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Jill I. Littrell

Georgia State University, littrell@gsu.edu

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CHILDREN IN FOSTER CARE AND EXCESSIVE MEDICATIONS

*Jill Littrell**

Georgia State University
School of Social Work
Atlanta, GA

ABSTRACT

Children in foster care system are more likely to receive diagnoses of major mental illness and to be medicated with powerful medications such as antipsychotic drugs. Reasons for the increased risk of the actual mental illnesses and for the diagnoses of illness among children in foster care are reviewed. The reliabilities of various diagnoses are considered. The legitimacy of the rationale for early medications to prevent later disability is discussed. The very real hazards of medicating with antipsychotics, anticonvulsants, stimulants, mood stabilizers and antidepressants are reviewed. A discussion of advocacy efforts occurring around the United States on behalf of medicated children in the foster care system is presented. Finally, changes being instituted by the federal government through the Department of Health, Education, and Welfare and the Government Accounting Office (GAO), following the hearing of December 1, 2011 convened by Senator Thomas Carper, are discussed.

CHILDREN IN FOSTER CARE: A VULNERABLE POPULATION

Medicating Foster Children

In the last decade, the use of antipsychotic medications for adults and children has increased dramatically. Domino and Swartz (2008) compared prescriptions for antipsychotic medications in 1996-1997 with prescriptions for antipsychotics in 2004-2005. The rate of adult office visits resulting in antipsychotics rose from 0.6% to 1.3% while the rate for children rose from 0.2% to 0.7%. Moreover, Comer, Mojtabai, and Olfson (2011) documented the recent rise in the use of atypical antipsychotics to treat anxiety disorders. Antipsychotics are also currently being used to treat antidepressant resistant depression and ADHD (Crystal, Olfson, Huang, Pincus, Gerhard, 2009; Fullerton et al., 2011) and insomnia

* E-mail: Littrell@gsu.edu

(Sinaikin, 2010). The increase is especially large among children in foster care. A study of 16 state Medicaid programs in 2007 found that 1.6% of children younger than 19 were receiving antipsychotics while 12.37% of children in foster care were receiving antipsychotics (Medicaid Medical Directors Learning Network, 2010, p. 14). dosReis et al. (2011) examined psychotropic prescriptions for 16,969 children under 20 years of age in a Mid-Atlantic state Medicaid program. All of the children in the sample had been given a mental health diagnoses. For the children in foster care not awaiting adoption, 19% were being medicated with multiple antipsychotic drugs and 24% of children who were in foster care awaiting adoption were being treated with multiple antipsychotics. Similar patterns of greater use of psychotropic drugs of many classes were found in a number of additional studies comparing rates of medicating foster children to other children (Breland-Noble et al., 2004; DosReis et al., 2001; Raghavan et al., 2005; Raghavan and McMillen, 2008).

Most recently, on December 1, 2011, Senator Tom Carper held a hearing to discuss the Government Accounting Office's study of the psychiatric treatment of children in foster care. The Government Accounting Office (Kutz, 2011) issued a report on the medication of children in foster care in five states during 2008. Across states, children in foster care are 2.7 to 4.5 times more likely to be medicated than children receiving Medicaid. Infants younger than 1 are medicated, albeit possibly with Benadryl (Salo, 2011). Doses exceeding the maximum levels approved by the FDA were found in several states. Across states, 0.11 to 1.33 percent of children are being treated concurrently with over five medications. According to the GAO panel "our experts also said that no evidence supports the use of five or more psychotropic drugs in adults or children, and only limited evidence supports the use of even two drugs concomitantly in children (Kutz, 2011, p14)."

Increased Risk for Mental Illness in Children in Foster Care

Greater prevalence of a number of mental illnesses might be expected in a population of foster children. First, many mental illnesses have a hereditary component. Parental mental disorder may constitute the reason why a child is in foster care. Because a child shares hereditary risk with a parent, greater prevalence of particular disorders can be expected for children in foster care. Second, disorders such as major depression, PTSD, and anxiety disorders are exacerbated by stressful conditions. The National Survey of Child and Adolescent Well-Being finds that 70% of children in foster care have a history of child abuse and/or neglect, more than 80% had biological parents with impaired parenting skills, and 40% had witnessed domestic violence (Burns et al., 2004; Leslie, Kelleher, Burns, Landsverk, and Rolls, 2003; Stahmer et al., 2005). Once in the foster care system, 63% of foster children are placed out of home for a duration of less than two years and during those two years live in, on average, three different placements (US DHHS, 2007). Thus, stressful conditions prior in early life and unstable living situations once in the foster care system can be expected to exacerbate emotional problems. Third, loss of a biological parent alone can be expected to result in depressive and anxiety symptoms as well as Post Traumatic Stress Disorder (PTSD) in children. Indeed, the GAO (2011) report noted that "57% of foster children were diagnosed with a mental disorder—nearly 15 times that of non-foster children receiving Medicaid assistance."

Issue of Legitimacy of Diagnosis

In an earlier time making a correct diagnosis was important because diagnosis was a guide to selecting the proper treatment. However, as previously documented, currently major depression, ADHD, anxiety disorders, and sleep disorders are being treated with atypical antipsychotics. DosReis et al. (2011) found that of the foster children in their sample receiving an antipsychotic, 53% had a diagnosis of ADHD, 34% had a diagnosis of depression, 21% had a diagnosis of bipolar, while only 5% had a diagnosis of schizophrenia. In examining factors that contributed to the greater likelihood of receiving multiple antipsychotics concomitantly, being male, being African American and having diagnoses of conduct disorder, autism, bipolar, psychosis, and schizophrenia increased the probability. Many of the children in the sample being treated with antipsychotics were also receiving antidepressants, stimulants, and mood stabilizers. In current practice, correspondence between diagnoses and particular treatments no longer describes practice. DosReis et al. (2011) speculated regarding the rationale for using multiple antipsychotics concurrently. They suggested that an insufficient response to one drug might prompt the addition of a second drug rather than increasing the dosage of the first drug or, perhaps, adding a second drug for a sleep problem might have provided a rationale. They also considered that “a proportion might lack a reasonable clinical rationale (p.1464)”. Whatever the reason, antipsychotics seem to be being dispensed for a wide range of diagnoses.

