

**Violence in the Twilight Zone:
Ictal Nystagmus and Paroxetine**
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Summary

A 22 year old Hispanic female (EV) with self-laceration, aggression, and suicidal ideation complained on admission of ocular movement. Several days later she developed an episode of conjugate oscillating horizontal nystagmus with loss of awareness. No further episodes of nystagmus or seizures were observed after discontinuation of the SSRI antidepressant paroxetine. Polypharmacy and brief patient contact limit evaluation and treatment of uncommon neurologic side-effects and emergent conditions. Heightened suspicion of SSRI-mediated disturbed violence is also warranted.

Case Report

Admission:

A 22 yr-old Hispanic female (EV) with mild mental retardation was admitted on involuntary status for remediation of repeated self-laceration, thoughts of suicide, and combative/aggressive behavior after a “fight” at her group-residence. Her admission took place two days after discharge from a five day stay at an inpatient psychiatric unit where paroxetine and aripiprazol were added to multiple psychotropic medications. She complained of uncomfortable eye movements.

Past History:

EV inflicted superficial skin cuts on both upper and lower extremities during and in-between periods of low self esteem and impulsive misbehavior from her early teen years. Prior diagnoses included psychosis NOS, recurrent major depression (4 yrs PTA/prior to admission); schizoaffective disorder; borderline personality (2 yrs PTA); and long-standing mild mental retardation. No EPS (extra pyramidal syndrome), nystagmus, or seizures were reported.

Admission meds (po/daily except where noted):

standing: lithium (300mg TID); divalproex sodium EC (500mg BID); clonazepam (2mg BID); aripiprazol (15mg BID); quetiapine (300mg and 500mg q hs); paroxetine (10mg q am); benztropine mesylate (0.5mg)

stat: haloperidol (5mg IM) and diphenhydramine (50mg IM) for agitation.¹

as needed: lorazepam (2mg q agitation); diphenhydramine (50mg q hs)

Course (nursing and staff notes):

day one: Intermittent head banging, superficial self-injury (lacerations)

day two: cheerful and flirtatious with a male peer; scratched left thigh after reminded about rules limiting sexual interaction. Mental status: dissociation of affect and thought (cheerful indifference), intermittent attention lapse, selective refusal to answer questions. No ocular dystonia, nystagmus, or other movement disturbance noted. Benztropine discontinued;

day three: tantrums, manipulative behavior, impulsive, redirectable (staff report). Mental status:

¹ divalproex (Depakene); clonazepam (Klonopin); aripiprazol (Abilify); quetiapine (Seroquel); paroxetine (Paxil); benztropine mesylate (Cogentin); haloperidol (Haldol); lorazepam (Ativan); diprenhydramine (Benadryl)

pleasant, lucid, not depressed or labile, expressed interest in favorite book. She denied relief from self-scratching (with comb or fingernails), but felt she “had to” do it. Ten minutes into the interview EV abruptly manifested a 5/second,² coarse,³ conjugate,⁴ horizontal,⁵ oscillating,⁶ nystagmus for five to seven minutes.⁷ During the episode she was unresponsive to immediate environment, questions, cues, or directions. Both eyes were open, pupils normal, with body seated upright and head facing forward. No body jerks noted. No tactile intervention attempted. After event EV denied recall of eye movements or loss of awareness. She evidenced no subsequent ill effects. Paroxetine was discontinued. Lithium increased to 600mg BID. Staff subsequently reported two “fake” seizure-like activities with “talking while shaking” and “shaking” while playing scrabble, smiling and talking. No further nystagmus or seizures observed.

day four: Divalproex EC reduced to 500 mg. Secluded for marked agitation and inability to contract against self-harm after repeatedly self-scratching neck and legs. Stat lorazepam (2mg). No further nystagmus or seizures observed

day five: self-scratched neck with comb, redirectable, compliant. No further nystagmus or seizures observed

day six: Behavior improved, mood stable. No further seizures or seizures observed. Discharged to group home, improved.

Laboratory tests and procedures:

admission lithium level 0.6 meq/1, TSH 2.11. No consults, EEG, or video telemetry ordered. MRI ordered (not completed at time of discharge)

Discharge

meds: lithium (600mg BID), divalproex sodium EC (500mg daily), clonazepam (2mg BID), aripiprazole (15mg BID), quetiapine (300mg q daily and 500 q hs)

recommendations: Followup by neurologist for review of possible seizure condition

² Rate approximated in retrospect

³ Coarse nystagmus is amplitude (moment, movement) greater than 3mm. In this instance it was cross midline and took up about 75% of available ocular movement range.

