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PROJECT TITLE: Defining Neurodevelopmental Domains in Children with Prenatal Solvent Exposure

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SUMMARY:
Organic solvents are inexpensive and commonly available substances of abuse that are found in accessible items such as spray paint, lacquer and glues, and which are often abused by young people in poverty. Solvents are highly lipophilic and can cross the plancenta resulting in fetal exposure. Case reports have suggested that children exposed in utero to solvents have developmental and/or physical features similar to those seen in children with a diagnosis of Fetal Alcohol Spectrum Disorder. This study will describe in detail the developmental and behavioral profile of children with prenatal solvent exposure. The student will use the database at the Manitoba FASD Centre and conduct a retrospective quantitative and qualitative chart review. The objective was to complete a chart review on a large clinical cohort of solvent exposed children with regards to dysmorphology, medical comorbidity and neurodevelopmental characteristics.

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BACKGROUND

Introduction

Organic solvents are inexpensive and commonly available substances of abuse that are found in accessible items such as spray paint, lacquer and glue, and which are often abused by young people in poverty[1]. Although it has been found that the abuse of solvents is common in some communities, it remains one of the least studied or discussed groups of abused substances[1]. Toluene is one of the most common constituents of abused solvents, and case records have revealed that in comparison with a control group of infants the toluene exposed children were more likely to be premature, of lighter birth weight, smaller birth length and had a smaller head circumference[2]. Published case reports of clinical assessment on these children has described delays in cognitive, speech and motor skills but further delineation of their neurodevelopmental profile is needed to facilitate early recognition of neurodevelopmental delays, referral to early intervention, and to identify areas for further research[1,2].

Epidemiology

The first indication of solvent abuse reported in Winnipeg was in 1964 when teenagers were found to be purchasing large quantities of nail polish remover[3]. The *Manitoba Pharmaceutical Association Review* and the *Manitoba Medical Review* alerted pharmacists and physicians of the problem and advised pharmacists not to display nail polish remover on open shelves and to restrict its sale in large quantities[3]. The *Poison Control Centre* of Winnipeg became involved two years later when appeals for factual information about 'glue-sniffing' were channeled to the centre from school nurses, principals, parents, social workers and teachers. Since that time there has been a consistent pattern of inhalant use reported in Canada, as described in the Canadian Addiction Survey, which has noted a rise of 0.5% in inhalant use in Canadians aged 15 years of age and older from 1994 to 2004[4]. In the United States, the American Drug and Alcohol Survey and the Monitoring the Future Study showed that inhalants were the second most common illicit drug among youth aged 12 to 17 in the 1990s, and that the rate of abuse has been increasing between 2002 and 2006[5, 6].

Solvent abuse is closely linked to social determinants of health, community and cultural factors. It is more prevalent in rural and isolated communities, in children that have dropped out of school, and those that have been abused physically or sexually[7, 8]. In Manitoba, a 2003 report from Paungassi First Nation notes that half of the children on reserve (less than 18 years of age) have used solvents[8]. Studies also suggest that inhalant abuse is increasing among females in the developing and developed world[4, 9]. More than 50% of solvent abusers are women in their childbearing years and up to 12, 000 pregnant women each year are abusing inhalants[9, 10].

Solvent Embryopathy

Solvents are highly lipophilic, and can cross the placenta resulting in fetal exposure at any time in the pregnancy[11]. With longer exposure, concentration and duration, the level of toluene

cumulatively increases in the fetal brain[11]. A number of cases of 'clinical toluene-abuse embryopathy' have been reported in offspring of toluene abusing women[2, 12, 13, 14, 15] . Given the persistent abuse of inhalants among young women of childbearing age, there is a justified concern about the long-term effects that the solvents are having on the developing fetus.

Occupational Exposure

Compared to voluntary direct inhalation, occupational exposure to solvents is typically controlled by workplace standards and presents a reduced (though not eliminated) risk of adverse fetal outcomes. Risk is dependent upon factors including the age of the woman exposed and the concentration of exposure[6]. Toluene abusers typically inhale 4000 to 12000 ppm in contrast to the workplace where exposure is usually limited to 500ppm[17]. Abuse of toluene is generally prolonged in comparison with the relatively limited duration of workplace exposure[16]. However despite these differences in exposure, various negative outcomes have been described with occupational exposure including urinary tract defects, gastrointestinal defects, and central nervous system defects[18].

