



THE TRANSMITTER

May 2016

Article Review

Prepared by: Cameron Dietiker, MD & Nijee Luthra, M, PhD, San Francisco PADRECC

Feasibility of external rhythmic cueing with the Google Glass for improving gait in people with Parkinson's disease.

Various external visual and auditory cues have been known to improve gait in people with Parkinson's disease. Modern mobile technologies like smartglasses, such as Google Glass, may provide a new method for delivering these cues. This study evaluated rhythmic visual and auditory cueing in a laboratory setting with a custom-made application for Google Glass. Twelve participants with a mean of age of 66.8 years and a mean disease duration of 13.6 years were enrolled. Several measurements of gait were compared including walking speed, cadence, stride length, stride length variability, and freezing of gait. These parameters were measured against three different types of external cues including metronome, flashing light, and optic flow as well as a control condition that did not involve any external cue. For each type of cue, participants completed several walking tasks of varying complexity. Sensors were attached to participants' feet, legs, and pelvis to capture motion data used to analyze gait. Two experienced raters scored the presence and severity of freezing of gait as recorded on video. During cueing, gait was noted to improve across several parameters, especially during more complicated walking courses. However, freezing of gait did not substantially improve. The metronome was more effective than rhythmic visual cues and was preferred by most participants. However, participants were overall positive about the convenience of using Google Glass to provide personalized mobile cueing to support gait. Potentially, this is an application that can be further developed and adjusted in the future to create more effective results. Smartglasses and other modern mobile technologies are offering new ways to approach gait problems in Parkinson's disease.

Journal of Neurology. April 2016. doi: 10.1007/s00415-016-8115-2. [Epub ahead of print]

CSF biomarkers associated with disease heterogeneity in early Parkinson's disease: the Parkinson's Progression Markers Initiative study.

The development of biomarkers to predict the progression of Parkinson's disease from its early stages and various characteristics of disease, which can vary substantially among different individuals, is an important area of research. Dr. Caroline Tanner at the San Francisco VA Medical Center PADRECC is one of many involved in the Parkinson's Progression Markers Initiative (PPMI), an ongoing international multicenter, prospective study to validate biomarkers in patients with Parkinson's disease. This study aimed to quantify cerebrospinal fluid markers, including alpha-synuclein (a-syn), amyloid-beta 1-42, total tau (t-tau), and tau phosphorylated at Thr181 (p-tau) in 660 PPMI subjects at baseline and correlated these data with measures of various clinical characteristics. Levels of a-syn, t-tau, and p-tau were significantly lower in patients with Parkinson's disease compared to healthy controls while amyloid-beta 1-42 levels were not. Levels of a-syn were significantly lower in patients with Parkinson's disease with non-tremor dominant phenotype, but other markers were not. Patients with Parkinson's disease who had the lowest amyloid-beta 1-42 or highest t-tau/amyloid-beta 1-42 and t-tau/a-syn quintile in Parkinson's disease patients were associated with more severe non-motor symptoms

compared with the highest or lowest quintiles, respectively. In a multivariate regression model, lower α -syn was significantly associated with worse cognitive performance. This data suggests that the measurement of cerebrospinal fluid biomarkers in early-stage Parkinson's disease may relate to disease heterogeneity, but longitudinal observations are needed.

Acta Neuropathologica. March 2016 . doi: 10.1007/s00401-1552-2. [Epub ahead of print]

Midlife milk consumption and substantia nigra neuron density at death.

Several environmental factors have been implicated to have a role in the development of Parkinson's disease, and one such factor is exposure to organochlorines and other pesticides. Prior postmortem studies in humans have found elevated levels of organochlorines in brain tissue, and more specifically, in the substantia nigra (SN) of patients with Parkinson's disease. Several long-term population-based studies, including one from the Honolulu-Asia Aging Study, have also shown an association between the intake of dairy products, including milk, and the future risk of Parkinson's disease. In this population from Hawaii, excessively high levels of heptachlor epoxide have been found in the milk supply. Dr. Caroline Tanner at the San Francisco VA Medical Center PADRECC was part of this current study designed to examine the relationship between midlife milk intake and Parkinson's disease incidence through associations with SN neuron density and organochlorine pesticide exposure in post mortem brains from the Honolulu-Asia Aging Study. Milk intake data was collected from 1965 to 1968 in 449 men aged 45–68 years with postmortem examinations from 1992 to 2004. Neuron density in sections of the SN and brain residues of heptachlor epoxide were measured. Results showed that neuron density was lowest in nonsmoking subjects who consumed high amounts of milk (0.16 oz/d). Although the number of Parkinson's disease cases was small, the percent of nonsmoking subjects with Parkinson's disease increased with amounts of milk consumed. After removing cases of Parkinson's disease and dementia with Lewy bodies, adjusted neuron density was 41.5% lower for milk intake of 0.16 oz/d vs milk intake that was less. Among those who drank the most milk, residues of heptachlor epoxide were found in 90% (9 of 10 brains) as compared to 63.4% (26 out of 41 brains) for those who consumed no milk. For those who were ever smokers, an association between milk intake and neuron density was less. Current findings suggest that milk intake may cause early nigral neurodegeneration prior to the onset of clinical Parkinson's disease and may involve a link with organochlorines. Further studies are needed to further establish whether the relationship between milk intake and Parkinson's disease.