⁴ Conjugate, i.e., both eyes moving in unison in the same plane

⁵ Horizontal, i.e., right-left plane

⁶ Oscillating nystagmus refers to unconscious movement of the eyes in each direction similar in speed and amplitude. “Oscillating” is preferred here to “pendular” (or “undulating”) due to slow arc-like (sinusoidal) movement sometimes associated with the latter. “Vibratory” suggests a “fine” (<1mm) rather than “coarse” (>3mm) movement. “Ocular flutter” is a rapid, brief in number (3-5), horizontal conjugate eye movement that decreases on fixation. Some examples of pendular nystagmus (none of which are similar to EV) can be seen on Dr. Timothy Hain’s *Otoneurology CD*: <http://www.dizziness-and-balance.com/sitecd.htm>

⁷ rate, amplitude, and duration of nystagmus estimated post-episode

Review:

Twilight states, psychomotor attacks, and temporal lobe epilepsy may underlie or contribute to commonly diagnosed psychiatric conditions.⁸ Absence attacks (petit mal epilepsy) can create lapses in memory, cognition and response; be confused with inattention, and create identity confusion, and personal distress. Migraine variants may present with nystagmus and altered consciousness.⁹ Psychogenic seizures may require 24-hr video-EEG telemetry for diagnosis¹⁰ and are notoriously difficult to distinguish from frontal lobe partial seizures (FLPS).¹¹

Epileptic nystagmus (EN)/ictal nystagmus (IN)¹² may occur alone or with other epilepsies.¹³ EN is a rare neurologic disorder which may be induced by substances and conditions which facilitate seizures in persons with constitutional or genetic predisposition (e.g., ion-channel defects¹⁴), trauma, drug/drug-withdrawal, infections, inner-ear/vestibular, and other neurologic conditions. EN is characterized by repetitive horizontal saccades (rapid foveal fixations) arising in the occipital or temporal-occipital cortex.¹⁵ Nystagmus may be the only motoric sign of seizure activity¹⁶ and may only be present during REM sleep.¹⁷

EN is associated in juveniles with absence seizure (Juvenile Absence Epilepsy, JAE). JAE has a female predominance (two to one), and an incidence of 2-8/100,000. Age of onset is roughly 8-26, sometimes manifesting first with automatisms and behavioral problems. Brief staring spells, motionless posture, non-responsive to queries, and lack of memory for attacks are

⁸ Strauss H, "Epileptic Disorders" in Arieti S, *American Handbook of Psychiatry*, ii (NY: Basic Books, 1977), 1120-1122

⁹ Lewis DW, Pearlman E *Pediatric Annals* 2005, 34(6):486-497

¹⁰ Leis AA, Ross MA, Summers AK, "Psychogenic seizures: ictal characteristics and diagnostic pitfalls" *Neurology* 1992, 42(1):95-99

¹¹ Saygi S, Katz A, Spencer SS, "Frontal lobe partial seizures and psychogenic seizures: comparison of clinical and ictal characteristics" *Neurology* 1992, 42(7):1274-1277

¹² Ictal implies seizure. Epilepsy refers to recurring seizures.

¹³ Kaplan PW; Tusa RJ, "Neurophysiologic and clinical correlations of epileptic nystagmus" *Neurology* 1993; 43(12):2508-1514

¹⁴ Mazzuca M, Lesage F, Lazdunski M, "Epilepsy and ion channels" *Epileptic Disorders* 1 Dec 2004; 6 Suppl 1:1-16

¹⁵ Garcia-Pastor A, Lopez-Estaban P, Peraita-Adrados R, "Epileptic nystagmus: a case study video-EEG correlation" *Epileptic Disorders* 2002; 4(1):233-28

¹⁶ Yilmaz A, Ulné K, Oguz KK, Saygi S, "Epileptic nystagmus in a patient with nonconvulsive status epilepticus" *Seizure* 2004; 13(3):183-186

¹⁷ Gire C, et.al., "Epileptic nystagmus: electroclinical study of a case" *Epileptic Disorders* 2001 January-March 3(1):33-37

characteristic. EEG spike and wave formation is only manifest during the seizure.

Horizontal nystagmus conditions include congenital and acquired or induced. Congenital nystagmus is usually a horizontal pendular nystagmus associated with reduced central visual acuity (cataracts, toxoplasmosis, macular or optic nerve hypoplasia, albinism, and amaurosis). Acquired or occupationally-induced nystagmus (e.g., miner's nystagmus), although sometimes horizontal, is typically rotatory and pendular) as an adaptation to persistent inadequate light.

