INHIBITION AS A MARKER FOR A FAMILIAL SUBGROUP OF ATTENTION DEFICIT HYPERACTIVITY DISORDER

by

Jennifer Crosbie

A thesis submitted in conformity with the requirements for the degree of Masters of Arts
Department of Human Development and Applied Psychology
Ontario Institute of Studies in Education of the University of Toronto

© Copyright Jennifer Crosbie 2000
The author has granted a non-exclusive licence allowing the National Library of Canada to reproduce, loan, distribute or sell copies of this thesis in microform, paper or electronic formats.

The author retains ownership of the copyright in this thesis. Neither the thesis nor substantial extracts from it may be printed or otherwise reproduced without the author's permission.

L’auteur a accordé une licence non exclusive permettant à la Bibliothèque nationale du Canada de reproduire, prêter, distribuer ou vendre des copies de cette thèse sous la forme de microfiche/film, de reproduction sur papier ou sur format électronique.

L’auteur conserve la propriété du droit d’auteur qui protège cette thèse. Ni la thèse ni des extraits substantiels de celle-ci ne doivent être imprimés ou autrement reproduits sans son autorisation.

0-612-49756-9
Abstract

Inhibition as a Marker for a Familial Subgroup of Attention Deficit Hyperactivity Disorder

Master of Arts 1999

Jennifer Crosbie

Department of Human Development and Applied Psychology

Ontario Institute of Studies in Education of the University of Toronto

Objective: to investigate whether deficient inhibitory control, as measured by the Stop-Signal Paradigm, delineates a more homogeneous subgroup of Attention Deficit Hyperactivity Disorder (ADHD). Method: Subjects were 54 ADHD children defined as having poor or good inhibition based on performance on the SSP. Poor and Good inhibition groups were compared on family history for ADHD, and measures of neurobiological and psychosocial risk. Results: a significantly higher rate of family history for ADHD was found in the Poor (48.1%) versus the Good (18.5%) inhibition group. No differences were found between the groups on index measures of neurobiological or psychosocial risk. Conclusions: findings provide preliminary evidence that classification using inhibition delineates a familial subtype of ADHD. No evidence was found that psychosocial or neurobiological factors accounted for the ADHD in the good inhibition group, or that environmental risks and inhibition act conjointly to increase the risk for ADHD in the Poor inhibition group.
Acknowledgments

I want to thank my thesis advisor, Dr. Russell Schachar, who assisted me in finding my way in the journey towards completion of this document. I would also like to thank Dr. Joseph Ducharme for acting as my committee member.

A special thanks my parents, whose unconditional support and encouragement made completion of this thesis possible.
# Table of Contents

Abstract .......................................................................................................................... ii

Acknowledgments ........................................................................................................ iii

Table of Contents .......................................................................................................... iv

List of Table and Figures .............................................................................................. v

Chapter I
   Introduction .................................................................................................................. 1

Chapter II
   Method ......................................................................................................................... 14
      Subjects .................................................................................................................. 14
      Groups .................................................................................................................... 14
      Measures ................................................................................................................ 15
      Procedure ............................................................................................................... 19

Chapter III
   Results ......................................................................................................................... 22

Chapter IV
   Discussion ................................................................................................................... 24
      References ............................................................................................................... 30

Tables ............................................................................................................................. 37

Figures ........................................................................................................................... 40

Appendix ......................................................................................................................... 44
List of Tables and Figures

Tables

<table>
<thead>
<tr>
<th>Table</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1a</td>
<td>Neurobiological Risk Index</td>
<td>37</td>
</tr>
<tr>
<td>Table 1b</td>
<td>Psychosocial Risk Index</td>
<td>37</td>
</tr>
<tr>
<td>Table 2</td>
<td>Summary of Subject Characteristics</td>
<td>38</td>
</tr>
<tr>
<td>Table 3</td>
<td>Prevalence of Family History of ADHD in Poor and Good Inhibition Groups</td>
<td>39</td>
</tr>
</tbody>
</table>

Figures

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 1</td>
<td>Distribution of stop signal reaction times (SSRT)</td>
<td>40</td>
</tr>
<tr>
<td>Figure 2</td>
<td>Prevalence of Family History for ADHD</td>
<td>41</td>
</tr>
<tr>
<td>Figure 3</td>
<td>Prevalence of Family History for ADHD, ADHD+CD and ADHD+RD Subjects</td>
<td>42</td>
</tr>
<tr>
<td>Figure 4</td>
<td>Mean number of neurobiological and psychosocial risk factors in Poor and Good inhibition groups</td>
<td>43</td>
</tr>
</tbody>
</table>
Chapter 1
INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is the most frequently diagnosed childhood psychiatric disorder. Prevalence rates in the general population are conservatively estimated to range from 3% -6% (Association, 1994; Bird et al., 1988; McGee, Feehan, Williams, Partridge, Silva and Kelly, 1990; Szatmari, Offord, and Boyle, 1989), and in clinically referred samples it is an estimated 50% (Offord et al, 1987; Offord, Boyle, Fleming, Blum, Grant, 1989). Developmentally inappropriate and impairing levels of inattentiveness, impulsiveness and hyperactivity are characteristic features of the disorder. Children with ADHD are at increased risk for the development of comorbid psychopathologies such as conduct disorder, anxiety, mood and learning disorders (Biederman et al., 1992). Follow-up studies have indicated that the disorder persists into adolescence and adulthood in approximately 30% of cases, with changes in the manifestation of the disorder occurring with age and gender (Mannuzza et al., 1991; Weiss, Hechtman, Milroy, Perlman, 1985).

Regardless of ADHD status in adulthood, individuals diagnosed with ADHD as children are at increased risk for the development of psychopathologies such as antisocial personality disorder and substance abuse, and are also at risk for educational and vocational disadvantages (Caspi, Moffitt, Newman, and Silva, 1996; Mannuzza, 1997; Mannuzza et al., 1998). These findings suggest that even when the appearance of the disorder has subsided, residual deficits may persist.

ADHD is a clinically and etiologically heterogeneous disorder. The following will review the studies involving genetics, neuroanatomy, neurobiological and psychosocial risk,
Inhibition as a Familial Marker for ADHD

and cognitive findings (specifically inhibition) within the ADHD population, highlighting the heterogeneity identified within the literature. This will be followed by a review of the difficulties with the present behavioural classification system and a discussion of the use of non-behavioural markers within the ADHD population to facilitate etiological research and understanding of the disorder. The present study proposes to investigate inhibition as a potential marker to delineate a more etiologically homogenous subgroup within the ADHD population.

Genetics

Research has indicated that genetic factors play a major role in the etiology of ADHD. Studies involving family, twin, and adoption have provided strong evidence for genetic involvement in the disorder (Faraone, Biederman, Keenan, & Tsuang, 1991; Faraone et al., 1995; Hudziak & Todd, 1993; Lombroso, Pauls & Leckman, 1994). Findings from family studies have consistently provided evidence of a higher incidence of ADHD among first and second degree relatives of ADHD individuals (Farone, et al., 1991; Farone et al., 1995; Hudziak & Todd, 1993; Lombroso et al., 1994). Siblings of children with ADHD have been found to have two to three times the risk of having ADHD (30%) when compared with siblings of normal controls (Biederman et al., 1992; Goodman & Stevenson 1989). Twin studies indicate that ADHD is a highly heritable condition with estimated contribution of additive genetic factors of approximately 60%, with the expected higher concordance for monozygotic then for dizygotic twins (Eaves et al., 1997; Edelbrock, Rende, Plomin & Thompson, 1995; Gilger, Pennington, & DeFries, 1992; Goodman & Stevenson, 1989). An
adoption study by Van den Oord et al (1994) studies indicate higher rates of ADHD or associated disorder among biological relatives of ADHD probands than adoptive parents, and estimated that genes account for 47% of the variance on measures of inattention on the Child Behavioural Checklist.

Molecular genetic evidence has indicated several possible roots for the genetic influence of the disorder. Various abnormalities, primarily affecting the dopamine system, have been identified for their possible role in the disorder. Genes within the dopamine system provide a clear choice as potentially involved in ADHD. The reduction of symptoms in ADHD brought about by pharmacological agents act primarily on the dopaminergic and noradrenergic systems, and the structures implicated by recent imaging studies - the fronto-striatal circuitry - are rich in dopamine innervation (Tannock, 1998). Comings et al (1991) identified A1 allele on the dopamine D2 Receptor gene. However, attempts to replicate this finding have not been reported. Several studies have found promising results for the implication of dopamine transporter (DAT) and D4 dopamine receptor gene (DRD4). An association between ADHD and the 480-bp allele of the dopamine transporter gene (DAT) was found by Cook et al (1995) using a family based association study. These results were replicated by Waldman et al (1996) in a population based study, and Gill Daly, Heron, Hawi & Fitzgerald, (1997) in a family based study. LaHosta et al (1996) found higher rates of 7-repeat allele of the DRD4 gene among ADHD children when compared to carefully matched control children. These results were maintained when the sample size used was increased by 50% (Sunohara et al, 1997). Similar results were found using a family-based association study of 52 families by Swanson et al (1998). The DRD4 family-based association was further
Inhibition as a Familial Marker for ADHD

reported by Bailey et al. (1997), Faraone et al. (1999) and Smalley et al. (1998). Although support for the DRD4 gene as the major gene in ADHD is encouraging, it is premature to make firm conclusions. The 7-repeat allele was not found by Castellanos et al. in their 1997 study. Furthermore, the allele is not found in all ADHD subjects, only 30 percent of the ADHD subjects in the LaHosta (1996) study had the 7-repeat allele. The three candidate genes that have been implicated as associated with ADHD are all within the dopamine system.

While the research to date has provided strong evidence for a genetic etiology, the specific mechanism by which these genes may influence development remains unclear. The fact that concordance for monozygotic twins is less than 100%, and that molecular evidence is variable, indicates that penetration of genetic influence is incomplete and that non-genetic factors play a role in the etiology of the disorder. It is possible that there is a group of ADHD individuals who have the disorder due to non-genetic factors, or a polygenetic predisposition that interacts with these non-genetic risk factors in a complex manner.

Neurobiological Abnormalities

Results of research involving neuroanatomical abnormalities have been strong, although as with the molecular research there is much variability within the findings. Research using neuro-imaging has identified a number of abnormalities in the brain structures of ADHD individuals implicating the fronto-striatal circuitry of the brain. Differences have been identified in the right prefrontal cortex (Castellanos et al., 1994; Filipek et al., 1997; Hynd et al., 1990), the basal ganglia, (Castellanos et al., 1994; Castellanos et al., 1996; Filipek et al., 1997), the corpus callosum, and the cerebellum (Baumgardner et al., 1996; Castellanos et al.,
Inhibition as a Familial Marker for ADHD

The efficacy of stimulant medications in ADHD (Jacobvitz, Sroufe, Stewart, Leffer, 1990; Schachar, Tannock, Cunningham 1996; Spencer, Biederman, Wilens, Harding, O'Dovvell, Griffins, 1996) further implicates these regions, as they are rich in dopaminergic and noradrenergic neurons. The research provides a body of evidence implicating fronto-striatal circuitry, however not all studies agree on the locus or lateralization of the observed impairments. Results to date are consistent in finding differences between ADHD subjects and normal controls but there are often differences in the precise nature of the abnormalities and formulation regarding their significance.