Neurology. March 2016. Volume 86: 512-519. doi:10.1212/WNL.0000000000002254

Committee Activities

Clinical Care Committee

- **Rotation of Committee Chair:** Leadership for the clinical care committee rotates amongst the PADRECCs. The Houston PADRECC leads the committee for May/June. The committee meets via conference call the first Tuesday of the month at 12pm (EST)
- **Standardize and Optimize Clinical Care:** The committee continues to discuss latest research on PD, new treatment strategies and a variety of clinical issues to improve patient care and outcomes. It also serves to provide clinical support to the consortium network by focusing on measures to standardize clinical care across the PADRECC network. Recent agenda items have included discussion on:

1. New PD treatments in the pipeline, including ND0612, which is a proprietary formulation of levodopa and carbidopa continuously administered subcutaneously and extended release Amantadine formulation. Discussions focused on reviewing the safety, tolerability and clinical efficacy data, presented at recent scientific meetings.
 2. Continued discussion focused on clinical experience sharing among the group regarding DUOPA™ (carbidopa and levodopa) enteral suspension delivered directly into the small intestine for the treatment of motor fluctuations for people with advanced Parkinson's disease and Rytary (carbidopa/levodopa IR/SA combination oral medication). Recent discussions have focused on learning optimal titrating schedules, strategies to manage complication, logistical and support issues
 3. Continued experience sharing regarding the use of various Neurotoxins across the PADRECC network with the objective to improve this specialized clinical practice and develop neurotoxin selection criteria for various conditions in the Veteran population.
 4. Practical aspects regarding the use of DAT scans; applications and pitfalls, including the issue of drug interference
 5. Palliative Care: Review of palliative care resources and practices in the PADRECCs
 6. Veteran's Choice Program: re-distribution of resources, optimal use of the program, impact on VA based sub-specialty care.
 7. Consortium Sites: Strategies to improve communications, enhance educational and clinical support and develop research projects with the consortium sites.
 8. National Consortium Meeting in September: tentatively scheduled for Sept 19th, 2016, one day ahead of WPC in Portland. Seeking submissions of posters (need not be original.)
 9. New MRI body scanning protocols for DBS implanted patients
 10. Collaborative research ideas e.g. comparing Pimavanserin (Nuplazid) with other atypical anti-psychotics in the treatment of psychosis related to PD.
- **PADRECC Transmitter:** PADRECC clinicians provide reviews of recent movement disorder publications that are included in the PADRECC Transmitter

Education Committee

- **PADRECC/EES Movement Disorder Series:** The 4th audioconference for FY 2016 was held on **May 12, 2016** "*Complementary & Alternative Medicine (CAM) in PD*" by Dr. Laurie K. Mischley, ND MPH, PhD Bastyr University Research Institute, Kenmore, WA. The audioconferences are archived on the National website www.parkinsons.va.gov under the Movement Disorder Series tab. Please see the **Dates to Remember** section below for a listing of upcoming FY 16 audio conferences.
- **National Newsletter:** The newsletter is currently being assembled.
- **“Mood Disorders in PD: What’s New:”** This enduring material project was done in collaboration with EES and is an on-line TMS self-study program that offers CME credit for a 3 year period. This program provides VHA healthcare professionals with a broadened medical awareness of Mood Disorders in PD. The program is available on TMS:

https://www.tms.va.gov/learning/user/deeplink_redirect.jsp?linkId=ITEM_DETAILS&componentID=14771&componentTypeID=VA&revisionDate=1343926380000

- **National Website Maintenance:** The committee performs monthly maintenance checks of the National Website to ensure information is current and up-to-date.
- **Education Needs Assessment:** An education needs assessment is being developed and will be disseminated to Consortium Members who attend the National Consortium Meeting in September in order to steer future education initiatives of this committee.
- **PADRECC Transmitter:** The committee continues to assemble and distribute this e-newsletter every other month.

Dates to Remember

June 19-23, 2016

2016 Movement Disorder Society International Congress

Berlin, Germany

www.mdsccongress2016.org

September 8th, 2016

EES/PADRECC Movement Disorders Series

Topic: Palliative Care and PD

<http://www.parkinsons.va.gov/>

September 19th, 2016 (*tentative*)

National VA PD Consortium Conference

Portland, Oregon

Additional information to follow

September 20-23, 2016

4th World Parkinson Congress

Portland, Oregon

<http://www.wpc2016.org/>