ALABAMA ACADEMY OF NEUROLOGY

AAN 2023 Abstract Entries

Abstract 23-01

Title: Nonketotic Hyperglycemic Hemichorea as a Presenting Sign of Drug-induced Diabetes

Presenting Author: Alexander Hedaya, PGY3, Department of Neurology, University of Alabama at Birmingham Heersink School of Medicine, Birmingham, AL, USA. Birmingham VA Medical Center, Neurology Service, Birmingham, AL, USA.

Additional Author(s): Michael Lyerly, Department of Neurology, University of Alabama at Birmingham Heersink School of Medicine, Birmingham, AL, USA. Birmingham VA Medical Center, Neurology Service, Birmingham, AL, USA.

Introduction/Background: Diabetes mellitus is an endocrine disorder which affects multiple organ systems and has far-reaching neurologic complications, the most common of which is neuropathy. Nonketotic hyperglycemic hemichorea-hemiballism is an acquired form of hemichorea which is a rare complication of diabetes mellitus and presents a diagnostic challenge due to its infrequency.

Description: Here, we report a case of nonketotic hyperglycemic hemichorea-hemiballism as the sentinel sign of newly-diagnosed diabetes mellitus. A 67-year-old male with a past medical history of bipolar disorder, schizophrenia, seizures, and hypertension presented with 3 days of acute onset right-sided hemichorea. 19 months prior, he was asymptomatic with a hemoglobin A1C of 6.5%. 3 months prior to presentation, he had increased his nightly quetiapine of 200mg nightly, which he had reportedly been taking for 12 years, to 300mg nightly. On presentation, he had unilateral right hemichorea, worse with movement, more prominent in right arm than right leg, and mildest in the right neck. Labs showed glucose of 476 mg/dL, 1+ urine ketones, and hemoglobin A1C of 15.1% and 15.9% on recheck. His CT head without contrast showed bilateral, left greater than right, basal ganglia hyperdensities. A diagnosis of nonketotic hyperglycemic hemichorea was made. Treatment with insulin returned the patient to near-normoglycemia, resulting in a dramatic reduction in involuntary movements within 12 hours. Resumption of a reduced dose of quetiapine 100mg nightly eliminated his residual symptoms. He was discharged on metformin and insulin and has remained minimally symptomatic, with decrease of hemoglobin A1C to 6.4% in just 4 months.

Discussion and Conclusion: This case highlights the importance of recognizing rare neurologic complications of diabetes mellitus. In this patient with longstanding schizophrenia, his antipsychotic dose-increase preceded nonketotic hyperglycemic hemichorea-hemiballism, suggesting that his hyperglycemia was drug-induced. While glucose control resulted in dramatic reduction of hemichorea, resumption of an antipsychotic led to elimination of abnormal movements, demonstrating the role of dopamine antagonism as a second-line therapy following initial glycemic control. In light of the many direct abnormal movement disorder side-effects of antipsychotics, recognition of an unusual presentation of diabetes mellitus led to rapid diagnosis, treatment, and resolution of symptoms in this patient.

References:

Chua CB, Sun CK, Hsu CW, Tai YC, Liang CY, Tsai IT. "Diabetic striatopathy": clinical presentations, controversy, pathogenesis, treatments, and outcomes. Sci Rep. 2020 Jan 31;10(1):1594. doi: 10.1038/s41598-020-58555-w. PMID: 32005905; PMCID: PMC6994507.

Ryan C, Ahlskog JE, Savica R. Hyperglycemic chorea/ballism ascertained over 15 years at a referral medical center. Parkinsonism Relat Disord. 2018 Mar;48:97-100. doi: 10.1016/j.parkreldis.2017.12.032. Epub 2017 Dec 29. PMID: 29305082.