Neurobiological and Psychosocial Risk

Numerous neurobiological and psychosocial risk factors, especially those acting early in life during the period of rapid perinatal brain growth, have been identified as associated with ADHD (Lou, 1996). These factors include fetal exposure to alcohol and drugs (Aronson, Hagberg, & Gillberg, 1997; Schneider, Roughton, & Lubach, 1997), tobacco (Milberger, Biederman, Faraone, Guite, Tsuang, 1996), disrupted parent-child attachment (Jacobvitz & Sroufe 1987), low birth weight (Breslau et al., 1996), and perinatal obstetrical complications (Milberger, Biederman, Faraone, Guite, & Tsuang, 1997). ADHD or aspects of the syndrome such as cognitive deficits have also been found to arise from traumatic brain injury in children (Fletcher, 1997, Max, 1998). Barkley (1990) identified low maternal education, low social class and single parenthood as important factors in ADHD. Biederman et al 1995 found that exposure to parental psychopathology (particularly maternal), chronic conflict and decreased family cohesion were more common in ADHD families than in control
families. Specific pregnancy, delivery and infancy complications were investigated by Sprich-Buckminster et al (1993) and Milberger, et al (1997). They identified a number of factors associated with ADHD including maternal bleeding, smoking, family problems, illicit drug use during pregnancy and fetal distress. While the specific risk factors identified in the two studies varied slightly, both studies highlighted that the risks associated with ADHD tended to be those that reflect chronic exposure to risk (i.e. smoking, family problems) rather than acute risk exposure.

The association of these neurobiological and psychosocial risks and ADHD suggests that they may play a role in the etiology in some cases of the disorder. The presentation of ADHD, or its symptoms, may not result from any one particular risk factor, but rather from an interaction of any combination of these risks. This interaction makes it difficult to assess accurately the specific role of any single factor, and indicates the need to investigate an index of risk factors (Biederman et al, 1995), as well as the interaction of genetics and environmental influences.

**Genes and the Environment**

The separation of possible environmental (neurobiological and psychosocial) and genetic influences is important for etiological research. The association of these environmental risks and ADHD suggests that there may be an ‘acquired’ subtype of the disorder, or that genetic and environmental risks act conjointly to increase the risk for ADHD. A two-factor model proposes that genetic and environmental factors interact to increase the risk for ADHD, predicting that both genetic and environmental factors would be present in
ADHD individuals (Kinney, Levy, Yurgelun-Todd, Tramer & Holzman, 1998; Kinney, Yurgelun-Todd, Wateraux & Matthyse, 1991). A separate ADHD model predicts that either genetics or environmental risk is sufficient for ADHD to occur; there are separate etiological routes, resulting in genetic (familial / heritable) and environmental (acquired) subgroups of the disorder.

Limited research has been carried out directly investigating the interaction of environmental and genetic influences in ADHD. Milberger, Biederman, Faraone, Guite, Tsuang (1997) investigated the gene-environment interaction using family history as a proxy for the genetic form of the disorder. The study investigated pregnancy, delivery, and infancy complication (PDICs) in an ADHD population with and without familial form of the disorder. While the authors found an association between PDICs and ADHD in the entire sample (as discussed above), they found no interaction between PDICs and the familial form of the disorder in predicating ADHD status. The authors concluded from this finding that there was no interaction between genetic and environmental factors in occurrence of the disorder.

**Current Theories of ADHD - Inhibition**

Current formulations of ADHD focus on various aspects of executive function - the delaying, future oriented, and intentional control processes of the cognitive system which include preparing, maintaining, stopping, adjusting and switching responses (Denckla, 1996; Shue & Douglas, 1992; Sonuga-Barke & Taylor, 1992). One particular executive process, inhibition, has been implicated as the fundamental executive function deficit ADHD (Barkley, 1997; Quay, 1997, Pennington & Ozonoff, 1996, Schachar & Tannock, 1993). According to
Inhibition as a Familial Marker for ADHD

This theory deficient inhibitory control impairs the ability of ADHD children to engage in other executive control strategies to optimize their behaviour. The direct cascading effect of deficient inhibition affects behaviour, working memory, self regulation, internal speech, and reconstitution (the ability to restructure behaviour) (Barkley, 1997; Quay, 1997). In the presence of a deficit in inhibition, individuals with ADHD would act without thinking and therefore miss out on the benefits of these control strategies.

Inhibition and executive functions directly involve the neural systems that include the orbital pre-frontal cortex and the sub-cortical structures which the prefrontal cortex send prominent efferent projections (Cohen & Servan-Schrieber, 1992; Dehaene, Posner, Tucker, 1994; Mesulam, 1981; Posner & Driver, 1992). The involvement of these neural substrates in inhibition is confirmed by neuro-imaging, electro-physiological and neuro-pathological studies in humans (Corbetta, et al., 1993; McDowell, Whyte & D'Esposito, 1997; Pardo, 1990; Casey, et al. 1995; Casey et al, 1997), as well as lesion studies in primates (Goldman-Rakic, 1987). Recent investigation using ADHD subjects have provided further connection between inhibition and these areas. Casey et al (1997) used magnetic resonance imaging (MRI) to examine the relation between specific fronto-striatal structures and performance on three response inhibition tasks in ADHD and normal control children. They found that children with ADHD exhibited the expected deficits on the inhibition tasks and that task performance correlated only with those anatomical fronto-striatal measures observed to be abnormal in ADHD (prefrontal cortex, caudate, and globus pullidus, but not the putamen). A recent functional MRI (fMRI) study by Rubia et al (1999), using the stop task (see below) as a measure of inhibition, found ADHD individuals showed lower power of response in the right
inferior cortex and the left caudate during administration of the stop task. These areas are directly associated with the fronto-striatal areas implicated in ADHD, providing a viable neurobiological connection between inhibition and ADHD.

Although inhibition has been studied using a variety of measures, recent investigations of inhibition have been widely carried out using the Stop-Signal Paradigm (Stop Task) (Logan and Cowan, 1984). The Stop-Signal Paradigm is a laboratory measure requiring a rapid ongoing motor response and the sudden cessation of that response following a specified signal (tone). Using the Stop-Signal Paradigm, a deficit in inhibition among ADHD children has been demonstrated and extensively replicated with both community and clinical samples (Jennings, Van der Molen, Pelham, Debski & Hoza 1997; Osterlaan and Sergeant 1996; Pliska, Borcherding Spratley, Leon & Irick, 1997; Purvis & Tannock, 1997; Schachar & Logan, 1990; Schachar & Tannock, 1995). Schachar and his colleagues have demonstrated and twice replicated a deficit in inhibition in ADHD children (Schachar & Logan 1990; Schachar, Mota, Tannock & Logan, 1999 in press; Schachar & Tannock, 1995). Children with ADHD consistently demonstrate longer Stop-Signal Reaction Times (SSRT) than controls, even when differences in 'go' reaction time (general slowing) are taken into account. Findings have most recently been replicated using a shorter, tracking version of the stop signal paradigm, with subjects diagnosed according to DSM-IV (Schachar, et al, 1999 in press).

While findings of ADHD children with deficient inhibition have been robust, inconsistencies within the data confound interpretation and point to the heterogeneity within the findings. A key aspect of the Stop Task data is that not all ADHD children perform poorly on the task. There is great variability among ADHD individuals in their performance,
some ADHD children perform very poorly on the task indicating deficient inhibition, while others appear to have no difficulty at all. Stop task data involving comorbid subgroups is similarly variable; some data indicates that comorbid subgroups show an inhibition deficit comparable with ADHD children (Schachar & Tannock, 1995), and other data indicates that the comorbid ADHD subjects show no significant deficit (Schachar & Logan, 1990; Schachar, Mota, Logan and Tannock, 1999 in press).

**Problematic Behavioural Phenotype**

Research has provided ample evidence to cause doubt in the reliability and validity of the current methods of diagnosis. A necessary element of investigation of any disorder is a reliable and valid diagnosis. Reliance on the use of behavioural phenotypes as a means of diagnosis and subtyping within the ADHD population is problematic. Agreement between parents and teachers is low (Sandberg, Day and Trott, 1996). Ratings of ADHD symptoms are subject to various biases or ‘halo effects’, such that non-compliant children receive higher ratings of ADHD symptoms than do compliant children even in the absence of ADHD behaviours (Abikoff, Courtney and Koplewicz, 1991; Schachar, 1985). Contrast effects are apparent, especially in parental ratings in which mothers exaggerate the differences between their twins (Eaves, 1997). The number of changes that have taken place over the years regarding the number, duration, impairment and pervasiveness of symptoms highlights the arbitrary nature in which the thresholds and criteria for diagnosis are determined. Subtle shifts in the criteria substantially alter which individuals meet, or fail to meet diagnosis at any one time. Sensitivity and specificity analysis indicates that DSM-IV criteria are not equally
predictive of the diagnosis (Faraone et al., 1993) or of impairment (Mota, Schachar 1999, in press). Research in ADHD is further complicated by the delineation of numerous subtypes based on phenomenology (e.g. DSM-IV inattentive, hyperactive-impulsive and combined subtypes), and comorbidity (e.g. conduct disorder and reading disabilities).

**New Phenotype Definition/ Genetic Markers**

Research involving ADHD is hampered by the heterogeneity of the disorder and inaccuracy in the behavioural phenotype. These two key factors contribute to the variability within family, twin, adoption and molecular genetic research, as well as within research involving cognitive deficits and environmental risks. There is strong genetic and biological evidence pointing to the heritable nature of the disorder, with a focus on inhibition as the underlying deficit. There is also strong evidence for the impact of neurobiological and psychosocial factors in the etiology of the disorder. The uncertainty in the behavioural phenotype highlights the need for more objective non-behavioural markers such as laboratory measures of neuro-cognitive deficits that will function as new phenotype markers to identify more etiologically homogeneous subgroups. A new phenotype definition or ‘psychiatric genetic nosology’, as defined to by Tsuang et al., “seeks to classify patients into categories that correspond to distinct genetic entities by addressing the problem of diagnostic accuracy; the degree to which a diagnosis correctly classifies people with and without a putative genetic illness” (Tsuang, Faraone, Lyons, 1993 p.1). They point to functional deficits and specific pathology of particular brain regions and neural networks, and are therefore vital to our understanding of the disorder and provide a key distinction for etiological research. Progress
In identifying the genetic mechanisms involved in ADHD will be hampered if cases of ADHD caused by non-genetic factors are included (false positives) or if cases with a genetic source are excluded incorrectly (false negatives). The identification of a new phenotype marker could play a vital role in defining a more homogeneous subtype of affected individuals, and increase the power to distinguish primarily environmental and genetic influences.

Inhibition is a clear candidate as a new phenotype marker for ADHD. Inhibition provides a direct link to brain function and it has a clear neurobiological model that corresponds to the neurological areas implicated in ADHD. Results using the Stop task have indicated a consistent inhibition deficit in ADHD children, but only in a subgroup of affected individuals. The connection of inhibition with the areas found to be associated with ADHD in both genetic and neurobiological research indicates that inhibition may be a marker for a subgroup of ADHD individuals with a genetic predisposition. The use of inhibition as a new phenotype marker could facilitate the identification of a more etiologically homogeneous subgroup, advancing investigation of the mechanisms involved in the occurrence of ADHD, and provide information regarding the basic nature of the disorder.

