Graduate Student Journal of Psychology
2005, Vol. 7

Teachers College, Columbia University ISSN 1088-4661

Child and Adolescent Depression: Should Antidepressants Be Used in Treatment?

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This paper examines the controversy over the use of selective serotonin-reuptake inhibitors (SSRIs) in the treatment of children and adolescents. Arguments for and against the use of SSRIs with pediatric populations are evaluated. Supporting SSRI treatment are findings that SSRIs are effective, the potential accessibility of medication, and findings that SSRIs have played a role in the overall decline in adolescent suicide rates. Arguments against the use of SSRIs among child and adolescent populations include findings of associated increases in suicidality and of potential impulsivity and violence in response to the medication. Arguments against treating children and adolescents with SSRIs also include the complications of side effects, dosage, and duration of treatment, and concerns over an approach limited to the neurobiological level. The role of psychotherapy, both alone and in combination with SSRI treatment is discussed.

The controversy over the use of antidepressants in the treatment of children and adolescents has received a great deal of media attention following the Food and Drug Administration's (FDA) September 2004 decision to require a "black-box" warning label for the use of these medications with pediatric patients. While such a decision does not contraindicate the treatment of pediatric patients with such medications, the black box represents the most serious type of warning label, cautioning strongly about the risks associated with a medication. In the case of antidepressant use in children and adolescents, the risk involves a potential increase in suicidality (i.e., suicidal ideation and behavior).

Many of the same arguments for and against the black-box warning can serve as arguments for and against the use of antidepressant medications in children and adolescents. The goal of this paper is to address the specific question of whether or not a particular class of antidepressant medications, selective serotonin-reuptake inhibitors (SSRIs), should be used in the treatment of children and adolescents with depression[1]. Research evidence supporting the efficacy of SSRIs in reducing the symptoms of depression among children and adolescents represents the strongest argument in favor of their use in pediatric treatment. In addition, greater accessibility to these medications (as compared to psychotherapy) among children and adolescents may also support their role in treatment. Finally, findings that suggest that SSRIs are associated with a decrease, rather than an increase, in completed suicides among children and adolescents lend support to their use in reducing actual incidences of suicide among depressed children and adolescents.

Although the evidence supporting the treatment of children and adolescents with SSRIs is persuasive, so too are the arguments against the use of this medication with pediatric populations. The most powerful evidence against the use of these medications in the treatment of children and adolescents comes from research demonstrating that the medication is associated with an increase in suicidality (e.g., Jureidini et al., 2004; Newman, 2004). Furthermore, there are findings that SSRIs may be linked to an increase in agitation, impulsivity, and violence among pediatric patients (e.g., Glass, 2004). Those who argue against the use of SSRIs in children also point out that the findings supporting their efficacy are quite small in magnitude as compared to the increased risks of suicidality. Pharmacological treatment of depression in general also brings concerns over side effects, questions of dosage and length of treatment, and treatment decisions for relapses, which are of heightened concern in the treatment of growing and developing children. Another argument against the treatment of children and adolescents with SSRIs lies in the limitations of approaching a psychological disorder solely on the neurobiological level. In other words, even if SSRIs are highly effective, pharmacological treatment of depression fails to address the feelings of depression on a psychological level and to foster the development of coping mechanisms. Such

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[1] The scope of this paper is limited to an examination of the treatment of children and adolescents with SSRIs and excludes the other major class of antidepressants that has been used in the treatment of this population, including tricyclic antidepressants (TCAs). Research on the latter suggests that they are no more effective than placebo in the treatment of children and adolescents (Carr & Boyd, 2003), and that they are associated with danger of overdose (Mahler, 2004).

mechanisms can play a critical role as patients wait for medication to become effective, as they face future Major Depressive Episodes, and as they grapple with the vicissitudes of life. This limitation of pharmacological treatment will be discussed and evaluated along with recent evidence supporting the efficacy of psychotherapy among child and adolescent patients.

Evidence Supporting the Treatment of Children and Adolescents with SSRIs

Efficacy

A number of recent studies offer support for the effectiveness of SSRI medications in the treatment of child and adolescent depression (e.g., Wagner et al., 2003; Treatment for Adolescents With Depression Study (TADS) Team, 2004). Although small when compared to the number of studies of antidepressant treatment among adult patients, the recent research findings offer persuasive evidence of the efficacy of SSRIs among child and adolescent patients. Wagner et al. (2003) demonstrated that depressed children and adolescents treated with sertraline (Zoloft) showed significantly greater improvement than did those treated with a placebo. Specifically, Wagner et al.'s research involved two identically designed studies conducted at multiple hospital, practice, and academic settings in the US, India, Canada, Costa Rica, and Mexico. Participants included 376 children and adolescents between the ages of 6 and 17, who were randomly assigned to the double-blind sertraline or placebo treatment conditions.

