## BIOGRAPHICAL SKETCH

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NAME: David A. Peterson

eRA COMMONS USER NAME (credential, e.g., agency login): dap_neuroscience

POSITION TITLE: Associate Research Scientist

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| University of Colorado, Boulder, CO (Boettcher scholar) | B.S. | 12/1990 | Electrical Engineering |
| University of Colorado, Boulder, CO | B.S. | 12/1990 | Business Administration |
| Colorado State University, Fort Collins, CO | Ph.D. | 7/2007 | Computer Science (Neuroscience emphasis) |
| University of California, San Diego | Post-doc | 12/2012 | Movement disorders |

### A. Personal Statement

I have a broad background in engineering, computer science, neurobiology, and movement disorders. During my ***doctoral program***, I applied signal processing and neural network algorithms to several forms of complex biological data sets, from hamster taste bud recordings to DNA microarrays to high-dimensional EEG recordings. I also initiated and led multiple novel experimental programs using EEG in applied cognitive neuroscience. Specifically, I evaluated the merit of blind signal separation and machine-learning based feature selection methods in an EEG-based brain-computer interface designed to provide an alternative channel of communications to patients with late stage amyotrophic lateral sclerosis. I also used EEG to investigate the neural correlates of verbal learning, including the differential effects of a musical mnemonic intervention in multiple sclerosis. I mentored junior graduate students that assisted with these projects, training them in the behavioral and EEG elements of the experimental design and execution, and facilitating their learning the relevant literature. In one case, this culminated in a peer-reviewed journal publication for a Master's student (Moore et al. 2008). In my ***postdoctoral research*** at UCSD with Dr. Howard Poizner, I began to specialize in movement disorders with a focus on the role of dopamine in learning. We compiled a comprehensive review on the role of striatal dopamine-mediated synaptic plasticity as a potential pathogenic factor in dystonia. We also conducted experiments demonstrating that dopaminergic deficits are associated with impaired instrumental rewarded learning in Parkinson's disease.

I have participated in several formal and informal training programs to prepare me for an independent research career in interdisciplinary approaches to movement disorders. These included the International Congress of Parkinson's Disease and Movement Disorders in 2013, 2015, and 2018, annual Dystonia Coalition meetings since 2011, and the Aspen course "Comprehensive Review of Movement Disorders" in 2013. I also participated in the Okinawa Computational Neuroscience Course in 2013, and attended the San Diego Lab Management Symposium, one of the hallmark training programs for newly independent investigators sponsored by a consortium of San Diego research institutions, including UCSD, the Salk Institute, the Sanford Burnham Prebys Medical Discovery Institute and the Scripps Research Institute. Collectively these have prepared me to lead large multi-party projects and given me a neurologist's perspective on dystonia that allows me to bridge the gulf that otherwise exists between computational neuroscientists and clinical movement disorders.

In an independent research program as an Associate Research Scientist with UCSD's Institute for Neural Computation and the Salk Institute's Computational Neurobiology Laboratory (both led by Dr. Terry Sejnowski), I have been initiating steps toward my overarching long term goal: to develop a theoretical framework for the dynamic role of abnormal sensorimotor learning in the pathogenesis of dystonia, and how those processes might be inverted to provide novel therapeutic strategies. One element of that framework at the behavioral level is that the relative timing of motor functions becomes disordered. Thus I have a line of research employing computational approaches to measure motor symptoms in movement disorders with an unprecedented combination of temporal precision, objectivity, and ease of use in the clinical setting. This part of my research program is focused on developing novel rating scale tools that will help provide objective and more precise quantification of motor symptoms critical not only for basic research into pathophysiological mechanisms but also clinical research into differential diagnosis, longitudinal monitoring, and severity assessment for treatment optimization. For the most common forms of focal dystonia – cranial and cervical – I have been developing and investigating the utility of computer vision and machine learning tools. These tools – which we are collectively referring to as the Computational Motor Objective Rater (CMOR) – use digital video of the face to quantify head position and movement as well as activity in facial muscles. With funding from the Dystonia Coalition in the form of a career development award and a pilot project, we demonstrated that these measures of eye closure exhibit convergent validity with clinical measures of symptom severity in blepharospasm (BEB), the most common type of cranial dystonia (Peterson et al. 2016 Neurology). This line of research has been extended with support from the CDMRP program in our IIRA project to investigate a similar approach for capturing abnormal head posture, range of motion, and head tremor in cervical dystonia (CD). More recently as PI for the Dystonia Coalition's Clinical Research Project on developing objective measures of severity, we are extending and consolidating these past efforts to also develop computational video-based severity measures for BEB and laryngeal dystonia.