Developmental Toxicity

Studies provide convincing evidence that gestational toluene exposure causes fetotoxicity. Toluene is known to cross the placenta and has been found in animal fetal-placental compartments up to 24 hours after the animals were first exposed[12]. Rat studies have found toluene exposed pups weigh significantly less than a control group, have deficits in behavioral endpoints such as the righting reflex and forelimb grip strength, and have smaller brains when exposed to high levels of toluene[6, 12,17,19]. Embryo lethality and dysmorphic features such as a cleft palate and missing digits have also been reported[10,18,19,20]. Soft tissues anomalies have been described including delayed cardiac development and cryptochidism[20].

A common mechanism of craniofacial teratogenesis for toluene and alcohol has been suggested based on analysis of patterns of malformations, most notably a 'deficiency of craniofacial neuroepithelium and mesodermal components due to increased embryonic cell death[10]. Reasons for similar malformations include a similar mechanism of teratogenesis, the same level of maternal toxicity, solvents potentiating the effects of alcohol or other drugs, or a common phenotypic endpoint[10].

Case studies describing developmental outcomes of toluene exposure associate this exposure with hyperactivity and attention deficits[6,16,18]. One animal study found a decrease in response rates, and therefore greater impulsivity, in the higher concentration toluene exposed rats[6]. This suggests a decreased level of motivation in the exposed rats, or an alteration in the perceived level of a reward, as a function of organic brain damage from toluene exposure[6]. Another animal study describes delayed central nervous system development as a result of the teratogenicity of solvents[10]. In a prospective study of 14 solvent exposed children 6 (42.8%) were delayed in cognitive or motor skills on formal developmental assessment[2]. Furthermore, 5(35.7%) of these children were observed to be delayed in speech[2].

Fetal Solvent Syndrome

Fetal Solvent Syndrome was first described by Toutant and Lippmann in 1979[15]. They described a fetus exposed to solvents as having a small head size, facial dysmorphology and low birth

weight[15,16]. Since that time, dysmorphic features including narrow bi frontal diameter, short palpebral fissures, deep-set eyes, small midface, flat nasal bridge, small nose and fingernails, and abnormal muscle tone have been reported[10]. Case reports have described developmental, behavioral and phenotypic features of solvent exposed children[2, 10]. Prematurity, low birth weight less than the 10th percentile, and neonatal complications such as polycythemia, renal tubular acidosis requiring bicarbonate, and other metabolic abnormalities such as hypocalcaemia have been recorded[2]. Case reports have documented delays in cognitive, motor, and speech skills[11]. Reported behavioral characteristics include hyperactivity, inattention, and aggressive or self-harming behaviour[6,17]. There has been no large case sample repository of solvent exposed children.

The goal of the present study was to develop a developmental and behavioral profile of solvent exposed children. The objective was to review a large clinical cohort of solvent exposed children with regards to dysmorphology, medical comorbidity and neurodevelopmental characteristics.

METHODS

This was a retrospective quantitative and qualitative chart review based on an 11-year clinical dataset kept between April 1999 and August 2010. This database was kept at the Manitoba Fetal Alcohol Spectrum Disorder (FASD) Centre in Winnipeg, MB. The Manitoba FASD Centre is affiliated with both Winnipeg Children's Hospital and the Rehabilitation Center for Children. It provides comprehensive multidisciplinary diagnostic assessments for alcohol and drug-exposed children with input from developmental pediatricians, clinical geneticists, occupational therapy, speech language pathology, and social work. Approval for the current study was obtained from the Health Research Ethics Board at the University of Manitoba.

Data Collection

The Centre's database includes information on exposure history, demographics, medical assessment and diagnosis. All charts noting any solvent exposure were queried and selected for review. In total 169 charts were reviewed. Each child was assigned a non-identifiable record number. Information retrieved from the charts included demographic data, type of exposure (solvent only or solvent and alcohol/other drug), associated diagnosis (Fetal Alcohol Syndrome (FAS), partial FAS (pFAS), Alcohol-Related Neurodevelopmental Disorder (ARND), normal, or 'other'), and complications including metabolic abnormalities (metabolic acidosis), withdrawal, solvent odor, and growth delay. Dysmorphic features were assessed by the geneticist and recorded using the 4-Digit Diagnostic Code[21]. The 4-Digit Diagnostic Code was developed in Seattle, Washington to describe the growth, facial dysmorphology, brain domain impairment, and prenatal exposure associated with alcohol abuse[21]. The 4-Digit Code is a Likert scale ranging from 1 to 4 where 1 represents no impairment, 2 represents a mild impairment, 3 represents a moderate impairment, and 4 represents a significant impairment, each specifically defined for the 4 areas described[21].