ALABAMA ACADEMY OF NEUROLOGY

AAN 2023 Abstract Entries

Abstract 23-02

Title: Exploring Correlation between Local Gyrification Index and Clinical Symptoms in Patients with Parkinson's Disease experiencing Freezing of Gait

Presenting Author: Alan Gardner, Undergrad-4, University of Alabama at Birmingham

Additional Author(s): Alan Gardner, Saul Gurgua Lopez, Virendra Mishra

Introduction/Background: About 50% of all Parkinson's disease patients develop freezing of gait (FoG). Currently, there are no objective ways to recognize FoG in clinical settings. T1-weighted (T1) MRI morphological investigations can provide information about area, volume, and thickness alterations; however, most lack conclusive results. Information about cortical folding can be determined using the local gyrification index (LGI). Despite being proposed for almost ten years, LGI has only recently been used to understand freezing of gait in Parkinson's disease patients. We hypothesized that LGI is correlated with clinical and FoG symptoms.

Methods: Of the 53 participants that we recruited at our site, 16 participants were PD-FoG, 21 participants were PD-nFoG, and 16 participants were HC. Proper diagnosis of FoG in the participants involved direct observation of FoG by a movement disorders specialist during a physical therapy task designed to elicit FoG. Using a 3T Siemens Skyra MRI scanner, the participants were scanned with the T1 MRI acquisition parameters resolution=1mm3, TR/TE=2300/2.96ms. Using FreeSurfer 7.0 to process the data, we computed LGI in accordance with the instructions that Freesurfer has described. To confirm the accuracy of the data and the quality of the reconstructed cortical surfaces, a manual and automatic quality check procedure was carried out. We collected mean LGI values from each region identified in the Desikan-Killiany atlas. After regressing age, gender, handedness, levodopa equivalent daily dose, unified Parkinson's Disease Rating Scale, and intracranial volume, statistical correlations were performed in FSL using the PALM toolbox. The results were considered significant at familywise error corrected (FWE) $pcorr<0.05$.

Results: Our analysis showed a significant difference at FWE $pcorr<0.05$ when looking at the correlation between LGI and clinical symptoms. Differences in the LGI of the left fusiform were correlated with decreased neuropsychological test scores (AVL01_List_A_Delayed_Recall_Raw and BVM01_Lrn_Raw) for PD_FoG when compared to PD_nFoG and HC. Likewise, differences in the LGI of the left hemisphere superior parietal cortex were correlated with decreased physical therapy test scores (OFF_FOG_TOTAL-PT) for PD_FoG when compared to PD_nFoG.

Discussion and Conclusion: Our analysis showed correlations between LGI and clinical measures.

ALABAMA ACADEMY OF NEUROLOGY

AAN 2023 Abstract Entries

Abstract 23-03

Title: MRI Correlates of Subjective Cognitive Complaint in a Subset of Participants with PD from the PPMI Database

Presenting Author: Saul Gurgua Lopez, First year Neuroengineering PhD, University of Alabama at Birmingham

Additional Author(s): Corina Catiul (University of Alabama at Birmingham), Virendra R Mishra (University of Alabama at Birmingham)

Introduction/Background: Our objective is to investigate whether subjective cognitive complaint and progression to cognitive complaint in patients with Parkinson's disease (PD) is reflected in Magnetic Resonance Imaging (MRI) measurements in a data sample from the Parkinson's Progression Markers Initiative (PPMI) study.

Cognitive impairment is one of the most important and debilitating non-motor symptoms in patients with PD. According to recent studies, persons with subjective cognitive complaint are more likely to progress to mild cognitive impairment (MCI). Hence it is important to understand whether we can quantify subjective cognitive complaint to facilitate early diagnosis of PD-MCI.

Methods: In this pilot study, we only selected those participants with a PD diagnosis, that had at least three consecutive yearly cognitive assessments, and had a diagnosis of cognitive complaint at any of those timepoints. From them, we chose the participants whose cognitive status changed either from normal cognition to cognitive complaint, or who started with cognitive complaint and maintained this status, without reversing to normal cognition. We identified 9 participants that started normal and converted to cognitive complaint (Age: 67±8 years (mean ± SD), 16±2 YOE, and 77.7% male) and 7 participants that started and remained in cognitive complaint status (Age: 68±6 years, 16±2 YOE and 42.8% male). Using FreeSurfer, we analyzed their T1 MRI images acquired at baseline for cortical measures. Statistical comparisons were conducted using XLSTAT. The groups were tested for normality using the Jarque-Bera test. Because the samples were uneven and not normally distributed, Mann Whitney test was used to compare the two groups. P-value <0.05 was considered significant.