Prior to treatment, participants' diagnoses of Major Depressive Disorder were confirmed and their symptoms were evaluated using the Children's Depression Rating Scale-Revised (CDRS-R) and the Clinical Global Impression of Severity of Illness (CGI-S). Participants received medication for a period of 10 weeks, with some adjustments permitted to attain effective dosages. The CDRS-R and CGI-S assessments were given multiple times throughout the duration of the study to evaluate responses to the medication. Significantly higher levels of improvement were found among patients treated with sertraline on both measures. On the CDRS-R, the sertraline group experienced a decrease in mean depression scores from week one to week ten of 22.84 points, whereas the placebo group experienced a mean score decrease of 20.19 points. On the CGI-S, the mean score decreases were 1.22 in the sertraline condition and 1.01 in the placebo condition.

The findings of Wagner et al.'s (2003) studies reveal a significant improvement among pediatric patients treated with sertraline as well as a large placebo effect. Studies of antidepressant treatment of adults and the small group of other studies of children and adolescents also reveal similar, sizeable placebo effects. Yet, the significant findings should not be discredited for a number of reasons. First, it is possible that in a number of ways, psychotherapy may also have played a role in the improvement of patients in both conditions. Specifically, though not permitted to be treated with cognitive-behavioral therapy (CBT), participants were allowed to continue other types of psychotherapy in which they had been engaged prior to joining the study. In fact, 8 placebo condition participants were in psychotherapy during the study and 29 had been in psychotherapy prior to the study; for both groups, Wagner et al. suggested that the benefits of extra-study psychotherapy may have been responsible for improvement in symptoms. Additionally, Wagner et al. pointed out that for all participants, because of the frequency of sessions for medication adjustment, monitoring, and symptom assessment (almost weekly throughout the study), an informal therapeutic interaction may have taken place between participants and investigators. Varley (2003) posits that "these findings suggest that children may be more responsive than adults to nonspecific measures of support that are included in the placebo response, particularly because children and adolescents are in a more dependent and reactive developmental state" (p. 1092). It is important to recognize that a small significant effect of sertraline was found above and beyond these potentially psychotherapeutic effects.

A second reason Wagner et al. (2003) offer for the large placebo effect is the high level of variability within conditions; participants were treated in different types of treatment centers, by different investigators, in different countries, and within different cultural contexts. A third reason for the high placebo effect, which the researchers did not mention, is that patients may have been moving out of the depths of depression over time. A condition for participation was that criteria for a Major Depressive Episode must have been present for at least 6 weeks prior to joining the study. The 6-week presentation of symptoms was followed by a 2-week screening period before the 10-week trials took place. In general, Major Depressive Episodes can last 4 months or longer, if left untreated (DSM-IV-TR). This, combined with the fact that the length of the episode included a minimum of 18 weeks (and possibly longer, since 6 weeks of pre-participation symptoms was the minimum requirement), makes it seem possible that some participants may have begun improving naturally. Despite the large placebo effect, the improvement of children and adolescents in the sertraline treatment condition was significant and supports the use of at least one SSRI in the treatment of child and adolescent patients.

Studies of other SSRIs offer additional evidence of their efficacy in treating child and adolescent patients, but they also point out the need to assess these medications individually. Although clustered together because of their known role in inhibiting the reuptake of serotonin, each medication appears to operate on a distinct pathway, as revealed in its effects on multiple neurotransmitters, side effects, and the differential responsiveness of patients. In addition to the above findings on the efficacy of sertraline, a recent major study by the Treatment for Adolescents With Depression Study (TADS) Team (2004) supports the use of

fluoxetine (Prozac). This study (which will be discussed subsequently in more detail in the context of psychotherapy) revealed that fluoxetine was superior to both placebo and CBT alone, but that the best outcome (and the only statistically significant finding) involved the combination of fluoxetine and CBT. By contrast, several unpublished studies recently suggested that another SSRI, paroxetine (Paxil), was not significantly more effective than a placebo, and that the medication (now contraindicated for use with pediatric patients) may pose particular risk of suicidality (Wooltorton, 2003; Mathews & Windham, 2004).

