Carnegie Mellon University

Annual Progress Report: 2011 Formula Grant

Reporting Period

July 1, 2013 – June 30, 2014

Formula Grant Overview

The Carnegie Mellon University received $943,032 in formula funds for the grant award period January 1, 2012 through December 31, 2014. Accomplishments for the reporting period are described below.

<u>Research Project 1: Project Title and Purpose</u>

Correlated Structure in Motor Cortical Populations – Motor control is one of the most important tasks the brain performs, and disorders of motor control affect millions of people. Although a wealth of psychophysical studies have led to good descriptions of the phenomenological processes underlying motor control and adaptation, the neural implementations of these processes are not well understood. One problem is that motor control is inherently a neural population phenomenon: movements are generated by groups of neurons that must work in a coordinated fashion to produce precisely timed muscle activation patterns. Using brain-computer interfaces, we will study how various features of the motor task act to shape the correlation structure of cortical population activity.

Anticipated Duration of Project

1/1/2012 – 12/31/2014

Project Overview

Volitional motor control is inherently a neural population phenomenon: to generate movements, neural activity from collections of neurons across multiple brain areas must be coordinated to result in precisely timed muscle activation patterns. This coordination is expressed by statistical dependencies in the tuning of groups of neurons, the so-called *signal correlation*, which arises from network constraints such as common inputs into groups of neurons. In motor control, these common inputs relate to the cognitive and behavioral factors underlying movement generation. By studying how signal correlations relate to various features of the task, like feedback or redundancy, we can probe how these parameters coordinate population activity in motor cortex and, ultimately, shape motor planning.

This project is a coupling of experimental and computational approaches to characterize the flexible correlation structure of motor neuronal populations. We will have monkeys implanted with chronic multielectrode recording arrays perform a combination of motor tasks including arm reaching and brain-computer interface (BCI) cursor control. Data from these tasks will be used to build a statistical model that fits the correlation structure as a function of both volitionally controllable driving inputs and task-dependent sensory feedback. Ultimately, the lessons we learn from the formulation of these models will improve our understanding of the cognitive and computational principles of motor control, and unite the neural encoding of movement with behavioral theories of motor control.

Specific Aim 1: Dissociate volitional from non-volitional dependencies in correlation patterns.
Specific Aim 2: Describe how correlation patterns change as a function of task redundancy.

Principal Investigator

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Other Participating Researchers

Andrew Schwartz, PhD – employed by the University of Pittsburgh

Expected Research Outcomes and Benefits

We anticipate several potential outcomes and benefits resulting from this study. (1) This research has direct implications for improving neural prosthetic devices, which have the potential to improve the quality of life for a substantial population of patients living with neurological movement disorders. Results from this study will be leveraged to current, ongoing clinical trials. (2) Robotic controllers generally lack the flexibility and robustness exhibited in physiological motor control. By furthering our understanding of the basic mechanisms of motor control, our findings could improve the design and performance of general autonomous control systems across a wide variety of applications. (3) Graduate students supported by this grant will be extensively cross-trained in both computational and experimental approaches to systems neuroscience, placing them at the forefront of a rapidly growing field. (4) Methodologies developed during this study will be directly incorporated into the classes taught by the Principal Investigator.

Summary of Research Completed

<u>Milestones for reporting period:</u>

- Present Aim 1 preliminary results at conference.
- Finish Aim 2 experiments.

- Implant electrode array into hemisphere 2 and start Aim 1 experiments using neurons from second hemisphere.

Research accomplished during this reporting period

Last reporting period we acquired a non-human primate and were in the process of training him to perform arm reaching tasks. In this project period, we completed the training and performed surgery to implant a chronic multielectrode recording array in primary motor cortex (M1). The surgery was a success, a sample of recordings from the array are shown in Fig. 1.

Since our theoretical work has progressed more quickly on Aim 2 than on Aim 1, we started collecting data from the experiments outlined in Aim 2. To examine the effects of task redundancy on neural recruitment in M1, we have been collecting data in a novel reaching task where the subject needs to make movements constrained to varying numbers of dimensions. An example of initial findings in this direction is given in Fig. 2.

In off-line data analysis on previously collected data, we tested the hypothesis that changes in neural tuning observed during changes in task redundancy are coordinated across neurons. The data do not support this hypothesis: rather, it appears the changes in each neuron are independent of the changes in other neurons, a finding that is not predicted by current theories of how populations of neurons work together to encode movement. These results were reported at the Computational Systems Neuroscience (Cosyne) annual meeting in Feb. 2014:

> Rasmussen, Schwartz, and Chase (2014) Dynamic range adaptation in motor cortical neurons. Cosyne.

