

Antidepressant Discontinuation Syndrome: Diagnosis, Prevention

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Discontinuation symptoms can occur with all antidepressant classes, and you will see many articles referring to SSRI discontinuation syndrome. The reason is that SSRIs are by far the most commonly prescribed antidepressant class.

This syndrome consists of usually mild and reversible symptoms that can be grouped into six categories.

As a general guideline, management involves restarting antidepressant medication.

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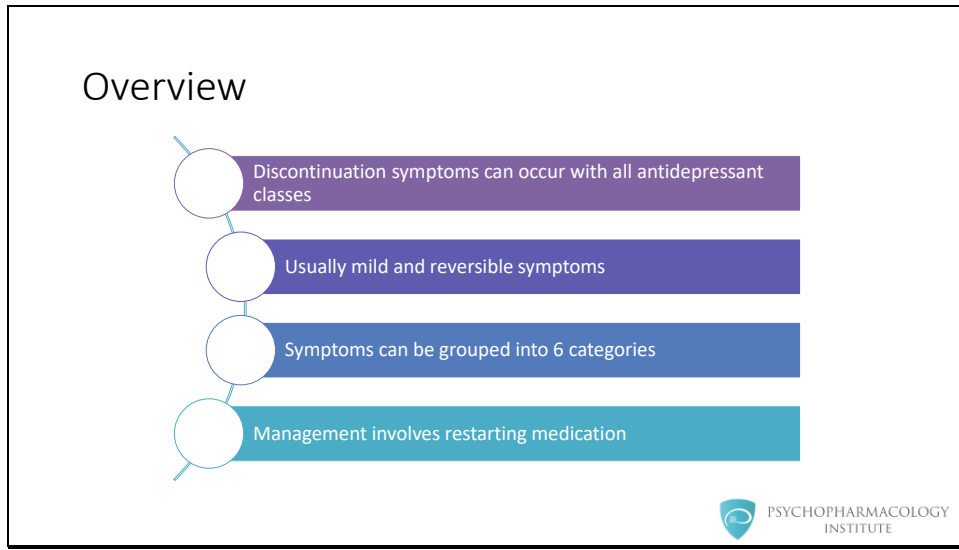
Antidepressant Discontinuation Syndrome

Flavio Guzmán, MD



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In this presentation we discuss the antidepressant discontinuation syndrome.



Let's see an overview of this topic.

Discontinuation symptoms can occur with all antidepressant classes, and you will see many articles referring to SSRI discontinuation syndrome. This has to do with the fact that SSRIs are by far the most commonly prescribed antidepressant class.

This syndrome consists of usually mild and reversible symptoms that can be grouped into six categories.

As a general guideline, management involves restarting antidepressant medication.



Clinical Relevance



Are antidepressants addictive?

- Discontinuation vs withdrawal
- No evidence of antidepressant craving

Haddad, P. M., & Anderson, I. M. (2007). Recognising and managing antidepressant discontinuation symptoms. *Advances in Psychiatric treatment*, 13(6), 447-457.

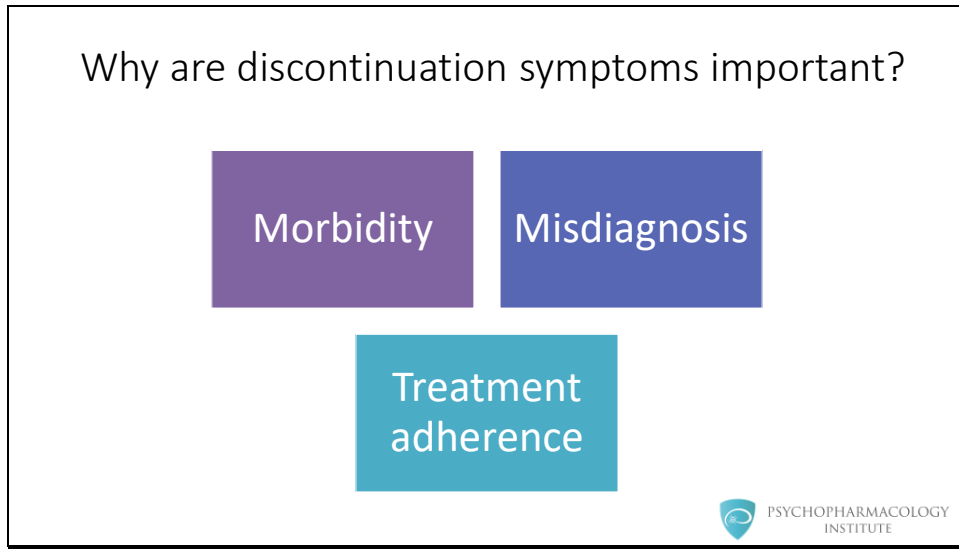


The first question we are addressing here is: Are antidepressants addictive?