Although the body of research on SSRI treatment of depression in children and adolescents is quite small, there are several important findings and implications. First, some studies have demonstrated significant levels of improvement among pediatric patients with depression (e.g., Wagner et al., 2003). Second, even in purely psychopharmacological studies, frequent interactions with a clinician may have psychotherapeutic benefits for adolescent and child patients (Wagner et al., 2003); this finding commands greater research attention to psychotherapeutic treatment of depression among children and adolescents. Furthermore, although large placebo effects and the therapeutic overlap were viewed as limitations in Wagner et al.'s (2003) study, such limitations may have serendipitously offered greater insight into the nuances of the treatment. Third, each SSRI operates differently, and rather than drawing general conclusions about the efficacy of the class of drugs in treating pediatric cases of depression, critical evaluations of each individual medication are needed. The need for specific research is embedded within a larger need for more studies on the use of SSRI medications with children and adolescents, to permit a better understanding of the efficacy and other benefits, and the risks associated with each of them.

Accessibility

Another consideration in this debate focuses on the accessibility of various treatments. Pediatric patients are largely dependent on parents or caregivers for treatment approval and decisions, initial insight into their difficulties, and transportation to and from treatment appointments. When it comes to getting treatment for depressed pediatric patients, might parents be more likely to seek treatment involving SSRIs than psychotherapy? Won Tesoriero (2004) suggests that many children and adolescents suffering from depression may receive treatment from pediatricians or primary care physicians because such treatment is more readily available and less stigmatized than treatment with a psychiatrist or psychologist. The issue of accessibility appears to be a serious one, given that there are about 7,000 child and adolescent psychiatrists in the U.S. (compared to about 60,000 pediatricians), and that, in the early 1990s, there was a need for 33,000 child and adolescent psychiatrists (Won Tesoriero, 2004). The problems of accessibility appear to be exacerbated among children in families of low socioeconomic status, children without health insurance, African Americans, and very young children (Olfson, Gameroff, Marcus, & Waslick, 2003). The possibility that accessibility factors and the stigma associated with having depressed children would lead parents to obtain prescriptions from a pediatrician, rather than transporting their child to numerous psychotherapy sessions, offers some support for the treatment of children and adolescents with medication to assure that they receive some form of help.

Through a collection of health-service use data, Olfson et al. (2003) found that whereas more depressed children and adolescents received psychotherapy than antidepressant medication (about 75% and 60% of those treated, respectively), the number of psychotherapy visits attended was found to be quite low. While clinical trials suggest 15 to 25 sessions over a period of 6 to 16 weeks, children and adolescents being treated for depression averaged fewer than eight sessions a year, with many undergoing only one or two visits (Olfson et al., 2003). Thus, the possibility arises of parental disincentives towards psychotherapy, including both the stigma associated with child depression and the logistical difficulties of transporting a child to numerous appointments. However, Won Tesoriero (2004) points out that following the black-box warning given to antidepressants this past September, parents are finding that many pediatricians and primary care physicians are no longer willing to prescribe medications. Thus, parents are finding it increasingly difficult to find one of an already small number of child and adolescent psychiatrists to prescribe the medication.

Although there may have been (and may still be) some advantages of treatment with SSRIs, there appears to be an important role for qualitative research to achieve an in-depth understanding of the factors that influence the parents and caretakers of children and adolescents with depression. Such research could lead to an understanding of their plight that goes beyond speculation and could guide practitioners and researchers in the development of and education about effective psychotherapeutic, psychopharmacological, or combined treatments.

Decrease in Child and Adolescent Suicide

In addition to the efficacy and accessibility of SSRIs, further support for the use of SSRIs in the treatment of children and adolescents with depression involves a potential association between treatments involving these medications and a decrease in suicide rates among adolescents. Brent (2004) points out that after a long history of increasing rapidly, suicide rates among adolescents have been falling for the past 10 years. Although a large part of the decrease can be accounted for by stricter gun control, Brent suggests that corresponding improvements in the detection

and treatment of depression and the use of SSRIs may have played a role. Brent cautions that there is a relationship between suicidality and completed suicide and that the possibility of SSRIs causing increased suicidality presents an important risk. Yet, he argues, such a risk suggests the need to carefully monitor adolescent patients being treated with SSRIs, rather than to avoid a form of treatment that appears to be effective in reducing depression and that may support an overall decrease in adolescent suicide rates.