Also in off-line data, we have been attempting to further our understanding of neural correlations and coordination during movement by investigating the information carried by populations of neurons about movement parameters. Results of this analysis for arm speed and direction of movement were published this year in an article that acknowledges CURE funding:

> Golub, Yu, Schwartz and Chase (2014). Motor cortical control of movement speed with implications for brain-machine interface control. J Neurophysiol. 112:411-29.

Although data collection has started, progress on the experimental side of this project is running slightly behind schedule. We will be requesting a one year no-cost extension so that we may complete the experiments.

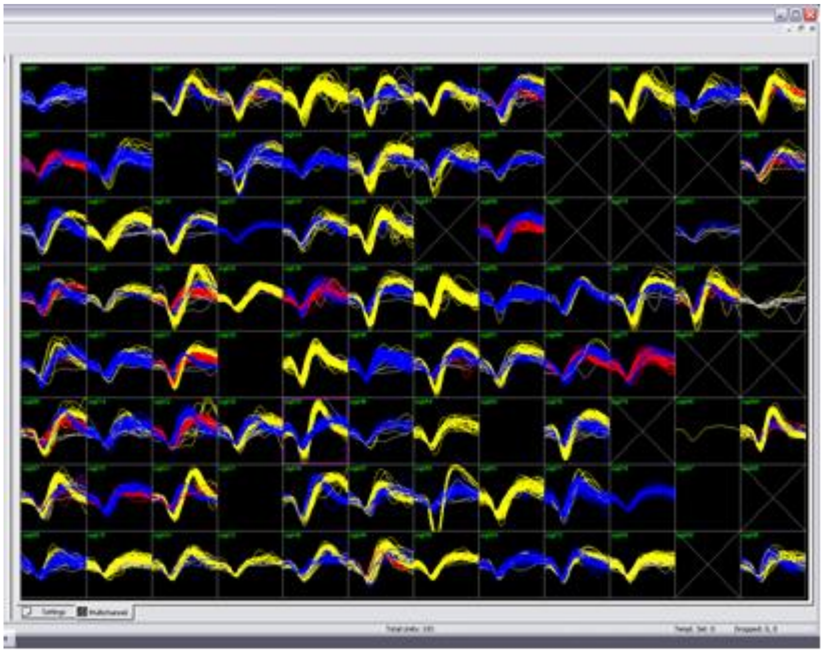

Figure 1: Screen shot of recordings from the multielectrode recording array chronically implanted in the primary motor cortex of the monkey on this project. Recordings are shown roughly two months post-surgery. Most channels show clear signs of action potentials emitted from well-isolated neurons.

