According to a review of neurobiological studies, considerable progress has been made in understanding the neurobiology of conduct disorder (CD) and oppositional defiant disorder (ODD), together referred to as the disruptive behavior disorders (DBDs). The disorders can be understood in a conceptual framework of deficits in 3 mental domains: punishment processing, reward processing, and cognitive control. This conceptualization in terms of functional domains allows for the consideration of environmental factors, such as parenting and peer group characteristics.

Lack of punishment fear in children can reduce the effectiveness of aversive conditioning that is crucial in learning to avoid undesirable behavior. In DBDs, this learning process can be impaired due to a lack of appropriate punishment by adults and by diminished punishment sensitivity in the child. In children and adolescents with DBDs, reduced sensitivity to punishment has been associated with altered autonomic nervous system function, as shown in studies of electrodermal fear conditioning, and with reduced cortisol reactivity to stress, altered serotonergic and noradrenergic neurotransmission, and, with less consistent evidence, deficits in the regulation of emotions by the amygdala. Failure to make the connection between inappropriate behavior and punishment has been observed beginning in early childhood in children who develop DBDs.

Impaired reward processing can manifest as reduced sensitivity to pleasant stimuli in young patients. The results include thrill- or sensation-seeking, such as engaging in risky or antisocial behavior and illicit drug use. Reduced sensitivity to rewards may impair the teaching of appropriate behavior. Neurobiologic correlates of this deficit include autonomic nervous system markers and decreased dopaminergic function. The orbitofrontal cortex may also play a predisposing role.
In contrast to punishment and reward processing, which are influenced by limbic brain structures, conscious control of behavior is the province of frontal cortical structures. Executive function—the explicit control of thought, emotion, and action—includes such processes as planning, inhibition of inappropriate responses, flexibility in changing circumstances, and making decisions. DBDs are associated with structural deficits and impaired function of the paralimbic system: the orbitofrontal cortex, superior temporal lobes, and cingulate cortices. Impairment in executive function has been shown in children with DBDs, especially in situations involving reward and punishment.

Symptom clusters in ODD and CD differ somewhat, contradicting the common belief that ODD is a less severe or transitional form of CD. A defiant/headstrong behavior cluster (e.g., argues with adults, deliberately annoys people) may be specific to CD, while ODD may be a mixed disorder of behavior and emotion, characterized by an irritability behavior cluster generally associated with anxiety and mood disorders.


From University Medical Center Utrecht; and Utrecht University, The Netherlands. Source of funding not stated. The study authors did not disclose potential conflicts of interest.

Gene Modifies Effect of Childhood Abuse

In young women, a polymorphism of the cannabinoid receptor gene was predictive of a relationship between childhood physical abuse and the eventual development of anhedonia and anhedonic depression.

Methods: The study was conducted in a sample of young U.S. women and then repeated in Australian women with heroin dependence. The U.S. study subjects were 1041 participants in an ongoing twin study, born between 1975 and 1985, and aged 18–29 years at the time of follow-up. The Australian participants were 1428 young women, aged ≥18 years, who had undergone opioid replacement therapy for heroin addiction, and 506 neighborhood controls. In both studies, a history of childhood physical abuse and emotional symptoms was assessed using the Semi-Structured Assessment for the Genetics of Alcoholism. Women were genotyped for the rs1049353, a gene that encodes the human cannabinoid receptor and that was previously shown to moderate stress adaptation in animal models.

Results: In the U.S. study, which used a dichotomous measure of childhood physical abuse, rates of anhedonia (22%), major depression (18%), and past abuse (9%) were as expected in a young female population. Childhood physical abuse was strongly associated with anhedonia, but this effect was modified by the cannabinoid receptor genotype. In the 501 women homozygous for the major allele, there was a strong association between abuse and anhedonia (odds ratio,* 5.09). Among these women, anhedonia was present in 57% with a history of childhood abuse and in 21% without such a history. In women who were homozygous for the minor form or heterozygous, there was no association between childhood abuse and anhedonia. A similar interaction was shown between abuse, genotype, and major depressive disorder, but this relationship was largely explained by the presence of anhedonia as a symptom of depression.

In contrast with the U.S. women, a continuous measure of childhood abuse was used in the Australian sample. Analysis of these women essentially replicated the U.S. results, both for the stress-buffering effect of the gene on the relationship of childhood abuse to anhedonia and on the direct relationship to anhedonia rather than depression.

Discussion: Several other candidate genes have been investigated as possible mediators of the effects of stress, including the monoamine oxidase-A gene and a gene that regulates glucocorticoid sensitivity.
coid receptor sensitivity. Results of the present study suggest that future genetic studies should focus narrowly on anhedonia when examining the effect of childhood adversity on depression.

Agrawal A, Nelson E, Littlefield A, Bucholz K, et al: Cannabinoid receptor genotype moderation of the effects of childhood physical abuse on anhedonia and depression. *Archives of General Psychiatry* 2012;69 (July):732–740. From Washington University School of Medicine, St. Louis, MO; and other institutions. Funded by the NIH; and other sources. The study authors did not disclose potential conflicts of interest.

