms among paint workers exposed to mixtures of organic solvents. **Environmental Research** Vol. 61; pp. 107-16.

Walkowiak J., Altmann L., Kramer U., Sveinsson K., Turfeld M., Weishoff-Houben M., Winneke G. (1998) Cognitive and sensorimotor functions in 6 – year- old children in relation to lead and mercury levels: Adjustment for intelligence and contrast sensitivity in computerised testing **Neurotoxicology and Teratology** Vol. 20 (5); pp. 511-521.

Watanabe C., Satoh H. (1996). Evolution of our understanding of methylmercury as a health threat. **Environmental Health Perspectives.** Vol: 104 (Suppl. 2); pp. 367-379.

Wechsler D. (1974). **Wechsler Intelligence Scale for Children – Revised**. Psychological Corporation, New York.

Weiss B. (1979) The behavioral toxicology of metals **Federation Proceedings** Vol. 13; pp.22-27.

Welp E., Kogevinas M., Andersen A., Bellander T., Biocca M., Coggon D., Esteve J., Gennaro V., Kolstad H., Lundberg I., Lynge E., partanen T., Spence A., Boffetta P., Ferro G., Saracci R. (1996) Exposure to styrene and mortality from nervous system diseases and mental disorders **American Journal of Epidemiology** Vol. 144(7); pp.623-633.

White R. F., Feldman R.G (1987) Neuropsychological assessment of toxic encephalopathy. **American Journal of Industrial Medicine.** Vol.11(4); pp.395-398

White L., O'Donnell C. (2001) Working children and accidents: Understanding the risks. **Child care and Health Development** Vol. 27; pp 23-34.

White R.F., Proctor S.P. (1997) Solvents and neurotoxicity **The Lancet** Vol. 349; pp. 1239-1243.

White R.F, Proctor S.P, Escheverria D, Schwikert J, Feldman R.(1995). Neurobehavioural effects of acute and chronic mixed solvent exposure in the screen printing industry. **American Journal of Industrial Medicine** Vol. 28; pp. 221-31

WHO (1985) **Chronic effects of organic solvents on CNS and diagnosis criteria** Report 5; Copenhagen

WHO (1988) **Consultation on chronic effects of organic solvents on the CNS: Development of core protocol for international collaborative study.** Copenhagen Nov. 15-18.

WHO (1986). **Operational guide for the WHO NCTB**. Office of Occupational Health; Geneva – Switzerland pp. 5 - 25.

WHO (1987). **Children at work: Special health risks.** WHO Technical Report Series 756. Geneva – Switzerland

Wickens, C.D., Carswell, C.M. (1997) Information Processing. In Salvendy G. (ed), **Handbook of Human Factors and ergonomics, 2nd edition**. Wiley: New York; pp. 130-149.

Williamson A., Feyer A., Rassack N. (1988) **The information processing and performance test battery** National Institute of Occupational Health and Safety – Human Performance Analysis Unit: Sydney, Australia.

Williamson A. (1990). The development of a neurobehavioural test battery for use in hazard evaluations in occupational settings. **Neurotoxicology Teratology** Vol. 12; pp. 509-514.

Williamson A.M. (1995) Neurobehavioural test batteries: current status, critical evaluation and new directions **Toxicology Letters** Vol. 82-83; pp. 203-209

Williamson A.M. (1996a) Historical overview of computerised behavioral testing of humans in Neurotoxicology **Neurotoxicology and Teratology** Vol. 18(4); pp. 351-357.

Williamson A.M. (1996b) The role of confounding variables in the assessment of neurobehavioural effects of chronic solvent exposure **Neurotoxicology** Vol. 17(3-4); pp. 761-768.

Williamson A, Winder C. (1993). A prospective cohort study of the chronic effects of solvent exposure. **Environmental Research** Vol. 62; pp. 256-71.

Winneke G., Collet W., Lilienthal H. (1988) The effects of lead in laboratory animals and environmentally-exposed children. **Toxicology** Vol. 49(2-3); pp. 291-8.