While individual physicians are engaging in off-label use of various drugs such as antipsychotics for various diagnoses in children and adults, the Federal Drug Administration continues to approve drugs for particular diagnoses rather than as general purpose panaceas. Assuming that diagnoses are still relevant in clinical practice, two diagnostic categories, which are not in the DSM-IV-R but have gained a modicum of perceived legitimacy, will be discussed: Pediatric Bipolar and Pre-psychosis.

Pediatric Bipolar

Before the last decade, there was wide agreement that Bipolar Disorder did not emerge prior to late adolescence or young adulthood (Anthony and Scott, 1960; Goodwin and Jamison, 2007, p. 188; Loranger and Levine, 1978). Whereas in 1996, pediatric bipolar was the least frequent diagnosis in hospitalized children, by 2004, it was the most frequent diagnosis for hospitalized children (Blader and Carlson, 2007). How did the diagnosis of Pediatric Bipolar gain acceptance? In the 1990s, Joseph Biederman, a child psychiatrist at Harvard, and his colleagues, began publishing articles indicating that many of the children who were being diagnosed as having ADHD and/or conduct disorder, also met criteria for Bipolar Disorder (see Biederman, Mick, Faraone, Spencer, Wilens, and Wozniak, 2000; Biederman et al., 2003). In order to bolster his case for children actually having Bipolar disorder, Biederman and colleagues and others assessed the parents of those children who met criteria for Bipolar disorder (see review of studies in Littrell and Lyons, 2010a). Many of these parents also met criteria for Bipolar Spectrum diagnoses. Since Bipolar is widely accepted as a heritable disease, the findings in parents were purported as evidence for the legitimacy of the claim that these children really were bipolar and they would emerge as adults with Bipolar Disorder.

Flaws in the argument. Biederman was able to make the case that the parents of the children who were being diagnosed with bipolar were also bipolar because of changes in the DSM-IV. In 1994, the diagnosis of Bipolar II was added to the *Diagnostic and Statistical Manual-IV* of the American Psychiatric Association. In the 1994 manual and the current 2000 version of the manual, whereas a diagnosis of Bipolar I requires that a patient meet criteria for an episode of mania, a diagnosis of Bipolar II only requires meeting criteria for hypomania. The same behaviors are listed for both mania and hypomania. The difference is that mania must last for a week whereas only four days are required for hypomania and, most importantly, if the behaviors result in functional impairment, then the diagnosis of mania is given rather than hypomania (see DSM-IV-TR, 2000, p. 368). The fact that hypomania does not result in significant functional impairment (DSM-IV-R) and the fact that hypomania is very common in the general population (Udachina and Mansell, 2007; Wicki and Angst, 1991) augured that the diagnosis of Bipolar would sky-rocket. Indeed, Moreno, Laje, Blanco, Jiang, Schmidt, and Olfson (2007) have documented a 38% increase in adult bipolar diagnoses from 2002-2003 compared to 1994-1995.

The problem with the diagnoses of Bipolar I and Bipolar II is they are two distinct disorders. In an early study, tracking those with Bipolar II diagnoses over time found that they were very unlikely to meet criteria for mania in later life (Coryell et al., 1995). Studies examining the family members of those with Bipolar I and Bipolar II, established that relatives of those with Bipolar I, for the most part, met criteria for Bipolar I and relatives of those with Bipolar II, for the most part, met criteria for Bipolar II (e.g., Coryell et al., 1984; see Littrell and Lyons, 2010a for review). The alleles for various genes increasing the risk for Bipolar I are not shared by those with Bipolar II (Judd et al., 2003; Vieta and Suppes, 2008). Moreover, distinct trajectories describe the course of the two disorders over time (Judd et al., 2003). Thus, the common label “bipolar” for those meeting criteria for Bipolar I and Bipolar II is very misleading.

In the studies examining the parents of children with Pediatric Bipolar, researchers failed to distinguish whether the parents met criteria for Bipolar I or Bipolar II (Littrell and Lyons, 2010a). Thus, the inference that children meeting criteria for Pediatric Bipolar had a genetic predisposition for Bipolar Disorder I based on the findings from studies of their parents was not legitimate and very misleading.

There were additional reasons for questioning whether children being diagnosed as Pediatric Bipolar would ever become Bipolar I adults. Many retrospective studies of adults with well-characterized Bipolar I suggested that they had exhibited depressive symptoms but not mania symptoms as children. For most adults with Bipolar I, a diagnosis of Major Depression preceded the emergence of mania. Moreover, there were a number of longitudinal studies of the children of parents with well characterized Bipolar I Disorder. Typical of these studies is work of Anne Duffy and colleagues. In a recent publication, Duffy, Alda, Hajek, and Grof (2009) reported that in their now young adult children of parents with Bipolar I, mania never emerged prior to 12, the mean age for the emergence of mania was 17, and in those in whom mania emerged, it was most often presaged by depressive symptoms in childhood. Thus, the children being diagnosed with Pediatric Bipolar, whose behavior overlapped with Attention Deficit/Hyperactivity, were obviously from a different population. (See Littrell and Lyons, 2010a, for citations and a review of the material referred to in this section.)

While psychiatrists are employing the Pediatric Bipolar diagnosis with great regularity, the various Committees established to develop diagnoses for children in the forthcoming DSM-V report are considering diagnoses of Temper Dysregulation Disorder with Dysphoria and Severe Mood Dysregulation (DSM-V Mood Disorders Workgroup; DSM-V Childhood and Adolescent Disorder Work Group, 2011) to supplant the Pediatric Bipolar label. Both antidepressants and stimulants can precipitate manic behavior (Delbello et al., 2001; Ghaemi, Hsu, Soldani, and Goodwin, 2003; Martin et al., 2004; Spetie and Arnold, 2007). The workgroups have noted that alternative terminology, a mere change in wording, could reopen the question of appropriate treatment for children currently being labeled Pediatric Bipolar. The committee recognized that for persons to whom the label “bipolar” is applied, “current convention renders treatment with antidepressants or stimulants relatively contraindicated without concurrent mood stabilizers or antipsychotics, (p. 6).” The discussions of the DSM-V workgroups reveal the degree to which confusion reigns as to how to identify legitimate diagnoses and what constitutes good treatment.