*See Reference Guide.

### Parents' Decisions About ADHD Medication

A focus-group study identified multiple factors that influence parents' decision to initiate medication for a child with ADHD. Typical themes found in the focus groups included ambivalence about stimulant medication, divergent opinions on how much information is enough, and trying alternative treatments before deciding to use medication.

**Methods:** The focus groups were conducted at a child psychiatry clinic in a suburban Northeastern teaching hospital. Participants were the parents or caregivers of children, aged 5–12 years, who had received a diagnosis of ADHD. Eligible parents of 96 children were asked to participate, but data collection was ended after the first 5 groups, with 27 participants, because the results were homogeneous and there was little likelihood of uncovering further new information. Focus groups were 2 hours long and conducted by child psychologists with experience in the method. Transcripts of the discussions were analyzed.

**Results:** The parents were a mean age of 45 years, and the children were a mean age of 9 years. The majority of the parents (82%) had at one time pursued medication, and 70% of the children were currently taking stimulants. Each focus group contained some parents who had decided to forego or discontinue medication.

Three main themes emerged from the discussions:

- Medication adherence was defined variably. Parents initially reported high compliance, but deviations, such as skipping or reducing a dose on days without structured plans, often emerged with further discussion.

- Participants reported positive attitudes, mainly about the immediate and long-term effects of medication, as well as concerns, primarily about stigmatization, safety, and undesirable modification of the child's personality. Another common theme that emerged was that parents often wanted to defer initiation until the child had tried treatments such as behavior modification, social skills training, or nutrition therapy.

- Attitudes about medical providers varied. Many parents reported appreciating professionals who made them feel a part of shared decision making, while remaining mindful that the parents should be the ultimate decision makers. Some parents wanted comprehensive information about ADHD, while others only wanted to know what was absolutely necessary. Expertise, empathy, and compassion were the qualities most highly valued in health professionals.

**Discussion:** The study authors recommend that professionals thoroughly assess parent attitudes to medication before recommending drug treatment. More individually targeted communication about medication may help minimize the long delay that appears to be part of the decision process.

Coletti D, Pappadopulos E, Katsiotas N, Berest A, et al: Parent perspectives on the decision to initiate medication treatment of attention-deficit/hyperactivity disorder. *Journal of Child and Adolescent Psychopharmacology* 2012;22 (June):226–237. From the Zucker Hillside Hospital, Glen Oaks, NY; and other institutions including Pfizer, Inc. Funded by the NICHD. Several study authors disclosed financial relationships with commercial sources.
Psychopharmacology of "Anxiety Triad" Disorders

Anxiety disorders often first emerge during childhood and adolescence and adversely affect relationships and school function, as well as increase the child’s risk of suicidal ideation. These disorders are underdiagnosed and undertreated in youths. Neuroimaging, genetic, and physiologic markers currently under investigation may lead to improved understanding of the disease and patient-specific treatments.

Clinical trials in youths with non-PTSD, non-OCD anxiety disorders have focused on the "anxiety triad"—separation anxiety disorder (SAD), generalized anxiety disorder (GAD), and social phobia. These 3 disorders are highly comorbid, physiologically distinct from other anxiety disorders, and similarly responsive to drugs and cognitive behavioral therapy (CBT). There have been clinical trials of medications and CBT in youths with pure forms of the disorders, comorbid forms, and mixed populations. Most trials of psychotherapy have evaluated CBT, with positive results. Other forms of psychotherapy remain understudied in youths with anxiety disorders, even treatments that are effective in other pediatric mental disorders.

SSRIs are considered first-line medication for pediatric anxiety disorders. Preliminary evidence also supports the use of SNRIs, such as venlafaxine, in GAD and social phobia. Tricyclics are not recommended for the anxiety triad disorders. Benzodiazepines have not been well studied, but limited evidence suggests they may be useful adjuncts to SSRIs in the acute treatment phase. There have been few studies of long-term use of any medications for pediatric anxiety, but limited evidence suggests that ongoing use provides continued efficacy with manageable side effects. The literature has shown significant positive synergy for medication and psychotherapy, and current treatment guidelines recommend a multimodal approach.

Recent research suggests that SSRIs and CBT work by modulating fear circuits in the anterior limbic region of the brain. These findings may lead to studies that predict treatment response based on neural responses to tasks observed on functional MRI. Genetic markers with potential to predict response have also been identified—e.g., genes that encode a particular variant of the glutamate receptor or the serotonin transporter gene. Biosignatures—panels of genetic, neuroimaging, and/or physiologic markers—may be used in the future to individualize treatment. Given that 20–30% of youths with anxiety disorders do not respond to SSRIs and CBT, drugs with other mechanisms should be evaluated. These include glutamatergic modulators (e.g., D-cycloserine, memantine, minocycline) and anti-adrenergic drugs (e.g., guanfacine, clonidine), some of which are under investigation in adults with anxiety disorders.

