Toward Understanding Hyperactivity

According to a Harvard study, both inhibitory control and postural dysfunction contribute to the hyperactive component of ADHD. Their differing responses to methylphenidate suggest they may be attributed to different neural circuitries.

**Methods:** Sixty-two boys aged 9–12 years currently or previously treated with methylphenidate (Ritalin) for combined-type ADHD were included in the study along with 62 randomly selected age-matched controls without ADHD. While performing a 15-minute cognitive attention task, patients’ inhibitory control and head movements were recorded using an infrared motion detection system. Inability to maintain head position was considered a sign of postural instability probably related to cerebellar abnormalities. Boys with ADHD were tested at least 18 hours after their last methylphenidate dose and then again 2 hours after receiving a single 0.4 mg/kg dose. Control subjects underwent a single testing session.

**Results:** Compared with healthy controls, the boys with ADHD exhibited significantly more movement during the 15-minute test, indicating inhibitory dyscontrol. After methylphenidate administration, inhibitory control problems resolved. Scores on a measure of postural instability were nearly 5-fold higher in the boys with ADHD. Nearly all children with ADHD (84–90%) had evidence of postural instability during their first testing session, compared with none of the controls. Although improved with methylphenidate administration, boys with ADHD continued to show some postural instability.

Ohashi K, Vitaliano G, Polcari A, Teicher M: Unraveling the nature of hyperactivity in children with attention-deficit/hyperactivity disorder. Archives of General Psychiatry 2010;67 (April):388–396. From Harvard Medical School; and McLean Hospital, Belmont, Mass. Funded by Copley Pharmaceuticals; and OPTAx Systems Inc. Several study authors disclosed commercial relationships that could pose conflicts of interest.

Thalamic Abnormalities in ADHD

Most brain studies in ADHD have focused on the basal ganglia and cortex. However, trauma to the thalamus can produce ADHD symptoms, and stimulants produce electroencephalographic changes that begin in the thalamic nucleus. Taken together, these findings suggest the thalamus may also be involved in the pathophysiology of ADHD.
Methods: A cohort of 105 children and adolescents (46 with ADHD and 59 without) aged 8–18 years underwent high-resolution brain MRI imaging studies. Whole brain volume and surface morphology of the thalamus were measured.

Results: Significant differences were found between youths with and without ADHD in whole brain volumes but not in overall thalamic volumes. Among those with ADHD, the 31 patients receiving stimulant treatment had larger thalamic volumes than those with untreated ADHD. Regional surface volumes in the pulvinar were significantly smaller in those with ADHD overall than in comparison subjects. However, stimulant-treated patients showed pulvinar enlargement compared with patients with untreated ADHD, suggesting stimulant medications may attenuate some of the brain morphology changes associated with ADHD. Patients with severe hyperactivity showed differing regional thalamic volume patterns than those with more severe inattention.

Discussion: These results support the pathophysiological function of the thalamus, particularly the pulvinar, in ADHD. The pulvinar region controls response to auditory and visual stimuli, and structural changes in this region may underlie misdirection of attentional resources associated with ADHD.

Ivanov I, Bansal R, Hao X, Zhu H, et al: Morphological abnormalities of the thalamus in youths with attention deficit hyperactivity disorder. American Journal of Psychiatry 2010;167 (April):397–408. From Mount Sinai School of Medicine, New York, N.Y.; and other institutions. Funded by the Tourette Syndrome Association; and other not for profit sources. One study author disclosed commercial relationships with pharmaceutical industry sources; no other author has relevant financial relationships that might pose a conflict of interest.

Differential Diagnosis in OCD

Childhood OCD is characterized by persistent, recurrent, intrusive thoughts (i.e., obsessions) and/or repetitive ritualistic acts (i.e., compulsions) that cause marked distress or interfere with functioning. These symptoms overlap with other diagnoses including tic disorders, generalized anxiety, autism, and schizophrenia spectrum disorders, and differentiating between them is critical to proper treatment. An expert review provides some guidance on the assessment and diagnosis of OCD in young patients.

