

Title page

Title: SSRI and SNRI withdrawal symptoms reported on an internet forum

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ST and JM had the original idea for the research. ST and DO developed the methodology and performed data collection. TS and JM carried out the analysis and wrote the first draft of the paper.

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Abstract

BACKGROUND:

Antidepressant withdrawal symptoms are well-recognised, but their potential duration remains uncertain.

OBJECTIVE:

We aimed to describe the characteristics of withdrawal associated with two popular classes of antidepressants, including duration.

METHODS:

We analysed the content of a sample of posts on an antidepressant withdrawal website. We compared the characteristics of withdrawal associated with SSRIs and SNRIs, including time of onset, duration and nature of symptoms.

RESULTS:

110 posts about SSRI withdrawal, and 63 concerning SNRI withdrawal, were analysed. The mean duration of withdrawal symptoms was significantly longer with SSRIs than SNRIs: 90.5 weeks (standard deviation, SD, 150.0) and 50.8 weeks (SD 76.0) respectively; $p=0.043$). Neurological symptoms, such as 'brain zaps,' were more common among SNRI users ($p=0.023$). Psychosexual/genitourinary symptoms may be more common among SSRI users ($p=0.054$).

LIMITATIONS:

The website aims to help people with antidepressant withdrawal, and is therefore likely to attract people who have difficulties. Length of prior use of antidepressants was long, with a mean of 252.2 weeks (SD 250.8).

CONCLUSIONS:

People accessing antidepressant withdrawal websites report experiencing protracted withdrawal symptoms. There are some differences in the characteristics of withdrawal associated with different classes of antidepressants.

Keywords: Antidepressant, SSRI, SNRI, Antidepressant withdrawal, Online report

SSRI and SNRI withdrawal symptoms reported on an internet forum

Introduction

Antidepressant use is high and increasing. In 2012, 13% of the population of the United States were prescribed antidepressants, a figure that had almost doubled since the year 2000 [1]. The majority of these prescriptions were for antidepressants classified as SSRIs or SNRIs. There are similar trends across the world [2], with the number of prescriptions for antidepressants in the United Kingdom more than doubling since 2005 [3].

There is now clear evidence that a variety of symptoms can result from the discontinuation of all antidepressant classes [4]. They have been observed to be more common in drugs with a shorter half-life, such as venlafaxine and paroxetine, and if the antidepressant had been taken for eight weeks or longer before withdrawal [5]. Common symptoms following SSRI withdrawal include dizziness, nausea, fatigue, anxiety, headache, electric shock-like symptoms, sweating, insomnia and nightmares [6]. There is comparatively less research on SNRI withdrawal, however, and little data on the nature of the symptoms from the user's perspective.

Symptoms are most commonly reported after sudden cessation of the medication, but can also occur following gradual tapering of the dose [4]. The time of onset of withdrawal symptoms is currently considered to be within a few days of stopping or reducing the antidepressant [5,7]. Onset of withdrawal symptoms after a week is considered unusual [4].

The length of time for which withdrawal symptoms can persist remains uncertain and somewhat controversial. Antidepressant users have been reporting the occurrence of protracted withdrawal states lasting months and even years, for some time [8]. However, patient information issued by professional organisations suggests that SSRI and SNRI withdrawal symptoms last for up to 6-8 weeks [9,7]. Some authors suggest that severe and prolonged

withdrawal symptoms represent 'medically unexplained symptoms' and dispute that they have any relation to antidepressant discontinuation [10]. However, psychiatric literature has started to report cases with longer durations of symptoms [6,8].

This study examines self-reports of SSRI and SNRI withdrawal symptoms by users of an online forum designed to help people withdraw from antidepressants. It aims to increase our knowledge about the characteristics of antidepressant withdrawal associated with these two popular classes of antidepressant, including the potential duration of symptoms.

Method

Self-reports of antidepressant withdrawal symptoms were found on <http://survivingantidepressants.org/> [11]. This website advertises itself as offering 'Peer support for [antidepressant] tapering and withdrawal syndrome'. The information for this study was found in the 'Introduction' area of the website, an online chatroom where individual users introduce themselves to the online community. Users are encouraged to include a variety of details in the signature area displayed for each of their posts. This typically contains a medication history, including antidepressant names, doses, durations of use and dates of changes; and details and dates of withdrawal symptoms. The structure of this introductory section ensures that each post is associated with a unique antidepressant user.

