

to reduce stress and anxiety, but then developed a compulsive and addictive use independently of her obsessions. Diagnostic criteria for addiction and markers of severity are almost all applicable to this particular craving and dependence without ingestion; yet, bleach abuse and dependence could not be considered as independent of OCD. This observation raises questions, then, about the shared physiopathology of both disorders under a different angle than that of a classical comorbidity. We suggest that, for these treatment-resistant symptoms, in our patient in particular and in those with severe and complex OCD in general, innovative therapies should be explored, e.g., new pharmacological agents such as baclofen<sup>4</sup> or deep brain stimulation.<sup>5</sup>

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# S-(+)-ketamine-induced dissociative symptoms as a traumatic experience in patients with treatment-resistant depression

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Ketamine, an NMDA receptor antagonist, is a rapid-acting antidepressant and anti-suicidal agent.<sup>1</sup> However, most clinical trials assessing its antidepressant action involve RS-(±)-ketamine, which is considered a more dissociative drug than S-(+)-ketamine.<sup>2</sup> In this report, we describe

severe psychotomimetic side effects after S-(+)-ketamine infusion therapy in two patients with treatment-resistant depression (TRD), contrasting with previous evidence that S-(+)-ketamine is less prone to inducing these side effects.

**Case 1.** A 43-year-old married man, educated at the vocational level, presented with a 2-year history of TRD with no previous report of dissociative or psychotic symptoms. The patient had not responded to citalopram, venlafaxine, mirtazapine, or augmentation trials with lithium and quetiapine. After a severe suicide attempt and refusal of electroconvulsive therapy (ECT), the patient was treated with an S-(+)-ketamine infusion (0.25 mg/kg, IV over 10 minutes) in July 2014, while still on mirtazapine and quetiapine. His baseline Montgomery-Åsberg Depression Rating Scale (MADRS) score was 40. After 24 hours, the MADRS score was 28 (30% improvement). The patient reported marked dissociative symptoms during infusion and described the procedure as a terrible experience: “There was a devil and he removed my heart with his own hands; it was terrible.” One week after the infusion, he persistently re-experienced recurrent dissociative thoughts and nightmares. Three weeks after the infusion, he was in remission from both depression and dissociation, but still hesitant to mention the psychotomimetic experience. At that time, he asked his psychiatrist: “to get out of limbo, I should go to hell?”

**Case 2.** A 66-year-old, college-educated married man was diagnosed with severe long-standing TRD. There were no previous reports of dissociative or psychotic symptoms. The patient had not responded to venlafaxine, citalopram, duloxetine, or augmentations with bupropion, aripiprazole, quetiapine, pramipexole, and agomelatine. The patient’s family would not accept ECT, and lithium was avoided due to a unilateral nephrectomy. He was treated with S-(+)-ketamine infusion (0.25 mg/kg IV over 10 minutes) in August 2015; mirtazapine and olanzapine were maintained. His baseline MADRS score was 48, declining to 31 after 24 hours (35% change). During the S-(+)-ketamine infusion, the patient developed dissociative symptoms that were experienced as traumatic. He felt a strange sense of bodily disintegration “into atoms. [...] It was death. I died... am I here? My body exploded.” He avoided talking about the experience, and dissociative and psychotic behavior persisted for almost 4 weeks.

We reported two cases of severe psychomimetic effects in TRD patients associated with rapid infusion (10 minutes) of S-(+)-ketamine, the ketamine formulation most widely used in Brazil. Thus, we raise the hypothesis that S-(+)-ketamine is not sufficiently less dissociative than RS-(±)-ketamine to the point of justifying rapid infusion, as has been common practice in Brazil.