Winneke G. (1995) Endpoints of developmental neurotoxicity in environmentally exposed children **Toxicology Letters** Vol.77; pp. 127-136.

Winneke G., Lilienthal H., Kramer U. (1996) The Neurobehavioural toxicology and teratology of lead **Archives of Toxicology** S18; pp. 57-70.

Winneke G., Bucholski A., Heinzow B., Krämer U., Schmidt E., Walkowiak J., Wiener J.A., Steingrüber H-J. (1998) Developmental neurotoxicity of polychlorinated biphenyls (PCBS): cognitive and psychomotor functions in 7-month old children **Toxicology Letters** Vol.102-103; pp. 423-428.

Woolf A.D., Alpert H.R., Garg A., Lesko S. (2001) Adolescent occupational toxic exposures. **Archives of Pediatrics and Adolescent Medicine – A National Study** Vol. 155; pp. 704-710.

Woolf A.D. (2002) Health hazards for children at work **Clinical toxicology** Vol. 40 (4); pp. 477 – 482.

Xiao J.Q, Levin S.M. (2000) The diagnosis and management of solvent – related disorders. American Journal of Industrial Medicine Vol.37; pp. 44 – 61

Zhou W, Liang Y, Christiani D.C. (2002) Utility of the WHO Neurobehavioural Core Test Battery in Chinese Workers – A Meta-analysis. **Environmental Research** Vol. 88; 94-102

Zeitz P., Kakolewski K., Imtiaz R., Kaye W. (2002) Methods of Assessing Neurobehavioural Development in children exposed to methyl Parathion in Mississippi and Ohio **Environmental Health Perspectives** Vol. 110(S6); pp. 1079-1083.

Zierold K.M., Garman S., Anderson H. (2004) Summer work and injury among middle school students aged 10-14 years. **Occupational and Environmental Medicine** Vol 61; pp. 518-522.

Zupanic M., Demes P., Seeber A. (2002) Psychomotor performance and subjective symptoms at low level toluene exposure. **Occupational and Environmental Medicine** Vol. 59; pp. 263-268.

LIST OF PUBLICATIONS FROM THIS THESIS

Journal Articles

Saddik B., Williamson A., Nuwayhid I., Black D. (2005) The effects of solvent exposure on memory and motor dexterity in working children **Public Health Reports** Vol. 120(6); pp.657-663.

Saddik B., Nuwayhid I., Williamson A., Black D. (2003) Evidence of neurotoxicity in working children in Lebanon **Neurotoxicology** Vol. 24 (4/5); pp. 733-739.

Conference Presentations

Saddik B., Nuwayhid I., Williamson A., Black D. (2005) **The relationship between solvent exposure and neurobehavioral performance in working children in Lebanon** Paper presented at the 9th International Symposium on Neurobehavioural Methods in Occupational and Environmental Health – Gyeongju, Korea.

Saddik B, Nuwayhid I, Williamson A, Black D (2003) **The effects of solvent exposure on memory and motor dexterity in working children – Further analysis** – Paper presented at the 9th Meeting of the International Neurotoxicology Association – Dresden, Germany.

Saddik B, Nuwayhid I, Williamson A, Black D (2002) **Assessing neurotoxicity of working children in Lebanon – A preliminary analysis** – Paper presented at the 8th International Symposium on Neurobehavioural Methods in Occupational and Environmental Health – Brescia, Italy

APPENDIX A – STUDY'S INFORMATION SHEET

The University of New South Wales/ American University of Beirut

Assessing Neurotoxicity of Working Children in Lebanon

Subject Information Statement and Consent Form

Subject Selection

You are invited to permit your child to participate in the study, Assessing Neurotoxicity of Working Children in Lebanon. Your child has been selected amongst other working children in your area. This study will help identify the chemical exposures working children are exposed to, and the consequences these exposures have on their neurological and neuropsychological development.

