

New Research in Depression and Anxiety

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Introduction

Depression and anxiety are some of the most common disorders of childhood and adolescence. New research in these areas explores important issues, such response to antidepressant medication, understanding the impact of early stressful experiences on later depression, symptoms in children of mothers with depression, and the impact of gender differences on depression and suicide.

Major Depressive Disorder and Response to Sertraline in Children and Adolescents

Although selective serotonin reuptake inhibitors are considered the pharmacotherapy of choice for children and adolescents with major depressive disorder (MDD), there is still no detailed analysis of how well these drugs are tolerated in this population. The study by Donnelly and colleagues^[1] examines 371 children receiving blinded treatment for up to 10 weeks and 221 treated in a 24-week, open-label extension study. Efficacy was evaluated using the Children's Depression Rating Scale -- Revised (CDRS-R) total score on children (age, 6-11 years) and adolescents (age, 12-17 years). Patients were included in the study if they had baseline CDRS-R scores of at least 45 and a diagnosis of MDD for at least 6 weeks before entry into the double-blind, short-term arm of the study. Safety was assessed by adverse events, changes in laboratory tests, and vital signs. Although some adverse events were found to occur more frequently in sertraline-treated patients (eg, insomnia, diarrhea, anorexia), there were no clinically significant changes in laboratory values, and the drugs were found to be safe in these age groups. Sertraline treatment showed statistically better efficacy in adolescents with MDD and numerically, but not statistically, significant improvement in children during the blinded portion of the study. Both age groups showed continued symptom improvement through the open-label study. These results support the use of selective serotonin reuptake inhibitors in children and adolescents with MDD.

Early Stressful Experiences and Dysthymia

Using epidemiological data, researchers from the Instituto Nacional de Psiquiatria in Mexico City^[2] performed a study to understand the association between dysthymic disorder (DD) and stressful experiences before the age of 15 years. The criteria included familial and social environmental experiences and used epidemiological data.

A community sample of 1932 adults was screened using the University of California at Fresno Composite International Diagnostic Interview. Comparisons from a final group (N = 1452) were made among those diagnosed as having DD (N=104; 27 males, 77 females), those who self-reported stressful early familial and social experiences (n = 104; 27 males, 77 females), and those who had no psychiatric diagnosis (n = 1348; 550 males, 798 females). Analysis was made using SPSS 7.5 and EPI Info 5.01 statistical software.

The study showed that men experience more stress in relationships than do women in all areas. Some of these areas included relationships with parents, social situations, work, and responsibilities. All results were statistically significant ($P < .001$). The study also showed that these factors represent more risk for men than women. Those with DD had a stronger association to stressful situations.

Symptoms in Children of Depressed Mothers

A study by Broitman and colleagues^[3] was designed to assess the rates and types of psychiatric symptoms in children of depressed mothers (DEP) compared with those of nondepressed mothers (NDC). Using the Schedule for Affective Disorders and Schizophrenia for School Aged Children (KSADS) Present & Lifetime version, a group of children ages 8 to 11 years (N=42) and their mothers were sampled. Advanced psychology graduate students who were unaware of the mother's mood status visited the subjects at their home and administered the KSADS. After diagnosis was established by combining the reports of both the mother and child, the results were determined by a clinical psychologist based on the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*.

The study found a significantly higher occurrence of mood, anxiety, and disruptive disorders in children of DEP than the children of NDC. According to the investigators, "More than 20% of children of DEP have both internalizing and disruptive disorders diagnoses." The children of DEP had more symptoms on the threshold level but not subthreshold-level symptoms on the KSADS screener.

Results showed that a mother's depressive status should be evaluated, because it is associated with increased risk among children. This extends beyond risks for childhood depression but includes anxiety and disruptive symptoms as well.

Maternal Depression and Impact on Children: STAR-D Study

A study by King and colleagues^[4] describes the Sequenced Treatment Alternatives to Relieve Depression (STAR-D) study, a multisite study of the impact of maternal depression remission or symptom reduction on children. The initial samples of 68 mother-child pairs were recruited from the STAR-D study from 7 centers. The mean ages of mother and child were 37.5 years (SD, 6.8 years) and 11.3 years (SD, 2.8 years), respectively. The age range for children was 8 to 17 years. Ethnicity distribution was as follows: white, 57.4%; black, 42%; Hispanic, 7.4%; and Hawaiian, 1.5%.