It is noteworthy that, despite being reported as a traumatic event by patients, these experiences cannot be diagnosed as such according to the DSM-IV criteria; acute stress disorder (ASD) is characterized by symptoms of negative mood, intrusion, dissociation, avoidance, and arousal that last from 3 days to 1 month, usually during or subsequent to a traumatic episode not correlated with the physiological effects of a substance.<sup>3</sup>

A core aspect related to ketamine use is its safety and tolerability, especially with respect to cardiovascular risks,

abusive misuse, and psychotomimetic side effects.<sup>4</sup> In the cases described herein, we suggest that rapid infusion of S-(+)-ketamine may offer less tolerability compared to the racemic formulation. However, the infusion rate used to treat these patients may explain, at least in part, the poor tolerability observed. Therefore, we maintain that ketamine administration should only be performed in the inpatient setting, with supporting services and monitoring available,<sup>5</sup> using a slow infusion over at least 40 minutes.

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# An index to examine the sexual HIV risk of psychiatric service users based on sexual partners

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Numerous studies report higher HIV infection rates among psychiatric patients than in the general population.<sup>1</sup> Relative to other HIV-affected populations, they have higher rates of HIV-related risk behaviors in fewer sexual occasions, including multiple partners, partners of unknown or positive HIV status, sex in exchange for money, shelter or goods, and low condom use rates.<sup>2</sup> We present a new HIV risk index (RI)<sup>3</sup> that takes into account differential risk associated with these factors.

Anal/vaginal receptive sex is riskier than insertive practices. Sex acts with partners of unknown/positive HIV status are riskier than those with HIV-negative partners, regardless of partner type.<sup>4</sup> Lastly, sex acts with steady, casual, and exchange partners are associated with different HIV risk.<sup>5</sup>

Our RI assigns differential risk to each sex act and sums risk across sex acts. The differential risk consists of three risk coefficients: 1) partner (type and HIV status); 2) vaginal sex (insertive or receptive) per sex occasion; and 3) anal sex (insertive or receptive) per sex occasion. Risk coefficients for vaginal/anal directionality are based on CDC transmission risk values,<sup>6</sup> while coefficients proposed for partner type were determined on the basis of expert opinion and face validity (Table 1).

RI is estimated for each sex partner (RI<sub>n</sub>); the sum of all RI<sub>n</sub> corresponds to the total RI score. We provide three examples to demonstrate the new RI in comparison to focusing only on condomless sex proportions.

**Example 1.** A man had four anal sex acts, one insertive and three receptive, all condomless, with a casual male HIV-unknown partner. Taking into account the three risk coefficients, this person would have an RI = 0.90\*(0.11\*1 + 1.38\*3) = 3.83. Based solely on the proportion of condomless sex occasions, this person's risk would be classified as 100%.

**Example 2.** A man had three vaginally insertive acts, all condomless, with a casual HIV-negative partner. This person would have an RI = 0.10\*(0.04\*3) = 0.01. His risk

**Table 1** Risk coefficients by sex partner type and HIV status, sex occasions

Sex partner RC		
Partner type*/HIV status	Heterosexual	MSM
Steady		
Positive	1.00	1.00
Negative	0.01	0.01
Unknown	0.50	0.50
Casual		
Positive	1.00	1.00
Negative	0.10	0.10
Unknown	0.75	0.90
Exchange		
Positive	1.00	1.00
Negative	0.25	0.25
Unknown	0.90	0.90
Sex occasions RC <sup>†</sup>		
	Vaginal-RC	Anal-RC
Receptive	0.08	1.38
Insertive	0.04	0.11

RI formula: RI<sub>n</sub> (Partner N) = RC [Partner type and HIV status] \* (RC[vaginal sex] \* number of condomless vaginal acts + RC[anal sex] \* number of condomless anal acts)

MSM = men who have sex with men; RC = risk coefficient; RI = risk index.

\* Steady partner: someone participants think of as a steady or main partner (spouse, girlfriend/boyfriend, lover, fiancée); casual partner: someone participants had sex with for love or fun, but did not think of as a main or steady partner; exchange partner: someone participants had sex with in exchange for something (money, drugs, alcohol, cigarettes, a place to sleep), whether the transaction was clearly negotiated or implied.

<sup>†</sup> Sex occasions risk coefficients are based on epidemiological data provided by CDC.<sup>6</sup>