Difficulty in evaluating the link between SSRIs and suicidality lies in understanding what the data can actually mean in practice. According to the former head of the FDA division that examines psychiatric medications, "You don't know whether the phenomena you're looking at are good surrogates for actual suicide" (Mathews & Windham, 2004, D3). In particular, the confusion arises from research findings of an increase in suicidal ideation and attempts, but no incidences of completed suicide associated with treatment with SSRIs. The instances of completed suicide are revealed, not in research studies, but in individual case studies, often provided by parents who speculate after a child's death that the SSRI played a role. Both Brent's (2004) reminder of the relationship between suicidality and completed suicide and features of the design of recent studies demand that the risk of completed suicide be further assessed. In particular, ethical limitations of research prohibit the inclusion of adolescents at the highest suicide risk as subjects in the research (Glass, 2004). For example, in Wagner et al.'s (2003) studies of children and adolescents treated with sertraline, "[p]atients who had previously attempted suicide or who were judged to pose a significant suicidal or homicidal risk" were excluded from participating in the study (p. 1034). The exclusion of such participants could lead to an underestimation of the suicidality risks associated with SSRI treatment.

The empirical data supporting the SSRI-associated increase in suicidality and a case study involving a suicide following the initiation of SSRI treatment will be presented below in a discussion of evidence against the use of SSRIs with children and adolescents. Supporters of the use of SSRIs in children and adolescents portray the suicidality findings as evidence of a small but serious risk associated with the medication, as opposed to the perhaps greater risk of removing the SSRI treatment option. Specifically, Boland and Keller (2004, as cited in Glass, 2004) state that "Although some concerns about potentiating suicidal behavior may remain, these should be balanced over the clear risk of suicide in patients with untreated depression" (Boland & Keller, 2004, p. 856, as cited in Glass, 2004, pp. 861-862). Similarly, Brent (2004) concludes that an appropriate balance needs to be found "between the risk of suicidality and another, greater risk: the risk that lies in doing nothing" (p. 1601). The key element missing from these statements, which will be discussed below, involves the role of psychotherapy, both alone and in combination with SSRI treatment and in specifically addressing the risk of suicidality.

Evidence Against the Treatment of Children and Adolescents with SSRIs

Suicidality

The most powerful argument against the treatment of depressed children and adolescents with SSRIs lies in findings that these medications may lead to suicidality among pediatric patients. Evidence from both clinical research trials and individual case studies reveals the potential that SSRIs may produce or exacerbate suicidal thinking and behavior. The seemingly paradoxical finding has been explained by the phenomenon of "rollback" (Mahler, 2004). Specifically, while in the initial depths of a Major Depressive Episode, a person may have thoughts about wanting to die, but may be unable to elaborate on these thoughts or to act on them given the decreased energy associated with the depression. As the SSRI begins to work (but before the person's mood has reached pre-episodic levels), the person may experience enough of an increase in his or her energy level to think seriously about, or act on, a plan to commit suicide.

The case against the use of SSRIs with pediatric patient populations can be made in part by an examination of some of the same research trials used to demonstrate the efficacy of SSRIs. For example, Jureidini et al. (2004) point out that analysis of the data in Wagner et al.'s (2003) study reveals the problematic increase in suicidality associated with sertraline. In particular, 9% of children and adolescents in the sertraline condition (as compared to 3% in the placebo condition), experienced adverse effects serious enough to lead them to withdraw from the study. Further analysis of the individual adverse events was not reported, but might be informative in confirming the extent to which they included suicidal ideation or attempts. Additionally, Jureidini et al. draw attention to Wagner et al.'s findings involving adverse events among patients who remained in the study, which included more instances of serious adverse events involving suicidality. Among patients in the sertraline condition, two suicide attempts and three instances of suicidal ideation were revealed as compared to two suicide attempts and no instances of suicidal ideation among patients in the placebo condition. The numbers are small and the conclusions unclear, but the possibility that sertraline caused an increase in suicidal ideation among these patients (and among those who withdrew participation) remains.

Newman (2004) presents an argument supporting the black-box warning for SSRI use with pediatric patients. Specifically, Newman describes findings from an analysis of unpublished studies coordinated by the FDA and reviewed by suicide experts at Columbia University. These experts blindly evaluated a series of narratives about adverse events that took place during clinical trials and made determinations as to whether or not each should be coded as an instance of suicidality. Without knowing whether they were reading narratives involving participants receiving

antidepressant medication or placebo pills, these raters found over twice as many incidences of suicidality among participants taking antidepressants versus those in placebo groups. However, a main criticism of this analysis was that the studies supplying the original data were not uniformly designed, were not specifically designed to study suicidality, and were not required to be of high quality. For Newman, however, this makes the findings all the more convincing, given that the probability of their chance occurrence would be 1 out of 20,000 ($p = 0.00005$) by his calculation (Newman, 2004, p. 1596).

