Olfactory Hallucinations as a Unique Presentation of Anti-Depressant Discontinuation Syndrome

Shweta Varade MD
Lehigh Valley Health Network, Shweta.Varade@lvhn.org

Casey Judge DO
Lehigh Valley Health Network, Casey.Judge@lvhn.org

Megan Leary MD
Lehigh Valley Health Network, Megan_C.Leary@lvhn.org

Preet Varade MD
Lehigh Valley Health Network, Preet_M.Varade@lvhn.org

Published In/Presented At

Varade, S. Judge, C. Leary, M. Varade, P. (2019, May 7). *Olfactory Hallucinations as a Unique Presentation of Anti-Depressant Discontinuation Syndrome*. Poster Presented at: The American Academy of Neurology (AAN) Annual Meeting, Philadelphia, PA.

Olfactory Hallucinations as a Unique Presentation of Anti-Depressant Discontinuation Syndrome

Shweta Varade, MD, Casey Judge, DO, Megan Leary, MD, Preet Varade, MD
Lehigh Valley Health Network, Allentown, Pa.

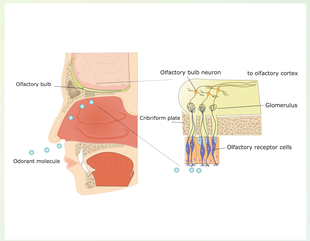
INTRODUCTION:

Discontinuation syndromes have been reported following abrupt cessation of anti-depressants that include Selective Serotonin Reuptake Inhibitors (SSRIs) and Tricyclic Anti-depressants (TCAs). Commonly reported symptoms include insomnia, nausea, imbalance, sensory disturbance, and hyperarousal. Less frequently, shock-like sensation, delirium, and mania have also been documented. Visual and auditory hallucinations are even rarer and have thus far been described in only one case report. Olfactory hallucinations, however, have not been reported as a manifestation of discontinuation syndrome to the best of our knowledge.

CASE PRESENTATION:

A 49 year old woman with a past medical history of Diabetes Mellitus Type II, coronary artery disease, hypertension, hyperlipidemia, and tobacco abuse presented with complaints of dizziness, episodes of transient alterations in consciousness, and "horrific smells" of mold and fire. Initial neurological examination was normal with the exception of decreased attention, concentration, and memory. Computerized Tomography (CT) of the head was negative for acute findings. She was offered admission for further workup but declined, however, returned the following day with the same complaints as well as amnesia and confusion. Her neurological exam remained unchanged. Further workup included Magnetic Resonance Imaging (MRI) of the brain which was negative for any structural abnormalities, prolonged electroencephalogram (EEG) which did not reveal any evidence of epileptiform discharges, and cerebrospinal fluid analysis that was unremarkable.

After discussing the risks and benefits, she was discharged home on anti-convulsants due to concern for seizures, despite a negative EEG. She returned to the emergency department the following day again with recurrence of symptoms. Further history revealed that the patient had abruptly discontinued paroxetine two weeks prior to presentation. The anti-convulsant was discontinued and she was restarted on paroxetine and discharged home. At a follow up visit with her primary care three days later, she reported cessation of any olfactory hallucinations.



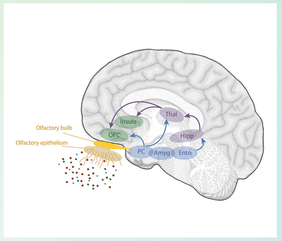


Image 1 (left): Anatomical representation of olfactory system

Image 2 (right): Structures involved in the processing of olfactory information. Olfactory information is carried to the primary olfactory cortex (olfactory nucleus, piriform cortex, olfactory tubercle, amygdaloid complex, and enterorhinal cortex) and then projected to the thalamus, orbitofrontal cortex, insula cortex, and hippocampus.

