Obstetric complications in children with Attention Deficit/Hyperactivity Disorder and Learning Disability

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ABSTRACT: This study aims to determine whether children with ADHD and learning disabilities (LD) have a significant history of obstetrical complications when compared to children with ADHD but without LD. Methods: Sixty-four children aged 6 to 12 years diagnosed with ADHD were assessed for a history of obstetrical complications using the Kinney medical and gynecological questionnaire. Learning ability was appraised using the Wide-Range Achievement Test (WRAT-R) for anglophone students and the "Test de Rendement Français" for francophone students. Results: Children with ADHD and a learning disability in mathematics had a higher rate of neonatal complications of great severity (p = 0.01) than children with ADHD and no disability in mathematics. Children with ADHD and a learning disability in reading also had a preponderance of neonatal complications of high severity (p = 0.02) compared to their peers with ADHD and no learning disability in reading. Children with ADHD and learning disability tend to have a significant history of neonatal complications, which validates the theory that complications in early life could adversely affect a child's academic ability later in life. This further confirms the importance of the perinatal and postnatal periods in CNS development of brain regions essential for mathematics and reading ability.

KEY WORDS: ADHD, learning disabilities, obstetric complications

INTRODUCTION

Attention-deficit hyperactivity disorder (ADHD) is a widespread psychiatric disorder in the pediatric population, affecting 6% to 9% of elementary school students (1). The cardinal features of ADHD are hyperactivity, impulsivity and inattention. Hyperactivity manifests as "a child who cannot sit still, climbs around when others are seated, and talks when others are talking" (1).

The etiology of ADHD is unclear at the present; however, it is known that ADHD has strong genetic determinants as indicated by family (2) and adoption (3) studies. Of special importance are twin studies (4) showing that ADHD heritability is high, ranging from 75 to 90%. The above studies state that non-shared environmental factors i.e., factors/events that are unique to one member of the family, account for the rest of the variance in ADHD phenotype (10-25%). In many cases, non-shared environmental effects have been found to out-weigh shared environmental effects. Thus, shared environmental effects that are typically thought to be life-shaping (such as family life) have less of an impact than non-shared effects on ADHD phenotype (5). Non-shared effects include events in pre-natal development and random variations in the genetic program of a child.

Case-control studies have shown that there is an increased risk of ADHD in children who have suffered pregnancy, labour/delivery and neonatal complications (6), a finding further supported by Ben-Amor et al (7).

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Learning disability (LD) encompasses problems with reading, spelling, vocabulary and arithmetic. Mathematics is mainly represented in regions of the parietal and frontal lobes. Disruption of neural circuits in these areas result in difficulties with number concepts, counting skills, arithmetic skills, procedural calculations, memory and visual-spatial skills (8). Broca's area, Wernicke's area, visual cortex and angular gyrus are parts of the brain involved in reading. Lesions in these areas can lead to deficiencies in vocabulary storage, reasoning, concept formation, and interpretation (9).

LD, as does ADHD, affects 6 to 9% of the pediatric population (10). Although the degree to which these two populations overlap could be as high as 45% (11), genetic epidemiological studies suggest that these two disorders are independently transmitted in families (12).

Although the neurocognitive mechanisms underlying these two disorders may be different (13), it has been suggested that children with ADHD and LD may have common frontal lobe dysfunction (14). Such disruption in areas involved in learning ability and sustaining attention is likely due to a combination of factors, including genetic and non-shared factors. Obstetric complications falling under the category of non-shared environmental factors have been found to be significantly greater among children with ADHD when compared to their siblings with no ADHD (7).

The goal of our study is to determine whether children with ADHD and comorbid learning disability tend to have had a greater history of obstetric complications when compared to children with ADHD only. Thus, it aims to look at whether obstetric complications are a factor in the etiology of ADHD and learning disability as an entity.

METHODS
Setting
All children participating in this study were recruited from the Disruptive Behavior Disorders Program (DBDP) and from the outpatient clinics at the Douglas Hospital, a psychiatric teaching hospital of McGill University in Montreal, Canada.

Subjects
Inclusion criteria:
Sixty-four children aged between 6 and 12 years diagnosed with ADHD were included in the study. The children and their parents were given a detailed explanation of the research protocol. Parents signed informed consent and children also gave consent for participation.