## B. Positions and Honors

### Positions and Employment

| | |
|---|---|
| 1991-1994 | Management Consultant, Business Networks Group, Accenture |
| 1998-2005 | Graduate Research Assistant, Department of Computer Science, Colorado State University |
| 2003-2007 | Graduate Research Assistant, Program in Molecular, Cellular, and Integrative Neuroscience |
| 2007-2012 | Postdoctoral Scholar, Institute for Neural Computation, University of California San Diego |
| 2009-2011 | Consultant to Eugene Izhikevich, Brain Corporation |
| 2010-2012 | Postdoctoral Scholar, Computational Neurobiology Laboratory, Salk Institute |
| 2012-2014 | Chair, Trainee Committee, Temporal Dynamics of Learning Center, UCSD |
| 2012-2018 | Assistant Project Scientist, Institute for Neural Computation, UCSD |
| 2014-2016 | Co-Scientific Program Director, Temporal Dynamics of Learning Center, UCSD |
| 2015-2019 | Member, Scientific Advisory Board, Tourette Association of America |
| 2018-2021 | Associate Project Scientist, Institute for Neural Computation, UCSD |
| 2021- | Associate Research Scientist, Institute for Neural Computation, UCSD |

### Honors and Awards

| | |
|---|---|
| 2002 | Nominated to Upsilon Pi Epsilon, International Honor Society for Computer Science |
| 2004 | Travel Fellowship Award, Conference on Research in Computational Molecular Biology |
| 2008 | Travel award, Movement Disorders Society |
| 2010 | Trainee Award, NSF Temporal Dynamics of Learning Center |
| 2010 | Travel stipend, Dystonia Coalition's 2nd annual meeting |
| 2012 | Travel award, Conference on Clinical Research for Rare Diseases |
| 2013 | Career Development Award, Dystonia Coalition |

## C. Contributions to Science

1. Phenotypic characterizations of cervical dystonia

One of the most common forms of focal dystonia is cervical dystonia (CD). In these studies, we evaluated associations between motor symptoms, pain, and quality of life aspects of CD. We also critically evaluated past attempts to use clinical ratings to quantify the efficacy of the sensory trick in CD. In addition to elucidating novel characteristics of CD, these studies set the stage for our computational video-based objective measures of motor symptoms in CD with CMOR.

Cisneros E, Vu JP, Lee HY, Chen Q, Benadof CN, Zhang Z, Pettitt EA, Joshi SK, Barbano RL, Jankovic J, Jinnah H, Perlmutter JS, Berman BD, Mahajan A, Goetz CG, Stebbins GT, Comella CL, **Peterson DA**. (2021) Does raising the arms modify head tremor severity in cervical dystonia?, *Tremor Other Hyperkinet Mov* doi: 10.5334/tohm.623.

Vu JP, Lee HY, Chen Q, Cisneros E, Barbano RL, Goetz CG, Jankovic J, Jinnah HA, Perlmutter JS, Berman B, Appelbaum MI, Stebbins GT, Comella CL, **Peterson DA**. (2020) Head tremor and pain in cervical dystonia, *Journal of Neurology* doi:10.1007/s00415-020-10378-5.

Cisneros E, Stebbins GT, Chen Q, Vu JP, Benadof CN, Zhang Z, Barbano RL, Fox SH, Goetz CG, Jankovic J, Jinnah H, Perlmutter JS, Adler CH, Factor SA, Reich SG, Rodriguez R, Severt LL, Stover NP, Berman BD, Comella CL, **Peterson DA**. (2020) It's tricky: Rating alleviating maneuvers in cervical dystonia, *Journal of Neurological Sciences* doi:10.1016/j.jns.2020.117205.