Pre-Psychosis

Considerable research has focused on the identification of markers that presage the development of psychosis. The hope was to be able to intervene early in the process and prevent schizophrenia. Allen Frances (2010b; 2011c), Co-Chair of the DSM-IV, articulates his objection to Pre-Psychosis in the forthcoming DSM-V. He argues that predictors of psychosis are not yet sensitive or specific. Indeed, Thompson, Nelson, and Yung (2011), developers of criteria for predicting future psychosis, reported that only 64.5% of those who developed schizophrenia were identified by their battery and for those scoring high, 35% were false positives. Examining persons in the high risk category, only 39.4% transitioned to psychosis during the 28 month follow-up interval. Thus, even given the best tools for identifying persons who will become psychotic, false positives are high. Allen Frances argues that given the state of the art, labeling children as “pre-psychotic” would not only be stigmatizing but would also result in unneeded medications.

Post Traumatic Stress Disorder

Many of the symptoms exhibited by children in foster care who are being medicated overlap with symptoms of PTSD. Hyper-alertness, irritability, and emotionality have been noted in Veterans returning from Iraq (Tyre, 2004). Thus, behavioral disturbance can be expected in those suffering trauma. Certainly, all children in foster care meet criteria for trauma: all have been removed from their biological families. Presently, reliable methods for distinguishing responses to trauma from other disorders in children have not been proffered. It is notable that the American Academy of Child and Adolescent Psychiatry (Gleason et al., 2007) specifically advises that PTSD in children should be treated with talk therapy and should not be medicated.

CAN EARLY PHARMACOLOGICAL INTERVENTION

Change the Course of a Disorder?

Bipolar

Kiki Chang and colleagues (2010; Chang, Howe, Galleli, and Miklowitz, 2006; Chang and Kowatch, 2007) have been proponents of the idea that early pharmaceutical treatment of Bipolar Disorder can prevent the emergence of severe symptoms. For his rationale, Chang references the kindling theory proffered by Robert Post (2007). The kindling theory posits that some process occurs in the brain when individuals are symptomatic which alters the physical characteristics so that severe symptoms are easier to elicit afterwards. If symptoms can be blocked, the kindling process can be precluded and the brain will remain healthy. That is the theory. Do the data support the theory?

In his many publications Chang fails to acknowledge some relevant facts. First, Goodwin and Jamison (2007), in their classic work on Bipolar, find little evidence for the kindling hypothesis that greater initial symptoms play a causal role in creating later symptoms (see Goodwin and Jamison, 2007, p. 152). With regard to early treatment changing the course of the disorder, Baldessarinni and colleagues have examined the impact of early treatment on the course of the Bipolar disorder and conclude that early treatment has no impact on subsequent frequency or severity of mood episodes (Baethge et al., 2003; Baldessarini, Tondo, Baethge, and Bratti, 2007). Finally, in Post's research on kindling which involved inducing seizure activity in rodents, suppression of seizures with anticonvulsants did not alter later sensitivity to provoking seizures, in fact, lamotrigine and carbamazepine facilitated kindling (Post, 2004; Weiss, Clark, Rosen, Smith, and Post, 1995; Postma, Krupp, Li, Post, and Weiss, 2000). Thus, the logic behind the rationale for early treatment is not supported by the facts. As we will be discussed in a later section, all of the drugs for Bipolar have severe deleterious effects on health. Thus, delaying treatment as long as possible seems a worthy goal.

While evidence is lacking for early treatment altering long term outcome, Whitaker (2010) has questioned whether pharmacological interventions for Bipolar I in adults, in fact, impairs long term outcome. Although drugs are approved by the FDA on the basis of evidence of efficacy, it should be noted that drug efficacy studies observe patients for about eight weeks. There have been no studies with random assignment to treatment and placebo with long term follow-up over years. An early naturalistic study with a ten year follow-up by Winokur et al. (1994) concluded that medications were not significantly related to outcome for patients with Bipolar.

Without the availability of random control studies to assess long term outcome of treatment, one can contrast the pre-drug literature on outcomes for Bipolar Disorder with current long term studies. This is what Whitaker did in his book. With regard to evaluation of patients before drugs, Rennie (1942) found that 93% of patients with mania recovered from their initial episode in an average of several months. Twenty-one percent never relapsed. Of those who did relapse, 30% remained remitted for at least 10 years with an average duration of remission of 20 years. Thus, after an initial period of bipolar symptoms, 51% were remaining well for a significant period of time. Later studies of those with Bipolar I in the post drug era find that only 2.1% of persons are asymptomatic during a 12.8 year follow-up; 80% of those who recover relapse within 1.7 years; 23% are continuously unemployed and

another 35% are erratically employed (Harrow, Goldberg, Grossman, and Meltzer, 1990; Judd et al., 2002). Examining outcomes for those with Bipolar II, Judd et al. (2003) concluded that Bipolar II is an even more chronic condition than Bipolar I.

Psychiatrists have also provided global assessments of outcomes for Bipolar Disorder. A review of early studies prompted Winokur, Clayton, and Reich (1969) to conclude there “was no basis to consider manic depressive psychosis permanently affected those who suffered from it” (p.21). This contrasts with the dismal prognosis, provided by the Judd et al. (2002) findings in the longest follow-up study of medicated patients in the post-drug literature discussed previously. Zarate, Tohen, Land, and Cavanagh (2000) have also noted the contrast between earlier and current outcomes: “In the era prior to pharmacotherapy, poor outcome in mania was considered a relatively rare occurrence. However, modern outcome studies have found that a majority of patients with bipolar evidence high rates of functional impairment” (p. 309). The contrast between early conclusions on Bipolar Disorder with current outcome studies should have prompted the hypothesis that drugs create a worse outcome. Rather, the conclusion made by psychiatrists is that in modern times we conduct more sensitive research and thus can develop more realistic expectations of prognosis.

