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Anorexia Nervosa and Mercury Toxicity

TO THE EDITOR: Neuropsychiatric symptoms as a result of mercury poisoning following the excessive consumption of large predatory fish (methyl mercury levels >1 ppm) are well documented but often misdiagnosed.

Mercury toxicity secondary to the excessive consumption of tuna was observed in a 47-year-old woman with a 30-year history of anorexia nervosa. The patient's prolonged abuse of laxatives resulted in a small bowel obstruction and rectal prolapse 7 years prior to the detection of mercury intoxication. The rectal prolapse was treated with total proctocolectomy and ileostomy. A low fiber diet was recommended thereafter, and the patient commenced a diet consisting of two cans of tuna and one muffin daily for the subsequent 7 years until she came to our unit for observation and treatment of anorexia nervosa.

The patient presented with a 1-month history of depressive symptoms, refusal to eat, fatigue, weakness, anxiety, insomnia, irritability, and "confusion." She weighed 73.7 lbs, which was approximately 53% of her ideal body weight, and was afraid that her bowels would stop working. She reported increased sensitivity to loud noise and ringing sounds in the absence of auditory stimuli. A neuropsychological assessment revealed less than normal scores for processing speed, working memory, and attention. Her premorbid IQ was estimated within the 61st percentile. Her current full-scale intelligence quotient score was within the 45th percentile, with a verbal intelligence quotient score within the 75th percentile and a performance IQ score within the 30th percentile. Her memory was stronger for verbal information (scoring in the 50th percentile) relative to nonverbal information (scoring in the 4th–10th percentile). Psychiatric examination revealed longstanding symptoms consistent with anorexia nervosa, but due to her most recent symptoms of irritability and weakness as well as her neuropsychological deficits, a mercury level evaluation was obtained.

The patient's plasma mercury levels were markedly elevated at 74 mcg/dl (normal=<10 mcg/dl) on two repeated measurements. A complete blood count, electrolytes, amylase, and lipase were all unremarkable, but liver enzymes showed slight elevation. The patient underwent chelation therapy, with succimer 10 mg/kg t.i.d. for 5 days and then 10 mg/kg b.i.d. for the following 14 days. The mercury toxicity motivated her to change her diet and broaden her food repertoire. Although her attitudes toward food with high residue did not change, the patient became afraid of eating any type of fish.

More than 200 neuropsychiatric symptoms have been attributed to mercury poisoning in the medical literature (1–3). Our patient's symptoms, including low mood, irritability, insomnia, cognitive impairment, and fatigue, may have been primarily mood symptoms, a consequence of severe malnutrition, or are attributable to mercury poisoning. Interestingly, mercury poisoning as a result of dental amalgam fillings may cause an anorexic syndrome (anorexia hydrargyrum) (4). To our knowledge, this is the first report of mercury intoxication secondary to anorexia nervosa. We are currently following our patient to monitor her psychiatric and neurological response to chelation. Longitudinal observation and treatment of malnutrition and depressive and anxiety symptoms may clarify the extent to which our patient's symptoms were attributable to mercury intoxication.

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Intranasal Zaleplon Abuse

TO THE EDITOR: Nonbenzodiazepine hypnotic agents were developed to minimize the adverse effects of benzodiazepines. These hypnotics bind to the α_1, α_2, and α_3 subunits of the gamma-aminobutyric acid type A ($GABA_A$) receptor complex. Zaleplon preferentially binds to the α_1 subunit. These compounds offer less abuse liability relative to benzodiazepines, although this is debatable under certain circumstances (1). We present the case of a patient who abused intranasal zaleplon in order to experience a "high" feeling.

"Mr. A" was a 28-year-old man with a 13-year history of polysubstance abuse (cannabis, cocaine, and heroin). He had been abusing mainly cocaine over the past 5 years and had unsuccessfully tried several treatments to achieve abstinence 1 year prior, following a prolonged stay in a monastery. As a result of sleep difficulties, he was prescribed zaleplon (10 mg/night) as needed. Over the next 3 months, the dose was gradually increased to 70–80 mg/day. Subsequently, he noticed that zaleplon had a mood uplifting effect. To boost this effect, he started taking the drug intranasally by snorting seven to eight pulverized capsules. The patient mentioned that intranasal zaleplon produced a euphoric feeling resembling that of cocaine, although less intense and of a shorter duration. This pattern of abuse persisted for almost 1 year, and withdrawal symptoms (anxiety, ner-

vousness) emerged whenever he tried to reduce its use. He was offered inpatient detoxification treatment, which he declined.