Results: We found that participants who presented with cognitive complaint at baseline had lower cortical thickness in the right and left middle temporal cortex and the left medial orbito-frontal cortex ($p<0.05$) than the group that started with normal cognition. There were no statistically significant differences between any other cortical areas between groups.

Discussion and Conclusion: Our pilot analysis suggested that cortical thinning can be an early indicator of cognitive complaint; this parameter could be explored further to identify possible links with cognitive domain deficits. Analysis of additional MRI measures is currently underway.

References:

Jones JD, Rivas R, Luna K, Ryczek CA, Thomas KR. Subjective cognitive complaints are important in PD-MCI criteria: Associations with CSF markers and cognitive decline. Parkinsonism Relat Disord. 2023;106:105221. doi:10.1016/j.parkreldis.2022.11.013

AAN 2023 Abstract Entries

Abstract 23-04

Title: Cryptococcal Meningoencephalitis and Immune Reconstitution Inflammatory Syndrome in a patient on Tocilizumab Therapy: A Case Report

Presenting Author: Nina Navalkar, PGY3, UAB Neurology Residency

Additional Author(s): Khurram Bashir, MD - UAB Medicine; Vanessa Sui, MD - UAB Medicine

Objective: To describe a case of cryptococcal meningoencephalitis complicated by immune reconstitution inflammatory syndrome (IRIS), vasculitis, ischemic strokes, and hydrocephalus.

Background: Cryptococcus neoformans is the most common cause of fungal meningitis worldwide and typically affects individuals with defects in cell-mediated immunity.

Description: A 71-year-old female with giant cell arteritis on daily prednisone and monthly Tocilizumab infusions presented with worsening headaches for 2 weeks and new-onset confusion for 3 days. Initial workup revealed hyponatremia (sodium 125 mmol/L) and community acquired pneumonia. She was treated with antibiotics, but her mental status rapidly declined necessitating endotracheal intubation. MRI Brain demonstrated multifocal areas of diffusion restriction in the bilateral cerebral and cerebellar hemispheres, basal ganglia, and brainstem with diffuse leptomeningeal enhancement. Cerebrospinal fluid (CSF) studies revealed an elevated opening pressure of 28 cm H2O, positive CSF cryptococcal antigen, and CSF fungal cultures grew cryptococcus neoformans. She was started on empiric liposomal amphotericin B and flucytosine before the cryptococcal antigen and cultures resulted. Despite treatment, her neurological status continued to decline with repeat MRI showing new ischemic infarctions, subarachnoid hemorrhages, and leptomeningeal and parenchymal enhancement. Digital subtraction angiography revealed cerebral vasospasm and possible vasculitis. Repeat lumbar puncture demonstrated persistently elevated opening pressure, continued pleocytosis, and increased protein. She was continued on antifungal therapy and received IV methylprednisolone for IRIS. She additionally underwent ventriculoperitoneal (VP) shunt placement. Despite these interventions, her clinical status continued to deteriorate and she was palliatively extubated.

Discussion and Conclusion: This patient presented with cryptococcal meningoencephalitis in the setting of immune suppression from prednisone and tocilizumab, a monoclonal antibody that targets the IL-6 receptor. Despite early and appropriate treatment, she continued to worsen with multiple complications including IRIS, a dysfunctional inflammatory response to infection precipitated by immune recovery. In patients treated appropriately for cryptococcal meningoencephalitis, a failure to respond should raise concern for complicating conditions.