The aim of the following study was to investigate if deficient inhibition functions as marker to delineate a more homogeneous subgroup of ADHD. The primary hypothesis of the study was that inhibition serves as a marker for a familial subgroup of ADHD; we would expect that ADHD children with deficient inhibition would have a significantly higher prevalence of family history for ADHD then those with normal or good inhibition. The
second hypothesis was that those with good inhibition would have increased exposure to environmental and/or psychosocial risk factors when compared to those with deficient inhibition. This hypothesis supports a separate etiology model of ADHD, indicating an alternative, non-genetic etiological route for the good inhibition group.
Chapter II

METHOD

Subjects

Subjects were selected from a sample of 88 ADHD Children. Children were excluded from the study if they had a history, or showed evidence of, neurological disorders such as epilepsy, chronic or serious medical problems, history or evidence of psychosis, clinically significant mood or anxiety disorder, or a verbal or performance IQ of less than 80. Inclusion criterion for the study was that individuals ranged in age from 7 to 12 years, had a confirmed diagnosis of ADHD, and valid Stop Signal Reaction Time (SSRT) scores (see below). All children were free of medication for 48 hours preceding testing. The parents of all children gave written consent for the children to participate in the study and all subjects gave verbal assent.

Groups

The experimental groups were determined from the sample of 88 ADHD children. Stop Signal Reaction Times (SSRT) were divided into thirds to determine extreme high and extreme low SSRT scores (Feldt, 1970). The high and low groups were then matched for sex and age. The resulting groups contain a total of 27 subjects each (24 males and 3 females) and made up approximately the top and bottom third of the ADHD sample based on SSRT scores. Deficient inhibition was defined as those subjects with SSRT scores in the top third of the sample, and were identified as the Poor Inhibition group. The subjects with SSRT scores in the bottom third were identified as the Good Inhibition group. Both groups contained 3
females and 23 males. The Poor Inhibition group had mean age of 9.03 (SD= 1.34) and the Good Inhibition group had a mean age of 9.27 (SD= 1.45). The SSRT scores of subjects in the Good Inhibition group are comparable to normative data (Williams, Ponesse, Schachar, Logan & Tannock, 1999) indicating that the ADHD subjects in the Good Inhibition group have a level of inhibitory control similar to children of the same age in the general population (Figure 1).

Measures

Diagnostic Measures. Subjects were assigned a diagnosis on the basis of a semi-structured clinical diagnostic interview with the child’s parents (Parent Interview for Child Symptoms, PICS) (Schachar & Ickowics, unpublished, see Appendix A) and with each child’s classroom teacher conducted over the telephone (Teacher Telephone Interview, TTI) (Schachar & Tannock, 1990). Interviews were administered by clinicians trained to 90% inter-rater reliability. The PICS interview covers DSM-IV symptoms of ADHD, Conduct Disorder (CD), Oppositional Defiant Disorder (ODD), anxiety, mood and other single symptom and internalizing disorders. The TTI covers ADHD, CD, ODD and screen for other disorders. Both the PICS and the TTI ask the informant for detailed descriptions of the child’s behaviour in the home and school setting, respectively. The clinician rate each symptom on a 4-point scale of severity and frequency. Inter-rater reliability and convergent validity of these interviews are high (Schachar & Logan, 1990).

Participants were administered the Wechsler Intelligence Scale for Children –III (WISC-III, Wechsler, 1991) as a measure of intellectual functioning. They were also
administered three subtests that provided standard scores on reading measures: reading subscale of the Wide Range Achievement Test – Revision 3 (WRAT-3; Jastak & Wilkinson, 1993), Word Attack, and Word Identification from the Woodcock Reading Mastery Tests Revised (Woodcock, 1987).

Diagnostic Criteria. To be classified as ADHD, children have to meet DSM-IV criteria for ADHD (age of, onset, severity and type of symptom) defined as at least 6 of 9 inattentive or hyperactive-impulsive symptoms, or both. Children had to meet criteria for ADHD in the parent or teacher interview but also exhibit a minimum of 4 inattentive or 4 hyperactive symptoms according to the other informant to ensure that the pervasiveness criterion was meet.

CD was diagnosed if 2 or more DSM-IV criteria for CD were reported by parents or teacher. Reading disability was defined by a score 1.5 standard deviations below the mean of any one of the reading measures, or by scoring 1 standard deviation below the mean of two of the three reading measures.

Family history for ADHD. Information was provided during the PICS - General Information Module interview regarding the family history of psychiatric, emotional, learning problems, and ADHD, and a decision regarding presence or absence of disorder was made by the clinician. The interviewer was blind to diagnostic status of the child at the time of taking the family history and was blind to the results of the laboratory assessment of inhibition. A family history of ADHD was identified as present if ADHD was identified in the mother, father or sibling of the subject.
Neurobiological Risk Factors. The Ontario Child Health Survey Scales (OCHS) - Family and Household Form (Offord et al. 1987) were used to record maternal report of exposure to neurobiological risk factors. Factors were examined individually and combined into a single multivariate risk index as was recommended by Biederman et al., (1995). Factors included in the neurobiological risk index were the following; during pregnancy there was - bleeding, high blood pressure, convulsions, seizures, infection, severe nausea or vomiting lasting more then a few weeks, took medicine other then vitamins, smoked, used drugs or alcohol, mother was under severe emotional stress, baby was born two or more weeks early or more weeks late; at the time of delivery any of the following problems occurred - emergency cesarean section or operation, planned cesarean section, breech delivery, baby was jaundice, baby didn’t breath properly, baby needed incubator, other special care, baby was born two or more weeks early or two or more weeks late; has the child ever had - head injury with loss of consciousness, accidental poisoning requiring admission to hospital (see Table 1a).

Psychosocial Risk Factors. The OCHS - Family and Household Form (Offord, et al. 1987) questionnaire was used to record the child’s exposure to psychosocial risk factors. Factors were examined individually and then all were combined into a single multivariate risk index. Factors that were included in the psychosocial risk index were; subsidized housing, single parent, overcrowding, early separation before the age of two, two or more ‘live in’ partners in the last two years, mother or father treated for “nerves” or a nervous condition, moved more than once in the last 2 years, medical or health condition in mother or father preventing them from carrying out normal daily activities at home/job/school, mother or father has less then a secondary education, in the past twelve months any significant events taken
place (i.e marriage, divorce, loss job), when in a disagreement with spouse in the past six months one or both -smashed or threw objects, threatened to hit or injured partner, hit or injured partner, when child is bad or does something wrong spank child with a strap/brush/something else, shake or shove the child (See Table 1b).

Impairment. Impairment was assessed using the Ontario Child Health Survey Scales (OCHS) parent and teacher ratings based on norms for age and sex. Parents and teachers reported on a number of items concerning how their child's ADHD affects them at home, in school and in the community.

Apparatus and stimuli. The stimuli for the stop signal paradigm were presented on a desk-top computer equipped with headphones through which auditory signals were presented. The stimuli for the go task were the upper case letters X and O, presented in the centre of the screen for 1000 ms. Each trial was preceded by a 500-ms fixation point, presented in the centre of the screen and then extinguished. The screen remained blank for 1000 ms. Consequently, each trial included a period of 2.5 s in which the subject could respond to the primary task in accordance with the task’s demands. The stop signal was a 100 ms, 1000-Hz tone generated by the computer and delivered through headphones at a comfortable listening volume. Stop signals occurred unpredictably on 25% of go-task trials, and involved presentation of a tone (a stop signal) that instructed subjects to completely stop their response to the go task on that trial. Responses were recorded with a hand held response box with buttons labeled with either an “X” or an “O”.

Calculation of the SSRT uses a tracking algorithm designed to find a stop-signal delay that ties the race between the go process and the stop process. The algorithm increases stop-
signal delay if subjects inhibit successfully, and it decreases stop-signal delay if subjects fail to inhibit. If the increments and decrements are equal in magnitude (50 ms changes), the algorithm will converge on a stop-signal delay at which the subjects inhibit 50% of the time. At that point, the go process and the stop process finish at the same time, on average. Go reaction time and stop signal delay are observable. SSRT is unobservable, but it can be estimated simply by subtracting stop signal delay from mean go reaction time (Logan, 1994).

Procedure

Subjects were tested individually in a quiet room in the presence of an examiner who read a uniform set of instructions. The task was presented in 10 blocks, the first two of which were practice. Each block consisted of 32 trials; 24 go signal trials without stop signals and 8 trials that included a stop signal. The X and O comprising the go signals occurred equally often in each block. Stop signals were presented in 25% of trials and occurred equally often with each of the two go signal letters. In the first of 10 blocks, subjects were presented with the go and the stop signals but were instructed to ignore the stop tones and practice responding quickly and accurately to the go signal by pressing the appropriate response button identified by X and O labels. Children were instructed to keep separate fingers of their left hand on the X and O buttons throughout the experiment. In the second practice block, subjects were informed about the stop signal and instructed to stop their response to the go signal when they heard the stop tone. Subjects were encouraged to continue responding to the go signal as quickly and as accurately as possible if no stop signal was presented. They were told that stop signals occurred in such a way that sometimes it would be difficult to stop and sometimes not. Stop
signal delay was set initially at 250 ms and then reset to 250 ms at the beginning of the 8 experimental blocks. After the third and sixth experimental block, go reaction time was presented on the screen and subjects were reminded about the importance of maintaining the speed and accuracy of their responses to the go signal. Go reaction time, standard deviation of go reaction time and SSRT were calculated for each of the 8 experimental blocks and for the entire task.

Accuracy, probability of inhibition and SSRT of each subject in each test block were examined to determine whether the subject had generally complied with the requirements of the task. Unacceptable performance in any block was characterized by: inhibition on all or none of the stop-signal trials, fewer than 66% correct responses to the go task, or scoring an SSRT that was less than 50 ms. Only subjects with valid SSRT scores were included in the final analysis.

Analysis

Groups were compared on measures of impairment, IQ, comorbidity (CD,RD) and DMS-IV behavioural subtypes (inattentive, hyperactive-impulsive and combined). Odds-ratio (OR) statistic was used to compare prevalence of family history of ADHD in the Poor and Good inhibition groups. Family history was investigated for mother, father and sibling separately, as well as part of a combined family history variable. Groups were compared using one-way analysis of variance (ANOVA) to detect differences between groups on multivariate measures of neurobiological and psychosocial risk. For contrasts of categorical variables a likelihood chi square ratio was used. Family history for ADHD, the
neurobiological risk index, and the psychosocial risk index were entered into a logistic regression to determine which variables best predicted inclusion in the Poor and Good inhibition groups.
Chapter III

RESULTS

Poor and Good inhibition groups did not differ on levels of impairment, IQ, diagnosis of CD, RD, or on the rate of DSM-IV behavioural subtypes of inattentive, hyperactive-impulsive and combined (Table 2).

The prevalence of family history of ADHD was significantly higher in the Poor Inhibition group (48.1%) than in the Good Inhibition group (19.2%) (odds ratio of 3.9, CI=1.14-13.38) (Figure 2). A similar trend was found in the analysis with mothers (18.5% vs. 3.8 %; p=.079), fathers (25.9% vs. 15.4%; p=.342) and siblings (18.5% vs. 3.8 %; p=.079), however, these differences were not significant.

No significant difference were found between the Poor and Good inhibitors on the neurobiological and psychosocial risk indexes (figure 4). Analysis of individual neurobiological risk factors indicated 2 of 21 risk factors were significantly more common in the Poor inhibition group; maternal emotional stress during pregnancy ($X^2=7.29$, p=.007) and jaundice ($X^2=4.48$, p=.034). One of 21 psychosocial risk factors, mother limited in daily activating due to medical condition, was found to be significantly more common in the Poor Inhibition group, ($X^2=5.55$, p=.018).

The logistic regression involving family history for ADHD, neurobiological and psychosocial risk indexes indicated that the only variable that significantly distinguished membership in the two groups was a family history for ADHD (OR = 3.9, CI = 1.14-13.38).