In patients with a comorbid tic disorder, differentiating tics from compulsions can be difficult. Simple tics are relatively clear cut. More complex motor tics such as repeated touching or smelling of objects, which involve coordinated movement produced by a number of muscle groups, more closely resemble compulsions. Consideration of precursors and triggers can help determine if an action is a tic or a compulsion. It is important to determine if the action reduces anxiety/distress or relieves an urge as well as the consequences of refraining from completing the action. Distinguishing between tics and compulsions can have important treatment implications; although behavioral therapies for both draw on the same techniques, pharmacological treatments differ. Obsessions should also be evaluated since <2% of patients with OCD present with only compulsions.

Comorbidity with generalized anxiety disorder (GAD) is common in young patients with OCD, and patients with GAD may participate in subclinical ritualistic behaviors. Obsessions are more intrusive than GAD-related worry, which typically involves more normal routine experiences. OCD obsessions typically center on more unusual content and are often socially or personally unacceptable.

Stereotyped and fixated behaviors characterize autism spectrum disorders. Obtaining a complete developmental history including presence and onset of language delays and social difficulties can help differentiate between OCD and autism. There is also substantial overlap...
between behaviors associated with OCD and psychosis; however, the motivation behind the behavior varies greatly. Patients with OCD are likely to have insight into their obsessions and compulsions while those with schizophrenia have little or none. In addition, prepubertal onset of OCD is common, while schizophrenia typically develops later.

Lewin A, Piacentini J: Evidence-based assessment of child obsessive compulsive disorder: recommendations for clinical practice and treatment research. Child Youth Care Forum 2010;39:73–89. From the University of South Florida College of Medicine, Saint Petersburg; and the University of California Los Angeles. Funded by the Joseph Drown Foundation; and Friends of the Semel Institute. Dr. Lewin disclosed a relationship with both study sponsors.

PTSD Practice Parameter

An updated Practice Parameter is now available for child and adolescent posttraumatic stress disorder. The previous American Academy of Child and Adolescent Psychiatry statement was published in 1998.

DSM-IV criteria for a PTSD diagnosis require the patient to be exposed to a qualifying index trauma and at least 1 month later to exhibit at least 1 reexperiencing symptom, at least 3 avoidance symptoms, and at least 2 hyperarousal symptoms. The parameter acknowledges ongoing debate about the appropriateness of the 3 avoidance symptoms requirement for younger patients. PTSD symptoms in young patients can mimic ADHD, panic or other anxiety disorder, oppositional defiant disorder, major depression, and bipolar disorder.

Childhood PTSD can manifest as new-onset aggression, oppositional behavior, separation anxiety, or fears unrelated to the trauma, or as a regression in developmental skills. Factors associated with developing PTSD include female gender, having a previous traumatic exposure, greater exposure to the index trauma, parental psychopathology, and lack of social support. A child’s reaction to trauma may be influenced to a degree by genetic factors. The prevalence of PTSD in the general U.S. youth population is about 9%, but many more children experience subsyndromal symptoms and do not meet full criteria. These children have been shown to have functional impairments similar to those who meet full DSM criteria.

Best treatment practice for PTSD should begin with an age-appropriate screening instrument for patients and their parents. Screening instruments should be administered to parents or caregivers of children aged <7 years because they lack the capacity to recognize pathology. Widely used instruments include the Juvenile Victimization Questionnaire, the UCLA Posttraumatic Stress Disorder Reaction Index, the Child PTSD Symptom Scale, the Trauma Symptom Checklist for Children, and a subset of items of the Child Behavior Checklist. In-depth evaluation that considers differential diagnosis should follow a positive screen. Physical conditions (e.g., hyperthyroidism, migraine, seizure disorder, excessive caffeine intake, certain tumors) can produce symptoms that resemble those of PTSD and should be ruled out. Somatic symptoms such as headache and abdominal difficulties often accompany PTSD.