It should be noted that the efficacy of lithium for reducing bipolar symptoms in children ages 7-17 has been called into question (Dickstein et al., 2008).

Pre-Psychosis and Psychosis

In examining efficacy of early medicating of psychosis, two types of studies can be examined. The first literature considers studies asking whether early treatment for those exhibiting overt psychosis changes the long term outcome of the later course of psychosis. Most of the studies in this literature were on young adults and not children. Indeed, in a meta-analysis by Perkins et al. (2005), the mean age of those with first episode psychosis was 27.8, so direct relevance to children can be questioned. However, this literature does shed light on the effects of early treatment. Another set of studies has examined the impact of treatment intervention on those who only exhibit symptoms believed to be predictive of later psychosis and who may have relatives with psychosis. The issue of the efficacy of early treatment of those already exhibiting psychotic symptoms, for psychosis and the issue of preventing psychosis are examined separately.

Treating overt psychosis early. Two large meta-analysis (Marshall et al., 2005; Perkins, Gu, Boteva, and Lieberman, 2005) have concluded that in those individuals exhibiting delusional thinking or experiencing hallucinations, delaying treatment is associated with more negative outcome. However, both of these reviews identified significant caveats in drawing the conclusion that early treatment causes better outcome. In both the Perkins et al. and Marshall et al. reviews, those receiving delays in treatment were distinguished by greater negative symptoms. Some of the positive benefit of early treatment was attenuated after controlling for initial characteristics. Moreover, in both reviews difference in outcome between those receiving early and late treatment was modest, with Perkins noting that delay in treatment accounted for only 13% of the variance in outcome.

Preventing the emergence of psychosis. A number of investigators have evaluated interventions to reduce the transition to psychosis in samples selected for high risk. No clear benefit for psychotherapy, family interventions, or antipsychotic drugs was apparent

according to a review conducted by the Cocharane Collaboration (Marshall and Rathbone, 2011a, b). However, there was a suggestive positive result from the use of omega-3 fatty acid supplements. In a study by Amminger et al. (2010), 81 high risk subjects were randomly assigned to take omega-3s or placebo. They were evaluated on global functioning and level of symptoms at 52 weeks. Some of the patients in the omega-3 group and the control group were taking benzodiazepines or antidepressants but none were taking antipsychotics. By 52 weeks, 4.9% of the omega-3 group and 27.5% of the placebo group had transitioned to psychotic disorder (Amminger et al., 2010). Along with the just-cited suggestive evidence for efficacy of omega-3 in preventing the emergence of psychosis, there is evidence that omega-3 have strong antidepressant properties (Kiecolt-Glaser, 2010). Moreover, in a study of medical students, omega-3 supplementation did attenuate symptoms of stress (Kiecolt-Glaser, Belury, Andridge, Malarkey, and Glaser, 2011). Omega-3s are found in fish and walnuts. Dietary supplements are also available.

ADHD

Years ago, Judith Rappoport and colleagues (Sostek, Buchsbaum, and Rappoport, 1980) conducted a study in which she gave stimulants to all the children, both those with ADHD and those without. She found that attention and vigilance improved for all children administered the stimulant. Stimulants are noted for focusing attention and enhancing memory formation in adults (Hart, Ksir, and Ray, 2009; Soetens, D'Hooge, Huesting, 1993). Studies evaluating improvement in school performance, do find that children with ADHD do better with stimulants. However, the results of the Multisite Multimodal Treatment Study (MTA) shed light on long term outcomes. In this study, outcomes for children with ADHD who had never been medicated were contrasted with those who had been medicated, some of whom were continuing with medications and others who were not. In the long run over eight years, children with ADHD on drugs versus children never on drugs show no difference in results on school achievement. For the MTA study, Molina et al. (2009) noted even those who continued taking medications did not differ from the non-medicated on most measures, with the exception of some benefit for continued drug use on math performance.

Major Depression

The acknowledged fact, even among psychiatrists, is that antidepressants do not work very well even during the eight weeks of initial treatment in adults. Only two-thirds of patients respond to a trial of antidepressant (Thase et al., 2005; Tratner, O'Donovan, Chandarana, and Kennedy, 2002). One half of responders are acknowledged to be placebo responders. Of those who respond to drug, less than half achieve remission from depression (Calabrese et al. 2006; Nemeroff, 2001; Tratner et al. 2002). The previous statements are based on published studies in which the results of treated versus controls did reach statistical significance.

Small reliable differences can be detected when the sample sizes are large enough. On the other hand, in order to be able to recognize when occasionally observed differences are merely chance, and there is in fact no effect, all data must be entered. If some studies which do not show effects are excluded, then there is an increased likelihood that false statistical evidence of effects (particularly small effects) can appear among remaining studies. Irving Kirsch (2010) gathered all the data from antidepressant studies comparing drug to placebo that were reported to the FDA by the drug companies. Analyzing this more complete set of

the comparisons between drug and placebo groups, the statistical conclusion was that there was little difference between the groups. The average difference between those treated with an antidepressant versus those receiving placebo is 2 points out of 51 points on the Hamilton Rating Scale, a commonly used assessment measure (Kirsch, Moore, Scoboria, and Nichols, 2002). These results may have contributed to the recent remark by the current director of the National Institute of Mental Health, Thomas Insel (2009), who offered a bottom line on the effectiveness of psychotropic medications in general, when he said: "The unfortunate reality is that current medications help too few people to get better and very few people to get well" (p. 704).