The children in the study met DSM-IV diagnosis of ADHD based on detailed clinical assessment, school reports, and reports from referring agencies, parents and pediatricians. A panel of two experienced child psychiatrists substantiated the DSM-IV diagnosis of ADHD based on a clinical interview with the child and parents, information collected from the different sources, and a structured interview using the Diagnostic Interview Schedule for Children DISC-IV (15).

Exclusion criteria:
Children with an IQ less than 70 on the Wechsler Intelligence scale for Children-III (16), history of Tourette syndrome, Pervasive Developmental Disorder or psychosis were excluded from the study. 53% of the subjects were anglophone and the rest were francophone. With respect to race, 8.4% of the subjects were black, 1.1% were aboriginal, 1% were half-Asian, 3.2% were half-black and half-Caucasian, 1% were half-Hispanic and half-Caucasian, and 85.3% were Caucasian.

Evaluation of learning disabilities
To evaluate learning disability, subjects wrote the Wide-Range Achievement Test-Revised (17) or Test de Rendement pour Francophones (18) according to their mother tongue.

The WRAT assessed academic performance, and consisted of reading, spelling and arithmetic subtests. The standard scores obtained in these subtests were ascribed a grade level. The WRAT was designed such that comprehension is not a factor in achieved test scores, and is widely used to assess a child's scholastic ability (17).

The TRF measures the scholastic abilities of subjects whose primary language is French. There are different tests with level of difficulty corresponding to the three stages of schooling from grades 1 to 12. The student is given the test appropriate to his/her grade level. The student's scores in the vocabulary, written comprehension and arithmetic subsections are also translated into grade equivalents.

Table 1. Neonatal complications of severity 6 in ADHD children with MD compared to ADHD children without MD

| Number of Neonatal complications of severity 6+ | 0 | 1 | Total |
|-----------------------------------------------|---|---|------|
| Mathematics Disabled*                         | 15| 3 | 18   |
| Not disabled*                                 | 46| 0 | 46   |
| Total                                         | 61| 3 | 64   |

MD = Disability in mathematics
*Including children with and without reading disabilities
If there was a difference in reading or mathematics grade levels greater than or equal to two years with respect to expected grade level given the age of the child, the child was deemed to have a learning disability in the subject.

Assessment of obstetric complications

The Kinney medical and gynecological questionnaire (19) was used to interview mothers with respect to pre-, peri- or post-natal complications that may have occurred during their pregnancy as well as during labour and delivery. This questionnaire was also used to collect information on neonatal conditions. This questionnaire was complemented with medical files when available (60% of cases).

The McNeil-Sjostrom scale for obstetric complications (20) was used to score this questionnaire. These complications were classified into the following categories: prenatal (1st, 2nd and 3rd trimesters), labour/delivery, and neonatal (within the first 8 weeks of birth) complications, and total obstetrical risk.

Prenatal complications included vaginal spotting, absence of fetal movements. Labour and delivery complications included placental abnormalities, antepartum hemorrhages, drug toxic side effects (because of alcohol, tobacco and illicit substances), and fetal distress (assessed by abnormalities of fetal heart rate or meconium staining). Neonatal complications comprised suboptimal 5-minute Apgar scores, low birth weight, small head circumference (below 10th percentile), congenital defects such as patent ductus arteriosus, and medical complications such as pneumonia in the first 8 weeks of life.

The McNeil-Sjostrom scale allows for weighting of several hundred specific complications of pregnancy, labor and delivery and the neonatal period. These complications were assigned one of six severity levels corresponding to the ordinal degree of potential harm to the baby’s central nervous system:

- Level 1 - Not harmful or relevant;
- Level 2 - Not likely harmful/relevant;
- Level 3 - Possibly but not clearly harmful or relevant;
- Level 4 - Clearly potentially harmful or relevant;
- Level 5 - Clearly potentially greatly harmful/relevant;
- Level 6 - Great harm to the offspring

Statistical Analysis

Clinical and demographic characteristics of children with ADHD and learning disability in reading or mathematics were compared to those of children with ADHD only using repeated measure ANOVA. Using the two-tailed paired t-test, we checked for correlations between reading disability and each of the obstetric complication subcategories. The same analysis was done with respect to disability in mathematics.

RESULTS

Children with ADHD and a disability in mathematics (MD) were found to have a higher rate of neonatal complications of severity 6+ (p = 0.004) than those without a disability in mathematics.