The term withdrawal is often avoided, as it may imply that antidepressants are addictive or cause a dependence syndrome. As pointed out by Haddad and Anderson, the occurrence of withdrawal symptoms doesn't in itself indicate that a drug causes dependence. There is no evidence that patients crave antidepressants once they have stopped them.

So, one of the messages we can send our patients is that antidepressants are not addictive. This is important as fear of addiction can reduce treatment adherence.





Why should we care about antidepressant discontinuation syndrome?


In this slide I list three reasons: the first is morbidity. Even though discontinuation symptoms are rarely fatal, they are associated with discomfort and some degree of psychosocial impairment.

The second is misdiagnosis. Discontinuation symptoms can be confused with recurrence of psychiatric illness or other medical problems. We'll discuss this in the next slide.

The third is treatment adherence. After experiencing discontinuation symptoms, patients may be unwilling to use psychotropic medications in the future.




Misdiagnosis



- Adverse effect of a new medication
- Recurrence of the underlying psychiatric illness

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Let's focus now on the problem of misdiagnosis.

Discontinuation symptoms can be confused with adverse effects of a new medication. This may lead us to the incorrect conclusion that the patient can't tolerate the new medication. This can happen when switching antidepressants with different mechanism of action, for example, from paroxetine to bupropion.

Discontinuation symptoms can also be confused with recurrence of the underlying psychiatric illness. An example of this would be the following situation: a patient has achieved remission of depressive symptoms and the physician recommends stopping the antidepressant but doesn't advise how to do it. So, the patient stops medications abruptly, leading to discontinuation symptoms. If the prescriber is not aware of this abrupt interruption, then he or she might confuse this with depression recurrence.



Misdiagnosis



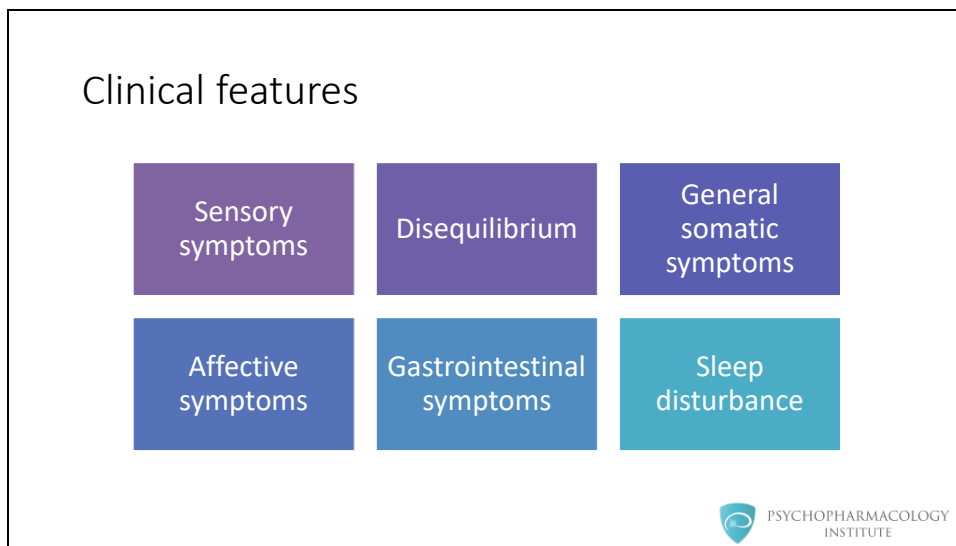
- Failure to respond to treatment
- Physical disorder

Haddad, P. M., & Anderson, I. M. (2007). Recognising and managing antidepressant discontinuation symptoms. *Advances in Psychiatric treatment*, 13(6), 447-457.



Discontinuation symptoms might also be confused with failure to respond to treatment, especially mental symptoms such as irritability or anxiety. Discontinuation symptoms can also be misdiagnosed as medical problems, this may lead to unnecessary referrals and evaluations by other specialists.






The discontinuation syndrome can be divided into six clusters of symptoms. Sensory symptoms, disequilibrium, general somatic symptoms, affective symptoms, gastrointestinal symptoms and sleep disturbance.


This syndrome was initially based on case reports, but the evidence expanded to include prospective studies, with randomized double-blind interruption periods.