References:

1. Aksamit AJB, Aaron L. Meningitis. Continuum. 2021;27:836-854.
Pescador Ruschel MA, Thapa B. Cryptococcal Meningitis. [Updated 2023 Jan 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-.
2. Pescador Ruschel MA, Thapa B. Cryptococcal Meningitis. [Updated 2023 Jan 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-.
3. Otto, S.B.J., George, P.E., Mercedes, R. et al. Cryptococcal meningitis and immune reconstitution inflammatory syndrome in a pediatric patient with HIV after switching to second line antiretroviral therapy: a case report. BMC Infect Dis 20, 68 (2020). https://doi.org/10.1186/s12879-020-4797-2

ALABAMA ACADEMY OF NEUROLOGY

AAN 2023 Abstract Entries

Abstract 23-05

Title: Electrical brain stimulation with minimally invasive electrodes to improve speech perception

Presenting Author: Serdar Akkol, PGY2, University of Alabama at Birmingham

Additional Author(s): Jose L. Herrero1,2, Elizabeth Espinal2, Noah Markowitz2, Ashesh D. Mehta1,2, Stephan Bickel1,2,3
1Feinstein Institutes of Medical Research, Northwell Health, Manhasset, NY, United States, 2Department of Neurosurgery, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY, United States, 3Center for Biomedical Imaging and Neuromodulation, Nathan Kline Institute for Psychiatric Research Orangeburg, NY

Introduction/Background: Electrical brain stimulation (EBS) will potentially become an important tool to ameliorate impairments in speech perception. Current EBS methods have advantages and disadvantages. While intraparenchymal EBS is invasive and presumably focal, transcranial electrical stimulation (TES) is noninvasive and delivers electrical current to wider areas, however it is not portable and much of the current is shunted through skin. Minimally invasive subdermal or cranial stimulation may address these issues.

Methods: Here, we tested the feasibility of EBS with two types of electrodes in 5 epilepsy patients undergoing intracranial monitoring: subdermal electrodes and cranial bolts that served as reference electrodes for clinical recordings and holding fixture for depth electrodes, respectively. We used matrix sentence speech-in-noise task, composed of semantically unpredictable five words, allowing the perceptual accuracy to be measured for each word. After achieving speech perception threshold of 60%, patients listened monoaurally to 20 sentences per condition (no-stimulation, 50ms or 200ms stimulation onset lag relative to sentence onset) presented randomly within block. Stimulation electrodes were located above superior temporal gyrus contralateral to the listening ear. Electrical stimulation parameters were 100Hz biphasic, charge balanced square wave pulses where amplitudes were modulated by the speech envelope with a maximum of 3mA. Patients were not aware of the stimulation.

Results: We found increased correct word perception accuracy in stimulation conditions, although not reaching statistical significance ($p=0.09$, RM-ANOVA), but we observed in 3 of 5 patients accuracy increased with longer lag (Accr200ms> Accr50ms> Accrno-stim).

Discussion and Conclusion: This study provides feasibility of minimally invasive electrodes for EBS to improve speech perception.

AAN 2023 Abstract Entries

Abstract 23-06

Title: Taking the Time to Assess Cognition in Parkinson's Disease: The Clock Drawing Test

Presenting Author: Hemant Srivastava, MS3, University of Alabama at Birmingham

Additional Author(s): Hemant Srivastava[1], Allen Joop[1], Raima A Memon[1], Jennifer Pilkington[1], Kimberly H Wood[1, 2], Marissa Natelson Love[1], Amy W Amara
[1]Department of Neurology, University of Alabama at Birmingham, Birmingham, AL, USA.
[2]Department of Psychology, Samford University, Birmingham, AL, USA.

Introduction/Background: Cognitive impairment is common and disabling in Parkinson's disease (PD). Cognitive testing can be time consuming in the clinical setting. One rapid test to detect cognitive impairment in non-PD populations is the Clock Drawing Test (CDT), which calls upon the brain's executive and visuospatial abilities to draw a clock designating a certain time.

Objective: Test the hypothesis that PD participants would perform worse on CDT compared to controls and that CDT would correlate with other measures of cognition.

Methods: This study evaluated two independent CDT scoring systems and differences in CDT performance between PD (N = 97) and control (N = 54) participants using a two-sample t-test. Pearson's correlations were conducted between the CDT and tests of sleepiness (Epworth Sleepiness Scale) and vigilance (Psychomotor Vigilance Test); executive function (Trails B-A); and global cognition (Montreal Cognitive Assessment). Receiver operating characteristic curves were used to determine cut points on the CDT that identify individuals who need additional cognitive testing.