Whereas efficacy of the antidepressants even in the short term is questionable, others have examined the long term outcomes on depression for those taking antidepressants contrasted with outcomes for depression in the pre-drug literature. Giovanni Fava (2003) was an early pioneer in this endeavor. He advanced the hypothesis that current treatments convert an acute problem into a disorder with a chronic course. Fava and Offidani (2011) reported a similar argument. Littrell (1994) also contrasted outcomes for depression prior to drugs and noted the same pattern of more frequent relapses in those treated with drugs. A recent evaluation by Andrews, Kornstein, Halberstadt, Gardner, and Neale, M. C. (2011) of outcomes with antidepressants compared to the depressed but unmedicated reached a similar conclusion. Although the explanations provided for the greater number of relapses over the long run in those taking antidepressants contrasted with those who do not have varied, the worse outcomes in those with drugs has been acknowledged by those who have looked at the data. Littrell (1994) offered drug withdrawal as an explanation for the high rate of depressive symptoms observed in those discontinuing antidepressant medications. Depressive symptoms emerge upon drug discontinuation even in those who were taking antidepressants for anxiety symptoms and who had not been previously depressed (Pato, Zohar-Kadouch, Zohar, and Murphy, 1988).

The efficacy of antidepressant drugs is particularly suspect for children and adolescents. Jureidini et al. (2004) conducted a meta-analysis of the six published randomized controlled studies they could find in the literature evaluating new antidepressants. According to the authors "On 42 reported measures, only 14 showed a statistical advantage for an antidepressant. None of the 10 measures relying on patient reported or parent reported outcomes showed significant advantage for an antidepressant, so that claims for effectiveness were based entirely on ratings by doctors (p. 880)". Two small studies did not find statistical significance. Among the larger studies, two found significant advantage, while two did not. With regard to effect sizes in the positive studies, "the effect size of 0.26 is equivalent to a very modest 3 to 4 point difference on the scale, which has a range of possible scores from 17 to 113 (p. 880)." Thus, the magnitude of the difference between antidepressant treated children's group versus placebo is very small, similar to published results in adults. Consistent with the unclear evidence of efficacy for antidepressants in children, Goodman, Murphy, and Storch (2007) noted that in only 3 of 15 outcome studies submitted to the FDA examining antidepressant efficacy in children for antidepressants were results significant. It should be noted that only fluoxetine/Prozac has been approved by the FDA for treating depression in children, although Prozac, Zoloft/sertraline, and fluvoxamine are approved for treatment of obsessive compulsive disorder.

The largest study of antidepressants in children was the "Treatment of Adolescents with Depression Study" which involved 13 academic centers and 327 adolescents ages 12 to 17

randomly assigned to Cognitive Behavioral Therapy, fluoxetine/Prozac, or a combination. At 12 weeks 73% had experienced a 50% drop in symptoms with combination therapy, compared to 62% with fluoxetine alone, and 48% with CBT. However, by 18 weeks, differences between CBT and fluoxetine were no longer significant. By 24 weeks, differences among treatments were no longer significant on percentages responding to treatment. By 24 weeks, approximately 89% could be counted as responders. In terms of relapses during the 36 months among those who were categorized as responders at 12 weeks, CBT had 3.1% relapses compared to 25.9% relapses in the Prozac group, and 11.5% relapses in the combination group (Rohde et al., 2008). At one year, a point when the researcher did not know what treatments the participants were receiving, a lack of difference among the groups remained. 82.2% of the combined group, 75.2% of the Prozac group, and 70.3% of the CBT group were categorized as responders defined as a 50% drop on scale scores. Recall that responding is not the same as being well. At one year, in terms of those who could be said to be well: 68% of the combined group, 67% of the Prozac, and 69% of the CBT group were described as remitted/well (TADS Team, 2009).

Suicidal events, defined as a suicide attempt, suicidal ideation, or preparatory action toward suicide, but not self-mutilation, were also measured in the TAD study. There were significantly more suicidal events during the 36 weeks with Prozac (14.7%) than with combination (8.4%) or than with CBT (6.3%) (TADS Team, 2007). For newly emergent suicidal events at 12 weeks, the interval during which most of the suicidal events occurred, the numbers were: 11.0% for Prozac; 4.7% for combination; 4.5% for CBT (TADS Team, 2007). Thus, the more rapid response to treatment with Prozac is offset by an increase in the risk for suicidal events.

DANGERS OF MEDICATIONS

Anti-Psychotics

Probably the worst side effect of drugs which block the action of dopamine is “brain tissue volume decrement.” Ho, Andreasen, Ziebell, Pierson, and Magnotta (2011) tracked first-episode psychotic individuals over an average of seven years. They took brain images over time. They documented a decrease in brain volume that was associated with the dosage of the medication. The effects obtained for both the older (neuroleptics) and the new (atypical) anti-dopaminergic drugs. Ho et al. acknowledged that because they did not observe random assignment to a control group of non-medicated individuals, they could not make a definitive statement that the drugs caused the brain volume decrement. It could have been that those receiving the higher dosages did not come from the same population of individuals. However, Ho et al. cited research with primates. Konopaske et al. (2007; 2008) randomly assigned primates to receive anti-dopaminergic drugs at levels in the therapeutic range for people for 27 months. Those animals who received the drugs exhibited a reduction in total weight of the brain, with greatest reduction in the parietal lobe (with a loss of between 11.8% to 15.2%). Moreover, a 14.2% reduction in glial cell (fat cells) numbers was reported. The glial cell reduction is notable because these cells release growth factors which are vital to maintain the health of the brain (Schwartz and Schechter, 2011; Ziv and Schwartz, 2008). Dopamine, the

neurotransmitter blocked by antipsychotic drugs, is a trigger for getting glial cells to release growth factors (Miklic, Juric, Carman-Krzan, 2004). The Konopaske studies are not the only studies in primates. Results similar to Konopaske et al.'s were found in a macaque study by Dorph-Petersen et al. (2005) who noted a 8-11% reduction in brain volume after 1.5 to 2.3 years of exposure to haloperidol (old neuroleptic) or olanzapine (new atypical).