Sensory symptoms



- Paresthesia
- Numbness
- Electric-shock-like sensations
- Rushing noise “ in head”
- Palinopsia (visual trails)



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Sensory symptoms include: paresthesia, numbness, electric shock-like sensations, rushing noise “ in head” and palinopsia, or visual trails.




Disequilibrium



- Light-headedness
- Dizziness
- Vertigo

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Disequilibrium symptoms include light-headedness, dizziness and vertigo.



General somatic symptoms



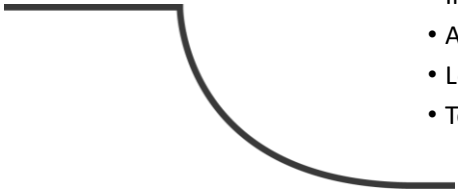
- Lethargy
- Headache
- Tremor
- Sweating
- Anorexia

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General somatic symptoms have been compared to a flu-like syndrome. This includes lethargy, headache, tremor, sweating and anorexia.




Affective symptoms



- Irritability
- Anxiety/agitation
- Low mood
- Tearfulness

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Affective symptoms that can be part of the discontinuation syndrome are irritability, anxiety, low mood and tearfulness.



Gastrointestinal symptoms



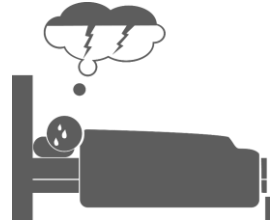
- Nausea
- Vomiting
- Diarrhea

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Gastrointestinal symptoms include nausea, vomiting and diarrhea.



Sleep disturbances



- Insomnia
- Nightmares
- Excessive dreaming

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The last cluster of symptoms is related to sleep disturbances, including: insomnia, nightmares and excessive dreaming.



FINISH:
A mnemonic for discontinuation symptoms

- F – Flu-like symptoms
- I – Insomnia
- N – Nausea
- I – Imbalance
- S – Sensory disturbances
- H – Hyperarousal

Warner, C. H., Bobo, W., Warner, C., Reid, S., & Rachal, J. (2006). Antidepressant discontinuation syndrome. *American Family Physician*, 74(3), 449-456.



There's also a mnemonic to help us remember the discontinuation symptoms. It's the word FINISH, F for flu-like symptoms, I for Insomnia, N for nausea, I for imbalance, S for sensory disturbances, and H for hyperarousal.



Primary TCA discontinuation syndrome

Lack of :

- Sensory abnormalities
- Problems with equilibrium

MAOI discontinuation syndrome

More severe: worsening of depressive episode, acute confusional state, anxiety symptoms, catatonia



The symptoms we discussed in the previous slides are commonly associated with the discontinuation of SSRIs and SNRIs. Specific symptoms for tricyclics and MAOIs have been described.

In the case of tricyclics, there is a lack of sensory abnormalities and problems with equilibrium. In the case of MAOIs, symptoms can be more severe, including a worsening of depressive episode, acute confusional state, anxiety symptoms and even catatonia.



Time of onset and duration



Onset:

- Generally in the first week
- Studies suggest a mean time of onset of 2 days after stopping

Duration:

- Spontaneous resolution between 1 day and 3 weeks after onset

Warner, C. H., Bobo, W., Warner, C., Reid, S., & Rachal, J. (2006). Antidepressant discontinuation syndrome. *American Family Physician*, 74(3), 449-456.



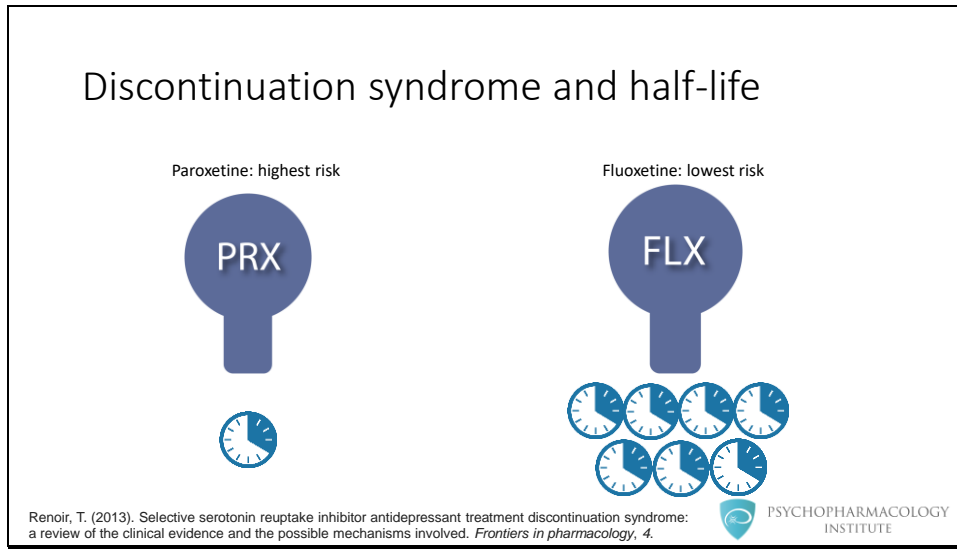
Let's see now the time of onset and duration.

