Carnegie Mellon University

Annual Progress Report: 2014 Formula Grant

Reporting Period

January 1, 2015 – June 30, 2015

Formula Grant Overview

The Carnegie Mellon University received $669,247 in formula funds for the grant award period January 1, 2015 through December 31, 2017. Accomplishments for the reporting period are described below.

Research Project 1: Project Title and Purpose

Spatiotemporal Codes Underlying Face Recognition – Considerable progress has been made in mapping the cortical basis of object processing (including faces, words and common objects), yet much less is known about the representational and computational underpinnings of this complex visual ability. In this project, we aim to examine the structure of objects representations as reflected by patterns of data in the human cortex obtained from magnetoencephalography (MEG). To this end, we will start by using faces as a model set of stimuli and will have participants make judgments about the similarity of faces while we collect MEG data. We will then map the brain regions underlying face identification, examine the representation of facial identity within these regions in terms of their spatial and temporal properties, and provide an account of face encoding relying on image-based features.

Anticipated Duration of Project

1/1/2015 – 12/31/2017

Project Overview

Many recent studies have yielded extensive evidence regarding the reliance of object processing (includes faces, words and common objects) on a network of cortical regions, with differential involvement of these regions in tasks such as face detection or individuation. Whereas the functional localization of face processing has been the predominant focus of the field, the precise mechanisms by which recognition is carried out at the neural level remain to be elucidated. The key question to be addressed in the current project concerns the mechanisms that permit face individuation—that is, the ability to discriminate and identify faces at the individual level, and the visual computations that support it. A second question concerns the deviations from these mechanisms in individuals with perceptual impairments and the nature of the alterations in the neural systems of these individuals.

Note: This project is funded, in part, under a grant with the Pennsylvania Department of Health. The Department specifically disclaims responsibility for any analyses, interpretations or conclusions.

Aim 1: Visualizing the spatiotemporal dynamics of neural representation of individual object identities

Aim 2: Analyzing the spatiotemporal dynamics of neural representations of object identity in individuals with deficits in object perception

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Expected Research Outcomes and Benefits

We anticipate several positive outcomes and benefits from this study. This project will uncover answers to basic science questions concerning the neural code that gives rise to rapid and successful object recognition. While we will use face recognition as an example, the findings will have broad relevance for our understanding of high level vision and its underlying neural correlates more generally. The end result, then, will be a deeper understanding of the computational and neural system that supports visual recognition. The findings of this research program will also shed light on the nature of the changes in neural coding in the cortex of adult individuals with impairments in visual recognition (either acquired through damage in adulthood or congenital/neurodevelopmental but manifest in adulthood, as well). Understanding how recognition occurs can help with the development of better training and intervention procedures for these individuals and can also shed light, more generally, on ways to enhance learning and to improve recognition skills through education. Last, we will make available all the MEG data as well as analytic pipelines for use by other scientists and researchers.

Summary of Research Completed

Aim 1: Visualizing the spatiotemporal dynamics of neural representation of individual object identities

This initial period has addressed Aim 1 of the proposal and has involved the development of the design of the experiment with which to characterize and examine the spatiotemporal dynamics of the neural representation of faces. Faces serve as a challenging test of any system as they, to a greater degree than other common objects, share elemental features such as eyes, a nose and a

mouth in a prespecified and fixed configuration. To this end, we have chosen a set of 91 young male faces (each of which is shown in a neutral and a happy expression) (see Figure 1). The faces are controlled so that they all match on luminance, contrast, global color, as well as on high-level (e.g. alignment) properties. In this experiment, participants completed a one-hour session in which they were familiarized with the face identities. We then collected the data from the MEG scanner. During the scanning, the participants performed a 1-back task on identity and, in addition, completed a 1-back localizer of faces, houses, scrambled pattern, objects, and words. Each face identity was presented approximately 100 times. Four participants completed this protocol thus far, each for approximately 12 hours of testing, and the very substantial amount of data are presently undergoing further analysis.