Newman argues further that such a finding stands in stark contrast to the efficacy data on SSRIs, in which significant effect sizes are small and sizeable placebo effects are revealed. Newman cites the small effect size in the TADS (2004) study of fluoxetine, in which the reduction of CDRS-R scores among patients receiving fluoxetine was 22.6 points versus 19.4 points among those receiving a placebo. These findings were similar to those of Wagner et al. (2003) (i.e., 22.84 in the sertraline condition and 20.19 in the placebo condition). As in Wagner et al.'s study, the TADS study left more information to be desired regarding the implications specifically related to suicidality. Again, the numbers are small, and drawing conclusions is difficult. Looking at the suicide-related events that did occur, no significant differences were revealed between the treatment groups. However, harm-related adverse events, a category broader than suicidality and including "any self-harm or harm to another person or property" revealed a difference: patients taking fluoxetine experienced more harm-related adverse events than did patients not receiving SSRIs (Glass, 2004, p. 862). The research studies, especially those involving experts' blind ratings of adverse events, suggest a potentially sizeable risk of suicidality associated with the treatment of children and adolescents with SSRIs. However, the data are limited by questionable research design and by the small number of data points (perhaps in part due to exclusion of high-risk patients from participation). Clearly, more research is needed to clarify whether or not the findings of increased suicidality among child and adolescent patients in a few trials can be generalized to the broader population of depressed children and adolescents.

Further evidence supporting the potential risk of suicidality posed by SSRI treatment of pediatric patients comes from the testimonials of relatives of those who have committed suicide following the initiation of SSRI treatment. According to Newman (2004), numerous individuals offered public testimony about such incidences to the FDA committee charged with the black-box label recommendation for these medications. Furthermore, Newman reports that "several of these cases involved patients who had shown no hint of suicidality before beginning treatment with the drugs" (Newman, 2004, p. 1596). The details of the case of Matt Miller, a 13-year-old boy who committed suicide a week after beginning treatment with sertraline (Zoloft), seem to suggest an association between the medication and suicide (Mahler, 2004). Matt did not appear to be at high risk for suicide; he had indicated on the Children's Depression Inventory one week earlier that although he thought about killing himself, he would not actually do it. Matt's parents are convinced that the medication led to Matt's suicide. Matt may have experienced rollback, getting enough energy back to convert suicidal ideation into a suicide. Alternatively, the medication may have induced a broader pattern of impulsivity and violence in the young patient, leading to his suicide (Mahler, 2004).

Impulsivity, Violence, and Hostility

Matt Miller's parents reported additional changes in Matt's behavior during the week he began taking sertraline. He became visibly agitated and seemed to have experienced a burst of energy, which he released through activities such as frequent bike riding. Searching for answers about his son's death, Matt's father came across

> …a phenomenon known as akathisia, or activation, a state of extreme agitation that can be induced by some psychotropic medications and can cause patients to behave in an uncharacteristically violent manner, which seemed to describe perfectly Matt's condition before his suicide. (Mahler, 2004, p. 62)

Matt's agitated behavior coupled with the violent means by which he chose to commit suicide (i.e., by hanging himself), suggested that beyond rollback, impulsivity and violence may have led to his decision to commit suicide (Mahler, 2004). Keeping in mind Matt's case, the findings of the TADS (2004) take on heightened significance. Specifically, the study's finding of a general increase in the broader category of harm-related adverse effects (Glass, 2004) might be consistent with a risk of activation among pediatric patients taking SSRIs.

The possibility that pediatric patients taking SSRIs might develop a pattern of impulsivity that can manifest itself in suicidality may have neurobiological underpinnings. Begley (2004) outlines findings related to the effects of SSRIs on the brains of children and adolescents. Specifically, treatment with SSRIs stimulates neurogenesis (the growth of new neurons), which may be more problematic to the child's developing brain than to that of an adult taking the medication. For example, this neurogenesis appears to restore the shrunken hippocampus (a brain region associated with emotion and memory) of the depressed adult's brain back to its original size (Begley, 2004). By contrast, the hippocampus does not show this shrinkage in the brains of depressed children and adolescents and therefore, "some scientists wonder whether the new neurons could destabilize fragile brain circuits in kids suffering from mental illness" (Begley, 2004). Furthermore, researchers are looking into differences in images of depressed children's prefrontal cortices (the region responsible for inhibition and impulse control) as compared to that of adults. The prefrontal cortex is still maturing in children and adolescents, and SSRI treatment may result in difficulties with impulse control.

Thus, SSRI medications may put children and adolescents at particular risk for impulsive and violent behavior, which among depressed children and adolescents seems likely to include suicidal behavior.