Experts have agreed that nonbenzodiazepine hypnotics have a reduced risk of abuse/dependence compared with benzodiazepines. However, this may not be the case when these drugs are taken for a prolonged period and in higher doses than recommended (1). To our knowledge, the present case is the first to describe intranasal zaleplon abuse for its stimulant and rewarding effect, which lends support to the concern of some investigators who maintain that individuals with a history of substance abuse may be at increased risk of abuse of these agents. Some studies showing that the physical dependence and reinforcing effects for zaleplon may be similar to those of benzodiazepines corroborate this reservation (2–4).

The underlying mechanism of zaleplon abuse and stimulating effect is unknown. However, following chronic exposure to benzodiazepines or benzodiazepine-like agents, alterations in $GABA_A$ receptor sensitivity occur, which contribute to the development of tolerance, dependence, and withdrawal. Moreover, a complex interaction (mostly a tonic inhibitory control) between the dopaminergic reward brain structures (ventral tegmental area, nucleus accumbens, ventral pallidum) and GABA function exists. It can be speculated that chronic and/or high exposure to $GABA_A$ receptor agonists could lead to a receptor inhibitory-excitatory switch in these reward-related areas that could contribute to addiction (5). Consequently, clinicians should be warned of the abuse potential of zaleplon, especially in multisubstance abusing individuals.

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A Case of fMRI-Guided rTMS Treatment of Coenesthetic Hallucinations

To the Editor: Hallucinations are the major first-rank symptoms in schizophrenia spectrum disorders and are commonly defined as a perceptual experience in the absence of sensory imput. However, these symptoms are rarely described outside of the auditory modality. We report the case of a patient with a positive diagnosis of schizoaffective disorder (according to DSM-IV-TR criteria).

"Mr. L" was a 33-year-old man who had been treated surgically 5 years previously for a testicular carcinoma. His regular clinical, biological, and imaging follow-up examinations did not show any signs of malignant extension. He developed coenesthetic hallucinations, experienced as electric shocks and alien objects moving inside his thorax, abdomen, and pelvis, for which treatment with antipsychotic and mood-stabilizing medications was unsuccessful. Through the use of new data-driven analyses (1), we observed a bilateral neural activity in the somatosensory and superior parietal cortices during coenesthetic hallucinations on a functional magnetic resonance imaging (fMRI) scan (Figure 1). Since repetitive transcranial magnetic stimulation (rTMS) has previously been used to treat auditory verbal hallucinations in adults (2) and children (3) with schizophrenia, Mr. L benefited from 10 daily sessions of fMRI-guided 1-Hz rTMS over the somatosensory cortex. A total of 10^4 pulses were delivered at 100% of the patient's motor threshold using the Magstim super-rapid stimulator, with a figure-of-eight coil positioned tangentially to the brain target. Low frequency rTMS has been shown to be effective in reducing neural excitability (2). The patient's rTMS sessions were successful in reducing the frequency and intensity of his coenesthetic hallucinations, measured using the Visual Analogical Scale (score: –55%; frequency: 73% to 18%; intensity: 84% to 30%). This improvement remained stable for at least 8 weeks and allowed a significant improvement in the patient's quality of life (improvement for Short Form-36–Physical Health subscores: from 35.5 to 65.1; improvement for Short Form-36–Mental Health subscores: from 21.8 to 53).

Our case demonstrates a link between the visceral symptoms of a patient's hallucinations and cortical somatotopic organization. This functional anatomical link is consistent with the results recently reported in the visual modality for a hallucinating patient with schizophrenia in whom neural hyperactivation was measured in category selective visual areas (4). To our knowledge, this is the first case report demonstrating the efficacy of neuronavigated rTMS in the treatment of coenesthetic hallucinations in a patient with schizoaffective disorder.

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