Description of study

If you decide to permit your child to participate in the study, an interview will be conducted to obtain general demographic data about you and your child. Following this interview, neuropsychological tests will be administered to your child. These tests are simple, non-invasive tests, which involve no risk to the child. Their purpose is to detect subtle neurobehavioural effects (such as memory, cognitive, attention and motor) which may be impaired with continued exposure to solvents and other chemicals. Other testing will include air sampling, where a small badge will be clipped on to your child's collar, to assess the amount of solvent exposure they are being exposed to during their work.
Testing will be carried out in a place that is convenient to you and your child.

Your child will be recompensed for time taken out of work and will be paid the equivalent hourly rate that s/he receive from their work.

Confidentiality

Any information that is obtained in connection with this study and that can be identified will remain confidential and will be disclosed only with your permission. If you give us permission by signing this document, we plan to discuss and publish the results as part of a Ph.D. thesis at the University of NSW, and in professional journals and professional conferences. In any publication, information will be provided in such a way that you cannot be identified.

Consent

Your participation is voluntary and your decision whether or not to participate will not prejudice your relationship with the University of NSW or the American University of Beirut in any way. If you decide to participate, you are free to withdraw your consent and to discontinue participation at any time without prejudice.

If you have any questions, please feel free to ask us. If you have any additional questions later, Ms Basema Saddik (ph 02 9385 2905) will be happy to answer them.
If you wish to make a complaint about the conduct of the project, you can contact the Ethics Secretariat, University of New South Wales on (61 2 9385 4234).

APPENDIX B – STUDY'S CONSENT FORM

The University of New South Wales/American University of Beirut

Assessing Neurotoxicity of Working Children in Lebanon

Subject Information Statement and Consent Form

You are making a decision whether or not to permit your child to participate. Your signature indicates that, having read the information provided above, you have decided to permit your child to participate.

Signature of parent/guardian

____

Please PRINT name

____

Date ______________________________

Signature of Investigator ______________________________

Please print name

Signature of Witness ______________________________

Please PRINT name ______________________________

Nature of Witness ______________________________

Revocation of Consent by Parent /Guardian or Child
I hereby wish to withdraw my consent for my child/ward to participate in the research proposal described above and understand that such withdrawal will not jeopardise any treatment or my, or my child/ward's relationship, with the University of New South Wales or American University of Beirut.

Signature ______________________________

Please PRINT name ______________________________

Date ______________________________

This section of revocation of consent should be forwarded to Dr Deborah Black, School of Community Medicine, University of NSW, Sydney NSW 2052. Phone 02 9385 2595, fax 02 9385 1513, email: deb.black@unsw.edu.au

APPENDIX C

Solvent Exposure Questionnaire

Demographic Data

Name of child: ______________________________

Date of Birth (mm/yy): ______________ Age: ______________

Sex: ____________

Address: ______________________________

Phone Number: ____________

Child's position in family- (biological rank and actual rank at present): ____________

Number of other children: Males/females ______________________

Father's occupation (detailed): ______________________

____

Father's educational level: ______________________________

Mother's occupation (detailed): ______________________

Mother's educational level: ______________________________

Level of education of siblings (or highest 2 if more than 2): ______________

____

Educational History of child: ______________________________

Educational level: ______________________________

Year left school: ______________________________

What school/s did you attend? ______________________________

Was it a public or private school? ______________________________

How many schools did you attend? ______________________________

Why did you leave school? ______________________________

Did you repeat any classes? If so what classes? ______________________

Are you attending any special schools (i.e., vocational, night schools)? Yes ☐ No ☐

If yes, specify: ____________________

Occupational history

Where do you work now? ____________________

Name of employer: ____________________

Address: ____________________

What do you do? (In detail) ____________________

____

____

How long have you been there? ____________________

Why are you working there? ____________________

____

What time do you usually start/finish work? ____________________

Do you have a break? (When and how many?) ____________________

____

What sort of tasks do you carry out? ____________________

____

Do you wear any protective equipment? ____________________

Overalls Yes ☐ No ☐

Gloves Yes ☐ No ☐

Dust masks Yes ☐ No ☐

Respirators Yes ☐ No ☐

Eye Protection Yes ☐ No ☐

Other Yes ☐ No ☐ If yes, Specify ____________________

Have you worked at other places? Yes ☐ No ☐

If so where have you worked? ____________________

What sort of work did you do? ____________________

____

____

Did you wear protective equipment where you worked last? ____________________

Overalls	Yes ☐ No ☐
Gloves	Yes ☐ No ☐
Dust masks	Yes ☐ No ☐
Respirators	Yes ☐ No ☐
Other	Yes ☐ No ☐ If yes, specify ____________________________

