Exposure Therapy for Single-Incident Trauma

A developmentally modified version of Prolonged Exposure therapy significantly reduced symptoms of posttraumatic stress disorder (PTSD), as well as anxiety and depression, in a small group of children with single trauma exposure.

Methods: Patients were 15 consecutively referred children (mean age, 11 years; 13 females) who had experienced a single event trauma (i.e., motor vehicle accident, circumstantial injury, sexual or nonsexual assault) ≥3 months in the past. All met criteria for PTSD based on the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS-PL). Comorbid conditions included generalized anxiety disorder; social phobia; specific phobia; panic disorder; oppositional defiant disorder; and parent-child relational problem. The mean time since the traumatic occurrence was 13.5 months.

All study patients underwent Trauma Mastery Therapy (TMT), a modified version of a manual-based cognitive behavioral exposure therapy for PTSD. The TMT protocol is modular, allowing clinicians to present ≥1 modules per session based on the patient’s individual needs. Treatment comprises psychoeducation and treatment planning, followed by exposure, and then relapse prevention. The number of treatment sessions varies from 7 to 16 based on the number of modules addressed in each. Patients were assessed after completion of each phase.

Results: At study end, 13 of the 15 patients (87%) no longer met K-SADS-PL criteria for PTSD. Mean patient-rated Child PTSD Symptom Scale (CPSS) scores decreased from 31 at baseline to 22 after psychoeducation, and further to 10 after exposure therapy. The mean final CPSS score at 1-month follow-up was <8. Improvements in the parent-rated version were similar. Both child- and parent-rated Child Depression Inventory scores decreased from about 15 points at baseline to 4 after treatment (p<0.01). Patients reported significant improvements in anxiety on the Multidimensional Anxiety Scale for Children (from 57 to 19; p<0.01). Although parents also reported improvement on this scale, the change was not statistically significant.
Discussion: The authors suggest the flexible modular approach of TMT may underlie its success, with exposure being the major contributing factor. Although the findings are preliminary, the positive results in this small series of patients suggest TMT may be a promising treatment for single-incident trauma in young patients.

Nevo G, Manassis K: An adaptation of prolonged exposure therapy for pediatric single incident trauma: a case series. *Journal of the Canadian Academy of Child and Adolescent Psychiatry* 2011;20 (May):127–133. From Sunnybrook Health Sciences Centre, Toronto, Ont., Canada; and other institutions. Funded by the Hospital for Sick Children, Toronto, Ont., Canada. The authors did not disclose potential conflicts of interest.

Executive Impairment and Stimulant Response

The effects of methylphenidate differed in youths with ADHD depending on the presence and severity of executive impairment. This finding suggests inattention symptoms may have multiple causes, possibly requiring different treatments.

Methods: Study subjects were 56 students, aged 6–16 years, who had been referred for double-blind trials of methylphenidate (*Ritalin*). ADHD diagnosis was based on a semi-structured diagnostic interview, DSM-IV criteria, and behavioral rating scales, and patients were required to have significant impairment in both home and school settings. Participants were observed during a baseline period, followed in random order by trials of placebo, low-dose methylphenidate (0.15 mg/kg b.i.d.), and high-dose methylphenidate (0.30 mg/kg b.i.d.). Each study period lasted 4 weeks. Neuropsychological tests were administered on the last day of each treatment phase. The outcome of interest was an executive impairment score calculated using multiple standardized measures administered by blinded raters. The effects of methylphenidate were analyzed in groups segregated by degree of baseline executive impairment.

Results: Methylphenidate had no effect on cognitive symptoms and little effect on behavioral symptoms in the 9 children with no apparent executive impairment. Methylphenidate had positive effects on both symptom clusters in each of the 10 youths with significant impairment. Patterns of response differed between the other groups. In the 21 patients with mild executive impairment, cognitive and behavioral symptoms showed no improvement at the low methylphenidate dose but significant improvement with the higher dose. The 16 patients with moderate executive impairment experienced significant and equivalent cognitive improvement with both methylphenidate doses. Behavioral symptoms in this group improved somewhat with the lower dose and significantly with the higher dose. A placebo effect on behavioral symptoms was observed in patients with no apparent executive impairment and in those with mild or moderate impairment.

