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Memory Reconsolidation for Treatment-Resistant Aggression and Self-Injurious Behaviors

To the Editors:

Aggression and self-injurious behaviors (SIBs) that cannot be effectively managed by available pharmacologic and behavioral interventions are an important and difficult clinical challenge. Presented below is a case (the first to our knowledge) where a memory reconsolidation paradigm was successfully used to lower the frequency of these episodes.

CASE

A 47-year-old man diagnosed with intermittent explosive disorder, polysubstance dependence (in a controlled setting), significant childhood neglect and abuse, and mild mental retardation (IQ of 56 per Wechsler Adult Intelligence Scale-Fourth Edition) was hospitalized in a state inpatient hospital with a long history of aggression and SIB. Aggressive behaviors included spitting, punching, and kicking staff and peers along with SIB of scratching arms, swallowing items, and banging, punching, or breaking glass windows.

There were no consistent predisposing factors to these behaviors, but he would sometimes state he did these behaviors when he felt lonely, wanted soda or money and had none, or when he was bored and wanted to be placed on constant observation. The patient developed and acquired these reinforcing properties over a long period, and clinical observation and interpretation suggested that this became a part of his pattern of interacting with others, serving to both modulate internal distress (as he had limited verbal capacity to express his feelings directly) as well as establish socioenvironmental control over others to get his desires met on the unit. These behaviors had kept him from being placed with community providers, and as a consequence, he had been hospitalized for over 7 years.

All previous attempts to mitigate these behaviors through medication (adequate trials of risperidone, haloperidol, olanzapine, quetiapine, topiramate, bupropion, paroxetine, trazodone, clonazepam, and naltrexone had been tried in combination and/or as necessary) and behavioral interventions (including weekly individual therapy, peer-based groups, transition care counseling, substance abuse counseling [including alcoholic anonymous meetings], multiple individualized coping skills treatments, and a differential reinforcement of other behavior schedule) did not have lasting results of decreasing the targeted behaviors.

Given the failure of these specialized pharmacologic and behavior treatments and after a through review of the patient's history, we began a trial of modafinil. This was chosen because of his addiction history, the habitual nature of these behaviors (which seemed to be rewarding and therefore could be perceived as a behavioral addiction), the novel mechanism of the drug,[1] and clinical research suggesting a modulating effect on addiction and processes requiring cognitive control.[1,2] He had a good initial response at 100 mg with a decrease in self-harm and had the dose increased to 200 mg after some of the problem behaviors returned after 6 weeks. He was maintained on this dose with good effect, and after the second month of treatment, he had no SIB and was recommended for a possible discharge to an appropriate outpatient facility.

At that time, he had a burst of aggression/SIB (which accumulated in 32 restraints in 2 months), and modafinil was tapered and discontinued by a treating psychiatrist because it was thought that this was possibly activating the patient given the potential stimulating properties of the drug. No other treatments (including multiple doses of different antipsychotics and behavioral techniques) could effectively manage these behaviors at this time.

Given the lack of efficacy of previous and current treatments and the seriousness of these behaviors, we discussed trying a new (and somewhat controversial) technique based on memory reconsolidation. Briefly, memory reconsolidation focuses on when memories are retrieved and are briefly open to a more physiologically malleable state where they can be either strengthened or weakened based on technique (please see Schwabe et al,[3] Lee,[4] and Nader and Hardt[5] for reviews). Importantly for this case, these methods have been found to effectively reduce addiction and emotionally laden memories in human populations.[3,6]

Propranolol, an adrenergic receptor antagonist, was chosen as the preferred method because it has been previously studied, cited widely in the literature,[3] and safe in this clinical context. The patient consented, and then the procedure was started on the unit (Fig. 1). A 1-time dose of 40 mg propranolol was given approximately 5 hours after an SIB episode in which he was restrained. After waiting 90 minutes (when peak levels of propranolol can be expected in humans after oral administration), we had him remember in as much detail as possible the things that led up to the episode, the actual incident, and his emotional response to the situation.