A developmental profile was qualitatively recorded under each of the 9 brain domains defined by the Canadian Guidelines for FASD Diagnosis and clinically used at the MB FASD Centre[22]. These domains included sensory processing, adaptive skills, fine motor and gross motor skills, language skills, behavioral assessments, academic achievement skills, cognitive skills and social

skills[22]. Cognitive and motor scores were recorded as a Developmental Quotient (DQ), which was calculated during clinical assessment by dividing a child's developmental age by their chronological age, or as the Intellectual Quotient (IQ) which was recorded in the chart when available.

Statistical Analysis
Data was analyzed for strength of association of solvent only exposed children in comparison to multiple substance exposed children using SPSS version 14 for Windows. Categorical variables were expressed as a percentage. Chi-squared tabulation was performed to test for differences between multiple substances exposed to those only exposed to solvents. Missing values were determined to be non-random and were excluded pairwise when appropriate. The level of significance was set at 0.05 for all statistical tests.

RESULTS

Demographics
Of the 169 charts reviewed, 25 (14.8%) were identified to have only solvent exposure (solvent only 'SO'), while 144 (85.2%) were exposed to solvents and alcohol +/- another drug (mixed solvent and other substance 'MS'). Subjects' demographic profiles (**Table 1)** revealed a group of individuals of varying ages and living situations.

Growth Parameters
There was no significant difference in length, weight or head circumference in the SO group vs the MS group. There was no difference between growth parameters of the solvent exposed group and the general population (**Table 2)**.

Dysmorphology and Congenital Anomalies
There were significantly more (P = 0.036) dysmorphic features recorded in the MS group than the SO group. Dysmorphic features were described by the 4-Digit Diagnostic Code and were considered positive when a child had short palpebral fissures, a flat philtrum, and a thin upper lip (**Table 3).** Other major congenital anomalies included 3 of the 169 (1.8%) solvent exposed children born with a cleft lip and palate, 1 (0.6%) born with an imperforate anus, and 15 (8.9%) born with congenital heart anomalies including Patent Ductus Arteriosus (5(3%)), Tetralogy of Fallot (3(1.8%)) and Ventricular Septal Defect (4(2.3%)). Minor congenital anomalies included the presence of café au lait spots (13 (7.7%)) and syndactyly (2(1.2%)) as well as sporadic reports of scaphocephaly, a dysmorphic auricle, microphthalmia and plagiocephaly.

Other Medical
Metabolic abnormalities at birth were recorded from the charts. 9(6.25%) of the MS exposed children were found to have metabolic abnormalities including hypoglycemia, hypocalcemia, hyperbilirubinemia, hypochloremia, or hyponatremia. There was no difference in the incidence of withdrawal or metabolic acidosis between the SO and MS exposed groups.

Neurodevelopmental Characteristics
22 (88%) of the SO group were described as having neurodevelopmental delay. Developmental quotients[a] were recorded for 140 of the 169 children, while an intellectual quotient was obtained in 29 children. Of the 29 children, 27 were MS exposed while the remainder had a SO exposure; there was no significant difference between the DQ's of the two groups **(Table 4)**. There was also no significant difference between the motor quotients of the two groups. There was a motor quotient recorded for 101 of the 169 children. The average motor quotient of the 101 children for which a motor quotient was identified was found to be 82 with a standard deviation of 14.5, with 15 (15 %) having a clinically significant delay, and 43 (42.6%) having a borderline delay.

Domains of Brain Function in Solvent Exposed Children (Table 5)
Summary characteristics of the 25 SO and 144 MS exposed children are described below according to the brain domains assessed including sensory processing characteristics, motor function, attention/hyperactivity, communication, cognitive function, academic achievement, memory, executive functioning, adaptive skills, and behavior/social skills. Characteristics were qualitatively recorded from multidisciplinary chart notes. Data for each domain was variably assessed for children in these groups and was recorded as available.

Sensory Processing
Information on sensory processing was recorded for 14 (56%) of the 25 SO exposed children and 98 (68%) of the 144 MS exposed children. Of the 14 SO exposed children for whom information was available 9 (64.3%) were described as having differences in auditory filtering verse 84 (85.7%) of the 98 MS exposed children. Other difficulties included differences in tactile sensitivity, sensation-seeking behaviors, being visually sensitive, seeking movement activities and having taste/smell sensitivity.