Chen Q, Vu JP, Cisneros E, Benadof CN, Zhang Z, Barbano RL, Goetz CG, Jankovic J, Jinnah HA, Perlmutter JS, Appelbaum MI, Stebbins GT, Comella CL, **Peterson DA**. (2020) Postural Directionality and Head Tremor in Cervical Dystonia. *Tremor Other Hyperkinet Mov*. 10. doi: 10.7916/tohm.v0.745.

Benadof CN, Cisneros E, Appelbaum MI, Stebbins GT, Comella CL, **Peterson DA**. (2019) Sensory Tricks Are Associated with Higher Sleep-Related Quality of Life in Cervical Dystonia. *Tremor Other Hyperkinet Mov* (N Y). doi: 10.7916/4q53-vt23.

2. Conceptual, theoretical, and computational frameworks for focal dystonia

The other most common form of focal dystonia is blepharospasm. In this study, we summarize past research on a "2-hit" model of blepharospasm pathogenesis that implicates an altered dopaminergic system in the striatum and abnormal "use patterns" as induced by peripheral manipulations that increase blinking. We then put forth a theoretical framework for the mechanisms responsible for the model, incorporating contemporary theories of basal ganglia function. We also outline a prescription for implementing a computer simulation of this system, and make experimentally-testable predictions amenable to investigation in future animal models.

**Peterson DA**, Sejnowski TJ. (2017) A Dynamic Circuit Hypothesis for the Pathogenesis of Blepharospasm. *Frontiers in Computational Neuroscience* 11:11. doi: 10.3389/fncom.2017.00011, PMC5340098

Within the field of neurology, the subfield of movement disorders has seen limited efficacy from traditional pharmacological treatments. Several new biomedical device technology developments, including for example deep brain stimulation (DBS), offer new hope for these patients. Yet most of these technologies have thus far been implemented in an open-loop fashion. In Broccard et al. 2015, we present a new noninvasive framework for rehabilitation in movement disorders, combining simultaneous imaging of the brain and body dynamics with model-free and model-based approaches for closed-loop paradigms.

Broccard F, Mullen T, Chi YM, **Peterson DA**, Iversen JR, Arnold M, Kreutz-Delgado K, Jung TP, Makeig S, Poizner H, Sejnowski TJ, Cauwenberghs G. (2014) Closed-loop Brain-Machine-Body Interfaces for Noninvasive Rehabilitation of Movement Disorders. *Ann Biomed Engineering*.doi: 10.1007/s10439-014-1032-6, PMC4099421

There is a large and fractionated literature on pathological aspects of dopaminergic and cholinergic transmission in dystonia patients and animal models, as well as a long tradition of viewing the basal ganglia, and in particular the striatum, as a critical node in the motor control networks that go awry in the disorder. In Peterson, Sejnowski, and Poizner 2010, we assembled a comprehensive review of the literature that highlights altered dopaminergic- and cholinergic-modulated synaptic plasticity in the striatum in dystonia. Since that review, one of the most marked genetic findings in dystonia (GNAL), points to altered intracellular signaling downstream from the D1-type dopamine receptor specifically in the striatum.

**Peterson DA**, Sejnowski TJ, Poizner H (2010) Convergent evidence for abnormal striatal synaptic plasticity in dystonia. *Neurobiology of Disease* 37(3):558-573, PMC2846420

3. Objective methods for measuring symptoms in focal dystonia

Two of the most common focal dystonias are cranial and cervical. In this study, we evaluated a novel, unobtrusive, objective method to measure symptom severity in blepharospasm, the most common form of cranial dystonia. Specifically, we confirmed two hypotheses: 1) that CERT could quantify eye closure from standard digital videos of blepharospasm patients recorded in a conventional clinical setting and 2) that CERT's measure of eye closure would correlate with clinical ratings of blepharospasm severity. Without any special requirements regarding lighting, CERT was able to register the face in each video frame over 99% of the time. CERT's eye closure measure was also positively linearly correlated with expert severity ratings using three clinical rating scales conventionally used with blepharospasm. Collectively the results pave the way for a new, convenient, objective method to robustly measure motor symptom severity in blepharospasm.