Family history was investigated in the comorbid ADHD+CD and ADHD+RD subgroups in both the Poor and Good inhibition groups (Table 3). Due to the small sample
size of the comorbid subgroups, the comorbid data was investigated informally. The
distinction of Poor versus Good inhibition predicted the presence of a family history for
ADHD in the ADHD+CD, ADHD+RD and pure ADHD (i.e. without CD or RD) subgroups
as it did for the entire sample (Figure 3). Comparable levels of family history for ADHD were
found for the entire Poor inhibition group (48.1%), ADHD +CD (50%), ADHD+RD (44%)
and pure ADHD (50%) individuals. Comparable level were also found in the entire Good
inhibition group (18.5%), ADHD +CD (25%), ADHD+RD (20%), pure ADHD (15.4%)
individual.
Chapter IV

DISCUSSION

The purpose of this study was to investigate inhibition as a marker for a more homogeneous subgroup of ADHD. Findings confirmed the primary hypothesis that classification of ADHD children according to inhibition served to identify a more homogeneous subgroup of ADHD children, with significantly more family history for ADHD. Children in the Poor inhibition group were 3.9 times more likely to have a family history for ADHD than children in the Good inhibition group. The findings provide preliminary evidence that inhibition may function to identify a genetically homogeneous subgroup of ADHD.

Exposure to neurobiological and psychosocial risks was reported in both the Poor and Good inhibition groups. However, no difference was found between the groups in the level of exposure. This finding does not support our hypothesis that the Good inhibition group may be an acquired subgroup of ADHD due to increased exposure to environmental factors. Results from the logistic regression indicated that family history for ADHD was the only factor that predicted inclusion in the Poor inhibition group. No interaction between family history and the neurobiological and/or psychosocial risk was found. This finding does not support a two-factor model which predicts that genetic and environmental factors act conjointly to increase the risk for ADHD, indicating that inclusion in the Poor inhibition group was not a result of an interaction of familial and environmental factors. These findings are similar to those reported by Milberger and his colleagues (Milberger, Biederman, Faraone, Guite, Tsuang, 1997; Sprich-Buckminster, Biederman, Milberger, Faraone and Lehman, 1993) who investigated familial versus non familial ADHD and the role of genetics factors.
(familial ADHD) and environmental risk (pregnancy, delivery and infancy complications - PDIC's). The Milberger et al. (1997) study found no interaction between PDICs and the familial form of the disorder in predicting ADHD status. The authors concluded from the finding that there was no interaction between genetic and environmental factors in occurrence of the disorder. Furthermore, these studies investigated whether the non-familial form of the disorder was more associated with PDIC's. They found no association in the 1997 study and a weak association in the 1993 study. The authors concluded that there does not appear to be association between the non-familial form of the disorder and increased exposure to PDIC's. This finding could be viewed as potentially similar to the present finding that there was no increased exposure to environmental risk in the Poor inhibition group, as the group has a low prevalence of family history for ADHD.

The conclusions that can be made regarding the level of neurobiological and psychosocial risk factors in the Good inhibition group are limited due to the lack of a normal control comparison. There was not an increase in the level of exposure to these risks when compared to the Poor Inhibition group, but it is not possible to determine if the groups were exposed to more of these factors then would be expected in the normal controls. Further investigation is warranted in ADHD children with good inhibition to determine what factors contribute to the development of the disorder in those individuals. Alternate possibilities may involve environmental risk factors not investigated in either of the two indexes used in this study, a cognitive deficit of a different type, or some other biological/genetic factor not associated with inhibition.
The findings of this study were not the result of differences between groups on measures of impairment, age, sex or IQ, nor were the differences an artifact of comorbidity. ADHD subjects in the Poor inhibition group, with and without comorbid CD and RD had an equally high risk of family history of ADHD. Previous studies by Schachar et al. investigated inhibition in several samples of ADHD and ADHD+CD. In two of these three samples the ADHD+CD subjects did not show a significant deficit in inhibition, suggesting that ADHD in the presence of CD may be a phenocopy of true ADHD (ADHD+CD is a phenocopy of ADHD without the underlying deficit) (Schachar & Logan 1990; Schachar, Mota, Logan and Tannock 1999 in press). In the third sample, the ADHD+CD subjects did show an inhibition deficit comparable with the ADHD subjects, suggesting a true hybrid of the disorders (Schachar & Tannock, 1995). Taken together, these studies indicate that the mixed ADHD+CD group may itself be a mixture; sometimes representing a hybrid involving true ADHD, and sometimes a only a phenocopy of ADHD (Schachar et al, 1999 in press). The results from the present study support the conclusion that the comorbid ADHD sample is itself heterogeneous in nature (in certain cases a hybrid and in others a phenocopy). The findings indicated that inhibition distinguished the comorbid ADHD+CD subjects into two groups as it did for the entire sample. Depending on their classification in the Poor or Good inhibition group, the combined ADHD+CD subjects had similarly high or low prevalence for family history of ADHD, when compared to the rest of the sample. The same pattern occurred in the ADHD+RD and the pure ADHD samples. This finding, although not investigated formerly, indicates that not only did inhibition delineate a familial subgroup within the entire sample, it also delineated a familial subgroup among the comorbid CD, RD and pure ADHD individuals;
the comorbid subjects with poor inhibition share the same familial (genetic) risk and those with good inhibition having potentially different etiological risk.

Familiality in this study was used as a proxy for genetic risk (Milberger, Biederman, Faraone, Guite & Tsuang, 1997; Sprich-Buckminster et al., 1993). Although familial transmission can also be the result of environmental factors, the strong genetic evidence for ADHD lends support for a genetic mode of familial transmission. The two groups showed significant differences in the familial prevalence of ADHD (48.1% vs 19.2%), but the rate of neurobiological and psychosocial factors did not differ between the groups, indicating that it is unlikely that the familiality was a result of environmental factors. The logistic regression involving family history for ADHD, neurobiological and psychosocial risk indexes indicated that the only predictor of inclusion in the Poor inhibition group was a family history for ADHD.

These data have provided evidence that classification using inhibition identifies a familial subgroup within an ADHD population. This evidence provides some support for inhibition as a potential phenotype marker for genetic analysis, however, there are several other aspects that need to be assessed to further evaluate its role. Tsuang, Faraone, Lyons (1993) summarized six characteristics important when selecting a new phenotype marker. 1. Specificity: the marker is more strongly associated with the disease of interest than with other psychiatric conditions. 2. State dependent: the marker is stable over time and not an epiphenomenon of the illness or its treatment. 3. Heritability: the indicator shows familial transmission. 4. Familial association: the marker is more prevalent among relatives of ill probands compared with an appropriate control group. 5. Co-segregation: the marker being
more prevalent among ill relatives of ill probands compared with the well relatives of ill probands. 6. Biological and clinical plausibility: clinically the marker bears conceptual relationship to the disease, possibly a resemblance to the presentation of the disease, as well as biological plausibility i.e. it assess brain regions believed to be impaired by the disorder (Tsuang, et al., 1993). Inhibition fulfills several of these criteria. Inhibition is more common to ADHD than any other psychiatric disorder, it is stable over time, and inhibition has clear biological and clinical plausibility to the disorder. Further research is necessary to determine whether inhibition meets the remaining criteria. A key aspect of such research would require measures of inhibition taken from the family member of ADHD probands and controls. If inhibition functions as a new phenotype marker then inhibition would need to be indicated as having a familial transmission, family members of ADHD probands would be shown to have a higher rate of poor inhibition then the family members of controls, and poor inhibition would be more prevalent in the family members with ADHD than in family members without ADHD.

The primary limitation of the preceding study was the use of a family history method rather than a more systemic family study approach. Another key limitation was that the small sample size of the groups did not allow for formal analysis on the comorbid CD and RD subgroups requiring the data be interpreted informally. Future research would benefit from including measures of inhibitory control on family members of ADHD probands as well as controls and their families. This data will greatly advance the ability to assess inhibition as a new phenotype marker for ADHD.

Findings indicate that inhibition does functions as a marker for a familial subgroup of ADHD. Identification of markers such as inhibition play a key role in defining a etiologically
homogeneous subgroup of affected individuals for genetic analysis, and increase the power to distinguish primarily environmental and genetic influences. Inhibition identifies the functional difficulties of ADHD and reflects the underlying neuropathological deficit of the disorder. Inhibition not only identifies a subgroup of ADHD children with a familial form of the disorder, but it provides a direct link to a viable genetic pathway for the disorder via a direct connection to the neuroanatomical regions (dorso-lateral prefrontal and associated subcortical regions) identified as abnormal among ADHD children. Classification using inhibition may benefit further research using neuro-imaging, electro-physiological and neuro-pathological by identifying those ADHD individuals with the underlying neuropathology.
REFERENCES


Inhibition as a Familial Marker for ADHD

53, 607-16


Corbetta, M., (1993). Positron emission tomography as a tool to study human vision and attention [comment]. Proceedings of the National Academy of Sciences of the United States of America, 90, 10901-10903


334-45.


Inhibition as a Familial Marker for ADHD


Inhibition as a Familial Marker for ADHD


Rubia K., Overmeyer S., Taylor E., Brammer M., Williams SC., Simmons A.,
Inhibition as a Familial Marker for ADHD


Inhibition as a Familial Marker for ADHD


Table 1a

**Neurobiological Risk Index**

During pregnancy:
- Bleeding
- High Blood Pressure
- Convulsions, Seizures
- Infection
- Severe nausea or vomiting lasting more than a few weeks
- Medicine other than vitamins used
- Smoked
- Used drugs or alcohol
- Mother was under severe emotional stress
- Baby born two or more weeks early or late

At the time of delivery any of the following problems:
- Emergency Cesarean section or operation
- Planned Cesarean section
- Breech or bum first delivery
- Baby jaundice or yellow
- Baby didn’t breathe properly
- Baby needed incubator
- Other special care

Was the baby born two or more weeks early

Was the baby born two or more weeks late

Has the child ever had:
- A head injury with loss of consciousness
- Accidental poisoning requiring admission to hospital

Table 1b

**Psychosocial Risk Index**

- Subsidized housing
- Single parent
- Number of people living in house greater than 6
- Before the age of 3, separated for from primary caregiver for extended period of time
- Two or more live in partners in the last two years
- Mother or father treated for "nerves" or a nervous condition
- Moved more than once in the last 2 years
- Medical or health condition in mother or father preventing them from carrying out normal daily activities at home, job or school.
- Mother or father has less than a secondary education
- In the past twelve months any of the following has happened to the primary caregivers: stopped full time schooling, lost job or was unemployed, got married, someone moved into home, had financial difficulties, separation from spouse, arrival of baby at home, someone moved out of our home, serious illness of someone dear, quit or fired from full-time work, started working or changed jobs, death of someone dear

When in disagreement with spouse in the past six months one or both of you:
- Smashed or threw objects (more than once)
- Threatened to hit or injured partner (more than once)
- Hit or injured partner (more than once)

When child is bad or does something wrong
- Spank child with a strap, brush or something else (sometimes - always)
- Shake or shove your child (sometimes - always)
Table 2  Summary of Subject Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Poor Inhibition</th>
<th>Good Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>males</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>females</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>age (mean yrs)</td>
<td>9.03</td>
<td>9.27</td>
</tr>
<tr>
<td>IQ</td>
<td>100</td>
<td>105.8</td>
</tr>
<tr>
<td>DSM-IV subtype (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>inattentive</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>hyperactive-impulsive</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>combined</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>comorbidity (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADHD+CD</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>ADHD+RD</td>
<td>9</td>
<td>5</td>
</tr>
</tbody>
</table>
Table 3  Prevalence of Family History of ADHD in Poor and Good Inhibition Groups

<table>
<thead>
<tr>
<th>Family History (%)</th>
<th>Poor Inhibition</th>
<th>Good Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>Total Group 27</td>
<td>Total Group 27</td>
</tr>
<tr>
<td>ADHD</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>ADHD+CD</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>ADHD+RD</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>13(48.1)</td>
<td>5(18.5)</td>
<td></td>
</tr>
<tr>
<td>6(46.2)</td>
<td>2(14.3)</td>
<td></td>
</tr>
<tr>
<td>3(50)</td>
<td>2(25)</td>
<td></td>
</tr>
<tr>
<td>4(44)</td>
<td>1(20)</td>
<td></td>
</tr>
</tbody>
</table>
Figure 1  Distribution of stop signal reaction times (SSRT)

* Based on normative data collected at the Ontario Science Center
(Williams, Ponesse, Schachar, Logan & Tannock, 1999)
Figure 2  
Prevalence of Family History for ADHD

![Prevalence of Family History for ADHD](image)
Figure 3  Prevalence of Family History for ADHD, ADHD+CD and ADHD+RD subjects
Figure 4  Mean number of neurobiological and psychosocial risk factors in Poor and Good inhibition groups

Neurobiological and Psychosocial Risk Factors in Poor and Good Inhibition Groups

- Good Inhibition
- Poor Inhibition

Mean Number of Risk Factors

Neurobiological  Psychosocial
Appendix

Parent Interview for Child Symptoms (PICS-4)
   General Psychopathology Module
   Disruptive Disorders Module
   General Information Module
GENERAL PSYCHOPATHOLOGY MODULE

ANXIETY DISORDERS

GENERAL INTRODUCTORY QUESTIONS:

Now, I am interested in exploring whether your child has been experiencing problems with excessive anxiety, nerves or worries. Children experience these symptoms in their own way.

