LETTER TO THE EDITOR

SSRIs-Related Behavioural Syndromes in Children and Adolescents

Ahmed Naguy MBBch, MSc

Key Words: SSRIs, behavioural syndromes

Dear Editor:

Selective Serotonin Reuptake Inhibitors (SSRIs) have become increasingly the mainstay of treatment for a wide array of depressive and anxiety disorders in Child and Adolescent Psychiatry (CAP) reflecting efficacy coupled with reasonable safety and tolerability- unlike its predecessors; tricyclic antidepressants (TCAs). Dire shortage of clinicians trained in Child and Adolescent psychotherapy renders SSRIs a default first-line treatment. FDA-approved SSRIs in CAP are sertraline, fluvoxamine, fluoxetine, and, escitalopram. Apart from expected somatic side-effect profile of SSRIs related to excess serotonin in the synaptic cleft stimulating post-synaptic 5HT2A, 5HT2c, and 5HT3 receptors, behavioural syndromes are now more frequently encountered in clinical practice that mandate special characterization. Here, I delineate eight of these syndromes- mostly based on clinical experience, as there is dearth of pertinent data in literature notably regarding CAP. Its neurobiologic correlates are yet to be defined.

1. **SSRI-Activation Syndrome** (Reinblatt, dosReis, Walkup, & Riddle, 2009):
   - It is more in CAP populations;
   - It is commonplace;
   - Tends to occur early-on during course of treatment;
   - Mostly manifests as agitation, dysphoria or akathisia, but with no striking mood changes;
   - It is not indicative of latent bipolarity;
   - And responds to dose reduction or slower titration.

2. **SSRI-Manic/Hypomanic Switch** (Joseph, Youngstrom, & Soares, 2009):
   - It is less common than the activation syndrome;
   - It is usually of later onset;
   - Manifests striking mood changes, with hyperactivity;
   - Might continue symptomatic after stopping SSRI;
   - And indicative of bipolar (III) disorder;
   - Cycle acceleration is also possible;
   - Stopping culprit agent is mandatory or cautious use under umbrella of mood-stabilization.

3. **SSRI-Discontinuation Syndrome** (Hosenbocus, & Chahal, 2011):
   - It occurs with prolonged use (at least 1 month);
   - Follows abrupt cessation;
   - It takes place within 1-7 days of stopping of offending agent;
   - Notably manifest when higher doses employed;
   - More likely with short half-life agents;
   - It presents in form of dizziness, insomnia, electric shock-like sensations, nightmares, flu-like symptoms;
   - Paroxetine is notorious in this regard;
   - Gradual tapering, benzodiazepine coverage or switch to fluoxetine is all helpful avoiding stopping it “cold turkey”.

4. **SSRI-Emotional Blunting** (Reinblatt, & Riddle, 2006):
   - It shows as apathy or indifference;
   - Might be related to resultant secondary dopamine deficiency with boosting 5-HT tone;

---

1Child/Adolescent Psychiatrist, Al-Manara CAP Centre, Kuwait Centre for Mental Health (KCMH)

Corresponding E-Mail: ahmednagy@hotmail.co.uk
Frontal lobe dysfunction has been postulated;
- It is of insidious onset;
- Seems to be dose-dependent (evident at high doses);
- Agents boosting DA drive are helpful e.g. stimulants or bupropion.

5. **SSRI-Unmasking Comorbidities**:
- It has been shown that effectively treating anxiety might reveal underling disruptive disorders or ADHD;
- Conversely, anxiety/depression can masquerade as “counterfeit ADHD”;
- It warrants treatment accordingly, with prioritized sequential approach based heavily on severity of symptomatology.

6. **Serotonin Syndrome (Kant, & Liebelt, 2012)**:
- It is likely especially if combined with other serotoninergic agents or in the setting of overdosing;
- Manifests as altered mental status (AMS), fever, gastro-intestinal (GIT) symptoms, hyperkinesias;
- 5-HT2 antagonists e.g. cyprhepatidine, α -2 agonist; dexmedetomidine, and supportive measures are the mainstay of treatment, besides stopping the offending agent.

7. **SSRI-related Suicidality**:
- Activation of suicidal ideations- paradoxical suicide is noted where mood symptoms improvement lag behind regaining of energy levels;
- FDA black box for those below 25 years- in 2004, based on data from 23 trials comprising 4300 patients, FDA issued this black-box warning of increased risk of suicidal thinking, feeling, and behaviour associated with antidepressants use in young population (Naguy, 2016);
- 2-fold increase compared to placebo; (4% vs. 2% respectively);
- And more when it is used for depressive than for anxiety or OCD disorders;
- Still, benefit of use clearly outweighs this theoretical risk as demonstrated by American College of Neuropsychopharmacology (Mann et al. 2006);
- AACAP developed practice parameters as regards frequency of close monitoring when initiating SSRIs in the first 12 weeks.

8. **SSRI-Withdrawal Mania/hypomania** (Goldstein et al., 1999):
- It is self-limited, paradoxical phenomenon;
- Has been reported in mood disorders (uni or bipolar);
- Might be related to nor-adrenergic (NE) overactivity and overriding cholinergic tone.

This list is not all-inclusive. It is ever-expanding as clinical data accrues. It merely sheds some light on oft-times under-recognized SSRIs behavioural syndromes. It beehoves clinicians be vigilant and mindful of these syndromes that might be a source of diagnostic confusion with syndromic relapse/recurrence and inform subsequent treatment directions accordingly. Hence, there is a pressing need to dissect the neurobiology of these syndromes and better define them as clinical entities.

**Acknowledgements / Conflicts of Interest**
The author declares no conflicts of interests, nor financial affiliations with pharmaceutical companies, or industry-sponsored research. The author extends his deepest gratitude to Dr Adel El-Zayid, MRCPsych (UK), Consultant Psychiatrist, and, Director General of KCMH for his invaluable scientific input to the manuscript.

**References**