A sample of posts was selected by collecting, in chronological order, posts in which the presence of withdrawal symptoms was reported, the medication being stopped or already ceased was clearly identified, and the withdrawal symptoms adequately described for the purposes of this study. For this study, posts involving withdrawal from SSRIs or SNRIs were selected, with subtypes of SSRIs and SNRIs grouped together. Posts in which authors were on

multiple psychotropic medications and were unsure which was causing their symptoms were excluded. One post where it appeared the author had used an SSRI and SNRI antidepressant simultaneously was excluded.

Each selected website user's withdrawal symptoms were listed, verbatim. These were manually ascribed to one of 8 symptom groups (neurological, psychological, gastrointestinal, musculoskeletal, respiratory, psychosexual/genitourinary, and other). The proportion of all users who experienced at least one of each class of symptom was computed and compared between drug types, along with the average number of symptoms within each symptom group experienced per person.

The reported duration of onset of withdrawal symptoms after medication reduction, the duration of withdrawal symptoms themselves, the mean duration of prior treatment and mean length of taper were all calculated for those people taking SSRIs and SNRIs, using the available data. Differences between groups were explored using non-parametric tests, due to the skewed nature of distributions.

Results

The sample consisted of posts by 174 individuals who had been taking SSRIs or SNRIs. 110 people reported withdrawal symptoms following SSRI use, specifically fluoxetine (N=9), escitalopram (N=35), sertraline (N=23), paroxetine (N=24) and citalopram (N=19). 63 people reported withdrawal symptoms following SNRI use, specifically venlafaxine (N=50) and duloxetine (N=13).

There was no statistically significant difference between mean durations of prior treatment or mean lengths of taper in the SSRI and SNRI groups. The combined mean length of prior

treatment was 252.2 weeks (standard deviation, SD, 250.8; N=146); the median was 156.0 (interquartile range, IQR, 50-416). Combined mean length of taper was 16.6 weeks (SD 25.9; median 4.0, IQR 0-20.0; N=79).

The mean time to onset of withdrawal symptoms following SSRI discontinuation or reduction (4.5 weeks, SD 13.0; median 1.3, IQR 0-6.0; N=66) appeared longer than for SNRIs (1.5 weeks, SD 3.0; median 0.3, IQR 0-1.3; N=46), however this difference did not reach statistical significance ($t=1.51$; $p=0.13$). The combined mean time to onset was 3.3 weeks (SD 10.2; median 1.0, IQR 0-3.4).

Withdrawal symptoms lasted significantly longer for those taking SSRIs than SNRIs. The mean duration of withdrawal symptoms in the SSRI group was 90.5 weeks (SD 150.0; median 34.0, IQR 8.0-104.0; N=97), and in the SNRI group 50.8 weeks (SD 76.0; median 28.0, IQR 4.5-62.8; N=40); $t=2.05$, $p=0.043$.

The duration of symptoms positively correlated with length of taper ($R^2=0.258$, $p=0.038$; N=65), but not with duration of previous treatment. Time to onset of symptoms was not associated with either.

Table 1 shows numbers and proportions of users experiencing at least one symptom in each class of withdrawal symptoms. The most common types of symptom in both the SSRI and SNRI groups were psychological, followed in descending frequency by neurological, gastrointestinal, musculoskeletal, and cardiovascular symptoms. Neurological effects were significantly more common among people who had withdrawn from SNRIs. There was a trend towards sexual and genitourinary effects being more frequent in people withdrawing from SSRIs; however, this difference did not reach statistical significance.

INSERT TABLE 1 HERE

Users' descriptions of neurological and psychological symptoms indicate experiences that are hard to classify using standard medical technology. Some, such as 'brain zaps' and electric shock-like sensations, have been noted before, but some are less familiar, such as 'brain sloshing,' 'vision lagging behind eye movements' and 'head like cotton balls stuffed in'.

Discussion

The data suggest that some people experience protracted withdrawal symptoms following both SSRI and SNRI withdrawal. The average duration of withdrawal symptoms among SSRI users was almost 21 months, and for SNRI users it was nearly 12 months. Among SSRI users, 50% experienced symptoms lasting 7.8 months or more, and for 25% symptoms lasted at least 2 years. For 50% of SNRI users, symptoms lasted at least 6.4 months, and for 25% they lasted for 14.4 months or more.

Reported time before onset of withdrawal symptoms was also longer than previously documented for people withdrawing from SSRIs/SNRIs. For 50% of SSRI users this was almost 9 days or more, and for 25% of users it exceeded 6 weeks. For those taking SNRIs it was closer to the duration previously reported, which likely reflects the short action of venlafaxine, the most commonly used agent in this group.

