RESULTS: Abnormalities Neurological Examination: Cranial Nerve (CN) Examination: CN II: bilateral pale discs. CN III, IV, VI: bilateral ptosis. CN IX, X: decreased gag reflex bilaterally. Motor Examination: Drift Test: positive left pronator drift, with right adductor digiti minimi sign and right cerebellar spooning. Sensory Examination: Ipswich Touch Test: decreased in left lower extremity. Temperature: decreased in left lower extremity. Rydel-Seiffer Vibratory Test: bilateral upper extremities 5 and bilateral lower extremities 3. Tandem Gait: unstable. Cerebellar Examination: Holmes Rebound Phenomena: positive with left greater than right. Reflexes: 1+ bilateral upper extremities, absent bilateral lower extremities. Neuropsychiatric Examination: Animal Fluency Test: 15 (abnormal). Clock Drawing Test: 3 (abnormal). Center for Neurologic Study Lability Scale: 16 (pseudobulbar affect).

CONCLUSION: Primary olfactory dysfunction with secondary inhibition of retronasal smell and perceived taste [Gruss 2015] can be an etiology. Such an olfactory dysfunction may reflect variation in nasal mucosal engorgement due to normal variability of the olfactory cycle [Eccles 1978]. This phenomenon is an unlikely due to the short duration ofepochs.

The cause of anosmia and ageusia in this patient suggests a central lesion involved in the processing of both smell and taste. Transient rapid symptoms associated with temperature change, as in Uhthoff's phenomenon seen in MS, can manifest with deficiency in special senses including visual field loss [Davis 2010]. Such also may be the origin for the chemosensory loss seen here. While this phenomenon may be induced by hot baths, more subtle temperature changes may also induce such symptoms [Romani 2000]. Given that olfactory threshold changes have been demonstrated in acute inflammatory changes in MS, such a temperature related etiology is more likely to manifest [Lutterotti 2011]. MS patients should be screened for chemosensory dysfunction, and those with chemosensory dysfunction should be assessed for demyelinating disease.

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Short Duration Monoballismus

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ABSTRACT: Study Objective: While monoballismus has been reported to be associated with hemorrhagic lesions in the subthalamic nucleus (Ohnishi, 2009) and multiple sclerosis (MS) (Rosa, 2011), the duration has been reported to be at least six days (Soysal, 2012). A patient with epochs of monoballismus lasting for 45 minutes is presented.

METHODS: Case Study: A 57 year old right handed female with attention deficit hereditary disorder predominantly inattentive on amphetamine sulphate, presented with two years of memory loss. For instance, after ordering food in restaurants, by the time the food arrives, she could not recall what she ordered. At the onset of this symptom, she noted three epochs of her left arm jerking for 45 minutes. The jerking would begin with low amplitude and low frequency and rapidly progress to the forearm and arm of greater magnitude and low frequency. With her right hand she would try to hold down her left arm without success. There was no associated paresis, sensory phenomena, headaches, dizziness, presyncope, loss of consciousness, or strong emotions. She admitted to frequent jamais vu.

RESULTS: Abnormalities: Neurological Examination: Mental Status Examination: Memory: Immediate Recall: 5 digits forward and 2 digits backwards. Cranial Nerve (CN) Examination: CN I: Alcohol Sniff Test 8 (hyposmia). CN XII: tongue tremor on protrusion. Motor Examination: Drift Test: positive right pronator drift. Gait Examination: Tandem Gait: unstable. Reflexes: 0-1 throughout. Neuropsychiatric Examination: Go-No-Go Test: 6/6 (normal). Animal Fluency Test: 15 (normal). Clock Drawing Test: 3 (abnormal). Center for Neurologic Study Lability Scale: 16 (pseudobulbar affect). Other: MRI with and without infusion: normal.