As shown in Figure 2, we can localize face selective activation on the cortical surface and are able to define regions of interest for further analysis. As shown in Figure 3, we can examine the time course at which faces are most uncorrelated (faces 1-91 on each of y- and x-axes and more yellow colors reflect higher dissimilarity i.e. more individuation). As evident, there is greatest dissimilarity in left and right posterior fusiform gyrus at approximately 150 ms post stimulus-onset. For 47 time points 10-470 ms after stimulus onset, andthese two regions-of-interest (ROIs) commonly implicated in face processing (right and left posterior fusiform gyrus [pFG]), we used linear SVM classification to measure neural discrimination of all possible face pairs, across facial expression. We then used multidimensional scaling to identify statistical dimensions underlying the neural discrimination data. For each dimension and time point, we constructed a "classification image" (CI), which displays visual information captured by the dimension. CIs were constructed by computing the difference between weighted averages of faces on each side of a given dimension, and then applying a permutation test to isolate statistically significant pixels. Across all face pairs, left and right pFG displayed the best classification performance at 180-200 ms. For both ROIs, the proportion of significant pixels in the CIs was highest at around 200 ms, with smaller peaks at around 100 and 350 ms. Hence, information about face identity was captured most clearly at around 200 ms. Pixel-wise correlations between CIs for the two ROIs were small to moderate (r range = -.01-.28), with correlations peaking at around 200 ms. This pattern suggests that left and right pFG carry partially overlapping information about face identity, with the greatest overlap at around 200 ms. Together, these results suggest that visual information about face identity is represented maximally, but not exclusively, at around 200 ms in pFG, and that the spatial properties of the information represented differ between left and right pFG.

This initial start to the project has made great strides and we are currently conducting a whole host of additional analyses to detail comprehensively the time course and spatial distribution of facial identity information in cortex.

Aim 2: Analyzing the spatiotemporal dynamics of neural representations of object identity in individuals with deficits in object perception.

Work on this second aim has not yet begun.

Figure 1: The 91 faces (neutral expression) selected as stimuli for the MEG study.

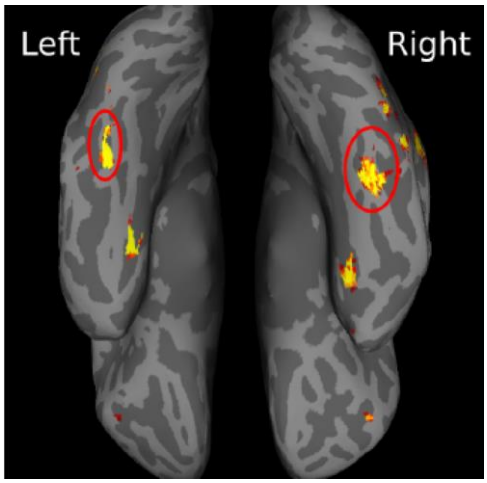

Figure 2: The ventral surface of an inflated brain of a single subject showing the left and right posterior fusiform gyri. The signal from these regions for each face identity at binned time points is shown in Figure 3.

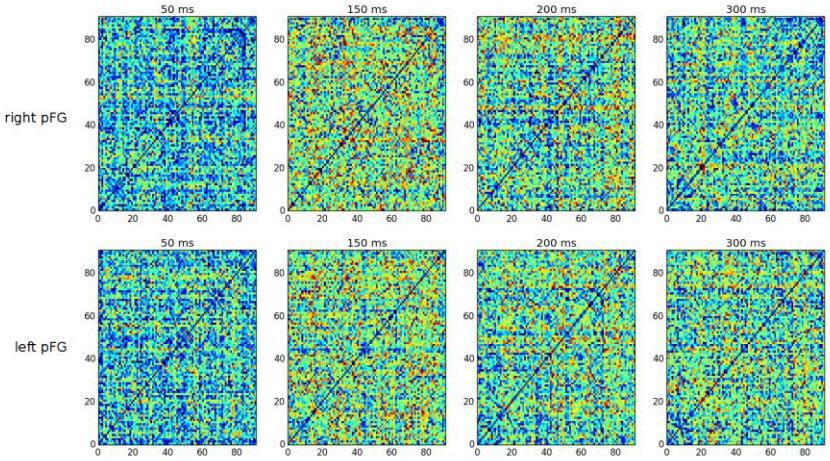

Figure 3: The dissimilarity matrix showing the dissimilarity of the MEG signals between two faces (on x- and y-axes) at 50, 150, 200 and 300 ms) in the right and left posterior fusiform gyrus.