Other Limitations of Psychopharmacological Treatment

Beyond the potential risks of an increase in suicidality, or a general increase in violence and impulsivity, there are several additional arguments against treating children with SSRI medications. First, general considerations of psychopharmacological treatments, such as side effects (ranging from the minor headache to suicidality), determination of dosage, and duration of treatment, require careful risk-benefit analyses for which the limited body of research may fall short of supplying sufficient data. Second, SSRI or psychopharmacological treatment of child and adolescent depression approaches the disorder only on the neurobiological, rather than the psychological level. As a result, SSRI treatment does not offer a child coping mechanisms or support, which may be of critical importance in the face of a recurrence. Unfortunately, the likelihood that children or adolescents experiencing Major Depressive Disorder will experience further Major Depressive Episodes is two to four times that of children and adolescents without depression (Wagner et al., 2003). Assuming a diathesis-stress model of depression, a child or adolescent with depression has some genetic predisposition or vulnerability to develop depression in the face of particular stressors. According to such a model, it would appear that treatment should take into consideration the exposure to the stressors that trigger the depression for a child or adolescent. Given their youth and the difficulties associated with adolescent development, it appears that treatment should address both current and potential future episodes. In such a treatment approach, SSRIs, in the absence of psychotherapeutic interventions that can foster coping skills, seem quite limited.

Combined Treatment of SSRIs and Psychotherapy

The recent research on the treatment of depression among adolescents reveals the efficacy of combination treatments including both SSRI medication and psychotherapy. In particular, the TADS (2004) demonstrated the efficacy of such combined treatments. The study involved 439 patients between 12 and 17 years of age who were randomly assigned to one of four conditions: fluoxetine alone, CBT alone, fluoxetine and CBT, and placebo. The outcome measure involved a reduction in symptoms of depression as measured by the change in CDRS-R scores over a 12-week treatment period. The most improvement came from the combination of fluoxetine and CBT, followed by the fluoxetine-alone group, then the CBT-alone group, and then the placebo. The only effect that obtained significance was the combined treatment over the placebo.

The value of psychotherapeutic treatment revealed by TADS (2004) went beyond the finding of the combined efficacy of CBT and fluoxetine. A more subtle effect was revealed in terms of the potential role of psychotherapy in reducing the risks of suicidality and generally impulsive and dangerous behaviors among adolescents treated with SSRIs. In particular, as compared to the fluoxetine plus CBT treatment group, the fluoxetine-alone group experienced more harm-related adverse events, including any self-harm or harm to the person or property of another (Glass, 2004). According to Glass, the TADS findings suggest the possibility of a protective effect of psychotherapy. Such a protective effect is a particularly important finding given concerns about the potential for SSRI treatment to induce suicidality and general impulsivity. Again, the numbers are small and thus, definitive conclusions are difficult to draw from this early research, including conclusions about whether findings about psychotherapy with adolescents generalize to the treatment of younger children. There appears to be a great need for future research clarifying whether or not there is indeed a causal association between SSRI treatment and suicidality and impulsive behavior. There is also a need for research on the potential benefits of the development of coping skills, support, and protection against suicidality offered by different forms of psychotherapy for depressed children and adolescents.

Discussion

There are no straightforward answers in the literature to the question of whether or not depressed child and adolescent patients should be treated with SSRI medications. Supporting such treatments are findings that SSRIs are effective in reducing or eliminating depression, potential issues of accessibility of medication over psychotherapy to children, and findings that SSRIs have played a role in the overall decline in adolescent suicide rates. Arguments against the use of SSRIs among child and adolescent populations come primarily from research and case study findings of associated increases in suicidality and findings of potential impulsivity, violence, or agitation in response to the medication. Furthermore, arguments against treating children and adolescents with SSRIs include the complication of an array of side effects of varying severity, issues of dosage and duration of treatment, and concerns over an approach limited to the neurobiological level, which provides no room for the development of coping skills or support.

The controversy over the use of antidepressant medications has been heightened by ethical concerns regarding unpublished data. Of particular concern was the discovery of internal documentation at a drug company instructing the withholding of data demonstrating that a particular SSRI, paroxetine (Paxil), was ineffective in the treatment of adolescents (Kondro & Sibbald, 2004). Furthermore, by conducting a meta-analysis of published and unpublished data on the use of SSRIs with children, Whittington et al. (2004)

found that, with the exception of fluoxetine (Prozac), the inclusion of unpublished data altered the overall findings such that the risks outweighed the benefits of treatment with several medications. Considering the overall limitations of small effect sizes in this growing area of research, and the potential suicidality risk, the disclosure of all findings appears critical.

