Nortriptyline-Induced Room Tilt Illusion

Bernard Sarmiento, MD, MBA[1,2], Melissa Vaz-Ayes[3], Matthew Gunther, MD[4], Adam Fusick, MD[5], Shixie Jiang, MD[3]

Department of Psychiatry, Massachusetts General Hospital[1]; Harvard Medical School[2]; Department of Psychiatry, University of Florida College of Medicine[3]; Department of Psychiatry, Stanford University School of Medicine[4]; Mental Health and Behavioral Services, James A. Haley VA[5]

INTRODUCTION

Room tilt illusion (**RTI**), or visual tilt, is a rare and transient perceptual disturbance resulting in a disorienting perspective where a patient's visual scene is tilted off the true vertical (usually by 90° or 180°)

- *Historical Context:*
  - First described in 1805 in a case where a woman treated for "hysteria" was experiencing hourly episodes where she saw the people around her standing on their heads[1]
- *Epidemiology:*
  - ~170 cases in the literature
  - In 656 patients presenting to an otology clinic for dizziness and/or vertigo, **1.2%** (n=8) had episodes of RTI[2]
  - Predominantly affects males (60.2%) with a mean age of 51.2 ± 20.3 years[3]
- *Characteristics:*
  - Primarily associated with central nervous system (CNS) disorders (61.4%)[3]
  - Most common etiology is **cerebral ischemia**, accounting for 27.7% of cases, particularly involving posterior fossa structures[3]
  - Other causes include multiple sclerosis, epilepsy, inner ear conditions, and migraines
    - Only one other case of medication-associated RTI (intravenous morphine w/ opioid toxicity)
  - Varies in duration, with episodes lasting from seconds to hours[4]
- *Potential Mechanisms:*
  - Sensory pathway dysfunction and/or disruption in **visual-vestibular integration** (an important element of the vestibulo-thalamo-cortical system): erroneous cortical integration of vestibular and visual cues resulting in erroneous visual scenes

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CASE PRESENTATION

- A 77-year-old male, married, veteran patient with a past psychiatric history of **major depressive disorder** and **generalized anxiety disorder** was transferred to a tertiary academic center for electroconvulsive therapy (ECT) for worsening and refractory depression with psychotic symptoms
  - Medical history was significant for atrial flutter (coumadin 5 mg daily), hypertension (losartan 25 mg daily and metoprolol 25 mg twice daily), and obstructive sleep apnea
- Mental Status Exam: Patient appeared thin, anxious, and severely dysphoric, but remained cooperative:
  - Soft speech with occasional hesitancy;
  - Depressed mood with a blunted and dysphoric affect;
  - Hyperreligious and nihilistic delusions;
  - Active auditory hallucinations in the form of the devil denigrating him and family;
  - Persistent suicidal ideation, with intermittent plan and intent;
  - Cognition was intact with a mini-mental state examination of 26 out of 30 (normal cognitive function).
- Complete physical exam and laboratory testing were unremarkable
- Psychotropic medications on admission were venlafaxine (150 mg daily), aripiprazole (10 mg daily), mirtazapine (30 mg nightly), and trazodone (25 mg nightly as needed)
- Patient cleared for ECT to target severe depressive episode, with refractory delusional content and perceptual disturbances → **Nortriptyline** was subsequently initiated as an augmentative agent due to minimal relief from ECT

CASE TIMELINE

Table 1: Overview of Patient's Psychiatric History, Clinical Presentation, Hospital Course, and Management, 2016-2019