In general what is your child like when it comes to:

- Things (s)he fears or avoids
- Worries and preoccupations?
- Shyness?
- Sensitive?
- Perfectionistic?

What triggers the anxiety or worry?

Is it related to a traumatic experience? What? When?

Is it related to the use of medication?
(e.g., for asthma, Ritalin or other stimulants, other medications, drugs?)

Is it related to a medical condition?
Life threatening and/or chronic illness, child is dependent on parents for care, etc.

INTRODUCTION:
I am now going to go through a list of different conditions and situations. We will see if (I already know) some of them apply to your child. The first deals with anxiety related to separation from care-givers.
SEPARATION ANXIETY DISORDER
Developmentally inappropriate and excessive anxiety concerning separation from home or from attachment figures as evidenced by three or more of the following:

DISTRESS WHEN SEPARATION OCCURS OR IS ANTICIPATED
Does your child (ever) get upset when you (or other people he is close to) go out without him/her? What about when (s)he is the one going out without you (visit friends, etc.)? How does (s)he react? Crying? Begging? Does (s)he have a similar reaction when a separation is anticipated? Is it recurrent and excessive?

LOOSING OR HARM BEFALLING ATTACHMENT FIGURES
Does (s)he worry that something will happen to you (or someone close) resulting in you (or that person) being harmed or that you (someone close) will leave and not come back Is it persistent and excessive?

UNTOWARD EVENT LEADING TO SEPARATION
Does your child worry a great deal that something might happen to him/her if (s)he is not by your side? Getting lost? Being kidnapped?

PERSISTENT SCHOOL RELUCTANCE OR REFUSAL
Does your child (ever) try to stay home from school because (s)he is afraid of being without you (or someone close)?

PERSISTENT AVOIDANCE OF BEING ALONE
Is your child comfortable in being separated from you briefly? Would (s)he be reluctant to being alone in his room (or in the basement) even if someone (s)he knows was elsewhere in the house. Does (s)he follow you around the house? Clingy?

PERSISTENT REFUSAL TO SLEEP ALONE
Does your child have trouble or is reluctant to GO TO SLEEP when you (or someone close) are not around? Does (s)he ever sleep away from home?

REPEATED NIGHTMARES OF SEPARATION
Does your child have bad dreams about being separated (taken away) from you? Or that something bad would happen to him/her, or to you? How many times did it happen. Get examples

PHYSICAL COMPLAINTS ASSOCIATED WITH SEPARATION
Does your child often complain of being sick (headaches, stomachaches, nausea, vomiting) when he is (or is about to go) away to school or to visit a friend (in a situation where you or someone close are not around)?

OTHER CHARACTERISTICS (DSM III-R)
How does (s)he react at the time of these separations? (tantrums? crying? pleading? physical symptoms?)

How does (s)he do when you are not around?
So sad or so preoccupied that withdraws or can't play or work? Wants to return home? Needs to call parents?
PANIC DISORDER
A panic attack is a discrete period in which there is a sudden onset of intense apprehension, fearfulness or terror, often associated with feelings of impending doom. Panic attacks are rare but not unheard of in pre-pubertal children.

Does your child (ever) get very scary feelings? Like something terrible was happening? Or times when (s)he complains of the heart beat going extra hard or too fast? Shaky, like fainting, or couldn't breath? Panicky?

When? Did it come all of a sudden? How long did it last? Did (s)he or you know why?

Four or more of the following symptoms developed abruptly and reached a peak within 10 minutes.
- palpitations, accelerated heart beat; sweating; trembling or shaking;
- shortness of breath; choking; chest pain; nausea or upset stomach;
- dizzy or faint; derealization or depersonalization; losing control or going crazy; fear of dying; paresthesias (numbness, tingling sensations);
- chills or hot flushes.

(circle or underline those present)

AGORAPHOBIA
The essential feature of Agoraphobia is anxiety about being in places or situations from which escape might be difficult or embarrassing. Not due to separation anxiety.

A. Has your child ever been afraid of being trapped or in a situation from where there is no escape like traveling in a bus (car, train, subway), enclosed or narrow places, elevators, large crowds, bridges, tunnels, etc.?

B. The above situations are avoided or endured with marked distress or anxiety about having panic-like symptoms?

SOCIAL PHOBIA
At least 6 months of marked and persistent fear of social or performance situations in which embarrassment may occur. It interferes with family, social, school functioning.

A. Has your child ever felt afraid of performing in front of people he does not know well because of possible humiliation? Like speaking in front of the class (answering a teachers question, show & tell); using a public washroom, gym-change room, shower; eating in the school lunch-room or restaurant?

B. Exposure to feared situation provokes anxiety in children the anxiety may be expressed by crying, tantrums, freezing and inhibited interactions to the point of mutism. Feared situations are avoided or endured with intense distress.

AVOIDANT DISORDER OF CHILDHOOD (DSM III-R Category)
A. Has your child excessively AVOID contact with people (s)he doesn't know well? How long (6 months to meet criteria) Interfere with functioning?

B. SOCIAL CONTACTS with familiar figures is desired. Warm and satisfying relationships with family.
SPECIFIC PHOBIA*
At least 6 months of marked and persistent fear of clearly specific objects or situations.
Symptoms interfere with family, social, school functioning.

A. Has your child ever felt excessive or unreasonable fears to a particular object or situation like animals, dark, heights, storms, water, loud sounds, clowns, injections, seeing blood, etc.

B. Exposure to phobic stimulus provokes anxiety response (panic); the phobic situation is avoided or endured with intense anxiety or distress.

*This condition is equivalent to Simple Phobia in DSM III-R

GENERALIZED ANXIETY DISORDER
Excessive anxiety and worry (apprehensive expectation), more days than not for a period of at least six months about a number of events or activities (such as school performance, friends, etc.).

Is your child a worrier? What does (s)he worry about?
Does (s)he seem to be worrying about one thing or another almost all the time? How long (6 months or more)?
Does (s)he worry about his performance in school or sports?
Relationship with friends, family, relatives?
Does (s)he worry about things before they happen?
Worries about not having said (or done) the right thing in the past?
Other worries?

Does your child have a hard time controlling the worry(ies).

The anxiety and worry are associated with at least ONE of the following symptoms:

They appear RESTLESS, KEYED UP or ON EDGE
Get TIRED EASILY, or always APPEAR TIRED
Difficulties CONCENTRATING or MIND GOING BLANK
IRRITABLE
MUSCLE TENSION
SLEEP DISTURBANCE (difficulty falling or staying asleep or restless unsatisfying sleep).
**ASSOCIATED SYMPTOMS (SCREEN FOR OVERANXIOUS DISORDER - DSM III-R)**

Excessive and unrealistic anxiety or worry for a period of six months or longer, as indicated by the frequent occurrence of at least FOUR of the following:

<table>
<thead>
<tr>
<th>CURRENT</th>
<th>LIFETIME</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Does your child WORRY EXCESSIVELY about what MAY HAPPEN in the future? **OVANX 1**

Does (s)he worry about whether or not they did OKAY IN THE PAST? **OVANX 2**

Whether or not (s)he is GOOD ENOUGH at school, in sports, with friends etc.? **OVANX 3**

Does (s)he often have PAIN OR PHYSICAL SYMPTOMS (i.e.: headaches, stomachaches, etc.) for which no physical basis can be established **OVANX 4**

Is your child easily EMBARRASSED, markedly SELF-CONSCIOUS **OVANX 5**

Does (s)he need REASSURANCE over and over again about all sorts of things **OVANX 6**

Is (s)he a child that can NEVER feel RELAXED, muscles look TENSE all the time? **OVANX 7**

**CONTINUE WITH GENERALIZED ANXIETY DISORDER**

**CLINICIAN TO RATE:**

The Hospital for Sick Children, Department of Psychiatry

Parent Interview for Child Symptoms IV (PICS-4) General Psychopathology Module

---

**GAD D**

The focus of the anxiety is not confined to having a panic attack (Panic Dis.), being embarrassed in public (Social Phobia), being contaminated (OCD), separated from attachment figures (SAD), or any other Axis I diagnosis.

**DISTRESS AND IMPAIRMENT**

The anxiety, worry, physical symptoms cause clinically significant distress or impairment

Is (s)he upset or distressed by the worries, anxious symptoms? **GAD E**

Does it interfere with school, social, family functioning

**NOT SECONDARY**

Not due to direct physiological effects of a substance (medication, drug of abuse), medical condition (e.g., hyperthyroidism) and does not occur exclusively during a Mood Disorder, Psychotic Disorder or Pervasive Developmental Disorder **GAD F**

**SECONDARY TO TRAUMA**

Are the anxiety and associated symptoms related to traumatic experiences?

- Acute Stress Disorder **ASD**
- Post-traumatic Stress Disorder **PTSD**
COMPULSIONS

Compulsions are repetitive, purposeful, and intentional behaviors, performed according to certain rules or in a stereotyped fashion. The behavior is designed to neutralize some dreaded event or situation (younger children may not articulate it). Common forms of compulsions are hand washing, counting and checking. However, there is an infinite range of possibilities.

Has your child ever felt that (s)he absolutely must do something over and over again (like washing their hands, even if they are clean; or checking locks, light switches; counting, balancing, making things even)

What about having to do something exactly the same way, each time? Does (s)he start all over again if (s)he makes a mistake.

What does (s)he do? Do you know why?
What would happen if (s)he doesn't do it? Does (s)he try to stop them?
How much of the time does (s)he have to do _______ (this actions)?
How long do they last?
Is (s)he upset or distressed by having to do __________ (the ritual)?
Does it interfere with school, social, family functioning

Use additional space in the back of page to describe

OBSESSIONS

Obsessions are recurrent and persistent thoughts, ideas, impulses or images that are actually experienced as intrusive, unwanted, senseless or repugnant. They should be distinguished from obsessive brooding or rumination which is characterized as organized thought about real or potentially unpleasant events. They should also be distinguished from thought insertion (the individual does not recognize it as a product of his mind but imposed from without).