Mental Issues Lead Pediatric Disabilties

According to 2008–2009 data from the U.S. National Health Interview Survey (NHIS), mental problems outweigh physical problems as a cause of disability in American children, for the first time since these data were collected. The 5 most common disabilities affecting U.S. children are now mental-health issues.

The overall prevalence of childhood disability has increased 4-fold since 1960, according to the NHIS. In the most recent survey, 8% of children aged <18 years were reported to have a health problem that limited their usual activity. The most frequently reported problem categories were: speech problems; learning disability; ADHD; other emotional, mental, and behavioral
problems; and other developmental problems. Parents of children with disability reported that these problems contributed to their child's disability about 20% of the time. Asthma was the 6th most prevalent problem and the leading cause of physical disability.

Many potential explanations for the shift have been suggested. Parents are pushing children to a higher standard of achievement, and many cannot acquire the emotional and cognitive skills as quickly as their parents would like. Parents may push for a struggling child to be diagnosed with ADHD so that the child's academic performance can be improved with stimulants and special accommodations. Physicians are diagnosing learning disabilities more often because of better diagnostic tools, lower diagnostic thresholds, and children's greater access to screening. Increased rates of premature birth and exposure to toxins during early life may have contributed to a true rise in prevalence of these disabilities, as may increasing rates of divorce and family conflict.

There is a mismatch between the needs of children with emotional or learning disabilities and the services offered by the current health care system. Only about half of these children receive any services. Many times a problem first recognized in early childhood may not receive any attention until older childhood, when it has grown too serious to ignore. In addition, there are too few child psychiatrists to address the needs of all children with mental disabilities. A shift toward preventing children’s mental disabilities, although difficult to implement, may be more effective than treating them.


**Pediatric Gender Identity Disorder**

The American Psychiatric Association first introduced gender identity disorders (GID) as a diagnostic category in 1980. Other than the DSM inclusion, the APA has released no other official statement on these diagnostic entities. At present, no organization provides recommendations for the treatment of GID, despite acknowledgement that mental health care is an important part of the multidisciplinary approach to this disorder. A literature review was conducted by an APA task force to determine if sufficient evidence exists to compile an evidence-based Practice Guideline on the treatment of GID.

A minority of children with GID will identify as transsexual or transgender in adulthood, even without treatment. Most will become comfortable with their gender over time. However, if GID persists into adolescence, it is more likely to continue into adulthood. Those with the onset of GID in adolescence are more likely to manifest significant comorbid psychopathology. These patients should be screened carefully to detect a history of trauma as well as for any disorder that may produce gender confusion (e.g., schizophrenia, mania, psychotic depression). When present, comorbid disorders must be addressed.

For various reasons (e.g., social stigma, likelihood of hormonal and surgical procedures), persistence of GID is considered undesirable. No long-term data are available suggesting that any treatment modality significantly affects later gender identity, and it is not currently possible to differentiate between preadolescent children in whom GID will persist and those in whom it will not.

Opinions differ on whether or not minimization of gender atypical behaviors and prevention of adult transsexualism are acceptable goals of therapy. Currently, the primary goal of psychotherapeutic treatment for childhood GID is to optimize the psychological adjustment and well-being of the child. Primary modes of therapy for pediatric GID include individual insight-oriented psychoanalytic or psychodynamic psychotherapy; protocol-driven psychotherapy such as behavior modification; parent and peer-relations focused therapy; and parent and child therapeutic groups. Additional interventions include support groups for primary caregivers,
community education, and school-based curricula; and instruction in techniques for building self-acceptance and resilience in the child.

Very few studies have systematically evaluated any intervention in GID, and no studies have systematically compared different interventions. Contingency management, including punishment of feminine behaviors, in young boys showed a short-term decrease in gender non-conforming behaviors, but long-term follow-up was not reported. Pharmacological suspension of puberty may allow the clinician and patient more time to explore the continuing evolution of gender identity, but the safe duration of suspension is unknown. Substantial brain maturation occurs during adolescence, and concerns have been raised over possible cognitive deficits associated with pubertal suspension.

Although the evidence is insufficient to draft a formal guideline, the task force did recognize the following as major tasks for mental health professionals working with children referred for gender concerns:

- Accurate evaluation of the gender concerns that precipitated referral
- Accurate diagnosis of gender identity related disorders according to the criteria of the most current DSM
- Accurate diagnosis of coexisting psychiatric conditions and problems in the parent–child relationship along with recommendations for their appropriate treatment
- Provision of psychoeducation and counseling to the caregivers about the range of treatment options and their implications
- Provision of developmentally-appropriate psychoeducation and counseling to the child
- When indicated, to engage in psychotherapy with the appropriate persons, such as the child and/or primary caregivers, or to make appropriate referrals for these services
- Education of family members and institutions about GID
- Safety assessment of family, school, and community environments, in terms of bullying and stigmatization, and development of protective measures.


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**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.