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Case Report Open Access

Hallucinogen Persisting Perception Disorder Following Therapeutic Ketamine: A Case Report

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Introduction

Intravenous ketamine, a dissociative anaesthetic, has been reported to alleviate major depression [1] and chronic pain [2] with minimal adverse effects [3,4], although perceptual disturbances are not uncommon [5]. Hallucinogen persisting perception disorder (HPPD) is an illness arising from the abuse of hallucinogens in which individuals suffer visual pseudohallucinations for months to years following exposure to LSD and similar drugs [6]. We now report a case of HPPD in a young man who received medically administered intravenous ketamine for treatment of a complex regional pain syndrome (CRPS).

Case Report

A 13 year old male piano student developed CRPS following a sacral injury. He had no history of substance use. At 15, chronic pain was treated with two continuous intravenous infusions of ketamine, each lasting a week, with maximal doses of 50 mg per hour. During each treatment he vomited and had visual and synesthetic hallucinations. Six months later he suffered the progressive onset of an array of visual pseudohallucinations and hypersensitivity to light and sound. Imagery included particles in the entire visual field seen in the air and on surfaces; large moving coloured blobs on surfaces; afterimages; trails of objects moving through his visual field, such as a tennis ball; objects changing their shape; and difficulty reading and playing the piano. He also suffered the incessant sensation of the euphoria he felt when given ketamine. These symptoms were reported as daily and constant on multiple follow-up visits over a three year period.

A psychiatric evaluation found no evidence of psychosis or depression. The mental status examination confirmed a deficit in short term memory. The patient described continual visual disturbances during the examination. Reality testing was intact.

There were no auditory hallucinations or delusions. Psychological testing confirmed a reading disorder. A quantitative EEG found evidence of an auditory processing disorder with irritability in the left temporal and occipital regions, including activation of the auditory system by visual stimuli, a putative marker for drug-induced synaesthesia.

Medications including divalproex sodium, several SSRIs, gabapentin and pregabalin were unsuccessful. Lorazepam 2 mg twice daily reduced, but did not ablate, his symptoms for two months. In that time he returned to the piano and was admitted to a university music program. Relapse followed as the patient apparently developed tolerance to the treatment. A similar pattern followed use of diazepam 10 mg a day. At the age of 18, he developed complex partial seizures which have been controlled with topiramate. However, the perceptual symptoms and ketamine euphoria have continued.

Discussion and Conclusion

Studies in subjects with HPPD suggest that the pathophysiology of the disorder involves either a slowly reversible or permanent disruption in the inhibition of visual information processing. This has been described from the use of LSD, MDMA, psychostimulants and a variety of botanical preparations of hallucinogens [7]. Evidence for visual disinhibition following LSD includes persisting afterimagery [8], abnormal flicker fusion testing, impaired dark adaptation [9], electrophysiological measures of cortical disinhibition [10] and increased measures of cerebral coherence, a putative measure of increased cortical activation [11]. To the best of our knowledge this report is the first association between ketamine and HPPD.

The mechanism by which ketamine antagonism of the NMDA receptor induces perceptual or psychotic symptoms is not known. Consistent in both animal and human studies, however, is the observation that ketamine increases activity of brain waves in the gamma (30 to 60 Hz) range. De la Salle et al. reported such an increase in gamma current density in the default mode network implicated in schizophrenia, as well as activation of gamma frequencies across the cerebrum [12]. This finding supports a disinhibition model of HPPD. In addition, GABA-A agonists such as midazolam reduce HPPD symptoms [13].

HPPD also appears to be associated with increased cerebral coherence, a measure of cortical connectivity [14]. Similarly, temporal lobe epilepsy involving the neocortex has been associated with increased coherence [15]. The role of ketamine in the generation or control of seizures is not known. But in our case, enhancement of cortical coherence with neurofeedback resulted in an exacerbation of HPPD.