Obsessions are often, but not limited to, contamination, aggressive or sexual content

Has your child ever had thoughts or fears that keep come into his/her mind over and over again, which (s)he can not stop and won't go away? or words or pictures? (e.g., fears of contamination, someone being harmed.)

What are they?
Does your child try to stop them?
How much of the time does (s)he have this thoughts? How long do they last?
Is (s)he upset or distressed by the thoughts?
Does it interfere with school, social, family functioning

Use additional space in the back of page to describe
### TICS

Tics are sudden, rapid, recurrent involuntary or repetitive movements or sounds.

<table>
<thead>
<tr>
<th>Motor Tics</th>
<th>Vocal Tics</th>
<th>Current</th>
<th>Lifetime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does your child have any repetitive, involuntary movements of eyelids, facial grimacing, shoulder, neck (other)?</td>
<td>What about repetition of sounds or noises like, whistling, coughing or clicking sounds, words, phrases?</td>
<td>TRANSIENT</td>
<td>TICS</td>
</tr>
<tr>
<td>MOTOR TICS</td>
<td></td>
<td></td>
<td>[ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Do the tics seem to appear in bouts? Many times a day? Nearly every day? How long? Free of tics for 3 months or more?</td>
<td></td>
<td>CHRONIC</td>
<td>MOTOR TICS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>[ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Is the child distressed by the tics? MARKED DISTRESS? Do they interfere with social, school, family function? SIGNIFICANT IMPAIRMENT?</td>
<td></td>
<td>CHRONIC</td>
<td>VOCAL TICS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>[ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Are the tics related to the use of medication (e.g.: stimulants)? Or neurological condition (e.g.: Huntington's chorea, post-viral encephalitis, etc.)?</td>
<td></td>
<td>TOURETTE</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>[ ] [ ] [ ] [ ]</td>
</tr>
</tbody>
</table>

Tic Disorders are distinguished from one another based on duration and variety of tics.

- Transient Tic Disorder: motor and/or vocal tics more than 4 weeks, less than 12 months.
- Chronic Motor or Vocal Tics: either motor or vocal tics, more than 12 months
- Tourette's Disorder: motor and vocal tics, more than 12 months

Describe

### STEREOTYPIC MOVEMENT DISORDER

Motor behavior that is repetitive, seemingly driven and nonfunctional. It interferes with normal activities or results in self injury

Does your child have repetitive grooming or nervous habits? Like nail biting, thumb sucking, head banging, rocking, self biting, skin picking, etc.?  

Does the behavior markedly interfere with normal activities or results in bodily injury requiring medical treatment?  

How long? More than 4 weeks?  

Is the behavior better accounted by a compulsion (OCD), a tic, Autism (PDD), Sub-average Intelligence?

Describe
Inhibition as a Familial Marker for ADHD

**HEALTH, PAIN SYMPTOMS**
Some children seem very preoccupied with their physical health, often complaining of physical symptoms, wanting medication or other treatments.
* No medical reasons for these complaints.
* Impairment in social, academic, family functioning

- MULTIPLE ORGAN/SYSTEM involvement, a lot of "patient" behaviour. Soma.iz
- LOSS OF VOLUNTARY muscle/organ FUNCTION. Conv.erm
- PAIN as the predominant focus of clinical attention. Psychological factors are judged to have an important role in onset, severity, exacerbation or maintenance. Psy. pain
- UNREALISTIC INTERPRETATION of physical signs or sensations. Not reassuring. Hypocho
- Preoccupation with an imagined or exaggerated DEFECT IN PHYSICAL APPEARANCE. Body

**SLEEP HABITS**
Now, I would like you to give me an idea of your child's sleeping habits.
When does (s)he go to sleep, how long does (s)he sleep, Are there any problems with her/his sleep? Does (s)he take naps or appears tired during the day?

Circle those present
- INITIATING SLEEP, MAINTAINING SLEEP, RESTLESS UNSATISFYING SLEEP, SNORING, APNEAS, NIGHTMARES, NIGHT TERRORS, SLEEPWALKING, SLEEP ATTACKS, OTHER

Use back of the page to describe

**EATING HABITS**
Describe your child's eating habits?
Note concerns regarding dieting, food restrictions, etc. (use back of the page if needed)

**ENURESIS**
Repeated (involuntary or intentional) voiding of urine during the day or night into bed or clothes.
2 episodes/month between ages 5 and 6, 1 episode/month older children, chronological age at least 5, mental age at least 4, not due to physical disorder

**ENCOPRESIS**
Repeated (involuntary or intentional) passage of faeces into places not appropriate for that purpose (e.g.: clothing, floor). The disorder may be overflow incontinence secondary to functional faecal retention at least one episode/month for at least six months, chronological age and mental age at least 4, not due to physical disorder
MOOD DISORDERS

This section begins with a general screen for dysphoric mood, irritability an anhedonia. If the screen is positive the interviewer should inquire about duration(s), onset(s) and offset(s) before assessing specific symptoms.

DEPRESSED OR IRRITABLE MOOD

- Establish the child's typical mood
  How would you describe your child's mood?
  Is (s)he mostly happy (or OK) child?
  or mostly sad (moody, down, mad, cranky, like crying)?.

- Establish presence of episodes of depressed or irritable mood
  Are there periods of time in which your child is mostly sad (down, etc.)
  When was the last time something like this happened?
  Was it an isolated event or have there been other episodes?

- Establish duration
  When sad (or down, etc.) how long would it last?
  How many hours a day? Days of the week? Weeks in a row?

- Establish onset and offset
  Do you know what triggers the sad (depressed, down, etc.) mood?
  How does it go away?

- Establish severity and impairment
  How much would the sadness (or being down, etc.) interfere with his life,
  schoolwork, friends, family life? How bad does it get?

- Establish history of past episodes
  Has there been another time when your child felt sad (cranky, mad, etc.)
  for ______ (at least 3 hours a day for 3 days in a week).
  Has (s)he ever felt that way for longer? What was the longest?
  How many weeks in a row? When was that? Any other time?

LOSS OF INTEREST OR PLEASURE

- Establish the child's typical interests and pleasurable activities
  What does your child usually do for fun?, Has (s)he been having as much
  fun as usual? What things are less fun than they used to be?
  Has (s)he been less interested in (bored with) friends or activities?

- Are there clear episodes of loss of interest or pleasure (anhedonia)?

- Establish duration

- Establish onset and offset

- Establish severity and impairment

- Establish history of past episodes
MAJOR DEPRESSIVE EPISODE:

Five (or more) of the following symptoms have been present during the same one week period and represent a change from previous functioning. At least one symptom is either: depressed mood (MDE 1) or loss of interest or pleasure (MDE 2).

DEPRESSED OR IRRITABLE MOOD most of the day, nearly every day, for at least one week?

DIMINISHED INTEREST OR PLEASURE in all or almost all activities (ANHEDONIA) for most of the day, nearly every day for at least one week?

APPETITE and WEIGHT
- During the time that your child felt ________
  - Was (s)he also feeling less hungry, eating less than usual (not dieting)
  - loosing weight (how much? clothes fit loose?)
  - feeling more hungry, eating much more than usual
  - gaining weight? (how much?)

SLEEP DISTURBANCE
- During the time that your child felt ________
  - Was (s)he having trouble falling asleep? - INITIAL INSOMNIA
  - waking up in the middle of the night? - MIDDLE INSOMNIA
  - waking up much earlier than usual? - TERMINAL INSOMNIA
  - or sleeping much more than usual? - HYPERSOMNIA

AGITATION / RETARDATION
- During the time that your child felt ________
  - Does (did) (s)he appear more agitated/restless than usual - AGITATION
  - or actually appear to move or talk more slowly than usual - RETARDATION

LOSS OF ENERGY / FATIGUE
- During this same time
  - Does (did) (s)he appear tired? Like (s)he has (had) less energy than usual?
  - Having to rest more?

WORTHLESSNESS/INAPPROPRIATE GUILT
- During the time that your child felt ________
  - Is (was) your child down on him/her-self; talking about being ugly, stupid, bad, worse than the other kids?
  - Believed (s)he is (was) the cause of bad things happening, or that deserves punishment?
CONCENTRATION / THINKING / INDECISION

Also, during this period of time in which your child felt ______
Is (was) it harder for him/her to keep his mind on things?,
harder to THINK OR CONCENTRATE?,
or having a hard time making up his/her mind, not knowing
what to do or what decision to make?

CURRENT       LIFETIME
MDE A8 [ ] [ ] [ ]

SUCIDALITY
Does (did) your child have recurrent thoughts of death (not just fear of dying)?
Thinking or talking about hurting him/her-self? - IDEATION
Voicing suicidal ideas, plans? - INTENTION

CURRENT       LIFETIME
MDE A9 [ ] [ ] [ ]

OTHER CHARACTERISTICS

LOW SELF-ESTEEM

CURRENT       LIFETIME
DYS B4 [ ] [ ] [ ]

HOPELESSNESS
Does (did) your child feel will (would) ever work our for him/her,
that everything goes wrong?, or that things will never get better?

CURRENT       LIFETIME
DYS B6 [ ] [ ] [ ]

REACTIVITY

During this period of time in which your child felt ______
Would your child feel better if something good happens or
feels sad (down, etc.) no matter what? DESCRIbe

CURRENT       LIFETIME

CURRENT       LIFETIME

EVIDENCE OF A PRECIPITANT
Inquire about significant life event, loss, illness, etc. DESCRIbe

CURRENT       LIFETIME

MIXED EPISODE?
Meets criteria for both MAJOR DEPRESSIVE and MANIC EPISODE (page 12)

CURRENT       LIFETIME
MDE B NO [ ] NO [ ]

IMPAIRMENT?
Unequivocal change in the child, affecting social (peer), family, school (academic)
functioning, which is not present when not symptomatic

CURRENT       LIFETIME
MDE C YES [ ] YES [ ]

SECONDARY?
Symptoms due to physical illness (endocrine disorders, etc.),
medication (clonidine, steroids, etc.) or street drugs.

CURRENT       LIFETIME
MDE D NO [ ] NO [ ]

BEREAVEMENT
Depression occurs within two months of the loss of a loved one
(uncomplicated bereavement).

CURRENT       LIFETIME
BEREAVE [ ] [ ] [ ]
MDE E
DYSTHYMIA

<table>
<thead>
<tr>
<th>CURRENT</th>
<th>LIFETIME</th>
</tr>
</thead>
<tbody>
<tr>
<td>DYS A</td>
<td>[ ]</td>
</tr>
<tr>
<td>DYS B1</td>
<td>[ ]</td>
</tr>
<tr>
<td>DYS B2</td>
<td>[ ]</td>
</tr>
<tr>
<td>DYS B3</td>
<td>[ ]</td>
</tr>
<tr>
<td>DYS B4</td>
<td>[ ]</td>
</tr>
<tr>
<td>DYS B5</td>
<td>[ ]</td>
</tr>
<tr>
<td>DYS B6</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

During a period of one year (or more) the child experienced DEPRESSED or IRRITABLE MOOD for most of the day, more days than not.

Presence, while depressed, of two or more of the following:

POOR APPETITE OR OVEREATING

INSOMNIA OR HYPERSOMNIA

LOW ENERGY OR FATIGUE

LOW SELF-ESTEEM

POOR CONCENTRATION OR DIFFICULTY MAKING DECISIONS

FEELINGS OF HOPELESSNESS

During the ONE YEAR PERIOD of the disturbance, the child has never without symptoms of Dys A and two of Dys B for more than two months at a time.