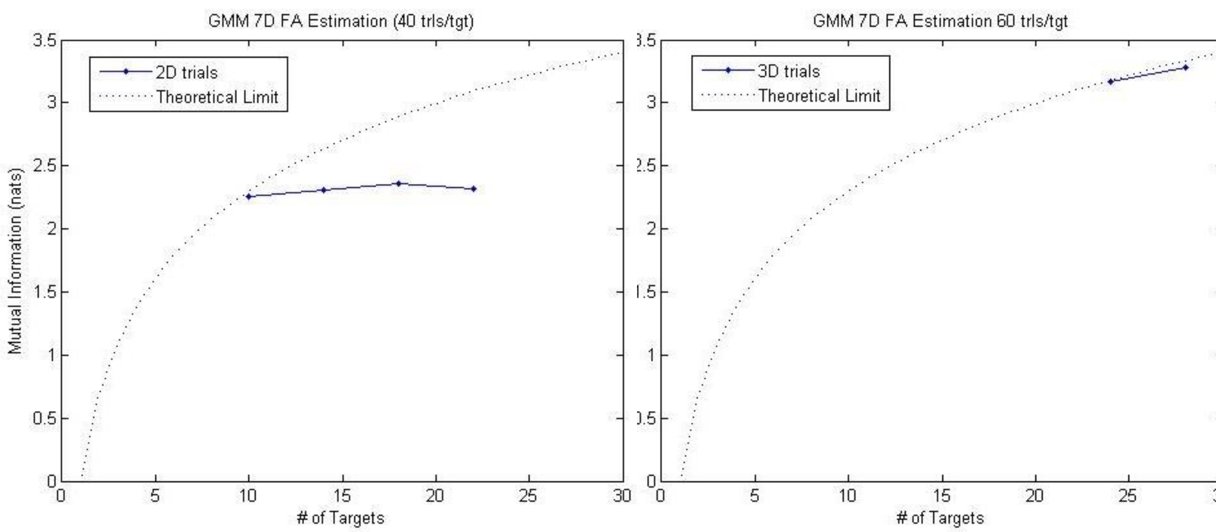

Figure 2: Estimates of the information carried by the neural population about target direction, when different numbers of targets are presented in two dimensions only (*left*) or three dimensions (*right*). Note that in the 3D case, the information carried by the population runs much closer to the theoretical upper limit (dotted lines), indicating that some task configurations are more efficiently encoded than others.

Research Project 2: Project Title and Purpose

Non-invasive Optical Imaging of Perceptual Learning and Development – The reliability and consistency of ordinary sight and hearing makes it natural to presume that perceptual systems are hard-wired and stable. Instead, however, they are highly dynamic and adapt flexibly to allow perceivers to discover regularities in the environment. In fact, over time perceptual expertise develops such that the brain's response to some classes of highly significant stimuli (faces, written words, speech) is markedly distinct. Our ultimate objective is to understand the learning mechanisms that serve the development of perceptual expertise to better understand developmental disorders (autism, dyslexia) and brain injuries that affect perception and to engineer devices to improve perception among those with impairments.

Anticipated Duration of Project

1/1/2012 – 12/31/2014

Project Overview

Our ultimate goal is to understand how perceptual systems are shaped by experience to develop perceptual expertise for some classes of stimuli. Humans exhibit such expertise for faces and native-language speech sounds and, later with developing literacy, for printed words. Human perceptual expertise for recognizing and categorizing these stimuli well exceeds the capacity of even the most sophisticated software for face and speech recognition. Understanding the learning mechanisms involved with extracting perceptual regularity from an inherently noisy and variable environment will provide insight about how to improve automatic machine recognition systems. It will also inform how to remediate perceptual problems arising from brain injury and developmental disorders and how to build effective rehabilitation programs for individuals with perceptual impairments.

The specific long-term aim is to address the development of perceptual expertise among pre-school aged children, a developmental window during which perceptual systems are thought to be highly malleable and during which time developmental disorders that impact perceptual expertise (autism, specific language impairment) tend to be discovered. The present research is unique and innovative because it allows for simultaneous measurement of brain and behavioral responses in young children who are unable to participate in many other forms of neuroimaging research, thus allowing us to probe the development of perceptual expertise. In the present project, we test the hypothesis that adaptation of an optical neuroimaging signal will serve as a more sensitive measure of children's phonetic representations than their behavioral responses and 2) that acoustic context will further shape these representations. At a broad level, achieving our aims will set the stage for Carnegie Mellon University's faculty to focus its research expertise toward innovative new approaches to studying the development of perceptual expertise and its health implications.

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Theodore Huppert, PhD – employed by the University of Pittsburgh

Expected Research Outcomes and Benefits

Perceptual learning is a robust phenomenon, measurable throughout the lifespan in humans and other species that is thought to support a variety of basic cognitive, perceptual and language functions. It is important because changes in the way that perceptual input is processed and represented impact all subsequent processing at higher levels. Understanding brain function as it relates to developing perceptual expertise for particular classes of stimuli will allow us to generate models of how perceptual learning can be harnessed to improve perceptual processing (such as training physicians to better detect tumors in visually-noisy scans) and remediate everyday perception when perceptual systems go awry. Deficits in perceptual learning are observed across a variety of brain disorders including schizophrenia for auditory processing, autism for faces and speech, specific language impairment and dyslexia for spoken language and words, and in response to traumatic brain injury, stroke, and seizure. Determining how to engineer systems to remediate brain disorders affecting perceptual processing requires an understanding of the relationship of brain function to perceptual learning and how perceptual expertise for specific classes of stimuli develops. Neuroimaging tools that can be used effectively to study the developing brain are necessary in this endeavor. The present project exploits functional near-infrared spectroscopy (fNIRS) as a neuroimaging technique suitable for use with children and therefore significant for measuring brain development. By understanding how the brain changes with development of perceptual expertise, we believe we can better understand the causes of perceptual symptoms for brain disorders.