Discussion: These findings support response inhibition associated with executive impairment as a primary deficit in ADHD. In the groups with moderate and significant cognitive impairment, the best methylphenidate dose for cognition was lower than the best dose for behavior. However, the authors caution that higher methylphenidate doses may impair cognition by limiting executive attention control and working memory functions. The differential dose-response relationship may explain why long-term treatment of ADHD has had limited success in improving academic achievement if prescribers are focusing on controlling behavior.

Study Rating—15 (88%): This study met most criteria for a randomized controlled trial. However, not all sources of study funding were disclosed.


*See Reference Guide.
Predictors of Suicide Attempt in Adolescent Depression

According to a secondary analysis of ADAPT (Adolescent Depression Antidepressants and Psychotherapy Trial) data, predictors for nonsuicidal self-harm differ from those for suicide attempt, and nonsuicidal self-injury, rather than previous suicide attempt, is the strongest predictor of subsequent suicide attempt.¹

Methods: Study subjects were 164 adolescents, aged 11–17 years, with major depressive disorder who participated in the ADAPT study of cognitive behavioral therapy, SSRIs, and specialist care in adolescents. Suicide attempts and suicidal and nonsuicidal self-harm were assessed at baseline and during 28 weeks of follow-up. Family functioning and severity of depression were also assessed.

Results: During the month before study entry, 58 adolescents (36%) had at least 1 episode of nonsuicidal self-harm and 28 adolescents (17%) had made at least 1 suicide attempt. During the 28-week follow-up, 60 participants (37%) had at least 1 episode of nonsuicidal self-harm and 50 participants (30%) attempted suicide. Multivariate analysis found previous nonsuicidal self-injury (odds ratio* [OR], 20.3), female gender (OR, 4.8), hopelessness (OR, 3.7), and anxiety disorder (OR, 3.7) independently and significantly predicted nonsuicidal self-harm. Nonsuicidal self-harm (OR, 3.2) and poor family functioning (OR, 2.1) were the only significant independent predictors of suicide attempt during follow-up. Severity of depressive symptoms also appeared to predict self-harm, but not suicide attempt.

Discussion: Nonsuicidal self-harm is generally considered less serious than suicide attempts. The results of this study suggest that self-harm and the factors that predict it deserve more attention because self-harm is a strong predictor of suicide attempt in adolescents with moderate-to-severe depression. Treating depression may reduce the risk of nonsuicidal self-harm, but family function should also be addressed in efforts to prevent suicide attempts.²


*See Reference Guide.

Antipsychotics for Non-Psychotic Disorders: Safety and Efficacy

Second-generation antipsychotics (SGAs) show similar efficacy in nonpsychotic disorders but differ in their safety profiles. The choice of a specific agent should be guided by the individual patient’s risk for expected adverse effects.

Background: In pediatric patients, only 14% of SGA use is for psychotic disorders; the rest is for disruptive behavior disorders, mood disorders, and, to a lesser extent, pervasive developmental disorders and mental retardation. Their use has increased significantly in patients as young as 2–4 years. The perception of relative safety has contributed to the growing use of SGAs to treat nonpsychotic disorders in children and adolescents.

Methods: A total of 32 randomized controlled trials of SGAs in the treatment of nonpsychotic disorders in patients under age 18 years were reviewed. None of the studies compared active medications. Because the studies lacked a common measure of efficacy, the authors calculated effect sizes* and the number needed to treat* (NNT) to compare efficacy outcomes. Adverse effects were compared using the number needed to harm* (NNH).
Results: The SGAs had comparable efficacy in nonpsychotic disorders, although the weight of evidence differed. Quetiapine was studied more extensively in bipolar disorder, and risperidone in pervasive developmental disorders. SGAs were effective in treating mania, extreme mood lability, irritability, and aggression, all with large effect sizes. (See table.)

SGAs were generally well tolerated in short-term clinical trials, but the adverse effects of greatest concern tend to develop after long-term exposure. Therefore, additional safety evidence was obtained from open-label comparative studies and schizophrenia clinical trials.

