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**Report to the FDA:**

**Observations on SSRI-Induced Behavioral and Mental Abnormalities  
in Children and Adults**

When evaluating the vulnerability of children or adults to SSRI-induced adverse drug reactions, the inquiry should be broadened from suicidality to include the overall problem of SSRI-induced mental and behavioral disturbances, such as manic-like syndromes, agitated depression, agitation, anxiety, akathisia, and insomnia. These phenomena can be understood as a continuum of stimulant adverse effects that, in their extremes, result in manic psychoses with violence and agitated depressions with suicide.

The overall pattern of SSRI-induced mental and behavior syndromes is well-documented and should discourage their use in children. For example, in brief clinical trials involving children, rates of SSRI-induced mania run as high as 4-6% and rates for SSRI-induced depression as high as 5%. In actual clinical practice involving longer drug exposures and less thorough monitoring, the rates are even higher (see the enclosed reviews).

Studies conducted with adults have grave implications for even more vulnerable children. Many clinical reports, clinical trials and epidemiological studies demonstrate increased rates of abnormal behavior, especially suicide, in adults in association with SSRIs.

In addition to several books\*, I have addressed these issues in two recently published peer-reviewed reports that are available on my website ([www.breggin.com](http://www.breggin.com)):

- (1) Breggin, P. "Suicidality, violence and mania caused by selective serotonin reuptake inhibitors (SSRIs): A review and analysis." International Journal of Risk & Safety in Medicine, 16, 31-49, 2003/4.

Two sections focus on children (pp. 40-42) and review clinical case studies, clinical trials, and epidemiological studies indicating significant rates of suicidality and other behavioral abnormalities. The paper reviews the literature and describes the SSRI-induced clinical syndromes that are associated with abnormal behaviors.

- (2) Breggin, P. "Fluvoxamine as a cause of stimulation, mania, and aggression with a critical analysis of the FDA-approved label." International Journal of Risk and Safety in Medicine, 14: 71-86, 2002.

Based on data collated from the FDA-approved label, including clinical trial data, Table I (p. 81) shows the unusually high rates of depression and other adverse reactions in children.

The above two reports were written specifically to address the kinds of issues that the panel will be examining. The scientific literature is much more extensive than generally realized and the syndromes rather well-documented and defined.

My clinical and forensic experiences and the scientific literature indicate that four syndromes encompass most of the phenomena and describe most of the individual cases:

(1) The production of a *stimulant continuum* that often begins with lesser degrees of insomnia, nervousness, anxiety, hyperactivity and irritability and then progresses toward more severe agitation, aggression, and varying degrees of mania. Mania or manic-like symptoms include disinhibition, grandiosity, sleep disturbances, and out-of-control aggressive behavior, including cycling into depression and suicidality.

(2) The production of a combined state of *stimulation and depression*—an *agitated depression*—with a high risk of suicide and violence. Often the overall depression is markedly worsened.

(3) The production of *obsessive preoccupations* with aggression against self or others, often accompanied by a worsening of any pre-existing depression.

(4) The production of *akathisia*, an inner agitation or jitteriness that is usually (but not always) accompanied by an inability to stop moving. It is sometimes described as psychomotor agitation or restless leg syndrome. The state causes heightened irritability and frustration with aggression against self or others, and often a generally worsening of the mental condition.

The above syndromes often appear in combination with each other. *Obsessive preoccupations* in particular are often displayed by the individual. Again based on my clinical experience and the scientific literature, these characteristics include:

1. A relatively sudden onset and rapid escalation of the compulsive aggression against self and/or others.
2. A recent (typically within two months) initial exposure to the medication, or a recent change in the dose of the medication, or a recent addition or removal of another psychoactive substance to the regimen.
3. The presence of other adverse drug reactions, often involving akathisia or stimulation along a continuum from irritability and agitation to agitated depression and mania.
4. Resolution of the syndrome after termination of the causative medication, often with a marked overall improvement in the individual's mental status.
5. An extremely violent and/or bizarre quality to the thoughts and actions.

6. An obsessive, compelling, unrelenting quality to the thoughts and actions.
7. An out-of-character quality for the individual as determined by the individual's history.
8. An alien or ego-dystonic quality as determined by the individual's subjective report.

Often the medications have been prescribed without sufficient monitoring and without the provision of adequate warnings to the patient and family about the risks of psychiatric adverse drug reactions.

Sometimes the syndromes will abate within days after stopping the SSRI but at other times they persist, leading to hospitalization and additional treatment over subsequent weeks or months. Reported rates for these four syndromes very widely but each of them appears to be relatively common. They frequently occur in individuals with no prior history of violence, suicidality, psychomotor agitation, or manic-like symptoms.

As a clinician and as a medical expert, I have been involved in dozens of criminal, malpractice, and product liability cases in which adults and children have committed violent and suicidal acts while taking SSRIs. In light of the scientific literature, the courts are giving more consideration to the role of SSRIs in producing abnormal mental states and behavior. When the patient is not informed in advance about the potential impairment of mental function and disinhibition of behavior, or when the prescription of the medication is negligent, the condition often qualifies as an involuntary intoxication under the law. The diagnosis in most cases is SSRI-induced mood disorder with manic features (292.84).

The medical profession and the public needs to be made more aware of the mental and behavior risks associated with SSRIs.

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\*Talking Back to Prozac (St. Martins, 1994), Brain-Disabling Treatments in Psychiatry (Springer, 1997), and the Antidepressant Fact Book (Perseus, 2001).