While brain volume reduction may be the most ominous side-effect of the antipsychotic drugs, brain volume reduction is not the only side effect. Atypical antipsychotics are notorious for inducing weight gain that does not plateau, type-2 diabetes, and an increase in fat levels in blood. Children are at elevated risk for developing metabolic side effects (Correll and Carlson, 2006; Safer, 2004; Sikich et al., 2004; Tohen et al., 2007; Woods et al., 2002). The older neuroleptic drugs have long been noted to be associated with Parkinson's symptoms (extra-pyramidal symptoms) in the short term, and permanent movement disorders (tardive dyskinesia) in the long run. The Clinical Antipsychotic Trial of Effectiveness study, a big government funded study, found that newer drugs were also associated with movement disorders, albeit to a lesser extent (Casey, 2006; Manschrek and Boshers, 2007; Miller et al., 2005). The FDA has also issued a warning indicating that the atypicals are associated with QT wave prolongation. Thus, fatal heart arrhythmias can occur (Psychiatric News Alert, 2011). Atypicals are also associated with lowered bone mineral density (Calarge, Zimmerman, Xia, Kuperman, and Schiechte, 2010).

Lithium

Lithium causes cognitive slowing in adults (Ghaemi, 2008; Pachet and Wisniewski, 2003); impairment is also observed in children (Geller et al., 1998; Silva, 1992). Other annoying side effects include: confusion, slurred speech, ataxia, frequent urination, enuresis, abdominal discomfort, nausea, and vomiting (Hagino et al., 1995). Twenty percent of patients experience weight gain (Chen and Silverstone, 1990). Lithium is associated with thyroid dysfunction (Goodwin and Jamison, 2007). Lithium can cause damage to the cerebellum (Goodwin and Jamison, 2007) and has been associated with cardiac arrhythmias (Ghamei, 2008).

Perhaps most troubling for medicating children is the risk of End Stage Renal Disease in those treated for an extended period of time (over 12 years). In a sample of 74 patients treated for 20 years, 12 reached End Stage Renal Disease (Presne et al., 2003). Presne noted that fifty percent of patients on lithium exhibit impaired renal concentrating ability (Presne et al., 2003). Even when medication is discontinued, kidney damage once started can continue (Markowitz et al., 2000), although kidney damage is related to the duration of lithium treatment (Bendz, Aurell, and Lanke, 2001). Extrapolating from these findings, if children are placed on lithium at age 6, some of them will need a kidney transplant at age 26. People develop an immune response to their transplants even when on immunosuppressants (Galliford and Game, 2009). Approximately, 19% of kidney transplants will be rejected within five years (Murphy, 2010, p. 259). Thus, lithium treatment in children can be expected to significantly shorten life span for some, if not many, of them.

Mood Stabilizers

The annoying side effects of valproate include sedation, nausea, and vomiting. Hematological side effects (anemia, low white counts) have been noted (American Academy of Child and Adolescent Psychiatry, 1997). Up to 89% of young women treated with

valproate develop polycystic ovarian disease, involving weight gain, facial hair, and menstrual irregularities (Isojarvi et al., 1993). Valproate increases risk for diabetes (Correll and Carlson, 2006). Both hepatitis and pancreatitis can be induced by valproate and carry black box warnings issued by the FDA (2009)

Depression can be induced and both carbamazepine and valproate have black box warnings for suicidal ideations (US FDA, 2008). Anticonvulsants such as valproate are noted for inducing cognitive impairment (American Academy of Child and Adolescent Psychiatry, 1997; Banu et al., 2007; Loring and Meador, 2004; Henin et al., 2009). Lamotrigine is another mood stabilizer. Lamotrigine is associated with Stevens-Johnson syndrome. Stevens-Johnson's syndrome entails life threatening blistering on all external body surfaces (Borchers, Lee, Naguwa, Cheema, and Gershwin, 2008).

Stimulants

Stimulants include amphetamines and Ritalin/methylphenidate. Adderall is a long acting form of amphetamines, while Concerta is a timed-release preparation of Ritalin. Stimulants have a black box warning for heart attacks in Canada and the U.S. (CanWestNews, 2008; Physician's Desk Reference, 2012). Stimulants do suppress growth in height possibly through inhibition of growth hormone (Faraone, Biederman, Morley, Spencer, 2008; Zhang, Du, Zhuang, 2010).

Stimulants can induce psychosis and are associated with sleep disturbance and suppression of appetite, and induction of motor tics (Physician's Desk Reference, 2012). Stimulants also suppress playfulness in animals (Beatty, Dodge, Dodge, White, and Panksepp, 1982). Animal research suggests that the purpose of play in youngsters, which is found cross species, is to facilitate social development and maturation of the orbitofrontal cortex and the Prefrontal Cortex (Bell, Pellis, and Kolb, 2010). Most of the research on stimulants has focused on the impact on concentration and school performance. Very little research has focused on social development. It is, however, known that stimulants can precipitate mania in the predisposed (DeBello et al., 2001).

As a part of the Individuals with Disabilities Education and Improvement Act of 2004, Schools cannot require children to take a stimulant to stay in school (see AbleChild.org web site).

Anti-Depressants

Selective Serotonin Reuptake Inhibitors carry black box warnings for agitation and suicidal ideation in children and adolescents (US FDA, 2007). Reinblatt, deReis, Walkup, and Riddle (2009) document that the SSRI, fluvoxamine, will induce "activation adverse events" including increased activity, impulsivity, insomnia, and disinhibition, in 45% of children. In adults, loss of libido and sexual dysfunction are common (Rosen, Lane, Menza, 1999). Studies examining the impact of SSRIs on puberty and or later adult sexual functioning are not available, although in adults sexual dysfunction can persist after drug discontinuation (Csoka, Bahrlich, Mehtanan, 2008). Studies with adults suggest that taking antidepressants for over a year is associated with weight gain (Fava, 2000; Raeder et al. 2006); an increase in C-Reactive Protein, a risk factor for cardiovascular disease (Hamer et al., 2011); type II diabetes (Kivimäjum et al., 2010; Raeder et al., 2006; Rubin et al., 2010); and metabolic syndrome (Dawood et al., 2007; Kemp et al., 2010); and cognitive impairment (Damsa et al., 2004; Fava, 2006). Brain imaging research investigating the emotional numbing effect of selective

serotonin reuptake inhibitors (SSRIs), finds that in persons taking SSRIs emotional response to both positive and negative stimuli are dampened (McCabe, Mishor, Cowen, and Hamer, 2010). Several studies have found that SSRIs are associated with suppression of growth hormone and suppression of growth (Weintrob, Cohen, Klipper-Aurbach, Zadik, and Dickerman, 2002) as well as decreased bone mineral density (Calarge, Zimmerman, Xie, Kuperman, and Schlechte, 2010).