The child experienced a MAJOR DEPRESSIVE EPISODE during the first year of the DYSTHYMIA disturbance.

Has the child ever experienced a MANIC EPISODE, MIXED EPISODE, HYPOMANIC EPISODE or CYCLOTHYMIC DISORDER.

Are symptoms superimposed on a chronic PSYCHOTIC disorder such as SCHIZOPHRENIA or DELUSIONAL disorder?

SECONDARY
Are symptoms due to physical illness, medication, or street drugs.

IMPAIRMENT
Unequivocal change in person which is not present when not symptomatic affecting social, academic, occupational functioning.
MANIC MOOD

I asked you about times when your child felt sad or down.
Now I want to ask you about different feelings.

- Does your child ever feel REALLY, REALLY GOOD, ALMOST TOO GOD, like (s)he is on TOP OF THE WORLD?
- Or like (s)he is TERRIFIC and there is NOTHING (s)HE CAN'T DO?
  When was that?
  Was there a reason?
  How long did it last (minutes, hours, days, weeks)?
  Have there been other times? When was the last time?

- How about other times when your child felt super angry, grouchy, cranky or irritable all the time?
  When was that?
  Was there a reason?
  How long did it last (minutes, hours, days, weeks)?
  Have there been other times? When was the last time?

- Does your child go through periods in which (s)he is full of energy, can't stop doing things and doesn't feel tired? Hardly needs any sleep?
  When? Why? How long did it last?

- Have there been other times? When was the last time?

Distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week (any duration if hospitalized)?

During the period of mood disturbance, three (or more) of the following have persisted (four if the mood is only irritable) and have been present to a significant degree:

INFLATED SELF-ESTEEM OR GRANDIOSITY

   During the time that your child felt ______

Does (did) (s)he feel especially self confident?
Could do anything?
Special? Stronger? Smarter? Special powers?

DECREASED SLEEP

   During the time that your child felt ______

Does (did) (s)he sleep less than usual, does (did) (s)he wake up feeling rested (or tired)

More or PRESSURED SPEECH

   During the time that your child felt ______

Does (did) (s)he talk more than usual? Faster, without stopping?
FLIGHT OF IDEAS/RACING THOUGHTS

During the time that your child felt ________

Does (did) (s)he feel his/her thinking is speeded up, as though thoughts were racing through his/her head.

Many thoughts and so fast (s)he could hardly keep track?

DISTRRACTIBILITY

During the time that your child felt ________

Does (did) (s)he have a lot more trouble concentrating?

Harder to pay attention because (s)he was easily drawn to unimportant or irrelevant external stimuli. Anything would get him/her off track.

Is the distractibility different from symptoms of inattention in ADHD:

Acute vs. Chronic?
Change from baseline?
Association with episode of elated mood?

INCREASE IN GOAL-DIRECTED ACTIVITY OR PSYCHOMOTOR AGITATION

During the time that your child felt ________

Has (s)he been doing a lot more with friends?
Is (was) (s)he accomplishing more work at school?
More interested in sex?
More restless than his/her usual, more energy?

EXCESSIVE INVOLVEMENT IN PLEASURABLE ACTIVITIES WHICH HAVE A HIGH POTENTIAL FOR PAINFUL CONSEQUENCES

During the time that your child felt ________

Does (did) (s)he engage in unrestrained spending (i.e. buying inappropriate presents for friends or family members), personal/sexual indiscretions, or foolish business investments?

MIXED EPISODE?

Meets criteria for both MAJOR DEPRESSIVE and MANIC EPISODE (page 12)

IMPAIRMENT?

Unequivocal change in person which is not present when not symptomatic affecting social, academic, occupational functioning.

SECONDARY?

Symptoms due to physical illness, medication or street drugs.

A mixed episode is characterized by a period of time (1week) in which criteria are met for both a Manic Episode or Major Depressive Episode (criterion A).
The child experiences rapid alternating moods (sadness, irritability, euphoria)

CYCLOTHYMIA

Evidence of episodes of illness lasting at least one year, characterized by numerous HYRPMANIC periods (not meeting criteria for mania) and numerous DYSTHYMIC (depressed) periods (not meeting MDE criteria). Never without symptoms for more than two months.

Absence of psychotic features

The Hospital for Sick Children, Department of Psychiatry
Parent Interview for Child Symptoms IV (PICS-4)
**PSYCHOSIS**

Have there been any periods when your child was preoccupied with strange, odd, unusual or bizarre thoughts that you couldn’t understand? Like (s)he was an important person but nobody else knew it? People were out to get him/her or try to poison him/her? Or that the world was coming to an end?

Has your child ever reported hearing voices of people not present, or seeing people or things that weren’t there? Or talked about communicating telepathically, or her/his thoughts being read by others? Or someone inserting thoughts in his/her mind?

Have there been times when his/her speech doesn’t make any sense? Incoherent?, Loose associations?

Catatonic behavior? Flat, inappropriate or incongruent affect?

Have these been accompanied by avoidance of social interaction, deterioration in school work, personal grooming?

**AUTISTIC SPECTRUM, P.D.D., SEMANTIC-PRAGMATIC LANGUAGE DISORDERS**

Have you (family members, teachers) had any concerns about your child’s ability to interact socially?

- poor use of non verbal behaviors (gestures, eye to eye gaze);
- failure to develop relationships appropriate to developmental level;
- limited interest in social reciprocity;
- marked difficulties understanding context of social situations, speech/language delay or peculiarity in use of language;
- unable to sustain conversation, unusual intonation;
- inappropriate use of words;
- restricted interests, stereotyped patterns of behavior.

**OTHER**

Any other issues or concerns?
THE HOSPITAL FOR SICK CHILDREN
DEPARTMENT OF PSYCHIATRY
PARENT INTERVIEW FOR CHILD SYMPTOMS (P. I. C. S. - 4)

GENERAL INFORMATION MODULE

copyright © 1995
R. Schachar, A. Ickowicz & R. Wachsmuth

CHILD'S NAME: ___________________________ DOB: _______ AGE: _______

DATE OF INTERVIEW: _______________ INFORMANT(S): ______________________ INTERVIEWER _______

01. Demographic Information
a. Family composition:

b. Who does the child live with? Where does (s)he live?
If parents are not together comment on custody, visitation, etc.

Do both Parents live in the Area? _______

c. Child's School: ___________________________ Child's Grade: [ ] [ ]

Type of program: Regular Classroom [ ]
Resource withdrawal [ ]
Special Education [ ]

02. Referral source: _________________________

2. School [ ] 5. Paediatrician [ ] 8. CAS [ ]
03. Presenting Concerns:
Describe, use back of page if more space is required

mark those that apply
excess of activity [ ]
inattentive [ ]
impulsive [ ]
academic prob. [ ]
defiant [ ]
aggression [ ]
deceitfulness [ ]
violation of rules [ ]
peer-social prob. [ ]
other [ ]

04. History of the presenting concerns:

04.1 Onset:

When was the first time that you became aware of these difficulties?
Was there ever a time when you had no worries?
What about your spouse/partner (if applicable)?
What about people outside the family (e.g., day care staff, teachers, etc.)?

AGE OF THE CHILD (IN YEARS) WHEN PROBLEMS WERE FIRST OBSERVED
(Describe, use back of the page if more space is required)

04.2 Who first identified the problem:
Parent [ ]  Teacher [ ]  Other (Describe) [ ]

04.3 What were the first manifestations:
(code all problems observed from onset)

overactivity [ ]  learning [ ]  anxiety [ ]
aggression [ ]  inattentiveness [ ]  shyness [ ]
defiance [ ]  impulsivity [ ]  social isolation [ ]
atachment issues [ ]  social judgement [ ]  developmental delay [ ]
other [ ]

(Describe, use back of the page if more space is required)
04.5 Course:
   How have the difficulties changed over time?
   Effect on Family, Peers, School
   What predicts better times and more challenging times?
   (Describe, use back of the page if more space is required)

04.6 Treatment:
   What has been done about the concern(s)?
   What has been useful so far?
   (Describe, use back of the page if more space is required)

04.7 Has medication ever been used to address the (behavioral, learning, emotional) problems?
   What?; When?; for How Long?; Effect?; Adverse Effects?
   (Describe, use back of the page if more space is required)

Is the child currently receiving any medication to address the (behavioral, learning, emotional) problems?
   What?; When?; for How Long?; Effect?; Adverse Effects?
   (Describe, use back of the page if more space is required)
Psychosocial and environmental Stressors

Almost all families have experienced stressful or traumatic events at one point or another. I am now interested in finding out if this has been the case for you, either recently or in the past?

(Give parent(s) an opportunity for a general description. Follow with a specific screening of these areas:

<table>
<thead>
<tr>
<th>Problems affecting the immediate family group:</th>
<th>Current</th>
<th>Precipitant</th>
<th>Past</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death in the family, life threatening illness, chronic illness-disability, separation/divorce, marital conflict, blended families, etc.)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trauma:</th>
<th>Current</th>
<th>Precipitant</th>
<th>Past</th>
</tr>
</thead>
<tbody>
<tr>
<td>Witness or victim of violence, abuse (spousal, physical, sexual)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Social supports:</th>
<th>Current</th>
<th>Precipitant</th>
<th>Past</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sole support parent, cultural and language barriers, access to services, etc.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relationship with school</th>
<th>Current</th>
<th>Precipitant</th>
<th>Past</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child’s relationship with teachers.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parent relationship with teachers/school.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parent’s occupational problems</th>
<th>Current</th>
<th>Precipitant</th>
<th>Past</th>
</tr>
</thead>
<tbody>
<tr>
<td>Job loss, change in job, work schedule, work conditions, etc.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Economic</th>
<th>Current</th>
<th>Precipitant</th>
<th>Past</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Housing</th>
<th>Current</th>
<th>Precipitant</th>
<th>Past</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moves, neighbourhood safety, dispute with neighbours-landlords, etc.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other</th>
<th>Current</th>
<th>Precipitant</th>
<th>Past</th>
</tr>
</thead>
</table>

** Precipitant: note if stressful event precedes the onset of the problem(s) of concern identified in page 2

** Past: History of the stress is positive but no longer active
04.4 **Precipitating factors:**
Did any stress or occurrence set off the (behavioral, learning, etc.) problems of concern?
(based on information from page 5; make a separate rating for each presenting problem)

<table>
<thead>
<tr>
<th>No = 1</th>
<th>Yes = 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>STRESS</td>
<td></td>
</tr>
</tbody>
</table>

04.8 **Perpetuating factors:**
Effect of stressors on maintenance of the problem(s) of concern

05 **Medical and Developmental History:**
(review of SDI Family & Household questionnaire)

05.1 **Overall rating of delay in development:**

<table>
<thead>
<tr>
<th>0</th>
<th>No delay</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Slight delay, transient</td>
</tr>
<tr>
<td>2</td>
<td>Moderate delay, persistent</td>
</tr>
<tr>
<td>3</td>
<td>Severe delay, persistent, interferes with social or academic development</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>8</th>
<th>Not known</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>Can't be rated</td>
</tr>
</tbody>
</table>

05.2 **Overall rating of past medical history:**

<table>
<thead>
<tr>
<th>0</th>
<th>No abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Slight difficulty, transient</td>
</tr>
<tr>
<td>2</td>
<td>Moderate difficulty, severe at time, without persistence</td>
</tr>
<tr>
<td>3</td>
<td>Severe difficulty, persistent disabling</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>8</th>
<th>Not known</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>Can't be rated</td>
</tr>
</tbody>
</table>

05.3 **Presently, is the child affected by a medical condition [different than the presenting problem(s)]?**

What? For how long? How is it being treated?