Risks of SGA-related weight gain and adverse metabolic effects were similar in children and adults. Although all SGAs can cause significant weight gain, olanzapine is the most likely to do so, with an NNH of 2–3, while aripiprazole is the least likely, with an NNH of 25–30. Risperidone and quetiapine had NNH estimates for significant weight gain of 7–8 and 10, respectively. Olanzapine also worsened glucose and lipid parameters to the greatest extent; risperidone adversely affected triglycerides but not glucose; quetiapine worsened a broad range of lipid parameters; and only aripiprazole did not adversely affect lipids or glucose. The authors recommend monitoring of weight, body mass index (BMI), and multiple glucose and lipid variables, beginning 3–4 months after the start of medication and semi-annually thereafter. Obesity, BMI, and a family history of diabetes or cardiovascular disorder should be considered when choosing an SGA.

All antipsychotic drugs can increase prolactin. Risk of hyperprolactinemia is highest with risperidone (NNH estimates range from 9 to about 50) and lowest with aripiprazole. Hyperprolactinemia tends to be dose-dependent and may subside with continued treatment; the clinical implications are not clear. Routine prolactin monitoring is not recommended, but patients should be followed for sexual adverse events.

Agents differ in their propensity to induce sedation: highest for quetiapine and lowest for aripiprazole. Tolerance to this effect usually develops early in treatment. Children are more likely than adults to have extrapyramidal adverse effects of SGAs, although there is little information suggesting different liability with different drugs. Reports of ECG abnormalities in pediatric patients taking ziprasidone make this agent a second- or third-choice drug in young patients.


*Drug Trade Names:* aripiprazole—*Abilify*; olanzapine—*Zyprexa*; quetiapine—*Seroquel*; risperidone—*Risperdal*; ziprasidone—*Geodon*

**Review: Psychocutaneous Disorders**

Disorders that combine psychiatric and skin manifestations have a wide spectrum of expression. It is important to recognize and treat the underlying psychopathology in children with psychocutaneous disorders. The most common underlying psychopathologies for primary...
psychiatric disorders with dermatologic manifestations are anxiety, depression, obsessive-compulsive disorder (OCD), and impulse-control disorder. Impulse-control disorder and OCD each may underlie the same repeated behaviors that damage the skin.

Trichotillomania, a repetitive irresistible urge to pull out one’s hair, is the most common psychocutaneous disorder seen in children and adolescents, primarily girls. It can occur at any age (mean age at onset, 9–13 years), but it may be a normal, self-limited habit in children under 5 years. Diagnosis is based on clinical presentation and usually confirmed by the patient’s acknowledgement or caregiver observation. Blunt accusation of the child can be harmful; instead the cause of hair loss should be discussed gently and the child should be given a chance to express his/her emotional needs. Psychotherapy and behavioral techniques like habit-reversal therapy are successful in the majority of patients. Clomipramine may be useful, and SSRIs may be tried if there are underlying anxiety or depressive symptoms.

Psychogenic excoriation refers to a range of symptoms characterized by repetitive skin picking. It is characterized clinically by symmetric linear excoriations on accessible parts of the body (the upper lateral back is usually spared), sometimes in association with preexisting lesions such as acne or insect bites. Treatment may include psychotherapy, behavioral therapy, sympathy, and pharmacotherapy. Few data are available on drug treatment of psychogenic excoriation in children. SSRIs, tricyclic antidepressants, atypical antipsychotics, and opioid antagonists have all been tried. Doxepin, an antidepressant that has anti-itching effects, might be tried if itching is present. Other anxiety-related psychocutaneous disorders include acne excoriee (picking of acne lesions), dermatophagia (skin biting), and onychophagia (nail biting). SSRIs, clomipramine, and doxepin have been used for acne excoriee. Hypnotherapy may reduce skin biting. Behavioral therapy, including habit-reversal training, may reduce nail biting, and SSRIs or clomipramine may be useful.

Other psychocutaneous disorders, such as factitious dermatitis and delusions of parasitosis, can also occur but are fairly uncommon in pediatric patients.

Al Hawsawi K, Pope E: Pediatric psychocutaneous disorders: a review of primary psychiatric disorders with dermatologic manifestations. American Journal of Clinical Dermatology 2011; doi 10.2166/11589040. From the Hospital for Sick Children, University of Toronto, Ont., Canada. This review was conducted with no external funding. The authors disclosed no conflicts of interest.