Summary of Research Completed

<u>Milestones for reporting period:</u> Collect data to test hypotheses with child participants; analyze data and prepare report(s) of results.

<u>Research accomplished during this reporting period</u>

In the present project year we achieved our objective to authorize near infrared spectroscopy (NIRS) as “minimal risk” for use in research with children and adults, as it is on other campuses internationally (and as are other neuroimaging techniques like functional magnetic resonance imaging, fMRI). This opens the opportunity to test children at the Carnegie Mellon Children's School in our experiments. The approval process involved a great deal of coordination, visits from international experts to discuss ethics with our review panel, and multiple meetings with the Carnegie Mellon University Institutional Review Board.

With approval to conduct research, we have begun training researchers ranging from graduate students to faculty in NIRS research, experimental design, and research protocols. We have benefited from the expertise of Dr. Theodore Huppert of University of Pittsburgh in leading these efforts. During the past year, we met our milestone of pilot testing our new NIRS system with adult participants. We were unable to enroll child participants during this period due to delays in moving our protocol through the process to certify NIRS as minimal risk and thereby suitable for testing children at the Carnegie Mellon Children's School. Now that we have full approval for research with adult and child participants we wish to expand the research by one year to complete this work.

We have also achieved scientific objectives. Dr. Marlene Behrmann's laboratory at Carnegie Mellon University has initiated a study of the hemodynamic response in the visual cortex as individuals (adult participants) view a series of achromatic grating patterns. The patterns have either a drifting or vibrating motion and vary in contrast. The ultimate purpose of this research is to investigate basic sensory-evoked responses in individuals with autism. The project has received Institutional Review and is underway.

Drs. Anna Fisher and Erik Thiessen of Carnegie Mellon University are collaborating to pursue NIRS as a measure of the development of selective sustained attention through the preschool and elementary school years. They address several key issues using a novel paradigm for assessing selective sustained attention in young children. A broad aim is to examine selective sustained attention and specify developmental trajectories of selective sustained attention in 2- to 7-year-old children thereby establishing a baseline contributing to the efforts of refining the cognitive phenotype of the Attention Deficit Hyperactivity Disorder (ADHD). The use of NIRS will bear on the often-hypothesized developmental changes in the contribution of exogenous and endogenous factors to selective sustained attention. In this project period, Drs. Fisher and Thiessen submitted a grant proposal entitled "Development of Selective Sustained Attention in Preschool and Elementary School Children," they trained their laboratories in NIRS protocols, established software to link their behavioral experiments to the time course of NIRS data collection, and developed a collaborative relationship with Dr. Theodore Huppert who is a local expert in NIRS. The project has passed Institutional Review and is ready to begin pilot testing with children.

Our scientific achievements also involved pilot testing behavioral protocols suitable for pairing with NIRS among both adult and child participants.

Through extensive preliminary research we have verified the effectiveness of a simple incidental training paradigm, the Systematic Multimodal Associations Reaction Time (SMART) task, in training listeners to categorize sounds. This task mimics critical aspects of learning in natural environments (multimodal associations, predictive relationships, indirect training, no explicit instruction or feedback), but its simple task demands are amenable for use among patients and children.

In the SMART task, participants must rapidly detect the appearance of a visual stimulus among four possible screen locations and report its position with a key press (Figure 1). A brief sound precedes the appearance of each visual target. Unknown to participants, each sound is an exemplar drawn from one of four distinct sound categories. In the first three blocks and the fifth experiment block the relationship between the sound category and the visual target location is fixed such that the sound category is consistently associated with one of the visual target locations (*Training Blocks*, 100 trials/block). In the fourth block, this association is destroyed by random assignment of sound categories to visual target locations (*Test Block – Random*). On each trial of each block, the task is rapid visual detection. However, if participants incidentally learn about the sound categories due to the consistent pairing of sound category exemplars with the location of the visual target in the Training Blocks, we expect reaction time to detect the visual target to be slower in the random Test Block when the relationship between sound and visual target is arbitrary. We refer to this implicit measure of auditory category learning as the *RT cost* ($RT_{Block4} – RT_{Block3}$). We also measure category learning and generalization to novel exemplars explicitly via an explicit sound categorization task that follows the SMART task. In this task, participants hear a sound exemplar drawn from the sound categories experienced during the visual detection task, but not heard previously. They indicate which box an "X" would be most likely to appear (although no visual targets appear in this task and there is no feedback about the correctness of responses). Each sound is presented 20 times in a random order. This presents the opportunity to collect both implicit and explicit measures of auditory category learning as well as to examine the extent to which the measures are in agreement. Our results (Figure 2) demonstrate the effectiveness of this indirect training task in producing robust nonspeech auditory and non-native speech category learning among typical adults. Each measure shows evidence of generalization of acquired category knowledge to novel category exemplars not heard in training, a hallmark of robust category learning. In all, the entire task takes about 40 minutes for control participants to complete. It is simple and easily administered. We expect patients and children to be slower to respond in the SMART task relative to control participants. What is unique about the SMART task is that it capitalizes on a simple, overt visual detection task to incidentally train participants to learn to learn auditory categories. It is extremely well-suited for use with NIRS due to its block structure.