Research Project 2: Project Title and Purpose

The Role of Lhx6-GPe Neurons in Basal Ganglia Function in Health and Disease – Motor symptoms of Parkinson's disease, a neurodegenerative disorder affecting nearly 1 million Americans, are attributed to hyperactivity of motor suppressing circuits in the basal ganglia. Focus of this project is plasticity of a subset of neurons, called Lhx6-GPe neurons, that critically regulate neuronal activity in this motor suppressing pathway and may represent novel targets to restore basal ganglia activity and motor control after dopamine depletion.

Anticipated Duration of Project

1/1/2015 – 12/31/2017

Project Overview

Parkinson's disease (PD) is the second most common neurodegenerative disorder, affecting nearly 1 million Americans. Its motor symptoms correlate with dysfunction of neural circuits in the basal ganglia, including increased synchrony and β-oscillations, thought to impede movement by disrupting temporal and spatial encoding properties of neurons. However, mechanistic explanations of how these widespread alterations in basal ganglia function arise through changes in activity of individual neurons are lacking. To address this knowledge gap, we leverage genetic and molecular tools to target and manipulate distinct populations of neurons in

the basal ganglia, to delineate their role in motor control in health and disease. For this project, we make novel use of a transgenic mouse line, Lhx6, to discover the behavioral and circuit-level functions of this understudied neuronal population. Lhx6-GPe neurons are genetically, physiologically, and anatomically distinct from other GPe neurons. Preliminary results from our lab show that in healthy mice, their over-activation with ChR2 produces an ADHD-like, hyperactive phenotype, not observed following stimulation of other populations of GPe neurons. Intriguingly, in dopamine-depleted mice, over-activation of Lhx6-GPe neurons does not affect movement, but their suppression, with Arch, restores motor function to levels nearing those seen in non-depleted mice. One explanation that could account for these observations is that Lhx6-GPe neurons participate in distinct neural circuits from other GPe neurons, whose over-activation is causally related to motor deficits in dopamine-depleted mice. To test this, we will first characterize, in detail, the synaptic inputs to Lhx6-GPe neurons and how they are altered by dopamine depletion.

Specific Aim 1: Identify changes to synaptic inputs of Lhx6-GPe neurons after dopamine depletion.
Specific Aim 2: Investigate how temporal dynamics of Lhx6-GPe neurons affects activity of striatal FSIs and pathological synchrony in PD.
Specific Aim 3: Determine the behavioral correlates of Lhx6-GPe neurons in control and dopamine-depleted mice.

Principal Investigator

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Other Participating Researchers

None

Expected Research Outcomes and Benefits

This project will examine the role of a genetically-defined neuronal population in the GPe in motor control in health and disease. Our experiments make novel use of an existing transgenic mouse line to test an innovative hypothesis about cellular mechanisms underlying pathological oscillations and network dysfunction in Parkinson's Disease (PD). Successful completion of these experiments will advance our understanding of the cellular and synaptic organization of neural circuits in the basal ganglia and could identify novel cellular targets to improve motor function in PD.

Summary of Research Completed

In the 3 months of work completed on this project, we have developed the necessary infrastructure to begin experiments described under Specific Aim 1: To identify changes to synaptic inputs of Lhx6-GPe neurons after dopamine depletion. Specifically, we have established a dopamine depletion paradigm by which we inject a toxin, 6-hydroxydopamine (6-OHDA) into the medial forebrain bundle (MFB). Within three days, this resulted in complete lesion of dopamine neurons on the side of injection, and this protocol worked to fully depleted dopamine (assessed with an immunohiostological stain for tyrosine hydroxylase) either unilaterally or bilaterally. We have also begun slice electrophysiology experiments to isolate excitatory synaptic inputs onto Lhx6-GPe neurons under control conditions. To distinguish Lhx6-GPe neurons from other cells in the GPe, we perform experiments in Lhx6-GFP mice. Using fluorescence-guided patching, we can perform whole cell voltage clamp recordings from Lhx6-GPe neurons during electrical stimulation of the internal capsules, the bundle of excitatory axons from the subthalamic nucleus (STN) to the GPe. We can isolate excitatory synapses from this projection and are now prepared to repeat these experiments in slices from dopamine-depleted animals.