Results: PD participants had worse performance on CDT compared to controls. The CDT was correlated with executive function (Trails B-A) and global cognition (Montreal Cognitive Assessment). The CDT correlated with vigilance (Psychomotor Vigilance Task) only in healthy controls. However, the CDT was not correlated with measures of sleepiness (Epworth Sleepiness Scale) in either group. A cut point of 9 on the Rouleau scale and 18 on the Mendez scale identified PD participants with cognitive impairment.

Discussion and Conclusion: The CDT is a rapid clinical cognitive assessment that is feasible in PD and correlates with other measures of cognition.

References: Aarsland, D., Bronnick, K., Williams-Gray, C., Weintraub, D., Marder, K., Kulisevsky, J., … Emre, M. (2010). Mild cognitive impairment in Parkinson disease: a multicenter pooled analysis. Neurology, 75(12), 1062–1069. https://doi.org/10.1212/WNL.0b013e3181f39d0e Agrell, B., & Dehljn, V. E. (1998). The clock-drawing test. Age and Ageing (Vol. 27). Retrieved from https://academic.oup.com/ageing/article-abstract/41/suppl_3/iii41/30862 Aprahamian, I., Martinelli, J. E., Neri, A. L., & Yassuda, M. S. (2009). The Clock Drawing Test: A review of its accuracy in screening for dementia. Dementia & neuropsychologia, 3(2), 74–81. doi:10.1590/S1980-57642009DN30200002 Basner M, Dinges DF. Maximizing sensitivity of the psychomotor vigilance test (PVT) to sleep loss. Sleep. 2011;34(5):581-91. Cosgrove, J., Jamieson, S., Smith, S., & Alty, J. (2015). The Relationship between Clock Drawing and Cognition in Parkinson's. Journal of Neurology, Neurosurgery & Psychiatry,

86(11), e4.82-e4. https://doi.org/10.1136/jnnp-2015-312379.172 Dinges DF. Microcomputer analysis of performance on a portable, simple visual RT task during sustained operations. Behavioral Research Methods, Instruments, & Computers. 1985; 17(6):652-5. Heerema, E. (2019). How the Clock-Drawing Test Screens for Dementia. VeryWell Health. Higginson CI, Wheelock VL, Levine D, Pappas CT, Sigvardt KA. Predictors of HVOT performance in Parkinson's disease. Appl Neuropsychol 2011; 18(3): 210-5. Jeong, H.-Y., Lee, J.-Y., PhD, M., Kyung, H., PhD, P. M., Ohphd, S., & Lee, J.-Y. (2016). Clock drawing test to screen for dementia in parkinsonian patients with low educational backgrounds. Neurology Asia, 21(4), 357–365. Retrieved from http://www.neurology-asia.org/articles/ neuroasia-2016-21(4)-357.pdf Mendez, M. F., Ala, T. and Underwood, K. L. (1992), Development of Scoring Criteria for the Clock Drawing Task in Alzheimer's Disease. Journal of the American Geriatrics Society, 40: 1095-1099. doi:10.1111/j.1532-5415.1992.tb01796.x Quental, N. B., Brucki, S. M., & Bueno, O. F. (2013). Visuospatial function in early Alzheimer's disease--the use of the Visual Object and Space Perception
(VOSP) battery. PloS one, 8(7), e68398. doi:10.1371/journal.pone.0068398 Rouleau, I., Salmon, D. P., & Butters, N. (1996). Longitudinal Analysis of Clock Drawing in Alzheimer's Disease Patients. Brain and Cognition, 31(1), 17–34. https://doi.org/10.1006/BRCG.1996.0022 Stella, F., Gobbi, L. T. B., Gobbi, S., Oliani, M. M., Tanaka, K., & Pieruccini-Faria, F. (2007). Early impairment of cognitive functions in Parkinson's disease. Arquivos de Neuro-Psiquiatria, 65(2b), 406–410. https://doi.org/10.1590/S0004-282X2007000300008 Watson, G. S., & Leverenz, J. B. (2010). Profile of cognitive impairment in Parkinson's disease. Brain pathology (Zurich, Switzerland), 20(3), 640–645. https://doi.org/10.1111/j.1750-3639.2010.00373.