The positive correlation between duration of symptoms and length of taper is likely to indicate that people experiencing difficult and protracted withdrawal symptoms reduce their antidepressants more slowly.

The prominence of psychological, neurological and gastrointestinal symptoms is consistent with the previous literature on SSRI and SNRI withdrawal [4], and lends this study face validity. The findings of higher rates of neurological symptoms with SNRI withdrawal, as well as the trend towards higher rates of psychosexual/genitourinary symptoms with SSRIs, have not been documented before and are likely to reflect the different pharmacological profiles of the different classes of antidepressant.

The verbatim description of symptoms revealed some unusual examples, not previously documented in the literature. The language used vividly illustrates the sometimes bizarre and highly distressing experiences that can follow SSRI and SNRI withdrawal.

Limitations

This study has a number of limitations. Most importantly, the website used was specifically designed to help people withdraw from antidepressants, and as such is likely to attract users who have had particular difficulties with the process of withdrawal. Moreover, the users of the site had used antidepressants for long periods, and results are likely to reflect this long duration of prior use.

The study does not, therefore, represent a prevalence study of occurrence of withdrawal symptoms, and does not describe the characteristics of antidepressant withdrawal among all users. Nevertheless, given the frequency of antidepressant prescribing, it is important that these adverse experiences are described and that differences between commonly used agents are recognised. This is especially important in view of evidence that people are taking

antidepressants for longer [12,13]. In 2011, 60% of antidepressant users in the US reported using them for more than 2 years [14].

It is also possible that symptoms were misattributed, exaggerated or influenced by reports by other people, and that they might be associated with confounding factors such as use of other medication or the presence of medical conditions. However, other research suggests that internet data can be used to provide reliable accounts of users' experiences of drug-induced adverse effects that are consistent with academic and professional literature [15].

Conclusion

Whilst its limitations should be borne in mind, this analysis of self-reported symptoms of SSRI and SNRI withdrawal highlights some important issues for clinical practice. The reported maximum duration of withdrawal symptoms was far in excess of the upper limit that is commonly quoted to patients, with both drug classes but particularly with SSRIs. Clinicians and patients need to be aware of this possibility when considering starting or stopping antidepressants.

The study illustrates some differences between antidepressant classes in the nature of subjective symptoms of SSRI and SNRI withdrawal, and the sometimes idiosyncratic ways in which they are described by individual patients. Knowledge of such descriptors may aid clinicians in understanding unusual presentations after antidepressant discontinuation.

Given the high and increasing rate of prescribing of antidepressants across western countries, this study suggests that further research into ways to alleviate prolonged adverse experiences following antidepressant withdrawal would be beneficial.

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Table (1 in total)

Table 1: Types of withdrawal symptoms

Symptom group	Examples (verbatim)	% of people experiencing at least one side effect		Fisher's Exact test (2-sided)
		SSRI (N=110)	SNRI (N=63)	
Neurological	Dizziness, 'brain zaps*', 'whoosh in ears', ringing ears, paraesthesia, 'needles under skin', sensitive to light, buzzing sound, burning sensation, restless legs, 'electric shocks', leg spasm, tremors, balance problems, 'tingly lips', 'blurry vision', 'vision lagging behind eye movements', 'brain sloshing'	66.4	82.5	P=0.023
Psychological	'Brain fog', anxiety, depression, feeling suicidal, irritable, feeling 'lousy', 'emotional numbness', pessimism, loss of hope, 'emotional pain', 'inner torment', anger, insomnia, obsessive thoughts, poor concentration and memory, panic, depersonalisation, paranoia, feeling 'wired', terrifying dreams, 'vivid nonsensical dreams', 'out of body sensation', 'overstimulated', 'head like cotton balls stuffed in'	93.6	84.1	p=0.062
Gastrointestinal	Nausea, bloated, diarrhoea, constipation, acid reflux, stomach cramps, appetite changes, sensitivity to food	42.7	46.0	P=0.751
Cardiovascular	Palpitations, chest pain, racing heart, high blood pressure, chest tightness, missed beats	15.1	11.1	p=0.499
Musculoskeletal	Jaw pain, aches and pains, body aches, muscle weakness, jaw clenching	20.0	14.3	p=0.413
Respiratory	'Flu' like symptoms, coughing, sinus problems, stuffy nose, laboured breathing	9.1	4.8	p=0.379
Psychosexual /Genitourinary	Urinary frequency, difficulty urinating, erectile dysfunction, numb penis	12.7	3.2	p=0.054
Others	Recurring infections, bad skin, hives	2.7	3.2	p=1.000

*Quotations indicate verbatim descriptions using non-standard terminology