Another interesting, recent development in the debate came in a recent revision to the FDA's warning about these medications (Polk, 2005). Specifically, in early February, 2005, the FDA removed a statement establishing a causal link between these medications and increased suicidality from its website and replaced it with a statement that reported an increase in suicidality found in short-term studies of these medications with children and adolescents. The replacement sentence was also placed in boldface in the black box warning on the medication insert, with the original (causal) sentence moved into a later section of the text that discusses suicide risk in more detail. Such a change in language serves to qualify the original FDA warning, and to point out that further research is needed to assess the true safety of the medication for children and adolescents.

At this time, the research data from studies of children and adolescents are few and there is a great need for further study to better understand child and adolescent depression, and to understand the relationship between the medication and possible outcomes of suicidality and impulsive or violent behavior. The case studies provided by the parents of children who have committed suicide during SSRI treatment demand a more in-depth, research-based evaluation of the treatment of children and adolescents with these medications.

The question of whether or not SSRIs should be used in the treatment of children also sheds light into the range of opinions of clinicians based both on experience and training. As a graduate student in clinical psychology, I have attempted to address the topic of the controversy surrounding the treatment of children and adolescents with SSRIs. In contrast, in his review of TADS (2004), which provided support for the role of psychotherapy in the treatment of depressed adolescents, Glass (2004) suggests that an "area of lingering controversy is the role of psychotherapy in the treatment of psychiatric disorders, including major depression" (p. 863). The depiction of child and adolescent depression as either a psychiatric or a psychological disorder, with different points of view and treatment implications of each, should not pose a threat to finding the most effective help for depressed children and adolescents. If anything, the early studies appear to suggest that the combination of psychotherapeutic and psychopharmacologic treatment may offer the most hope to patients.

Wilens, Spencer, Frazier, and Biederman (1998) offer a six-step framework for evaluating the treatment of children and adolescents with psychotropic medication. First, psychotropics should only be prescribed following a thorough diagnostic evaluation. Second, when used, pharmacotherapy should be integrated with other forms of treatment, such as psychotherapy, rather than suggested as an alternative form of treatment. Third, the severity and type of symptoms and the age of the child should be considered. Fourth, both the family and the child should be educated about treatment alternatives and the risks and benefits associated with the medication. Fifth, the child or adolescents' dosage should be kept as low as possible and treatment should be tapered if not effective and reevaluated after the child or adolescent has improved. Sixth, multiple practitioners (e.g., psychologists and psychiatrists or pediatricians) should work collaboratively in managing the psychopharmacologic treatment. Such a framework should guide the treatment of children and adolescents with SSRIs.

For now, a primary goal should be collaborative, interdisciplinary research to assess the true safety and efficacy of SSRIs in pediatric patients and to identify effective forms of psychotherapy. Until more research has clarified the safety of SSRI mediation for use with children and adolescents, they should continue to be prescribed only in severe cases of depression and after the parents, child, and clinician have learned about, understood, and considered other alternatives. Ideally, such medication would be prescribed and patients closely monitored by psychiatrists with specialization in the treatment of children and adolescents. However, as Won Tesoriero (2004) pointed out, there are simply too few of such professionals (with some 7,000 child and adolescent psychiatrists in the U.S. currently, versus an estimated need in 1990 for 33,000 such professionals). Won Tesoriero suggests that this shortage is associated with the limited federal funding for hospitals to offer the training this specialty requires. Because of the heightened concerns over the safety of antidepressant treatment of children and adolescents, it seems critical to address this shortage of child and adolescent psychiatrists. Perhaps this could be addressed by increasing the opportunities for psychiatrists to specialize, by offering training to the pediatricians who prescribe the medication, or by increasing collaboration between child and adolescent psychologists and those writing the prescriptions in an attempt to improve diagnosis, treatment plans, and monitoring of young patients.

Furthermore, when treating children and adolescents with SSRIs, concurrent psychotherapy should be strongly encouraged for several reasons. First, psychotherapy becomes critical to monitor risks related to suicidality and impulsivity. Second, psychotherapy can offer depressed children and adolescents support as they wait for the inhibition of enough serotonin-reuptake to occur and an improvement in mood to result. The support and development of coping skills offered by psychotherapy can be equally important throughout psychopharmacological treatment, during the tapering and removal of medication, and in the future as children and adolescents face other Major Depressive Episodes and cope with everyday life stressors.