Discontinuation symptoms occur generally during the first week after stopping the antidepressant. Studies suggest a mean time of onset of 2 days after stopping.

Regarding duration, spontaneous resolution occurs between 1 day and 3 weeks after onset, most commonly around 10 days.



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The discontinuation syndrome has been reported in relation to almost every SSRI, although there are increased reports in patients stopping paroxetine treatment. So far, half-life is the pharmacokinetic property that has been linked to risk of discontinuation symptoms.

Fluoxetine has a half-life of around 7 days, this makes it the SSRI with the lowest risk of this syndrome.



Differential diagnosis

Discontinuation	Depression Relapse
Dysphoria, appetite changes, sleep problems, fatigue.	
Dizziness, "electric shock" sensations, "rushing" sensations in the head, headache, nausea	
Rapid reversal of symptoms after restarting the antidepressant	

Warner, C. H., Bobo, W., Warner, C., Reid, S., & Rachal, J. (2006). Antidepressant discontinuation syndrome. *American Family Physician*, 74(3), 449-456.



How do we differentiate discontinuation symptoms from a depressive relapse?

They have in common symptoms such as dysphoria, appetite changes, sleep problems and fatigue.

It's practical to look for symptoms that are not seen in depression relapse, some examples are dizziness, "electric shock" sensations, rushing sensations in the head, headache and nausea.

Also, we can see a rapid reversal of symptoms after restarting the antidepressant.



Prevention and Management



Who is at risk?

- Patients who begin to feel better
- Women who discover they are pregnant

So who is at risk of discontinuing medication without letting you know?

Generally, patients who begin to feel better and are not comfortable with the idea of taking medication for a long time. Also, women who discover they are pregnant are more likely to abruptly stop medications, because of safety concerns.



How to discontinue antidepressants

- Warn patients about the possibility of antidepressant discontinuation syndrome
- May be possible to stop fluoxetine therapy without tapering

Here are some considerations on how to discontinue antidepressants. First, patient education is very important. We need to warn patients about the possibility of antidepressant discontinuation syndrome. Also, it may be possible to stop fluoxetine therapy without tapering, this hasn't been explored in studies specifically designed to address this observation.



What to do ?

1. Provide reassurance to the patient
 - Reversible, not life threatening, will run its course within 1 to 2 weeks

Warner, C. H., Bobo, W., Warner, C., Reid, S., & Rachal, J. (2006). Antidepressant discontinuation syndrome. *American Family Physician*, 74(3), 449-456.



So, what do we do with a patient suffering from discontinuation symptoms?

First of all, we provide reassurance. We do this by explaining that this syndrome is reversible, not life threatening, and that it will run its course within 1 to 2 weeks.



What to do ?

2. Consider restarting the medication with a slow dose taper

- If symptoms occur during tapering:
 - Consider restarting at the original dose and then taper at a slower rate.
- If slow tapering is poorly tolerated:
 - Consider substituting with fluoxetine

Warner, C. H., Bobo, W., Warner, C., Reid, S., & Rachal, J. (2006). Antidepressant discontinuation syndrome. *American Family Physician*, 74(3), 449-456.



Second, we restart the medication with a slow dose taper. What if symptoms occur during tapering? In this case we should consider restarting at the original dose and then taper at a slower rate. If slow tapering is poorly tolerated, we can consider substituting with fluoxetine.



Key points

- Discontinuation symptoms include flu-like symptoms, insomnia, nausea, imbalance, sensory disturbances and hyperarousal (FINISH)
- More commonly seen with paroxetine
- Restarting the antidepressant is generally enough

The key points are the following:

Discontinuation symptoms include flu-like symptoms, insomnia, nausea, imbalance, sensory disturbances and hyperarousal. We can use the mnemonic FINISH to keep these symptoms in mind.

This syndrome is more commonly seen with paroxetine.

From a therapeutic standpoint, restarting the antidepressant is generally enough as management strategy.