Ketamine, a schedule III drug which is an anaesthetic agent, can be prescribed by any physician. Enthusiasm for its use in treatment of refractory depression has yet to be tempered by a body of research establishing safety and efficacy [16]. The history of LSD in the 1960s followed such a course over time, in which a period of rising enthusiasm was followed by one of sober reconsideration as the risks and benefits were identified [17]. This report adds a note of caution to the process.

References

1. Zarate CA (2006) A randomized trial of an N-methyl-D-aspartate antagonist in treatment-resistant major depression. Arch Gen Psychiatry 63: 856-864.
2. Correll GE (2004) Subanesthetic ketamine infusion therapy: A retrospective analysis of a novel therapeutic approach to complex regional pain syndrome. Pain Med 5: 263-275.
3. Koffler SP (2007) The neurocognitive effects of 5 day anesthetic ketamine for the treatment of refractory complex regional pain syndrome. Arch Clin Neuropsychol 22: 719-729.
4. Perry EB (2007) The Yale Ketamine Study Group. Psychiatric safety of ketamine in psychopharmacology research. Psychopharmacology (Berl) 192: 253-260.
5. Krystal JH (1994) Subanesthetic effects of the noncompetitive NMDA antagonist, ketamine, in humans. Psychotomimetic, perceptual, cognitive and neuroendocrine responses. Arch Gen Psychiatry 51: 199-214.
6. Lerner AG (2002) Flashback and hallucinogen persisting perception disorder: Clinical aspects and pharmacological treatment approach. Isr J Psychiatry Relat Sci 39: 92-99.
7. El-Mallakh R, Halpern J, Abraham HD (2007) Hallucinogen and MDMA Related Disorders. In: Tasman A, First M (eds.). A Clinical Guide to the Diagnosis and Treatment of DSM-IV-TS Mental Disorders, 3rd edition, John Wiley, 2007.
8. Liu F (2012) Ketamine-induced neuronal damage and altered N-methyl-D-aspartate (NMDA) receptor function in rat primary forebrain culture. Toxicol Sci Oct 11.
9. Bosnjak ZJ (2012) Ketamine induces toxicity in human neurons differentiated from embryonic stem cells via mitochondrial apoptosis pathway. Curr Drug Saf 7: 106-119.
10. Okamoto Y, Tsuneto S, Tanimukai H, Matsuda Y, Ohno Y, et al. (2012) Can gradual dose titration of ketamine for management of neuropathic pain prevent psychotomimetic effects in patients with advanced cancer? Am J Hosp Palliat Care Jul 24.
11. Abraham HD, Duffy FH (1996) Stable quantitative EEG difference in post-LSD visual disorder by split-half analysis: Evidence for disinhibition. Psychiatry Res 67: 173-187.
12. de la Salle S, Choueiry J, Shah D, Bowers H, McIntosh J, et al. (2016) Effects of ketamine on resting-state EEG activity and their relationship to perceptual/dissociative symptoms in healthy humans. Front Pharmacol 7: 348.
13. El-Mallakh RS, Halpern JH, Abraham HD (2008) Substance Abuse: Hallucinogen- and MDMA-Related Disorders (Chapter 60). In: Tasman A, Maj M, First MB, Kay J, Lieberman JA, editors. Psychiatry. 3rd edition. London: John Wiley & Sons pp: 1100-1126.
14. Abraham HD, Duffy FH (2001) EEG coherence in post-LSD visual hallucinations. Psychiatry Res 107: 151-163.
15. Bartolomei F, Wendling F, Vignal JP, Kochen S, Bellanger JJ, et al. (1999) Seizures of temporal lobe epilepsy: Identification of subtypes by coherence analysis using stereo-electro-encephalography. Clin Neurophysiol 110: 1741-1754.
16. Schatzberg A (2014) A word to the wise about ketamine. Am J Psychiatry 171: 262-264.
17. Abraham HD, Aldridge A, Gogia P (1996) Psychopharmacology of the hallucinogens. Neuropsychopharmacology 14: 285-298.