We noted that ADHD children with a reading disability (RD) had a greater preponderance of labour and delivery complications of severity 6+ (p = 0.065), neonatal complications of severity 6+ (p=0.02) than those with no reading disability.

All variables were similar across the different study groups, except for IQ and age. The children with ADHD and MD tended to be significantly older than those without MD (p=0.001) although this was not the case for children with ADHD and RD compared with those without RD (p = 0.39). The children with ADHD and MD had a significantly lower IQ than those with no MD (p=0.016) and those with RD had a significantly lower IQ than those with no RD (p=0.002).

DISCUSSION

A substantial proportion of children with ADHD have comorbid LD. Both disorders have causal
The results of the study have shown that a history of neonatal complications tends to be significantly more prevalent among ADHD children with a learning disability. Low birth weight (LBW), considered a neonatal complication and defined as a birth weight less than 2.5 kg, has been identified in past research studies as a risk factor in ADHD (21). Stress during or following pregnancy is also a possible causal factor in learning disabilities (22). LBW children have been found to have delayed cognitive development (23) and subsequent RD and MD (24).

The main neonatal complications found to be prevalent among the children in our study were neonatal hospitalization, being in an incubator, requiring oxygen therapy, general anesthesia or surgery. These findings support earlier findings pointing to a higher prevalence of early-life stressful events among ADHD children (6). Such neonatal events have been shown to potentiate heightened locomotor activity later in life in animal models (25). A retrospective analysis of children who had been referred for ADHD found that many of them as infants had received Cardif Bag Resuscitation and a 1-minute Apgar score below 7 or a 5-minute Apgar score below 9 (26). This further supports the relationship between neonatal complications and ADHD.

Environmental or psychosocial stress has been shown to impede neurogenesis, especially that of the hippocampus, the center of learning and memory (27). Some human studies have proposed that hypoxic/ischemic brain damage secondary to perinatal asphyxia can lead to neurologic and intellectual dysfunction (28). In our study, the presence of severe (6+) neonatal complications among ADHD children with comorbid learning disabilities suggests that the global impact of the neonatal complication (such as hypoxia affecting brain development as a whole) leads to development of learning disability. Thus, greater severity of early-life stressful events tends to induce learning disability and ADHD, two disorders that have already individually been associated with neonatal complications.

Limitations
This study compared children with ADHD and learning disability to children with ADHD only; since it compared children of different families, it could not account for shared environmental factors.

In some other studies (14), a national standardized test was used to determine learning ability. This option was not available to us, as Canada does not administer such nationwide testing. When assessing learning disability, it is sometimes difficult to tell whether a child under the age of 8 has a learning disability for certain. In these cases, we assessed learning status using teachers’ and psychiatric evaluations.

In addition, we did not address comorbidity of psychiatric disorders, although this may affect the degree of learning disability.

The major limitation is the low number of cases having neonatal complications of extreme severity (three cases in MD and two cases in RD).

Clinical Implications
Early insult on the fetal brain during crucial periods of development may have long-lasting effects on cognition and behaviour. The etiology of ADHD and learning disability is thought to be a combination of genetics and environmental stressors. This study indicates that a condition that affects half of the pediatric ADHD population may be linked to early-life stressful events when they are particularly severe. These results further support that which has already been shown for ADHD and learning disability individually; that the happenings in the early life of a child are crucial to brain development and have implications for a child’s academic performance and functioning far into the future.

REFERENCES
1. Anderson J, Williams S, McGee R, Silva PA. The prevalence of DSM-III disorders in a large sample of pre-adolescent children from the general population. Arch Gen Psychiatry 44:69-81; 1987
2. Faraone SV, Biederman J, Milberger S. An exploratory study of ADHD among second-degree relatives of ADHD children. Am J Psychiatry 35:398-402; 1994
3. Cadoret RJ, Stewart MA. An adoption study of attention deficit/hyperactivity/agression and their relationship to adult antisocial personality. Comprehensive Psychiatry 32:73-82; 1991
4. Eaves LJ, Silberg JL, Meyer JM et al. Genetics and developmental psychopathology: 2. The main effects of genes and environment on behavioural problems in the Virginia Twin Study of Adolescent Behavioral Development. J of Child Psychology & Psychiatry & Allied Disciplines 38:965-980; 1997
5. McGuinff P, Martin N. Science, medicine, and the future. Behaviour and genes. BMJ 319:37-40; 1999.
6. Milberger S, Biederman J, Faraone SV, Guite J, Tsuang MT. Pregnancy, delivery and infancy complications and attention deficit hyperactivity disorder: issues of gene-environment interaction. Biol Psychiatry 41:65-75; 1997
7. Ben-Amor L, Grizzenko N, Doan J et al. Perinatal complications in children with Attention-Deficit Hyperactivity Disorder and their non-affected siblings. J of Psychiatry and Neuroscience 30(2): 120-126; 2005
8. Geary DC. Mathematical disorders: An overview for educators. International Dyslexia Association: Perspectives. 26:6-9; 2000.

