

SSRI discontinuation syndrome

When was the SSRI discontinuation syndrome first recognized?

Reports began to emerge soon after the SSRIs were introduced in the late 1980s. *How common is it?* The incidence and prevalence of this syndrome is not yet known. The few available discontinuation studies indicate minor forms of the syndrome may be common and severe forms unusual. A retrospective chart review of 171 clinic patients who discontinued an SSRI while under supervision, reported at least one new symptom in 20% and 14% of patients stopping paroxetine (Paxil) and fluvoxamine (Luvox), respectively. Abrupt discontinuation of fluvoxamine was associated with new symptoms in 12 of 14 subjects (86%) in a prospective, open-label panic study. In a randomized placebo-controlled trial of paroxetine for panic, 19/55 (34%) experienced withdrawal symptoms. Abrupt discontinuation of fluoxetine (Prozac) in a randomized placebo controlled study of 299 subjects did not appear to cause many symptoms. No published study of sertraline (Zoloff) discontinuation symptoms is yet available but there are several case reports.

What are the signs and symptoms of the SSRI discontinuation syndrome?

Neurologic symptoms (dizziness, vertigo, lightheadedness and gait instability) are most commonly reported, followed by somatic complaints (nausea, emesis, fatigue and headache) and not uncommonly, insomnia. Still characteristic but reported less frequently are shock-like sensations, paresthesia, visual disturbances, diarrhea, myalgias and chills. A range of nonspecific mental symptoms including agitation, impaired concentration, vivid dreams, depersonalization, irritability and suicidal thoughts have been reported. When allowed to run its course, the syndrome duration is variable (one to several weeks) and ranges from mild-moderate intensity in most patients, to extremely distressing in a small number.

What other factors should clinicians consider when identifying this syndrome?

The duration of SSRI use is usually 1 month with symptoms developing 2-5 days after SSRI discontinuation or dose reduction. When symptoms emerge in this context, clinicians should be encouraged to include the discontinuation syndrome on their list of differential diagnoses. Awareness of some of the more unusual symptoms, such as dizziness and shock-like sensations, and re-education of patients prior to stopping or tapering an SSRI, should prevent unnecessary and expensive medical investigations.

What is the mechanism behind this problem?

The biological mechanisms underlying this syndrome are not well understood, although an acute decrease in synaptic serotonin in the face of down-regulated or desensitized serotonin receptors has been postulated.

Who is at risk?

The SSRI discontinuation syndrome does not appear to discriminate based on age, sex, diagnosis or dose of SSRI (both low and high doses have been reported). As I mentioned, there appears to be less risk with the abrupt interruption of fluoxetine. Paroxetine is the SSRI most often mentioned in the case reports and the reason for this may be as simple as the fact that it is most frequently prescribed. An alternative explanation may involve paroxetine's affinity for cholinergic (muscarinic) receptors, causing cholinergic rebound on discontinuation. However, this explanation wouldn't account for the full spectrum of symptoms described.

Can it be avoided or treated?

Review of the SSRI discontinuation literature suggests that symptoms may occur even if the SSRI dose is tapered gradually. In half of 50 reported cases, an attempt was made to taper the SSRI, although details concerning the duration and rapidity of taper were not provided consistently. At this point, it is unclear whether tapering SSRIs will reduce the risk nor is it clear whether we should advocate the routine taper of SSRIs when stopping treatment. The only known effective treatment is the re-introduction of the SSRI which is associated with rapid resolution of symptoms. Unfortunately, the syndrome tends to recur in approximately 75% of patients when the same SSRI is later discontinued.