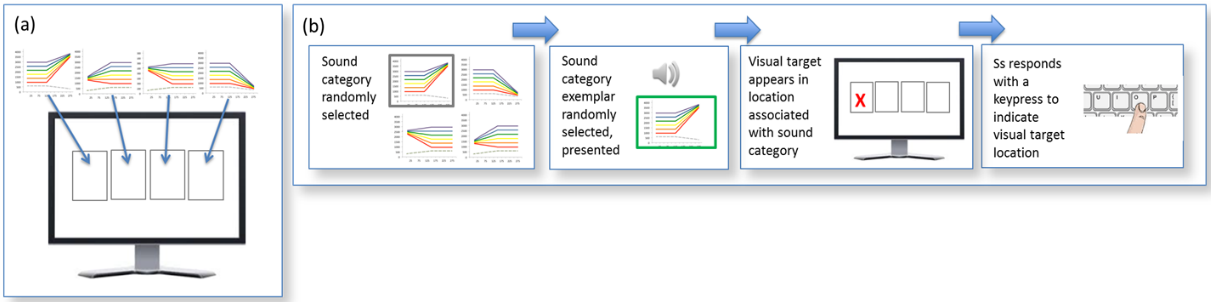

Figure 1. Overview of the Systematic Multimodal Associations Reaction Time (SMART) task. (a) There is a consistent mapping between auditory categories and screen locations, with acoustically-variable sound exemplars associated with the category-consistent visual location. (b) The order of events in an example trial of the task. A sound category is randomly selected and an exemplar from it is chosen and presented. This is followed the appearance of a red 'X' in the corresponding screen location. Participants then respond by pressing the key corresponding to the position of the 'X'.

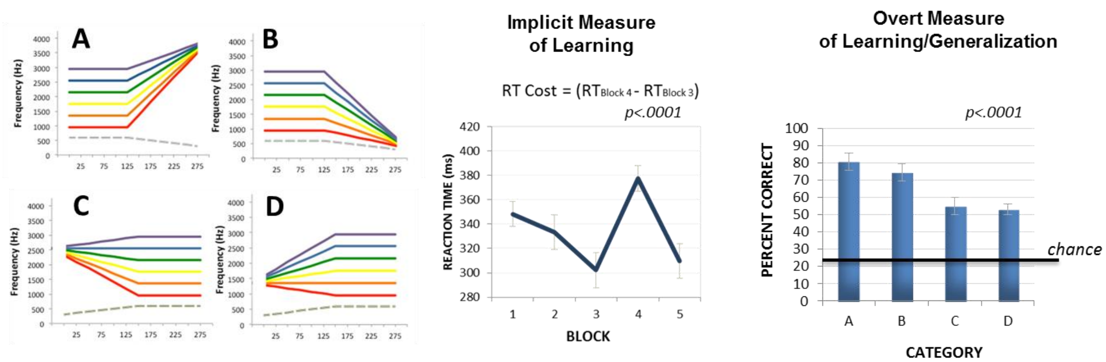

Figure 2. Two measures of category learning in the SMART task. Data are from typical adult listeners learning complex nonspeech auditory categories. **(Left panel)** The four categories (A, B, C, D) are defined by 6 unique sounds per category. Each colored component is paired with the lower-frequency grey component to create the exemplars. **(Middle panel)** Listeners incidentally learn the nonspeech categories across the first three blocks. This is evident in a significant RT Cost to visual detection when the association of auditory categories to visual detection locations is destroyed in Block 4. **(Right Panel)** Listeners generalize this learning to novel category exemplars in an overt category-decision task that immediately follows the SMART task. Generalization was above-chance for all categories.