TIMELINE	WINTER 2016	MAY-SEPTEMBER 2018	OCTOBER-DECEMBER 2018	DECEMBER 2018 (ADMISSION)	1ST HALF OF JANUARY, 2019	2ND HALF OF JANUARY, 2019	FEBRUARY-MARCH 2019	APRIL 2019
RELEVANT CONTEXT	Development of generalized anxiety disorder (GAD) following the death of his first wife	Treated as an outpatient with multiple anxiolytics, including benzodiazepines, and supportive counseling	Three involuntary hospitalizations in three months, including two hospitalizations at a VA hospital	Admission to tertiary academic medical center for electroconvulsive therapy (ECT) due to refractory symptoms	Fourth hospitalization	Fourth hospitalization	Fourth hospitalization	Discharged
PSYCHIATRIC SYMPTOMS	Excessive anxiety and worry about children and financial situation; associated with fatigue, irritability, difficulty concentration, and sleep disturbances; intermittent delusion of financial ruin	Worsening anxiety and development of severe depressive symptoms, including 30 lb. weight loss, anhedonia, avolition, fearfulness, guilt, hopelessness, and active suicidal ideation	Continued severe depression; development of psychotic symptoms including auditory hallucinations of the devil denigrating him and family and mood-congruent ideas of reference	Prior to admission, no real improvement to symptoms of severe depression and psychotic features of mood-congruent delusions and auditory hallucinations	Severe dysphoria w/ continued anhedonia, fatigue, guilt, and hopelessness; religious delusions of guilt and financial ruin, and active suicidal ideation	Little change to his overall mood, w/ profound dysphoria, continued suicidal ideation, and persistent delusions of financial ruin and impending arrest	Continued lack of mood improvement w/ passive suicidal ideation, anxiety, but increasing desire to go home	Improved depressive symptoms w/ minimal mood-congruent delusions of guilt, but devoid of any suicidal ideation
MANAGEMENT								
HOSPITAL COURSE	-	-	-	Admitted for ECT due to refractory symptoms; physical exam and laboratory testing unremarkable	After 8 sessions of ECT, with limited improvement to depression and hallucinations → TCA trial w/ nortriptyline was initiated	Stable vital signs over four weeks w/ unremarkable neurological examinations; CT and MRI of head were unremarkable	Lack of mood improvement led to discontinuing nortriptyline after four weeks → Lithium initiated, and aripiprazole titrated	Discharged with follow-up care: geri-psychiatry outpatient clinic, suicide prevention team, & treatment resistant depression clinic
PSYCHOTROPIC MEDICATIONS	❖ Multiple medication trials for MDD and GAD were employed as an outpatient and during three inpatient hospitalizations: sertraline, fluoxetine, venlafaxine, bupropion, buspirone, trazodone, aripiprazole, and quetiapine			Aripiprazole 10 mg; Venlafaxine 150 mg; Mirtazapine 30 mg; Trazodone 25 mg	Aripiprazole 10 mg; **Nortriptyline titrated to 50 mg;** ECT	Aripiprazole 10 mg; **Nortriptyline 50 mg**; w/ ECT	Aripiprazole 15 mg; Lithium 600 mg; Trials of methylphenidate & dexamethasone	Aripiprazole 15 mg; phenelzine 30 mg; trazodone 25 mg
ROOM TILT ILLUSION	-	-	-	-	❖ On 6th day of nortriptyline, and one day following titration to 50 mg, patient developed a **visual disturbance where it felt as though he was standing on the wall looking downwards as if his surroundings were tilted by 90 degrees** ❖ Episodes occurred in the morning, when fully awake, with no accompanying symptoms, lasting between 2 and 30 seconds ❖ Solely present for the four weeks he was on nortriptyline			For two months following nortriptyline discontinuation, **there was no recurrence of RTI**

DISCUSSION

- RTI involves dysfunction in the perception of verticality
- Verticality is processed through the integration of visual, vestibular, and somatosensory inputs within the vestibulo-thalamo-cortical system[5]
  - Disruption (i.e. infarct) in vestibular nuclei, thalamic nuclei, cerebellar pathways, and/or cortical projections can lead to RTI
- **Table 2** highlights the theoretical impact of tricyclic antidepressants (TCA) that may have led to the development of RTI in this patient
- As many patients who experience RTI are middle-aged to elderly, a thorough cerebrovascular workup, including imaging (i.e. MRI) and vascular studies, is strongly recommended, along with treatment of the underlying condition
  - The patient had several risk factors including age, hypertension, and an arrhythmia

Table 2: Tricyclic Antidepressants' Potential Effects on the Visual-Vestibular Integration System

Effect	Possible Mechanism of Action
Anticholinergic	Acetylcholine blockade at muscarinic receptors of the vestibular system can lead to perceptual dysfunction, with vertigo and imbalance[6]
Histaminergic	TCAs' affinity for antagonizing H_1 and H_2 receptors can lead to vestibular compensation disruption[7]
Potassium Channel Modulation	K+ receptors are thought to play a role in the function of vestibular hair cells[8]

CONCLUSIONS

- Pharmacological triggers of RTI remain underexplored in the literature, with this case being the 2nd medication-associated RTI occurrence
- Verticality integration dysfunction highlights the complexity of spatial processing within sensory neural pathways

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