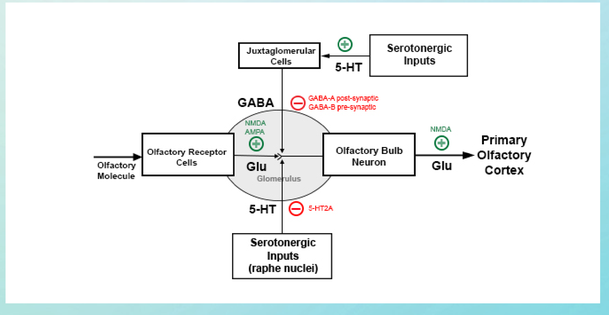


Image 3: Effects of serotonin on the olfactory pathway

DISCUSSION:

Discontinuation syndromes can occur with any SSRI but is more frequently noted with Paroxetine[2]. The syndrome can occur after treatment duration of as little as two months and tapering off of the medications has not shown to eliminate the risk of withdrawal symptoms[2], which can last as long as a few days to several weeks.[2]

There is a known link between depression and the perception of non-existent odors (phantosmia/parosmias or olfactory hallucinations), that are typically described as "unpleasant."[1] Abnormal functioning in the orbitofrontal cortex[4] has been thought to affect olfactory processes in depressive disorders, possibly due to anatomical proximity. In many cases, these symptoms can be treated with anti-depressants.[1]

It has been hypothesized that hallucinations as a discontinuation syndrome may be a result of the decrease in the available synaptic serotonin from downregulated serotonin receptors or due to secondary effects on other neurotransmitters.[2]

Sensory neurons release glutamate to activate post-synaptic targets in the olfactory pathway.[4] This is modulated by the GABA-B receptor which works to reduce neurotransmitter release in olfactory neurons.[4] Serotonin activates periglomerular neurons leading to an increase in GABA-B activity and thereby turning down the strength of odor input to the brain.[4] Thus patients who may be pre-disposed to phantosmia/parosmia may have a dampened sense of awareness of smell while they are being treated with anti-depressants such as paroxetine.

Conversely, there is a decreased level of GABA in the cingulate gyrus, right and left insula, and left amygdala in patients with depression.[5] A study in rhesus monkeys[3] determined a direct anterior retrograde pathway from the anterior cingulate gyrus to the primary olfactory cortex, which may activate the entire olfactory cortex to mediate the process of rapid attention to olfactory stimulus.[3] This suggests that in patients with decreased GABA activity, such as when anti-depressants are suddenly discontinued, it may be possible for them to experience a heightened awareness of phantosmias or parosmias.

CONCLUSION:

While anti-depressant discontinuation syndromes have been previously reported, there is little available data on the phenomenon of olfactory hallucinations as a symptom. In part, this may be due to the fact that parosmias/phantosmias are rarely reported spontaneously by patients and often not explicitly asked about by clinicians.[2] We present a unique case of a patient who experienced olfactory hallucinations shortly after discontinuing paroxetine.

REFERENCES:

1. Croy, I., et al. "Research Letter Enhanced Parosmia and Phantosmia in Patients with Severe Depression." Psychological Medicine, vol. 43, no. 11, 2013, pp. 2460–2464., doi:10.1017/s0033291713001773.

2. Fava, Giovanni A., et al. "Withdrawal Symptoms after Selective Serotonin Reuptake Inhibitor Discontinuation: A Systematic Review." Psychotherapy and Psychosomatics, vol. 84, no. 2, 2015, pp. 72–81., doi:10.1159/000370338.

3. García-Cabezas, Miguel Á., and Helen Barbas. "A Direct Anterior Cingulate Pathway to the Primate Primary Olfactory Cortex May Control Attention to Olfaction." Brain Structure and Function, vol. 219, no. 5, 2013, pp. 1735–1754., doi:10.1007/s00429-013-0598-3.

4. Hagiwara, Akari, and Venkatesh Murthy. "SEROTONIN AND SMELL." Harvard University - Department of Molecular & Cellular Biology, 5 Dec. 2018, www.mcb.harvard.edu/archive/serotonin-and-smell/.

5. Roberts, Steven. "Phantosmia and SSRI Discontinuation Syndrome." Nomadic Research Labs, 7 Mar. 2019, microship.com/phantosmia-and-ssri-discontinuation-syndrome/.

6. Saive, Anne-Lise, et al. "Schematic View of the Human Olfactory System." A Review on the Neural Bases of Episodic Odor Memory: from Laboratory-Based to Autobiographical Approaches, Frontiers, 2014, www.frontiersin.org/articles/10.3389/fnbeh.2014.00240/full.

7. Yasui-Furukori, Norio, and Sunao Kaneko. "Hallucination Induced by Paroxetine Discontinuation in Patients with Major Depressive Disorders." Psychiatry and Clinical Neurosciences, vol. 65, no. 4, 2011, pp. 384–385., doi:10.1111/j.1440-1819.2011.02211.x.

LVHN.org

Lehigh Valley Health Network