Attention/Hyperactivity
Information on attention/hyperactivity was recorded for 17 (68%) of the SO group, and 109 (75.7%) of the MS group. Of the 17 SO exposed children for whom information was available, 16 (94%) were described as having a short attention span and a high activity level and of the 109 MS exposed children 83 (76.1%) were found to display these behaviors. These individuals were also described as impulsive.

Language
Solvent exposed individuals were described as having a delay in receptive and expressive language. Information on language was recorded for 23 (92%) of the 25 SO exposed children and 134 (93%) of the 144 MS exposed children. Of the 23 children for whom information was available in the SO group,10 (43.4%) were found to have a receptive language delay and 18 (72%) were found to have an expressive language delay. Of the 134 children for whom information was available in the MS group 97 (72.3%) were found to have a receptive language delay and 99 (73.8%) in the MS group were found to have an expressive language delay.

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[a] A DQ of 100 signifies normal development, a score from 70-84 indicates borderline development, a score < 70 indicates a clinically significant delay.

Academic Achievement
In both groups children were described as having academic difficulties, having difficulty learning new concepts, being impulsive in class and wandering around the classroom.

Memory
Difficulties with memory functioning were described in all areas including short term, long term, sequential, auditory and visual memory.

Executive Functioning
Difficulties were described in all areas of executive functioning in both the solvent exposed groups. These deficits included difficulties with inhibiting inappropriate actions, initiating appropriate actions, shifting from one task to another, remembering a sequence of activities, and difficulties in planning and organizing.

Adaptive Skills
Information on adaptive functioning was recorded for 12 (48%) of the 25 SO exposed children and 75 (52%) of the 144 MS exposed children. Of the 12 SO exposed children for whom information was available, 10 (83%) were described as having difficulties with feeding and sleeping. 46 (61.3%) of the MS group had feeding difficulties with frequent gagging and choking and 36 (48%) had sleeping difficulties. Additional problems were noted in areas of social skills, self care, communication and self-direction.

Behavior/Social Skills
Information on behavior was recorded for 22 (88%) of the 25 SO exposed children and 121 (84%) of the 144 MS exposed children. In both groups, severe behavioral difficulties were described including aggression, anxiousness, impulsivity, self-harm, destructive behavior, and sexualized behavior. Self-harming behaviors included head banging and self-gagging.

There were 6 (4.2%) of the 144 MS exposed children and 1(4%) of the 25 SO exposed children who were described as demonstrating solvent seeking behavior (i.e. actively seeking out car fumes to inhale) in the absence of environmental exposure to solvent abuse.

DISCUSSION

This study documents the clinical profile of a large 11-year cohort of solvent exposed children and provides a description of the significant consequences of fetal exposure to solvent abuse. A developmental and behavioral profile of a subgroup of solvent only exposed children was further compared to the profile of mixed solvent and alcohol exposed children, specifically identifying delays in cognition, language, motor skills, adaptive skills and executive function with differences in attention and hyperactivity, sensory regulation and behavior. Understanding unique behavior of solvent exposed children, specifically solvent seeking behavior, will contribute to the understanding of the teratogenesis of this disorder as well as addiction itself.

Inhalant abuse is a pervasive but under-recognized problem of addiction found almost exclusively in adolescence[23]. It has been a popular drug of choice because of its accessibility, low cost and misperceived lack of addictive qualities[24]. In 2006 Manitoba introduced provisions to the Public Health Act which addressed the sale of intoxicating substances[25]. The Act made it illegal for retailers to knowingly sell products such as glue, gasoline and nail polish remover as intoxicants[25]. It made it mandatory to store these substances responsibly and control sales where appropriate in order to limit potential abuse of these solvents[25]. Stigma around inhalant abuse suggests that its use is underreported[16]. It is important that health care professionals take a comprehensive and sensitive history with women about their use of inhalants along with other substances of abuse including alcohol and drugs. Risk factors such as poverty that contribute to solvent abuse should be identified. This will help to identify those at risk and minimize the impact of solvent abuse in society.

This study describes the significant developmental deficits and potential long-term impact on cognitive and adaptive functioning resulting from prenatal solvent abuse. The solvent exposed groups demonstrated delays in cognitive and motor function as demonstrated by their DQ's (**Table 4)**. Data in this study shows that 24 (17.4%) of the solvent exposed children had a clinically significant cognitive delay (n=138), and 69 (50%) had a borderline cognitive delay (n=138). Expressive language delay was present in 117 (69.2%) of solvent exposed children (n=169) and a receptive language delay was present in 107 (63%). These findings are consistent with previously published case reviews and animal studies[2, 16, 17,18, 26]. Limited prospective studies with small reported numbers have also shown developmental delays including language and motor delays[2,10].