9. Sousa DA. How the special needs brain learns. Thousand Oaks, Ca: Corwin, 2001

10. Shaywitz SE, Shaywitz BA, Fletcher JM, Escobar MD. Prevalence of reading disability in boys and girls: results of the Connecticut longitudinal study. JAMA 264:998-1001; 1990.

11. Biederman J, Newcorn J, Sprich S. Comorbidity of attention deficit with conduct, depressive, anxiety and other disorders. Am J Psychiatry 148:564-577; 1991.

12. Faroone SV, Biederman J, Lehman BK et al. Evidence for the independent familial transmission of attention deficit hyperactivity disorder and learning disabilities: results from a family genetic study. Am J Psychiatry 150:891-895; 1993

13. Tirosh E, Berger J, Cohen-Ophir M, Davidovitch M, Cohen A. Learning disabilities with and without attention deficit hyperactivity disorder: parent's and teacher's perspective. J Child Neuro 13:261-270; 1998.

14. Lazar JW, Frank Y. Frontal systems dysfunction in children with attention-deficit hyperactivity disorder and learning disabilities. J Neuropsychiatry Clin Neurosci 10:160-167; 1998.

15. Barkley RA. Attention-deficit hyperactivity disorder: a handbook for diagnosis and treatment. New York: Guilford Press, 1990.

16. Wechsler D. Wechsler Intelligence Scale for Children, 3rd ed. San Antonio, TX: Psychological Corporation, 1991.

17. Jastak S, Wilkinson GS. The Wide Range Achievement Test, Revised. Wilmington, Del: Jastak Associates, 1985.

18. Sarrazin G. Test de Rendement pour Francophones. Toronto, ON: Harcourt & Brace, 1995.

19. McNeil TF, Cantor-Graae E, Sjostrom K. Obstetric complications as antecedents of schizophrenia: empirical effects of using different obstetric complication scales. J Psychiatr Res 28:519-530; 1994.

20. McNeil TF, Sjostrom K. McNeil-Sjostrom scale for obstetric complications. Department of psychiatry, Lund University, Malmo, Sweden. 1995

21. Breslau N, Brown GG, DelDotto JE et al. Psychiatric sequelae of low birth weight at 6 years of age. Journal of Abnormal Child Psychology 24:385-400; 1996.

22. McGrath MM, Sullivan MC, Lester BM, Oh W. Longitudinal neurologic follow-up in neonatal intensive care unit survivors with various neonatal morbidities. Pediatrics 106: 1397-1405; 2000.

23. Hartsough CS, Lambert NM. Medical factors in hyperactive and normal children: prenatal, developmental, and health history findings. American Journal of Orthopsychiatry 55:190-201; 1985.

24. Johnson, E. O., & Breslau, N. Increased risk of learning disabilities in low birthweight boys at age 11 years. Biological Psychiatry, 47: 490-500; 2000

25. Brake WG, Sullivan RM, Gratton A. Perinatal distress leads to lateralized medial prefrontal cortical dopamine hypofunction in adult rats. J Neurosci 20:5538-5543; 2000.

26. Chandola CA, Robling MR, Peters TJ, Melville-Thomas G, McGuffin P. Pre- and perinatal factors and the risk of subsequent referral for hyperactivity. Journal of Child Psychology & Psychiatry & Allied Disciplines 33:1077-1090; 1992.

27. Gould E, McEwen BS, Tanapat P, Galea LAM, Fuchs E. Neurogenesis in the dentate gyrus of the adult tree shrew is regulated by psychosocial stress and NMDA receptor activation. J Neurosci 17:2492-2498; 1997.

28. Lou HC. Perinatal hypoxic-ischemic brain damage and intraventricular hemorrhage. A pathogenetic model. Arch Neurol 37:585-587; 1980.

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