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LETTERS TO THE EDITORS

Maintenance use of ketamine for treatment-resistant depression: an open-label pilot study

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Singh et al.[1] reported that two or three weekly 40 min i.v. infusions of ketamine (0.5 mg/kg) are safe and effective for maintaining an acute response to ketamine during one month of treatment for resistant depression (TRD).

We present herein the results of an open label pilot study of 8 TRD patients who received 40 min infusions of ketamine (0.5 mg/kg) for 7 weeks after a positive acute response to three ketamine infusions. We employed a maintenance protocol at a lower frequency as follows: three initial infusions every other day for a week, an infusion 7 days after the last initial infusion and infusions every two weeks thereafter. This lower frequency was based on the 18-day median time to loss of response reported by Murrough et al.[2]

In this study, those who did not respond adequately to appropriate courses of at least two antidepressants were considered TRD patients. The subjects were two men and six women, aged 25-53 years, diagnosed with major depressive disorder. They had no unstable clinical diseases and they were not acutely psychotic. Three patients had a comorbid diagnosis of generalized anxiety disorder, one of whom also had a diagnosis of fibromyalgia. Two of the individuals had been hospitalized once after attempting suicide. The mean duration of illness in this sample was 16 years. At the time of the study, four of the patients were in polytherapy, three were in monotherapy and one had chosen to discontinue antidepressants because he considered them ineffective.

They signed an informed consent form and completed a Beck Depression Inventory (BDI) three times: pretreatment (mean BDI scores = 33.75), 3 days after the initial infusions (mean BDI scores = 10.25) and on day 60 (mean BDI sores = 10.75). All eight patients sustained the response until day 60.

During the infusions all of the patients had some degree of dissociative symptoms, ranging from a feeling of lightheadedness to feelings of being outside the body or in another dimension. These symptoms began after 15 to 20 min of infusion and quickly reduced in intensity after the end of the infusions. All the patients could be discharged with no complications 30 min after the end of the infusions. Like Singh et al.,[1] we also observed that the dissociative symptoms decreased with repeated doses. Two patients complained of nausea, which was successfully treated with intravenous ondansetron. Despite this, seven of the patients described the infusion experience as pleasant and only one as unpleasant. No delusions or hallucinations were reported during the study. There were no clinical emergencies.

Thus, the use of multiple infusions of ketamine to maintain its acute effects might be an effective and well-tolerated treatment approach for TRD patients. An infusion every two weeks appears to suffice. This may represent a simple, quick way to bring longer term benefits for TRD patients with an acute ketamine response. Hence, this may be an alternative as we await eventual FDA approval of intranasal esketamine or new drugs targeting the glutamatergic system.[3] However, controlled studies with larger samples are required to replicate our findings.

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Disclosure

The authors report no conflicts of interest.

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Skin picking disorder comorbid with ADHD successfully treated with methylphenidate

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Skin picking disorder (SPD) is characterized by repetitive picking and scratching of the skin, leading to tissue damage and substantial distress.[1] The few pharmacological studies on SPD treatment have yielded conflicting results[2] and more pharmacological evidence is needed to guide clinicians.

Attention deficit hyperactivity disorder (ADHD) is characterized by symptoms that express varying levels of inattention, hyperactivity and impulsivity. Case reports of ADHD treatment with psychostimulants suggest they can also act on comorbid disorders with impulsive features (kleptomania, pathological gambling and bulimia nervosa).[3] Erdogan et al.[4] reported that SPD patients had a high prevalence of comorbid ADHD, but this has not been investigated in other studies. The only case report of ADHD comorbid with SPD, by Lane et al.,[1] described

Table 1 Scores for depression, anxiety, impulsivity, inattention and hyperactivity questionnaires during treatment

	No medication	MPH SODAS 20mg	MPH SODAS 30mg
BDI	8	2	0
ASRS D	8	1	1
ASRS HI	3	0	0
BIS AT	22	22	21
BIS PLAN	36	35	29
BIS MOT	24	24	22
BIS TOT	84	81	72
STAI T	55	55	55
STAI S	62	62	60

ASRS D = Adult Self Report Scale – Inattention Symptoms; ASRS HI = Adult Self Report Scale – Hyperactivity and Impulsivity Symptoms; BDI = Beck Depression Inventory; BIS AT = Barratt Impulsiveness Scale – Attentional Subscale; BIS MOT = Barratt Impulsiveness Scale Motor Subscale; BIS PLAN = Barratt Impulsiveness Scale – Planning Subscale; BIS TOT = Barratt Impulsiveness Scale – Total Score; STAI S = State-Trait Anxiety Inventory – State Score; STAI T = State-Trait Anxiety Inventory – Trait Score.

a 9-year-old boy with a full-scale IQ of 77 who only experienced improvement when a behavioral intervention was associated with ongoing psychostimulant treatment. There are no case reports describing methylphenidate treatment in ADHD adults comorbid with SPD. Likewise, there are no reports in the literature of worsening SPD symptoms due to psychostimulant treatment in patients without ADHD.

We present the case of a 26-year-old college student who sought care because she could not control her scratching behavior. The patient reported starting the excoriation because she felt recurring insect bites on her skin. However, she described the itching as rapidly fading and that she continues excoriating without it. She only became aware of her behavior as she felt pain or bled. Most lesions were located on her thighs and legs. She was ashamed of her injuries and hid them by avoiding short clothes. Her dermatologist had already tried unsuccessfully to treat her SPD with fluoxetine and sertraline. Although she did not spontaneously self-report inattention and impulsivity symptoms, her family and friends frequently complained about them. The patient met DSM-5 criteria for both SPD and ADHD, and her husband and mother confirmed symptoms at clinically significant levels. We decided to treat ADHD first because of family and educational impairments and, after 1 month on 20 mg/day methylphenidate SODAS, she reported being able to focus on what she was feeling and that this aided her in inhibiting the impulse to scratch herself. She also stopped mentioning the itching sensation in her skin. After increasing MPH to 30 mg/day, she experienced further symptomatic improvement, and said that "did not even remember the injuries."

Table 1 presents self-report questionnaires measuring depression, anxiety, impulsivity traits and ADHD symptoms at baseline and when using 20 and 30 mg of MPH. These scores show that changes in inattention were most consistent with SPD decrease. During follow up assessments, the patient reported that her mood improved as her academic performance and social relations became less impacted by her ADHD. Although her Beck Depression Inventory scores decreased during treatment, her initial scores were already below the cutoff for clinical depression. The patient suspended medication by herself twice after the third month and resumed excoriating her skin, which again remitted with therapy.

Given the low efficiency of available pharmacologic agents for treating SPD (N-acetylcysteine, SSRIs), MPH might be an option for a subset of SPD patients. Since SPD can be defined as a repetitive behavior disorder due to impulsivity and inhibitory control deficits, and considering that the patient in this case report noticed that her scratching behavior was associated with mind wandering (inattention), we can suggest some hypothesis why the ADHD treatment helped improve SPD symptoms. Methylphenidate acts by inhibiting dopamine and noradrenaline reuptake, mainly in the *striatum* body, prefrontal cortex and *nucleus accumbens*. Thus, it can be posited that its action on prefrontal cortex could have helped reduce impulsivity, whereas its action on *striatum* body could have increased the attentional state. Thus, we suggest that increased attention span and decreased impulsivity could be mechanisms that, when achieved jointly, could decrease SPD symptoms. Further studies are needed to address whether methylphenidate benefits SPD individuals who do not have ADHD by improving cognitive functions (e.g. inattention or inhibitory control).

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