According to the authors, "Mothers were assessed at baseline and followed every 3 months until one year after remission (or 24 months if they do not remit)." Children were assessed every 3 months and assessments included the following measures: KSADS Present & Lifetime version, Child Behavior Checklist, Children's Global Assessment Scale, Social Adjustment Inventory for Children and Adolescents, and various techniques for family adjustment assessment. The STAR-D study collects measures of maternal depression, adjustment, and treatments.

The results showed the mean baseline Hamilton Depression Rating Scale score for mothers was 24.6, and the mean Children's Global Assessment Scale score for children was 70.4. The number of children who met criteria for MDD (8.8%), attention-deficit/hyperactivity disorder (ADHD) (17.6%), and various other anxiety disorders was significant. The STAR-D study shows promise in the better understanding of the impact of maternal depression remission on children.

Depression Screening and Pharmacogenomics

To better individualize dosing management of psychotropic medications for children and adolescents, pharmacogenomic strategies are being used. Accurate definition of cytochrome P450 polymorphisms status can be provided through microassay technologies. Many studies have shown that by using traditional polymerase chain reaction assays, one can demonstrate the predictable differences in the activity level of various P450 enzymes. However, new microassay methods have made the assessment of the allelic status of P450 genes more practical and affordable. A study by Mrazek and colleagues^[5] shows that the atypical polymorphisms have been linked to problematic psychotropic medication responses. In identifying these genotypes, better implementation of clinical dosing strategies may result.

Using a novel microassay technology, the determination of the alleles of the cytochrome P450 system were achieved. High allelic variability was shown in a sample of 12 children. Atypical 2D6 haplotypes were found in all 12 patients. A strategy for reduction of medication side effects is now feasible to help children who have genotypes associated with poor metabolism of 2D6 enzymes. More research is required to better understand the epistatic genotypic interactions before the most effective medication for a given patient can be determined.

Depression, Suicide, and Gender Differences

A study by Barbe and colleagues^[6] assessed depressed children, clinical symptoms, and comorbid disorders "with and without clinically significant suicidal ideation stratified by gender." A total of 35 children (ages 7-17 years) were recruited from inpatient and outpatient clinics, all with a MDD (current *DSM-III-R*). Using the KSADS, current MDD symptoms and lifetime comorbid psychiatric disorders were examined. Thirty-two percent of the depressed subjects were classified as suicidal (lifetime or current) based on having suicidal ideation with a plan (n = 43).

Results of this study showed that suicidal depressed (SD) children were markedly older than non-SD children ($P < .02$). With regard to age, there were significant interactions between suicidality and gender for hopelessness ($P < .03$), duration of MDD ($P < .03$), and comorbid oppositional disorder. In comparing SD females with non-SD females, the SD girls had more hopelessness ($P < .003$) for longer periods ($P < .02$) and were more apt to have comorbid oppositional disorder ($P < .02$ vs $P < .05$). It was also shown that SD girls experienced more hopelessness ($P < .03$) than SD boys.

Differences due to gender in this study were apparent, especially with regard to hopelessness, yet further study is required to determine if gender is a specific characteristic of SD.

Anxiety Disorders in Children

Childhood disorders are often categorized according to externalizing behavior problems vs internalizing behavior problems, such as anxiety. Teachers often play a critical role in identifying whether children have externalizing disorders such as ADHD. Are teachers effective in detecting internalizing problems such as anxiety disorders? One study^[7] examined elementary school children to evaluate their anxiety symptoms over development, gender differences in presentation, and teacher awareness of anxious kids. More than 400 children between second and fifth grade completed the Multidimensional Anxiety Scale for Children. Teachers were asked to identify the 3 most anxious children in each classroom. Significant findings were that girls reported more social anxiety, performance fears, and humiliation or rejection. Younger children had increased anxiety on the total score but also had greater subscale scores for separation/panic, harm avoidance, anxious coping, and perfectionism. In other words, these measures of anxiety decreased as children grew older. Teachers were able to identify more anxious children overall, especially those with observable fears related to humiliation, rejection, and separation. Further studies need to not only replicate these findings but also investigate the impact of early intervention in development of childhood anxiety disorders that may often persist into adulthood.