List medications (if applicable)
0.6  **Family History:**

06.1  **Family History of psychiatric, emotional, learning problems:**

Start with a general probe like:

Does this child remind you of anybody in your family?

- ADHD [ ]
- Learning [ ]
- Depression [ ]
- Mania [ ]
- Anxiety [ ]
- Psychosis [ ]
- Autism [ ]
- Subs. Abuse [ ]
- Impulsive Dis. [ ]
- Tics/OCD [ ]
- Prob. with law [ ]
- Other [ ]

Establish presence of positive history in first degree relatives:

I would like to explore now for presence of learning, behavioral, emotional and psychiatric problems in the immediate family.

Draw a genogram (family tree) of first degree biological relatives (parents, siblings, half siblings)

Is there evidence of ADHD in this child's

- MOTHER? [ ]
- FATHER? [ ]
- SIBLINGS? [ ]

Screen for positive history in extended family.

What about other emotional/psychiatric problems in other family members? Indicate positive findings and relationship to the child.

---

06.2  **Other relevant history:**

Describe (use back of the page)

Revised: 22/01/98
ATTENTION DEFICIT-HYPERACTIVITY DISORDER:

The essential feature that defines ADHD is a developmentally inappropriate, persistent pattern of difficulties with inattention, hyperactivity and impulsivity:

- **Inattention**: refers to deficits in either selecting what to attend or in sustaining attention (keeping attention focused) for as long as necessary to perform a task.
- **Impulsivity**: relates to individual difficulties restricting behaviors or delaying responses as the situation demands (i.e. blurtting out answers before questions have been completed, difficulty awaiting one's turn, etc.).
- **Hyperactivity**: relates to excesses in physical movement, especially movements that have a purposeless, poorly directed or driven quality.

Maladaptive and developmentally inappropriate symptoms have persisted for at least 6 months.

General introductory questions:

I am interested in getting a PICTURE or a series of SNAP SHOTS of how your child is or has been for the past 6 months:

First, I'd like to ask you about your child's behaviour in different situations

Not all children behave in the same way in all situations.

**IF THE CHILD HAS BEEN RECEIVING STIMULANT MEDICATION RATE BEHAVIOUR OFF MEDICATION.**

The first situation is: **AT PHYSICAL PLAY (OUTDOORS)**

What is your child's favorite outdoor activity?

What is (s)he like when playing these activities?

What about playing in the park, in the street, yard, beach?

Considering age, does (s)he often abandon one activity for another as though the novelty of the second activity is not its most important feature?

Can you give me examples of what you mean?

When was the last time you saw this sort of behaviour?

Probe for activity, distractibility, planfulness, concentration
In general terms, what is your child's level of activity?

Does (s)he RUN ABOUT OR CLIMB excessively?
(during inappropriate times or situations)

Often "ON THE GO" or acts as if "DRIVEN BY A MOTOR"

Does (s)he stick to each activity (s)he undertakes? or
Does (s)he SHIFT EXCESSIVELY from one activity to another?
(drawn by impulse to move on)

Does (s)he plan things out before starting? Or does (s)he jump right in?
Is (s)he cautious or reckless?
Would (s)he ride her/his bike into traffic without looking?

Does (s)he learn from experience?

Does (s)he ACT BEFORE THINKING?

Does (s)he often LOSE THINGS necessary for activities?

What if (s)he is playing with other children,
can (s)he WAIT for HER/HIS TURN
in games or other group situations?

Does (s)he BUTT INTO other's games?

Some children PLAY QUIETLY outside, others are on the NOISY side.
How would you describe your child?
PLAYING INDOORS AT GAMES

Playing Alone:
What are your child's favorite activities when playing alone indoors at home?
What about reading, hobbies, puzzles?
What is (s)he like when playing at these activities?
Can (s)he plan out an activity?
You are looking for a description of behaviour during an activity which requires sustained attention and mental effort.

<table>
<thead>
<tr>
<th>Question</th>
<th>ADHD IV-1E</th>
<th>ADHD IV-1F</th>
<th>ADHD III-R 7</th>
<th>ADHD III-R 8</th>
<th>ADHD IV-1A</th>
<th>ADHD III-R 9</th>
<th>ADHD IV-2C</th>
<th>ADHD IV-2E</th>
</tr>
</thead>
<tbody>
<tr>
<td>How organized is (s)he? Can (s)he get ORGANIZED for tasks and activities?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does (s)he AVOID TASKS REQUIRING SUSTAINED MENTAL EFFORT?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can (s)he CONCENTRATE RIGHT THROUGH until (s)he has FINISHED?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Or does (s)he often abandon one activity for another as though the novelty of the second activity is its most important feature?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the lack of persistence a result of DISTRACTIBILITY?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does (s)he SHIFT EXCESSIVELY from one activity to another?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How much ATTENTION does (s)he pay TO DETAIL?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does (s)he often LOSE THINGS necessary for the activity?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can (s)he PLAY QUIETLY?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does (s)he RUN ABOUT or CLIMB EXCESSIVELY? (during inappropriate times or situations)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Often “ON THE GO” or acts as if “DRIVEN BY A MOTOR”.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
PLAYING WITH THE PARENT

When you are playing a game with your child (e.g. cards, board game) and you try to explain something (rules, strategy, etc.), does (s)he seem to listen when spoken directly? (attention not compliance)

Does (s)he have difficulty staying seated? (gross motor)

What about following through on instructions?

Is (s)he often forgetful?

PLAYING WITH OTHER CHILDREN (INDOORS)

Does (s)he have difficulty awaiting turns in games or group situations?

Does (s)he butt into other children's games?

Does (s)he shout a lot in these situations? When (s)he has something to say or ask (hyper-reactive, excitable)?

Is (s)he mostly quiet or does (s)he talk excessively?

How does (s)he react to her/his own mistakes?

Does (s)he blame others?
TV

Does your child like to watch TV?
How does (s)he behave while watching TV?
How long does (s)he watch at one time (sitting)?
Does (s)he take it in?

Does (s)he have difficulty concentrating?

Is (s)he distractible while watching TV?

To what extent is (s)he fidgeting or squirming while watching TV?

HOMEWORK

In general what is your child's approach to homework (most of the time)?
Would you say that (s)he is motivated (or unmotivated) to do it?

Is (s)he disorganized?

How is your child when it comes to paying attention to details?

Does (s)he often leave the seat?
DINNER TABLE

What is your child like at the dinner table? Is (s)he expected to ask permission to leave the table? Many children find it difficult to sit at the table, can (s)he stay seated at the table?

Is (s)he FIDGETY? (fine motor)

Does (s)he TALK EXCESSIVELY?

Does (s)he BLURT OUT REQUESTS OR ANSWERS to questions being made?

STORE

What is it like when you take her/him out shopping?

Does (s)he need a lot of supervision? Does (s)he ACT BEFORE THINKING? (climbs on shelves, pulls things down)

Note: There are 3 additional items of ADHD in the ODD section

OPPOSITIONAL DEFIANT DISORDER

The essential feature of Oppositional Defiant Disorder is a recurrent and persistent pattern of negativistic, defiant, disobedient, and hostile behaviour towards authority figures. At least 4 Symptoms present in the last 6 months.

General introductory questions:

Does your child have any jobs, chores, or responsibilities at home?

What type of household rules do you have?

What expectations for household chores do you have of your child? (e.g.: washing dishes, keeping room tidy)

How does your child react to rules and responsibility? Bedtime, curfews, etc.?

Is (s)he cooperative and easy to get along with at home?

How does your child get along with other family and non-family adults?

Most of the time, when you make a request does (s)he comply or do you get the feeling that (s)he JUST DOESN'T SEEM TO LISTEN? (rate only if child is inattentive rather than disobedient)

Is it because (s)he has DIFFICULTIES FOLLOWING INSTRUCTIONS?

Does (s)he seem to be FORGETFUL? (e.g. routines, chores)
OPPOSITIONAL DEFiant DISORDER
(CONT.)

Does (s)he BREAK MINOR RULES?

Is your child the sort of kid who will argue over anything and everything?
ARGUMENTATIVE?

How does (s)he react if things don't go his/her way?
Does (s)he get ANGRY or RESENTFUL?

If (s)he doesn't get her/his way, does it ever go as far as a TEMPER TANTRUM?

Does (s)he try to get back at you? Is (s)he SPITEFUL or VINDICTIVE?

Is (s)he DELIBERATELY ANNOYING or PROVOCATIVE?

On the other hand IS (s)HE TOUCHY or EASILY ANNOYED?

How often would (s)he SWEAR or use OBScene LANGUAGE?
(out of keeping with the milieu?)
CONDUCT DISORDER

The essential feature of Conduct Disorder is a repetitive and persistent pattern of behaviour in which the basic rights of other or major age-appropriate societal norms or rules are violated, including aggression to people and animals, destruction of property, deceitfulness and theft. At least 3 Symptoms present in the last 12 months and one present in the last 6 months.

AGGRESSION TO PEOPLE & ANIMALS

Does (s)he OFTEN BULLY, THREATEN OR INTIMIDATE other kids? CD 0 / 1

INITIATED PHYSICAL FIGHTS? CD 11 / 2

Has USED A WEAPON that can cause SERIOUS PHYSICAL HARM to others? (e.g., bat, brick, broken bottle, knife, gun) CD 10 / 3

Has been PHYSICALLY CRUEL TO PEOPLE? CD 13 / 4

PHYSICALLY CRUEL TO ANIMALS? CD 8 / 5

Has STOLEN while CONFRONTING the victim? (e.g., mugging, purse snatching, extortion, armed robbery) CD 12 / 6

HAS FORCED SOMEONE INTO SEXUAL ACTIVITY? CD 9 / 7

DESTRUCTION OF PROPERTY

Has deliberately engaged in FIRE SETTING with the intention of CAUSING DAMAGE? CD 4 / 8

Has deliberately DESTROYED other's PROPERTY? (Vandalism) CD 7 / 9

DECEITFULNESS/THEFT

Has BROKEN INTO someone else's house, building or car? CD 6 / 10

Often LIES TO OBTAIN GOODS or FAVOURS, or to avoid OBLIGATIONS? (*cons* others) CD 3 / 11
Has STOLEN items of non trivial value WITHOUT CONFRONTING the victim? (e.g., shoplifting, forgery, etc.)

SERIOUS VIOLATIONS OF RULES

Often STAYS OUT AT NIGHTS despite parental prohibition?

Has RUN AWAY from home OVERNIGHT? (at least twice, while living with parents or surrogate home)

Is often TRUANT from SCHOOL? (beginning before age 13)
Inhibition as a Familial Marker for ADHD

**TYPE OF CONDUCT DISORDER.**
(To be completed by the clinician after considering all information available)

**Rate the child's aggressive behavior on the following dimensions:**

**Physical aggression**

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
</table>

Typically, aggressive behavior characterized by hitting, use of weapons, or objects.

No aggression.

**Verbal aggression**

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
</table>

Typically, aggression involves verbal attacks.

No aggression

**Reactive**

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
</table>

Aggression typically in response to provocation, rarely planned, impulsive.

**Proactive**

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
</table>

Aggression rarely a response to provocation, typically planned, rarely impulsive.

**Hostile**

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
</table>

Rarely an attempt to achieve a specific goal or obtain an object, typically an act designed exclusively to hurt another.

**Instrumental**

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
</table>

Typically an attempt to achieve a specific goal or obtain an object, rarely an act designed exclusively to hurt another.

**Comments:**

Revised 20/02/97

The Hospital for Sick Children, Department of Psychiatry
Parent Interview for Child Symptoms IV (PICS-4) Disruptive Disorders Module