After that session (30 minutes), we led him to the window and asked him if he wanted to hit it. He declined and stated he was tired. The rest of the week showed a dramatic reduction in SIB with only 1 short episode of hitting the window in which he was redirected without a restraint. We tried the propanolol session again the next week (with the same perimeters) after he was triggered in a trauma group by a peer and escalated with another restraint. He maintained a marked reduction in SIB incidents afterwards (a total of

FIGURE 1. Timeline of the SIB resulting in a physical restraint and subsequent memory reconsolidation paradigm employed using propranolol.

3 short restraints) and was discharged 3 months later even after a prolonged, and at times uncertain, discharge process. He was discharged on some of his long-standing medication—trazodone 100 mg every bedtime for sleep, clonazepam 1 mg thrice a day by mouth for anxiety, paroxetine 40 mg by mouth every morning for anxiety/aggression, and quetiapine 200 mg thrice a day as necessary for agitation.

DISCUSSION

This case highlights the potential to use memory reconsolidation for aggression/SIB. The mechanisms that could be responsible for the observed effects are beyond the scope of this case study, but prior work has shown that noradrenergic activity in the amygdala has important effects on emotional memory enhancement.[3,7,8] It is therefore possible that our patient had a reduction in amygdalar activity after administration of propranolol, and during memory reactivation, this translated into a decreased emotional salience of that memory. This more neutral memory could have therefore decreased the incentive (or rewarding properties) of the SIB. Given the exploratory nature of this report and the importance of effective treatments for SIB, memory reconsolidation warrants further research for this indication.

ACKNOWLEDGMENT

The authors would like to thank the clinical staff of Connecticut Valley Hospital for their care and support of this patient.

AUTHOR DISCLOSURE INFORMATION

Drs Matuskey and Sondik have no biomedical financial interests or potential conflicts of interest relevant to this submission.

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Dimenhydrinate Use Disorder With Chronic Psychosis

To the Editors:

Dimenhydrinate is a commonly used and easily obtained remedy for nausea that is well known as a substance of abuse.[1] We report a case of dimenhydrinate addiction and associated psychosis, which was misdiagnosed as treatment-resistant schizophrenia. The patient provided informed consent to publish this case report.

CASE REPORT

A 38-year-old woman was referred to the B. C. Psychosis Program, a provincial tertiary-care mental health unit for treatment-resistant psychosis, following poor response to therapy at a general hospital. Her referral diagnosis was chronic schizophrenia, and upon arrival, she had auditory, visual, and tactile hallucinations; persecutory delusions; moderate disorientation; and irritability. She also had sustained tachycardia. She was receiving haloperidol 1 mg daily, zuclopenthixol decanoate 250 mg intramuscularly every 2 weeks, propranolol 20 mg twice daily, and citalopram 40 mg daily. Positive and Negative Syndrome Scale score was positive, 26; negative, 29; general, 47; and total 102. Hospital records indicated her psychosis had begun 8 years previously at age 30 years and was characterized by prominent perceptual disturbances, persecutory delusions, and disorganization. Episodes of low mood and suicidal ideation were also noted. The patient had had 5 previous psychiatric admissions, but her psychosis had never completely remitted despite treatment with a variety of antipsychotics, including a 9-month clozapine trial during the year before index admission; it was discontinued because of tachycardia, hypotension, and sedation. The patient had a history of significant substance use including cocaine, methamphetamine, and cannabis leading up to her first psychotic episode, although she consistently denied any concurrent stimulant use since her first admission, and this was confirmed by occasional negative urine drug screens during the index and prior admissions. Her family history included several first-degree relatives with addictions and suicide but no psychosis.

The patient disclosed that she had been using high doses of dimenhydrinate (diphenhydramine and 8-chlorotheophylline), an over-the-counter nausea remedy, for epigastric discomfort and nausea associated with gastroesophageal reflux disease. She also asserted that it helped control her weight and provided euphoria and behavioral activation. She began using this medication "7 or 8 years ago," initially ten 50-mg tablets 3 to 4 days a week. During the year before index admission, she endorsed daily use of 20 or 30 tablets of dimenhydrinate. Records identified excessive dimenhydrinate use as a concern 2 years prior to admission, but the patient received no intervention.

Upon admission to the unit, access to dimenhydrinate was sharply curtailed. Her sensorium cleared, and her perceptual disturbances decreased in the first week even as haloperidol was discontinued. During the ensuing 2 months, zuclopenthixol