For proponents of SSRI use in children who are exclusively focused on examining depression and treatment on the neurobiological level, the potential role of psychotherapy in treatment remains a powerful one. Studies compar-

ing interpersonal therapy and SSRIs have demonstrated that psychotherapy produces similar (and possibly longer-lasting) brain changes to those produced by SSRI treatment (Friedman, 2002). Finally, the research so far on the treatment of child and adolescent depression reveals the benefits of psychotherapy both directly and indirectly. TADS (2004) demonstrated significant improvement among depressed adolescents only from the combination of an SSRI and psychotherapy, and a possible protective effect of psychotherapy related to impulsivity and suicidality. Wagner et al's (2003) work revealed the more subtle possibility that even in a study limited to psychopharmacological treatment, the informal, frequent psychotherapeutic interactions between investigators and pediatric patients may have led to substantial improvement. Together, such findings offer powerful evidence of the importance of psychotherapy in the treatment of depressed children and adolescents.

References

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed. text revision). Washington, DC: Author.

Begley, S. (2004, October 15). Developing problem: Why depression looks different in a kid's brain. *The Wall Street Journal*. Retrieved November 18, 2004, from Factiva database.

Brent, D. A. (2004). Antidepressants and pediatric depression—the risk of doing nothing. *The New England Journal of Medicine*, *351*, 1598-1601.

Carr, V. A., & Boyd, C. P. (2003). Efficacy of treatments for depression in children and adolescents. *Behaviour Change*, *20*, 103-108.

Friedman, R. A. (2002, August 27). Like drugs, talk therapy can change brain chemistry. *The New York Times*. Retrieved December 13, 2004, from ProQuest database.

Glass, R. M. (2004). Treatment of adolescents with major depression: Contributions of a major trial. *The Journal of the American Medical Association*, *292*, 861-863.

Jureidini, J. N., Doecke, C. J., Mansfield, P. R., Haby, M.M., Menkes, D. B., & Tonkin, A. L. (2004). Efficacy and safety of antidepressants for children and adolescents. *British Medical Journal*, *328*, 879-883.

Kondro, W., & Sibbald, B. (2004). Drug company experts advised staff to withhold data about SSRI use in children. *Canadian Medical Association Journal*, *170*, 783.

Mahler, J. (2004, November 21). The antidepressant dilemma. *New York Times Magazine*, pp. 58-65, 100, 118-119.

Mathews, A. W., & Windham, C. (2004, August 25). FDA findings bolster Prozac use by teens. *The Wall Street Journal*, pp. D1, D3.

Newman, T. B. (2004). A black-box warning for antidepressants in children? *The New England Journal of Medicine*, *351*, 1595-1598.

Olfson, M., Gameroff, M. J., Marcus, S. C., & Waslick, B.D. (2003). Outpatient treatment of child and adolescent depression in the United States. *Archives of General Psychiatry*, *60*, 1236-1242.

Polk, J. (2005, February 9). FDA backs away from antidepressant warning. Retrieved March 16, 2005, from http://www.cnn.com/2005/HEALTH/conditions/02/09/fda.antidepressant/index.html

Treatment of Adolescents With Depression Study (TADS) Team. (2004). Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for adolescents with depression study (TADS) randomized controlled trial. *The Journal of the American Medical Association*, *292*, 807-820.

Varley, C. K. (2003). Psychopharmacological treatment of major depressive disorder in children and adolescents. *The Journal of the American Medical Association*, *290*, 1091-1093.

Wagner, K. D., Ambrosini, P., Rynn, M., Wohlberg, C., Yang, R., Greenbaum, M. S., et al. (2003). Efficacy of sertraline in the treatment of children and adolescents with major depressive disorder: Two randomized controlled trials. *The Journal of the American Medical Association*, *290*, 1033-1041.

Whittington, C. J., Kendall, T., Fonagy, P., Cottrell, D., Cotgrove, A., Boddington, E. (2004). Selective serotonin reuptake inhibitors in childhood depression: Systematic review of published versus unpublished data. *The Lancet*, *363*, 1341-1345.

Wilens, T. E., Spencer, T. J., Frazier, J., & Biederman, J. (1998). Child and adolescent psychopharmacology. In T. H. Ollendick & M. Hersen (Eds.), *Handbook of child psychopathology* (pp. 603-636). New York: Plenum Press.

Wooltorton, E. (2003). Paroxetine (Paxil, Seroxat): increased risk of suicide in pediatric patients. *Canadian Medical Association Journal*, *169*, 446.

Won Tesoriero, H. (2004, October 7). New drug problem: Getting antidepressants. *The Wall Street Journal*. Retrieved November 18, 2004, from Factiva database.