A major problem with initiating treatment with antidepressants is that they are associated with severe withdrawal symptoms when the drug is discontinued. As previously discussed, depression emerges as a component of withdrawal even in those who were taking antidepressants for anxiety and were not initially depressed (Pato, Zohar-Kadouch, Zohar, and Murphy, 1988). Haddad (1997) indicates that 20-86% of sample report symptoms, after discontinuing the drug, which include dizziness, nausea, lethargy, headache, anxiety, tingling and burning sensations, confusion, tremor, sweating, insomnia, irritability, memory problems, anorexia. Stoukides and Stoukides (1991) provided a case report of man who had taken Prozac/fluoxetine for 6 months. Upon discontinuation, the man experienced muscle spasms and exhibited protruding tongue movements. Consistent with the case report, Ceccherini-Nelli et al. (1993) reported that of 10 individuals examined, seven exhibited withdrawal symptoms which included cardiac arrhythmia, resting tremor of the jaw, tongue, and upper extremities, insomnia, chills, sweating, nausea, headache. Along with other symptoms, Lejoyeux and Adés (1997) reported mania or hypomania, delirium, mood changes, dizziness, sensations of tingling and burning in limbs. Goldstein et al. (1999) and McGrath et al. (1993) also reported the emergence of mania upon withdrawal. Surprisingly, protocols for detoxing patients from antidepressants have not been published.

Assuming female foster children will grow up and have normal lives including becoming parents themselves, continuing with SSRIs during pregnancy is problematic. SSRIs increase the risk of autism (Croen, Grether, Yoshida, Odouli, and Hendrick, 2011) and decreased head circumference (Marroun et al., 2012). Withdrawal symptoms in the infant, heart defects, hypospadias (misplaced urethra opening in the male), and life threatening pulmonary hypertension in the new born have been reported for infants exposed to antidepressants during gestation (Chambers et al., 2006; Gentile, 2011; Udechuku, Nguyen, Hill, and Szego, 2010). Antidepressants also increase the risk for hypertension in the mother during pregnancy (Anick Berard 2012 British Journal of Clinical Pharmacology).

Research on Bipolar I has documented that early onset depression is often a precursor to the emergence of mania (Leverich et al., 2006). Thus, depression in a child is a risk factor for mania. Indeed, Goldberg et al. (2001) found that 19% of their young depressives converted to mania. It is further known that antidepressants can precipitate a mania (Ghaemi, Hsu, Soldani, and Goodwin, 2003). Indeed, antidepressants can precipitate mania in as many as 44% of those who exhibit fluctuations in mood (Akiskal, Djenderedjian, Rosenthal, and Khani, 1977). Thus, the relatively high risk of inducing mania is another danger of using antidepressant medications in young persons.

FORCES BEHIND DIAGNOSING AND MEDICATING CHILDREN

At the individual level, some of the incentive for providing strong diagnoses to children derives from the Medicaid system allowing more visits to those children with more extreme

diagnoses. Moreover, severe diagnoses may qualify a child for Supplemental Security Income from the Social Security System. Once particular diagnoses are provided, medication seems to follow automatically despite the guidelines of the American Academy of Child and Adolescent Psychiatry (Gleason et al., 2007) that for small children, other interventions should be tried first. The pressures toward diagnosis cannot, however, explain the higher doses of medications exceeding recommendations of the FDA and why so many children received multiple medications. Perhaps one has to look at how doctors are trained and to the financial ties to the pharmaceutical industry of the academic opinion leaders who are running the continuing education programs.

Senator Charles Grassley's committee investigated the ties between academic psychiatrists and the pharmaceutical industry. Both Charles Nemeroff of Emory University and Joseph Biederman of Harvard were sanctioned for failing to reveal the extent of their financial remuneration to their employers (Harris and Carey, 2008a/b). (Biederman, as mentioned previously, was the exponent for the diagnosis of Pediatric Bipolar.) In the Grassley Committee hearings, there was also concern expressed over the ghostwriting of articles and books by the pharmaceutical industry with prominent academicians appending their names to these publications (Grassley, 2010).

Notes of caution against the broad based use of antipsychotics have appeared in the literature. For example, Ho et al. (2011) indicate "our findings may lead to heightened concerns regarding potential brain volume changes associated with the sharp rise in atypical antipsychotic use in non-schizophrenic psychiatric disorders (p. 135)." Dos reis et al. (2011) caution, "Antipsychotic poly-pharmacy has demonstrated greater adverse effects with only marginal benefits" and "Given the lack of scientific evidence for such practice, the lack of data on the cumulative risks on child development, and the clear indications of the metabolic adverse effects with these agents, it is important to investigate concomitant antipsychotic use in this vulnerable child population." Comer, Mojtabei, and Olfson (2011), referring to the rise of atypicals in the treatment of anxiety disorders, indicate "Prudence further suggests that renewed clinical efforts should be made to limit use of these medications to clearly justifiable circumstances (p. 1064)". However, the words of caution provided in the journals may not be enough to drown out advertisements from pharmaceutical houses and the cacophony of opinion leaders tethered to industry.

There is a problem with the system for informing physicians. Doctors do have to accumulate continuing education hours to maintain their licenses. There is no formal mechanism for awarding credit for simply reading journals. Drug companies sponsor and select the speakers for the Continuing Education Programs. All the medical journals are replete with industry advertisements. Given the system for informing doctors, it is no wonder why many physicians, who were writing prescriptions for poly-pharmacy and dosages in excess of those recommended by the FDA, probably believed that they were following good practice.