CONCLUSION: Transient tonic-clonic movements of one limb have been described with focal epilepsy associated with diabetic non-ketotic hyperglycemia (Grant, 1985). A metabolic abnormality such as transient hypoglycemia or hyperkalemia can cause a focal dystonia (Soysal, 2012), which theoretically could manifest with monoballismus. This could be a somatic manifestation of underlying conflict, conversion disorder, or as a result of a physical manifestation of panic attack with hyperventilation and tetany (Mihai, 2008). This may be the first manifestation of a generalized cerebral disorder associated with chorea or ballismus such as Wilson's disease, or Huntington's Chorea (Mihai, 2008). It is possible that this is a variant of Alien Hand Syndrome with parietal lobe involvement (Shrestha, 2015). But this is unlikely given the absence of hemineglect or hemiagnosia. It is possible that amphetamines may have induced a monochorea. Chronic amphetamine use has been demonstrated to cause chorea (Klawans, 1974) and it theoretically could have

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caused ballismus movements in this case. In patients who present with short duration monoballismus, evaluation for subthalamic nuclei function, seizure disorders and other origins of ballismus are warranted.

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Cardiovascular Safety Assessment of Deutetrabenazine in Healthy Volunteers and Implications for Patients With Huntington Disease or Tardive Dyskinesia

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ABSTRACT: Introduction: Deutetrabenazine is approved for treating Huntington disease (HD) chorea and is being evaluated for tardive dyskinesia (TD).

OBJECTIVE: To assess the effect of deutetrabenazine on cardiac repolarization.

METHODS: A QT interval study was performed to evaluate effects of deutetrabenazine 12 and 24 mg on cardiac repolarization, as assessed by time-matched change from baseline, placebo-adjusted, in Fridericia-corrected QT interval (ΔΔQTcF). Moxifloxacin (400 mg) and tetrabenazine (50 mg) were the positive control and comparator, respectively. An exposure–response analysis was developed from this study to predict maximal effects on QTcF at maximum recommended dosing based on CYP2D6 status, an approach consistent with regulatory guidance at predicting QT interval effects.

RESULTS: Maximal ΔΔQTcF between the least-squares mean (90% two-sided confidence interval) of deutetrabenazine 12 and 24 mg (n = 45 in each group) were 2.8 (0.7–4.8) ms and 4.5 (2.4–6.5) ms, respectively. The ΔΔQTcF increase with tetrabenazine (n = 45) was 7.6 (5.6–9.5) ms. Assay sensitivity was verified with moxifloxacin (n = 47), which produced a maximal effect on ΔΔQTcF of 14.0 (11.9–16.0) ms. A linear model was developed that described a correlation between plasma concentrations from pivotal HD andTD trials (n = 101) and QT interval prolongation. Using that model and the individual predicted Cmax for HD and TD patients, the placebo-adjusted change from baseline inQTcF for deutetrabenazine at maximal recommended daily doses was found to be 5.4 (2.5–9.5) ms.

CONCLUSIONS: Patients receiving the maximal recommended doses of deutetrabenazine are predicted to have a QTcF increase below the level of regulatory concern.

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Effect of DR/ER-MPH on Early Morning and Late Afternoon/Evening Functioning in Children With ADHD: Analysis of PREMB-R Items From a Phase 3 Trial

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ABSTRACT: Objective: In a phase 3 trial of children with ADHD, DR/ER-MPH (formerly HLD200), a delayed-release and extended-release methylphenidate, improved ADHD symptoms and reduced at-home early morning and late afternoon/evening functional impairments versus placebo, as measured by the validated Parent Rating of Evening andMorning Behaviors-Revised, Morning (PREMB-R AM) and Evening (PREMB-R PM) subscales. This post hoc analysis evaluated the effect of DR/ER-MPH versus placebo onindividual PREMB-R AM/PM item scores.

METHOD: Data were analyzed from a pivotal, randomized, double-blind, multicenter, placebo-controlled, parallel-group, phase 3 trial of DR/ER-MPH in children (6-12 years) withADHD (NCT02520388). Using the 3-item PREMB-R AM and 8-item PREMB-R PM, both key secondary endpoints, investigators evaluated early morning and lateafternoon/evening functional impairment by scoring each item on a severity scale from 0 (none) to 3 (a lot). For post hoc analyses, treatment comparisons between DR/ER-MPH and placebo at endpoint were determined by using least squares mean changes from

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