Treatment of PTSD in young patients should include psychoeducation for both patients and parents, trauma-focused psychotherapy including CBT, and pharmacotherapy when necessary. Coercive therapies such as "restrictive rebirthing" and "holding" are not endorsed. Several trauma-specific psychotherapy protocols have been developed. These are generally based on teaching parenting skills; relaxation; affective modulation; cognitive coping and processing; mastery of trauma reminders; and prevention of future trauma. Trauma-focused CBT and the CBITS (Cognitive Behavior Intervention for Trauma in Schools) program have the strongest empirical support. The manualized Seeking Safety protocol and Eye Movement Desensitization and Reprocessing (EMDR) have also shown some efficacy. The SSRIs paroxetine and sertraline are the only medications approved for adult PTSD, and neither is
indicated for the disorder in children. However, preliminary evidence suggests they may reduce PTSD symptoms in children when used in combination with psychotherapy, and they may be particularly useful in patients with comorbid conditions. It should be noted that SSRIs can produce symptoms of activation, irritability, poor sleep, and inattention that may appear as PTSD hyperarousal in some children. A small number of studies have had some success with risperidone and the antihypertensives clonidine and propranolol. Hypothalamic-pituitary-adrenal (HPA) axis dysfunction may have a role in childhood PTSD and could present a future treatment target.

"American Academy of Child and Adolescent Psychiatry Practice Parameters are developed to assist clinicians in psychiatric decision making. These Parameters are not intended to define the standard of care and should not be deemed inclusive of all proper methods of care or exclusive of other methods of care directed at obtaining the desired results. The ultimate judgment regarding the care of a particular patient must be made by the clinician."


**Managing Inpatient Aggression**

Thirteen studies were reviewed of pharmacological management of aggression in hospitalized children and adolescents, and the authors offer some recommendations based on this limited evidence.

**Antihistamines** may be appropriate for treating behavioral instability and mild aggression. Diphenhydramine can be administered orally, intramuscularly, or intravenously and is usually well tolerated. Although use is common, the only controlled trial found it not superior to placebo at reducing aggression.

**Mood stabilizers** may be effective, but only lithium and carbamazepine have been studied in inpatient populations. Results with both agents have been mixed. Studies have shown a 3–4 week course may be necessary to improve aggression, making mood stabilizers an impractical choice during short hospital stays.

**Conventional antipsychotics** may help control aggression, but studies are limited and adverse effects including dystonia are common in young patients.

**Benzodiazepines** are considered by some to be the preferred treatment for pediatric aggression. However, they carry the potential for abuse and dependence and withdrawal syndromes can be problematic. They can also cause paradoxical reactions that include agitation.

**Atypical antipsychotics** have undergone the most study. Risperidone is considered the safest and most effective atypical antipsychotic for pediatric aggression, but most studies targeted chronic aggression in outpatients. A single study found it effective in inpatients. Ziprasidone has the largest evidence base for inpatients, possibly because it was the first available in an IM formulation, and it has compared favorably with olanzapine and with haloperidol. One small study found oral olanzapine reduced aggression in 3 of 5 treated children, but all patients experienced intolerable adverse effects. A single study evaluated aripiprazole and found it reduced aggression in young patients with conduct disorder. Studies of short-term inpatient quetiapine have not been conducted. Overall, the authors recommend standing use of risperidone or as-needed IM ziprasidone or olanzapine.
**Discussion**: As-needed medications for acute inpatient agitation should be used only after optimized therapy for the primary disorder and/or behavioral interventions have failed. When treatment is necessary, diphenhydramine at a weight-based dose of 25–50 mg may be used for mild aggression. When symptoms are moderate-to-severe, IM ziprasidone or olanzapine may be the best option and should be combined with seclusion/restraints when necessary.