Prospective, longitudinal studies often provide the most valuable information about development of psychopathology. If such data exist, there is often a gap of information about minority ethnic populations. Investigators followed up a group of more than 140 students for 7 years who were from a predominantly African American community.^[8] First grade children were classified as highly anxious if they scored in the top third with measures of Parent and Child-Report of Anxiety and Teacher Report of Shy Behavior. In contrast, the low anxious children scored in the bottom third of these same measures. Follow up with this same group was performed in the eighth grade and used standardized measures of academic, social, and psychological functioning. Only the teacher

rating of anxiety/shyness in the first grade was predictive of eighth grade academic performance. The highly anxious group was 3 to 4 times more likely to be at the bottom third level of eighth grade reading and math achievement tests. Parent ratings of the first graders were more correlated to later depressive symptoms, whereas child ratings were more associated with later anxious symptoms on the Internalizing Symptom Child Report in eighth grade. In contrast, there were no correlations with the externalizing symptom parent and teacher reports. This preliminary report supports the idea that early anxiety may be associated with later internalizing rather than externalizing symptom disorders. Despite a relatively small sample size and lack of formal diagnostic interviews, this study accessed information from multiple informants and followed up the same cohort longitudinally. Further work needs to investigate various ethnic populations to determine whether early intervention with highly anxious children has an impact on subsequent academic achievement, especially by targeting test or performance anxiety.

Crisis Intervention Services and Predicting Hospitalization

The goal of the study by Gray and colleagues^[9] was to evaluate the use of The Acuity of Psychiatric Illness Scale-Child and Adolescent version (CAPI) as a "predictor of psychiatric hospitalization." From May 2001 to January 2003, 468 children who came to a pediatric hospital and were seen for the first time by a crisis intervention worker were included in the sample. Clinical and demographic data were documented and the CAPI was completed at the end of the interview.

Univariate analyses on the 20 dichotomized items of the measure revealed significant relative risk ratios (RRs) for suicidal ideation (RR, 5.9; 95% confidence interval [CI], 3.3-10.7), self-mutilation behavior (RR, 2.9; 95% CI, 1.6-5.3), reality assessment (RR, 5.1; 95% CI, 2.5-10.7), depression (RR, 4.5; 95% CI, 2.5-8.0), anxiety (RR, 3.0; 95% CI, 1.7-5.4), and nutritional status (RR, 3.2; 95% CI, 1.7-5.8). Patients were most likely to be admitted if they had moderate or severe symptoms of these conditions rather than those with no or mild impairments.

It was found that the CAPI is a useful tool to help crisis workers evaluate when to request psychiatric services. Further testing is required, including "testing its predictive ability in a multivariate model."

Emotional Disorders and Abdominal Pain

A study by Campo and colleagues^[10] assessed whether recurrent abdominal pain (RAP) is associated with psychiatric symptoms and disorders and why it is prevalent in children and adolescents. A case-control study was performed using children and adolescents (ages 8-15 years) through a screening process conducted in primary care pediatricians offices. Children with RAP (cases; n = 42) and children without RAP (controls; n = 38) were interviewed using standard psychiatric procedures "blind to subject status, and self, parent, and clinician ratings of child psychiatric symptoms, temperamental traits, and functional status."

The study found that in 79% of the cases RAP was more likely to be diagnosed with an anxiety disorder and 43% with a depressive disorder. The cases also had a higher level of anxiety and depressive symptoms, temperamental harm avoidance, and functional impairment than controls. Cases associated with anxiety disorder (mean age of onset, 6.25 years; SD, 2.17 years) were markedly more likely to precede RAP (mean age of onset, 9.17 years; SD, 2.75 years) in those cases with associated anxiety.

The study found that children who present with RAP should be carefully assessed for anxiety and depressive disorders. Possible future treatments for RAP could be current treatments for anxiety and/or depressive disorders. More studies, including longitudinal, family, and psychobiological

studies, are needed to better understand the nature of observed associations among RAP, anxiety, and depression.

References

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