Both the SO and MS groups demonstrate significant behavioural comorbidity. Internalizing behaviours such as anxiousness and inattention, as well as externalizing behaviours such as aggression and impulsivity, are described in the solvent exposed children. Both groups had difficulties with attention, impulsivity and hyperactivity, with a clinical profile that was described as meeting the criteria for ADHD. Similar behavioral concerns described in the literature include hyperactivity, head banging, aggressiveness and attention deficits[16,18]. Animal studies describe impairments in behavioral maturity in rats exposed to solvents prenatally[17,25,27]. This suggests that abuse of solvents during pregnancy may produce long-lasting effects on behavioral development[27]. Socially inappropriate behaviors such as aggressiveness, hyperactivity, inattention and impulsivity negatively impact adaptive functioning including peer relationships, occupational success, and social stability. Children with solvent exposure have been shown to require adapted classrooms and in some cases stimulant therapy to improve attention[18]. Deficits in social skills lead to numerous secondary disabilities including depression, social isolation and failure in the workplace[28].

This study showed solvent exposed children scored poorly in areas of sensory-processing, adaptive skills and executive functioning. Sensory processing challenges can result in atypical behaviors and negatively influence social skills. This clinical profile describes difficulties with Activities of Daily Living compounded by issues with executive functioning making it challenging to plan, organize and sequence tasks. The need for specific therapy and daily supports to address these deficits is clearly indicated.

Solvent seeking behaviour is an atypical behaviour described in this study that may provide a window into the biology of addiction. While there are no reports of solvent or toluene seeking behaviour in the literature, alcohol seeking behavior has been described in rat studies, potentially associated with alterations in opiod or various neurochemical and neurocircuitry changes[29,30] . We speculate that prenatal solvent exposure may also result in disruptive effects on the neurocircuitry or anatomy of the developing fetus resulting in this behaviour. Solvent seeking behavior should be further researched to better understand its pathophysiologic mechanism and to potentially provide a theraputic route for mediating future addictive behavior and comorbidity.

Dysmorphology is also associated with prenatal solvent exposure suggesting an embryopathy dependent on timing and dose of exposure. In this study 73 (43.2%) solvent exposed children (n=169) demonstrated dysmorphic features. Dysmorphology associated with solvent exposure has been described in the literature. A single case report describing a neonate born to a mother known to be abusing solvents notes resultant microcephaly and a left sided cleft palate[15]. In another case series five pregnant women were admitted to hospital with renal tubular acidosis secondary to solvent abuse[16]. Of their five infants, two demonstrated craniofacial abnormalities[16]. In another study 7 (12.5%) of infants were described as having FAS-like facial features (thin upper lip, narrow palpebral fissures, smooth philtrum and a flat midface) [31]. There is a statistically significant dose response relationship described with maternal solvent exposure between fetal malformation and facial dysmorphologies[10,18, 24,32,33] . We suggest that solvent exposure may be playing an independent role in craniofacial teratogenesis.

The neurodevelopmental outcome of solvent exposed children appears to parallel that of prenatal alcohol exposure and underscores the need to comprehensively understand the outcomes of prenatal substance abuse. For example, the mechanism of craniofacial teratogenesis that results in facial abnormalities of solvent exposed children may be similar to that of alcohol[10]. In one study, 83% of toluene exposed infants were found to have features similar to FAS[16]. It is also possible that toluene may potentiate the adverse effect of alcohol when both are used in pregnancy[16]. A similar neurodevelopmental profile can be seen with language, attention, sensory, cognition, executive functioning, memory, and adaptive functioning domains[13,14,28,34,35,36,37]. The similarities of the findings between toluene exposed children and alcohol exposed children may have important implications concerning the pathophysiology of the toxic effect[16]. Whether there is a similar mechanism at play, or solvents potentiates the effects of other substances still has to be delineated.

This paper is limited by its retrospective database. Key compounding effects such as poor nutrition, other drug use, poverty, and family histories of learning disabilities or delays that would also impact a child's health or developmental status were not able to be collected. Past drug history is often self-reported or obtained from professional members of the community, and its accuracy is often variable. It has been suggested that there is additional stigma attached to the used of solvents, which may further limit its results[26]. Another limitation is the relatively limited scope of early database information. This study represents the largest dataset of solvent exposed children reported to date, however it remains relatively small sample.