ALABAMA ACADEMY OF NEUROLOGY

AAN 2023 Abstract Entries

Abstract 23-07

Title: Effectiveness and safety of deutetrabenazine in patients with chorea associated with Huntington disease

Presenting Author: Ashley White, MS-3, University of Alabama Heersink School of Medicine

Additional Author(s): Victor Sung, MD, University of Alabama Heersink School of Medicine

Objective: To evaluate real-world effectiveness, safety, and tolerability of DTBZ for chorea associated with HD.

Background: Huntington disease (HD) is an inherited autosomal dominant neurodegenerative disorder characterized by a triad of motor, cognitive, and psychiatric symptoms. Chorea is an abnormal, involuntary movement characterized by brief, irregular, non-rhythmic muscle contractions. Deutetrabenazine (DTBZ) and tetrabenazine (TBZ) are both VMAT2 inhibitors approved for the treatment of chorea associated with HD. Prior clinical trials have demonstrated that the molecular manipulation in DTBZ greatly reduced adverse effects by prolonging the plasma half-life of the drug as well as maintaining effectiveness. However, research has been limited on the safety and efficacy when comparing treatment of patients with DTBZ compared to treatment with TBZ in real world practice.

Methods: This was a non-interventional, retrospective chart review study from an HD Society of America Center of Excellence at the University of Alabama at Birmingham (UAB). The study population is a cohort of HD patients treated at UAB's Huntington's clinic from April 2017 through December 2021. During this period the DTBZ had become FDA approved, and patients were switching from TBZ either directly, after a gap, or were starting DTBZ for the first time. Due to this, changes amongst HD patients were tracked at the clinic and stratified into these three categories. Effectiveness of chorea treatment was assessed based off total maximal chorea (TMC) scores of each patient's baseline prior to DTBZ initiation and subsequent follow ups at the stable dose reached. Any adverse effects of DTBZ were recorded as well as the dose they occurred. Patient's experiences are followed up formally in 6-month intervals but are tracked throughout

Results: The mean (SD) age of the 80 patients in the study was 52.1 (12.6) years, and 45 (56.3%) were female. The mean (SD) last stable dose of DTBZ was 39.2 (21.3) mg/day (n=73). TMC score analysis focused on 3 groups of patients with both pre- and post-DTBZ initiation TMC scores who reached a stable dose (n=50): those with no prior tetrabenazine (TBZ) or DTBZ use (n=30), those with prior TBZ use with a gap before DTBZ initiation (n=8), and those with an "overnight" switch from TBZ to DTBZ (n=9). Mean (SD) pre-DTBZ initiation TMC scores were 11.1 (5.4), 18.3 (5.0), and 9.9 (3.3), respectively. Mean (SD) TMC score changes for these groups were −3.7 (4.5), −7.8 (2.8), and −2.1 (4.2). Decreases in TMC scores were observed for 24 (80.0%), 8 (100%), and 7 (77.8%) patients. Overall, 27 (33.8%) patients had ≥1 adverse event recorded between DTBZ initiation and the first visit with a TMC score after reaching their last DTBZ stable dose or DTBZ discontinuation for those without a stable dose, including sedation/somnolence/fatigue (n=14, 17.5%), diarrhea (n=3, 3.8%), falls/balance issues (n=3, 3.8%), akathisia (n=2, 2.5%), anxiety (n=2, 2.5%), depression (n=1, 1.3%), and parkinsonism (n=1, 1.3%).

Conclusions: Our center's use of deutetrabenazine supports the data from its pivotal trial for Huntington's disease chorea for TMC improvement and safety. The observed safety profile supports the known safety profile of DTBZ in this population, and common AEs included sedation/ somnolence/fatigue, diarrhea, and falls/balance issues. Though this real-world study of patients with HD-related chorea is based on a single center, and chart review studies are prone to selection bias and missing data, the design captured reasons for discontinuation.