Drug Trade Names: clomipramine—Anafranil; doxepin—Adapin, Sinequan

### Clozapine for Aggression in Autism

Results of a retrospective review suggest that treatment with clozapine can reduce the number of days with aggressive behavior in patients with autism spectrum disorder or pervasive developmental disorder (PDD).

**Background:** Risperidone and aripiprazole are the only medications FDA approved to control irritability in patients with autism. Both agents have been shown to reduce aggression, tantrums, and self-injurious behavior in this population, but 30–50% of patients do not respond to treatment. Several case reports of improved disruptive behavior in patients treated with clozapine prompted the present analysis.

**Methods:** Records were reviewed for all inpatients with autism (n=3) or PDD (n=3) who received clozapine for disruptive behavior at a single psychiatric hospital between 2002 and 2010. The 6 patients (4 females) had received the diagnosis of autism or PDD between the ages of 2 and 5 years. Most patients (n=4) began clozapine treatment as either an adolescent or young adult (aged ≤21 years). Commonly exhibited behaviors, as reported by nursing staff, included destroying objects (n=4) and assaulting others (n=4); and self-harm was observed in 1. All patients had been treated with conventional antipsychotics, and 5 of the 6 had received risperidone. The effects of clozapine were examined over 8–12 months.
**Results:** Prior to starting clozapine, the proportion of days with any aggressive behavior ranged from 10% to 35% (mean, 19%). The number of days with aggressive behavior was significantly reduced, nearly 2-fold, with clozapine to a mean of 11%. Object destruction and assault on others were both significantly reduced, but self-harm was not affected in the single patient with self-injurious behavior. The number of antipsychotic drugs was also decreased overall. Before clozapine patients received 0–3 antipsychotic drugs, but during the treatment period no patient received an antipsychotic other than clozapine. All patients were discharged from the hospital and moved to specialized care settings for patients with autism spectrum disorders. Clozapine was generally well tolerated. Constipation was common, affecting 5 of the 6 patients, but it was easily managed. No agranulocytosis or other life-threatening adverse effects were observed. Although metabolic syndrome developed in only 1 patient, the mean weight gain was large (>31 lbs). One patient experienced tachycardia after starting clozapine, but it was managed with a beta-blocker.

**Discussion:** Clozapine appears to produce significant improvement in disruptive behaviors. Although it was well tolerated in these patients, clozapine should not be used as first-line treatment for disruptive behavior in autism or PDD because of the potential for serious adverse effects. The authors suggest that in spite of study limitations (e.g., retrospective design, small sample), the present results indicate clozapine may be useful as a second- or third-line option.  

Beherec L, Lambrey S, Quilici G, Rosier A, et al: Retrospective review of clozapine in the treatment of patients with autism spectrum disorder and severe disruptive behaviors. *Journal of Clinical Psychopharmacology* 2011;31 (June): 341–344. From the Centre Hospitalier du Rouvray, France; and other institutions. The study was conducted with no external funding. The authors disclosed no competing interests.

**Drug Trade Names:** aripiprazole—Abilify; clozapine—Clozaril; risperidone—Risperdal

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**Reference Guide**

**Effect Size:** The effect size represents the amount of change in outcome that can be attributed to treatment, where 0.2 indicates a small effect, 0.5 a medium effect, and 0.8 a large effect. It is relatively independent of clinical significance and large effect sizes do not ensure treatment efficacy.

**Number Needed to Harm:** A measure of how many patients need to be exposed to a risk factor to cause harm in 1 patient that would not otherwise have been harmed. Lower NNH indicates more attributable risk.

**Number Needed to Treat:** Indicates how many patients need to be treated for 1 to benefit. The ideal NNT is 1, where everyone improves with treatment. The higher the NNT value, the less effective is the treatment.

**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.

**Study Rating:** A measure of how well a study conforms to quality standards. The study rating uses a checklist system based on the comprehensive Strength of Evidence Report from the Evidence-based Practice Center Program of the Agency for Healthcare Research and Quality (AHRQ). The rating checklists have been posted at www.alertpubs.com.