Deshmukh P, Kulkarni G, Barzman D: Recommendations for pharmacological management of inpatient aggression in children and adolescents. *Psychiatry (Edgemont)* 2010;7 (2):32–40. From University Hospitals Case Medical Center, Cleveland, Ohio; and Cincinnati Children’s Hospital Medical Center, Ohio. The study was conducted with no external funding; and the authors have no financial relationships relevant to the article.

**Drug Trade Names**: aripiprazole—Abilify; carbamazepine—Epitol, Tegretol; diphenhydramine—Benadryl, and others; haloperidol—Haldol; olanzapine—Zyprexa; quetiapine—Seroquel; risperidone—Risperdal; ziprasidone—Geodon

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**Childhood Psychotic Symptoms**

A Duke University investigation of a large cohort of preteen twins found psychotic symptoms are heritable and associated with many of the same risk factors as adult schizophrenia. The study provides "the most comprehensive picture to date of the clinical and theoretical significance of children’s self-reported psychotic symptoms."

**Methods**: To test whether children reporting psychotic symptoms share the same risk factors as adults with diagnosed schizophrenia, >2200 12-year-old twins followed from age 5 in a British longitudinal study were assessed for the presence of hallucinations and delusions. Children’s reports were judged as probable or definite psychotic symptoms by the interviewer and confirmed by psychiatric experts. Based on their contributions to adult schizophrenia, familiality; social, neurodevelopmental, home-rearing, and behavioral risk factors; and comorbid conditions were compared between the 125 children with at least 1 definite psychotic symptom and more than 2000 children without definite symptoms.

**Results**: Self-reported psychotic symptoms at age 12 were significantly associated with familial risk factors including maternal psychotic disorders, inpatient psychiatric treatment of family members, and family member suicide attempts (odds ratios* [OR] 1.8–2.5; p≤0.01 for all). Social factors associated with psychotic symptoms were urban residence and socioeconomic disadvantage (OR, 1.5–1.8; p<0.05). Children with psychotic symptoms were significantly more likely to have been born with low birth weight (p=0.04) and to have lower IQ and theory of mind scores (p<0.001). Significant home-rearing risk factors included maternal negativity (p=0.02), household chaos (p≤0.02), and maltreatment (p<0.001). Psychotic symptoms at age 12 were also significantly associated with premorbid antisocial behavior, ADHD symptoms, internalizing problems, social isolation, and educational difficulties at age 5 years (p≤0.04 for all). Compared with children without psychotic symptoms, those with definite psychotic symptoms had significantly more comorbid antisocial behavior, depressive and anxiety symptoms, and suicidal or self-harm behaviors (p<0.001 for all).

In the primary analysis, children with probable psychotic symptoms were grouped with the no-symptom children. When investigated separately, they showed intermediate scores between the symptom-absent and definite-symptom groups. Because the identified risk factors may not be specific to schizophrenia, the primary analysis was controlled for depression and neurological disorders (e.g., migraine, epilepsy). Neither significantly altered the pattern of associations.

**Discussion**: Neurodevelopmental theories of schizophrenia generally focus on negative symptoms. These results suggest positive symptoms should be considered in the model as
well. However, the prevalence of psychotic symptoms (6%) in this cohort was markedly higher than the population prevalence of childhood-onset schizophrenia, suggesting some but not all children with psychotic symptoms who are exposed to these genetic and environmental risks will convert to clinical schizophrenia.

This study has implications for both research and clinical practice. The findings suggest children with psychotic symptoms can be recruited for research into the pathogenesis of schizophrenia before prodromal symptoms surface and prior to the rapid neurodevelopmental changes that occur during adolescence. Clinically, the findings underscore the importance of assessing psychotic symptoms in preadolescents and the need to address the predisposing familial, social, neurodevelopmental, and other risks. Interventions at this early stage should be investigated.


*Reference Guide Item.

Reference Guide

Odds Ratio: A comparison of the probability of an event in two groups. An odds ratio of 1 implies that the event is equally likely in both groups. An odds ratio greater than 1 indicates that the event is more likely to occur in that group than in the comparison group.

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