ALARM AND ADVOCACY

Presently, Allen Frances (2009; 2010a/b), a Co-Chair of the DSM-IV, has led a rebellion against the Committees developing the DSM-V. Frances cautioned against the unintended consequences of the manner in which the DSM-IV criteria were stated, which led to the

epidemic rise in the diagnoses for ADHD and Bipolar Disorder (Frances, 2011c). In an interview with Gary Greenberg (2010), Allen Frances explained his activism, “kids getting unneeded antipsychotics that would make them gain 12 pounds in 12 weeks hit me in the gut. It was uniquely my job and my duty to protect them. If not me to correct it, who? I was stuck without an excuse to convince myself.” A petition, entitled “Open letter to the DSM-5”, on October 23, 2011, launched by the Society for Humanistic Psychology and several other American Psychological Association divisions, was posted on the Web (<http://www.ipetitions.com/petition/dsm5/>). The petition implores the DSM-5 committees to avoid further loosening of the criteria for being diagnosed with a mental disorder. Frances (2011a, b) has applauded the effort and has urged others to sign.

A number of physicians have written books detailing how the industry has provided lucrative fees to academic opinion leaders who present the materials carefully prepared by the pharmaceutical industry at continuing “education” conferences. Carl Elliott (2010) in *White Coat, Black Hat* details the lack of ethics in medicine generally and the heavy domination by pharmaceutical houses. Doug Bremner, an Emory psychiatrist who was once an opinion leader on the circuit marketing pharmaceuticals, has a web site where he discusses the side effects of various medications. Doug Bremner (2011), in the *Goose that Laid the Golden Egg* as well as on his website, details his legal entanglements with drug companies when he published a study connecting Accutane, a drug used in the treatment of acne, with increased risk for suicide. Phillip Sinaikin (2010), another individual once on the circuit for the pharmaceuticals, offers witness testimony to corruption of influential members of the psychiatric profession in *Psychiatryland*. Joanna Moncrieff (2003) also detailed the influence of the pharmaceutical industry in “*Is psychiatry for sale?*” Marcia Angell (2005), former editor of the *New England Journal of Medicine*, has written extensively about loss of credibility in the medical profession because of ties to industry. Recently, she (2011) offered a supportive review of Bob Whitaker’s (2010) *Anatomy of an Epidemic* in *New York Review of Books*. (Whitaker contrasts outcome pre and post drugs for antidepressants, mood stabilizers, and antipsychotics and finds that outcomes are worse with drugs.) She concurs that there is a paucity of data on the long term effects of psychotropic medications of any type for any age. Most of the “data” consists of industry funded studies which follow patients for eight weeks.

Others have focused more specifically on the heavy medications being used for foster children. The public broadcasting system program *The Watchlist* (2011) aired “The Medication of Foster Children”. Diane Sawyer ran segments on ABC news documenting the medication of children in foster care during the first week in December of 2011. Jeffery Thompson, a state Medicaid director in Washington state, organized the Medicaid Medical Directors Learning Network (2010) to investigate the practice of medicating foster children with strong medications. Senators Grassley and Landrieu developed the Senate Caucus on Foster Care Youth to investigate the issue of psychotropics (Samuels, 2011). James Gottstein of Psychrights sued the state of Alaska on behalf of foster children. Senator Carper of Delaware held a Committee meeting on December 1, 2011 to hear testimony of experts and to discuss the findings of the GAO on the five state survey on the extent of medicating children in foster care.

MOVING FORWARD

In September of 2011, Congress passed the Child and Family Services Improvement and Innovation Act. This law requires that states applying for certain federal child welfare grants establish protocols for the appropriate use and monitoring of psychotropic drugs prescribed to children. In the GAO's report to congress (Kutz, 2011), they indicated that compliance with the guidelines promulgated by the American Academy of Child and Adolescent Psychiatry requires obtaining informed consent for medical treatment. Unfortunately, the GAO report did not discuss who might be empowered to provide informed consent for foster children. In my personal experience, case workers and foster parents are quite intimidated by doctors and are reluctant to challenge a recommendation. This is consistent with Matt Salo's (2011) testimony before the Carper Sub-Committee indicating that states "had to abandon an attempt to strengthen the hand of foster care workers in these situations, when it became clear that BA/BS or MSW educated workers would face significant liability issue when disagreeing with prescribers." In fact, foster parents have been accused of medical neglect when they objected to medicating children in their care. Of course, expecting physicians to exercise good judgment has resulted in the extant situation.

On December 1, 2011 Senator Tom Carper of Delaware convened the Senate Sub-Committee on Financial Management, Government Information, Federal Services, and International Security. At this meeting, discussed early in this paper, the GAO announced plans to contact states to develop tracking systems to monitor the medicating of children in foster care. The federal government through National Association of Medical Directors may provide policies on best practice. Jim Gottstein (personal communication, 2011), of Psychrights, also suggests that doctors engaging in off-label prescribing for which there is paucity of justification in the research literature (that is, there is no medically accepted indication), are guilty of Medicaid fraud. Thus, the federal government can act to protect foster children by bringing charges of Medicaid fraud against both doctors and the pharmacies that fill the prescriptions. With regard to children in the general public, on August 1, 2011, Ron Paul has introduced "The Parental Consent Act" (HR2769) which will require informed consent from parents for participation in mental health screening.

Hopefully, more foster children will remain drug free given these new policies. However, assuming that the drugs were at least effective at sedating these children, other supports for foster parents will be needed. This may require more use of behavior therapy and psychotherapy. Evaluation of the cost effectiveness of these interventions should be made. Recently, Fullerton et al. (2011) noted an increase in Medicaid spending for persons with Major Depression which coincided with an increased reliance on atypical antipsychotics. Given the high cost of atypical antipsychotics safer treatment may even be cheaper.

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