Research Project 3: Project Title and Purpose

Technology to Support Life-logging – An emerging paradigm in healthcare is the use of mobile and wearable technologies for monitoring a person's health status remotely and in real time. In particular, there is an opportunity to understand a person's health-related events and functional ability to perform daily life activities. To succeed, there is a need to correlate data from body-worn sensors with the actions that the wearer is actually engaged in. That can be accomplished with machine learning algorithms trained on labeled data sets. This research will advance capabilities for people to collect "life-logs" that serve as the basis for such labeled data, i.e., ground truth data to train the algorithms. As such, this project supports future population-based applications.

Anticipated Duration of Project

1/1/2015 – 12/31/2016

Project Overview

The goal of this research is technology that facilitates collection of data about a person's daily activities – what and precisely when he/she is performing a particular activity – in a process commonly referred to as "life-logging." Specific aims and methods to achieve them are:
1. *Create a list of events (health signs and life activities) of interest that might be detectable by mobile, wearable or other sensors embedded in the user's environment.* We will consult with local clinicians who treat prevalent chronic diseases to build a preliminary list. Conditions of interest will likely include congestive heart failure (CHF), chronic obstructive pulmonary disorder (COPD), cancer and high risk of falling. For each event, we will assess the viability of reliably detecting it.

2. *Develop a prototype system of hardware and software for declarative life-logging.* By this we mean that the user will inform the system directly at or near the time of a particular activity that it is about to or just took place. We will explore a number of alternative interaction modes such as touchscreens and smart watches, building upon prior results and insights gained through development of systems to support ecological momentary assessment.
3. *Develop a prototype system for reflective life-logging* with which the user will interactively review raw data gathered over time to create a time-stamped life-log. We will build upon and refine an earlier prototype called MemExerciser that creates video life-logs semi-automatically, and combine it with techniques for adding contextual data that were used in another earlier prototype called IMPACT (for Improving Monitoring of Physical Activity using ContexT).
4. *Advance computer vision algorithms that recognize and classify human activities based on video streams acquired from body-worn, a.k.a. "first-person vision" (FPV) cameras.* We will build upon and combine bodies of work for recognition of household objects and recognition of hand movements to create algorithms for recognizing specific activities of interest. We will assess the performance of those algorithms and integrate them to the reflective life-logging platform.

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Expected Research Outcomes and Benefits

Our team is committed to management of prevalent diseases such as congestive heart failure (CHF), chronic obstructive pulmonary disorder (COPD) and cancer through the use of unobtrusive, real-time measurement of health status. We embrace the use of mobile and wearable sensors that continuously acquire data about a patient's functional abilities that can be analyzed and summarized for clinicians and the patient. There are many wearable devices, commonly referred to as fitness bands, now emerging on the market that can contain biosensors (e.g., movement, heart rate, skin temperature and skin conductance) and environment sensors (e.g., location, ambient light and ambient sound). Data from those sensors can be combined to reveal what and how the wearer is doing, as well as context. While those devices have been marketed as fitness products, hence toward people who are generally in very good health, there are opportunities to apply their capabilities to people who are not healthy. To do that, however, it is necessary to correlate sensors with actual patient behavior. An algorithm can learn such

correspondence if sufficient quantities of good-quality, time-synchronized data streams are available. The desired outputs of this project are tools for acquisition of patient behavior data and analyses of their suitability for use in healthcare. They will enable future studies in which they are applied to CHF, COPD, cancer and other patient populations for which it is desirable to have more and better data on health and well-being.

Summary of Research Completed

Due to unforeseen circumstances, initiation of this project was delayed until July 2015.