Do you do the same work everyday? (Describe your normal workday) ______________

____

____

____

____

____

____

____

____

Health related questions

Weight (kg) ______________________ Height (cm)____________________

Have you ever suffered from head injury with LOC (Loss of Consciousness)? Yes ☐ No ☐

If so, how long were you unconscious for? ________________________________

When was the last time you were unconscious? ________________________________

Have you suffered other injuries (i.e./ limb injury, eye injury, muscle injury)? Yes ☐ No ☐

(If yes, what type of injuries)? ____

____

Are you currently on medication? Yes ☐ No ☐

If yes, what is the name of medication and what is it for?___________________________

____

Do you smoke? Yes ☐ No ☐ (If yes how many cigarettes per day?) _________

Do you drink alcohol? Yes ☐ No ☐ (If yes how many bottles / glasses per day?) ______

Do you drink coffee? Yes ☐ No ☐ (If yes how many cups per day?) _________

Have you ever sniffed a substance? Yes ☐ No ☐
(If yes what kind and how many times?) ______________________________________

____

Do you suffer from epilepsy? Yes ☐ No ☐

Do you suffer from any psychiatric illness? Yes ☐ No ☐ (If yes what kind/s?) __________

____

Do you suffer from diabetes mellitus? Yes ☐ No ☐

Do you suffer from any peripheral (encephalopathy, carpal tunnel syndrome, chronic limb pain, other) or CNS (Central Nervous System) disorders? Yes ☐ No ☐ (If yes what kind)

____

Do you wear prescription glasses? Yes ☐ No ☐

Do you suffer from other visual problems? Yes ☐ No ☐ If yes, specify ________________

____

Neurotoxic symptoms

Do you feel light-headed or dizzy at work? Yes ☐ No ☐

Do you feel tired more easily than expected for the amount of work you do? Yes ☐ No ☐

Do you find it difficult to concentrate? Yes ☐ No ☐

Do you feel confused or disoriented? Yes ☐ No ☐

Do you have trouble remembering things? Yes ☐ No ☐

Have your relatives noted that you have trouble remembering things? Yes ☐ No ☐

Do you have to make notes to remember things? Yes ☐ No ☐

Do you find it hard to understand the meanings of things you read (books, magazines, newspapers)? Yes ☐ No ☐

Do you find it difficult to understand the meanings of things you watch on TV? (*focus on illiterate children*) Yes ☐ No ☐

Do you ever feel irritated? Yes ☐ No ☐

Have you had a seizure? Yes ☐ No ☐

Since you started work:

Have you been sleeping more often than is usual for you? Yes ☐ No ☐

Have you had difficulty falling asleep? Yes ☐ No ☐

Have you been bothered by inco-ordination or loss of balance? Yes ☐ No ☐

Have you had any loss of muscle strength in your arms or hands? Yes ☐ No ☐

Have you had difficulty moving your fingers or grasping things? Yes ☐ No ☐

Have you had any numbness or tingling in your toes for more than one day? Yes ☐ No ☐

Have you had headaches? Yes ☐ No ☐ If yes, how often and when do you usually have them?

____

Have you felt "high" from chemicals used at work? (*Define and explain high*) Yes ☐ No☐

Do your hands tremble? Yes ☐ No ☐

Do you often feel depressed for no particular reason? Yes ☐ No ☐

Other comments/related symptoms: ____

____

____

____

This is an interviewer-administered questionnaire, and will be administered to determine the child's exposure history and associated demographic and occupational history. The child will be especially prompted for type of work practices done and other information which will help determine the exposure levels.

CORRECTED LIB