**Peterson DA**, Littlewort GC, Bartlett MS, Macerollo A, Perlmutter JS, Jinnah HA, Hallett M, Sejnowski TJ. (2016) Objective video-based measures of eye closure severity in blepharospasm. *Neurology* 87(20) 2146-2153, doi 10.1212/WNL.0000000000003336, PMC5109937

Musician's dystonia is one of the most perplexing forms of dystonia, and in Peterson et al. 2013 *Neurology*, we completed a comprehensive review of motor function assessment in musician's hand dystonia, a motor control disorder which we hypothesize results from an aberrant feedback-based repetitive learning regime. It is by far the most comprehensive review of its kind in the field of musician's dystonia, representing an exhaustive examination of motor control measures used in over 135 articles previously published in the field. The paper critically and systematically evaluates the array of rating scales previously used in musician's dystonia interventional and pathophysiology studies.

**Peterson DA,** Berque P, Jabusch HC, Altenmuller E, Frucht SJ (2013) Rating scales for musician's dystonia: the state of the art. *Neurology* 81(6), 589-598, doi: 10.1212/WNL.0b013e31829e6f72, PMC3775681

4. Brain dynamics of learning and memory

There is an increasing appreciation for cognitive deficits in multiple sclerosis (MS). In Thaut et al. 2014, we investigated in 54 patients with MS whether a musical template for verbal learning not only improves learning and memory but also involves a different pattern of short-term, system-level brain plasticity measured with EEG as changes in oscillatory network synchronization. Given the practical significance of sequencing in verbal information, we specifically investigated whether music would improve learning and memory for ordered word lists. A musical mnemonic led to overall better word memory and better word order memory and recruits stronger oscillatory network synchronization in prefrontal cortical areas in MS patients during word learning.

Thaut MH, **Peterson DA**, McIntosh GC, Hoemberg V. (2014) Music mnemonics aid verbal memory and induce learning-related brain plasticity in multiple sclerosis. *Front Human Neurosci*, 8:395. doi: 10.3389/fnhum.2014.00395, PMC4056382

**Peterson DA**, Lotz DT, Halgren E, Sejnowski TJ, Poizner H (2011) Choice modulates the neural dynamics of prediction error processing during rewarded learning. *NeuroImage* 54(2):1385-1394.

5. Brain Computer Interfaces based on the electroencephalogram (EEG)

*Toward a new communication channel for patients with ALS*

In late stages of the disease, ALS patients lose motor function and therefore the ability to communicate with the outside world. In Yang et al. 2014, we developed and tested a new strategy for brain-computer interfaces (BCIs), which could offer a new channel of communication for ALS patients. Most BCIs are "synchronous" systems, in which the system sets the timing of the interaction and tries to infer what control command the subject is issuing at each prompting. In contrast, in "asynchronous" BCIs subjects pace the interaction and the system must determine when the subject's control command occurs. In this paper we proposed a new idea for a BCI that draws upon the strengths of both approaches. The subjects are externally paced and the BCI is able to determine when control commands are issued by decoding the subject's intention for initiating control in dedicated time slots. This strategy offers the potential to mitigate the signal detection challenges of fully asynchronous BCIs, while providing greater flexibility to the subject than traditional synchronous BCIs.


Yang L, Leung H, **Peterson DA**, Sejnowski TJ, Poizner H. (2014) Toward a Semi-Self-Paced EEG Brain Computer Interface: Decoding Initiation State from Non-Initiation State in Dedicated Time Slots. *PLoS ONE* 9(2): e88915. doi: 10.1371/journal.pone.0088915, PMC3931691

**Peterson DA**, Knight JN, Kirby MJ, Anderson CW, Thaut MH. (2005) Feature selection and blind source separation in an EEG-based brain-computer interface. *EURASIP Journal on Applied Signal Processing; Special Issue on Trends in Brain Computer Interfaces* 19: 3128-3140.

Garrett D, **Peterson DA**, Anderson CW, and Thaut MH. (2003) Comparison of linear, nonlinear, and feature selection methods for EEG signal classification. *IEEE Transactions on Neural Systems and Rehabilitation Engineering* 11(2):141-144.