One case of voluntary rapid conjugate horizontal oscillating nystagmus in conjunction with a nonepileptic seizure has been reported in the recent literature. In that instance a 56 year old woman post-temporal lobectomy for temporal lobe epilepsy, treated with lamotrigine and primidone, was admitted with gradual onset of psychosis and self-injurious behavior. During a monitored two hour seizure she was unresponsive, incontinent, with eyes closed. When her lids were forced open she showed brief (maximum five second duration), high frequency, low amplitude, "pendular" horizontal nystagmus which disappeared abruptly upon her own forced closure of her eye-lids. Event-concurrent EEG was essentially unchanged from past interictal monitoring.¹⁸

Paroxetine is a known risk factor in suicidal behavior, manic disinhibition, and the serotonin syndrome (which may include ocular myoclonus).¹⁹ Recent review suggests increased risk of aggression compared to placebo.²⁰ The manufacturer recommends its discontinuation in patients who develop seizures.²¹ Aripiprazole and quetiapine are rare causes of seizures and are "possibly contraindicated" in epilepsy.²²

Discussion:

EV's episode of horizontal oscillating nystagmus was distinct from a previously reported instance of voluntary nystagmus. EV's eyes were fully open, the nystagmus lasted 7-10 minutes, and was coarse rather than fine in nature. After the attack paroxetine was discontinued, lithium increased,²³ and divalproex reduced.²⁴ Further administration of prn and stat medications were

¹⁸ Davis BJ, "Voluntary nystagmus as a component of a nonepileptic seizure" *Neurology* 2 December 2000, 55:1937

¹⁹ Predictors of Serotonin syndrome: clonus (inducible, spontaneous, or ocular), agitation, sweating, tremor, and exaggerated reflexes. Dunkley EJ, Isbister GK, Sibbritt D, Dawson AH, Whyte IM "The Hunter Serotonin Toxicity Criteria" *Quarterly Journal Medicine (QJM)*, 2003; 96(9):635-42

²⁰ Healy D, Menkes D, Herxheimer, "Antidepressants and Violence: Problems at the Interface of Medicine and Law," *PLoS Medicine*. Sept. 2006, 3(9)(e372):478-487 www.plosmedicine.org. Public Library of Science is an open source, peer review publication.

²¹ "Paxil," *PDR* (Thomson, 2006), 1503-1504

²² aripiprazole and quetiapine, *Medscape* interaction checker. [Http://medscape.com](http://medscape.com)

²³ lithium is a rare cause of status epilepticus. It has no known pharmacokinetic interactions with antiseizure meds. Spina E, Perucca E "Clinical significance of pharmacokinetic

confounding factors. Standing medications may have been contributory. No further nystagmus attacks or seizure episodes were observed after discontinuation of paroxetine. After some initial deterioration in behavior, a significant reduction in self-laceration, suicidal thoughts, and episodic aggression followed.

In retrospect EV's differential diagnosis might include "twilight states" such as dissociated personality and fugue states, migraine variants, and seizure states including petit mal, temporal lobe epilepsy, frontal lobe partial seizures, and psychogenic epilepsy. No autonomic signs indicative of a serotonin syndrome were present. The solitary episode of horizontal oscillating (pendular) nystagmus, characterized here as "ictal" could also be termed "myoclonus."²⁵ No exam was undertaken for concurrent involuntary palatal movements. There was no otological or neurologic consult, video telemetry, E.G. or EEG monitoring. MRI was ordered but not conducted.²⁶

Conclusion

Neurologic side effects raise special concerns in patients subject to complex polypharmacy and problematic psychiatric diagnoses. In EV undiagnosed absence seizures might have formed the basis for her long-term psychiatric presentation. Suicidal and violent impulsive behavior, demand heightened scrutiny for specific sensitivity to psychotropics, especially the SSRI and SNRI class of antidepressants. The onset of a rare otoneurologic condition, ictal nystagmus, requires further assessment and comment

Summary:

A twenty-two year old Hispanic female with a history of mild mental retardation, aggression, and self-injury was admitted for recent behavioral, mood, and personality changes and suicidal ideation. During hospitalization she complained of involuntary eye movements and manifested one episode of oscillating horizontal conjugate nystagmus with lack of awareness, non-responsive to verbal intervention, with no memory for the attack. No further attacks were

interactions between antiepileptic and psychotropic drugs" *Epilepsia* 2002, 43 Supplement 2:37-44

²⁴ Divalproex sodium is the acknowledged gold-standard for treatment of absence seizures. Its effect on ictal nystagmus is undocumented. It was reduced here due to possible prolongation of absence attacks when given with clonazepam and unknown interactions with the neuroleptics quetiapine (already at maximum recommended dose) and aripiprazole.

²⁵ Ocular myoclonus is usually vertical, closely correlated with involuntary palatal movements, and perseveres through sleep. Myoclonus is generally classified as a movement disorder-tremor, and may be a side effect of SSRI's (selective serotonin reuptake inhibitors).

²⁶ MRI is recommended as early as possible in EN to rule out brain pathology with potential for remediation

observed after discontinuation of recently added paroxetine. Medication interactions may have conditioned both the seizure and the suppression of absence attacks.

Absence seizures can contribute to lapses in judgment, depressed self esteem, and aggression. Patients with limited and/or fluctuating mental capacity, dissociations of emotion, cognition and behavior, and a new onset focal oculomotor event such as nystagmus deserve careful neurologic review. Psychotropic medications, especially SSRI antidepressants, may also cause abrupt behavior, personality, and mood alterations with aggressive outbursts and suicidal impulsivity.