This study has outlined the neurobehavioural profile of a large cohort of solvent exposed children. By defining a neurobehavioral profile early intervention programs can be tailored to the needs of this population with the goal of improving outcomes for solvent exposed children. Further studies should continue to expand on this Fetal Solvent Syndrome profile and compare solvent exposure to multiple substance use exposure. Characteristic behaviors and developmental delays should be clarified in the solvent exposed group such as solvent seeking behaviors in order to better understand the teratogenicity of this substance of abuse.

Children with FSS require comprehensive multidisciplinary community based and educational supports. Children with prenatal solvent exposure need to be identified and referred to multidisciplinary diagnostic centers where an appropriate diagnosis can be made. The community and educators need to recognize FSS and allocate resources to this under identified population. Appropriate supports optimize opportunities for children with FSS and empower caregivers to advocate on the child's behalf.

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TABLES

TABLE 1
Demographic profile of solvent exposed children (n=169)

Demographic Profile	Solvent Only, n (%)	Mixed solvent, n (%)
Total	25 (14.8)	144 (85.2)
Sex		
Female	11 (44)	83 (57.6)
Male	14 (56)	61 (42.4)
Age in months		
0-35	7(28)	61 (42.4)
36-59	7 (28)	25 (17.3)
>60	11 (44)	58 (40.27)
Placement Type		
Foster Care	20 (80)	115 (80)
Birth Family	3 (12)	16 (11)
Adopted	2 (8)	13 (9)
Number of Placements		
0-1	10 (40)	73 (50.7)
2-4	11 (44)	52 (36.1)
>4	4 (16)	18 (12.5)
Unknown	0	1 (0.7)

TABLE 2
Growth parameters of solvent exposed children (n=169)

Growth Parameter	Solvent only (n=25), n (%)	Mixed solvent (n=144) n (%)
Length		
< 3rd percentile	0 (0)	2 (1.4)
3rd-10th percentile	3 (12)	21 (14.7)
>10th percentile	22 (88)	120 (83.9)
Weight		
< 3rd percentile	0 (0)	3 (2.1)
3rd-10th percentile	7 (28)	25 (17.4)
>10th percentile	18 (72)	116 (80.6)
Head Circumference		
< 3rd percentile	1 (4)	9 (6.3)
3rd-10th percentile	10 (40)	44 (30.8)
>10th percentile	14 (56)	90 (62.9)

Subjects with missing values were excluded.

TABLE 3
Dysmorphic features of solvent exposed children (n=169)

Dysmorphic features present:	Solvent only (n=25), n (%)	Mixed solvent (n=144) n (%)
Yes	6 (24)	67 (46.5)
No	19 (76)	77 (53.5)

TABLE 4
DQ's of solvent exposed children (n=140)

DQ	Solvent only (n=21), n (%)	Mixed solvent (n=117) n (%)
Normal development (85-100)	11 (52.3)	34(29)
1 SD (70-84)	8 (38.2)	61 (52.1)
2 SDs (<70)	2 (9.5)	22(18.9)

TABLE 5
Summary of neurodevelopmental findings reported in solvent exposed individuals (n=169)

Brain Domain[22]	Clinical Observations of Solvent Exposed Children (n=169)
Sensory processing	Differences in auditory filtering, visual sensitivity, tactile sensitivity, taste/smell sensitivity, underresponsiveness/seeks sensation, and vestibular sensitivity.
Motor	Fine motor difficulties described more frequently than gross motor difficulties. Some abnormal tone described. Delays in visual-perception skills. Difficulty with sequencing tasks
Attention	Overactivity, impulsivity and short attention span
Language	Difficulties described in receptive and expressive language with more difficulties in expressive in the SO group.
Cognitive	Average DQ of 86 +/- 10 in the SO group and an average DQ of 79.6 +/- 13 in the MS group
Academic Achievement	Below grade level Disorganized and restless Difficulty learning and transferring new concepts
Memory	Difficulty in all areas of memory
Executive Functioning	Limited in spontaneous organization Trouble with sequencing, shifting and initiating tasks. Described as delayed in working memory and cognitive flexibility
Adaptive Skills	Feeding difficulties with frequent gagging and choking. Sleep difficulties Delays in toilet training. Problems with social skills, self care, communication and self direction
Behavior/Social Skills	Described as aggressive, impulsive, anxious, showing self harming behaviors including head banging, showing destructive behaviors and sexualized behaviors, being disorganized, having attachment issues, and stubborn. Deliberately seeks out the smell of exhaust fumes.

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