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Final Report

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Introduction

The US Army Grant W911NF-14-0440 was active from 8-1-2014 through 12-31-2018. We have expanded the major goals of the grant since it began. Initially, the grant was centered on imagined speech. At that time, other approaches to imagined speech reconstruction using different non-invasive imaging methods such as EEG, fMRI, or fNIRS had been attempted without success. We had shown initial success in reconstructing phonemes using ECoG, and we believed that we could develop and apply new methods to characterize ECoG data to extend imagined speech reconstruction.

Early in the project, in close collaboration with our ARO PO, we expanded our goals to focus on the characterization of complex brain processes using ECoG data. While we still aimed to study imagined speech reconstruction, we also increased our emphasis on improved analysis methods while applying these methods to other cognitive and motor activities, including vision, attention, and finger movement. Despite this considerable broadening from the original proposal, we successfully:

1. Created new methods to characterize ECoG data;
2. Applied these methods to imagined speech as well as vision, attention, finger movement, and other activities;
3. Extended these achievements with clinical and scientific implications that could greatly increase project impact well after project completion.

The subsequent text details a myriad of verifiable accomplishments – including over two dozen peer-reviewed journal publications, eight book chapters, successful activities from students, and many other achievements. The remainder of this document is structured as follows. We review our accomplishments throughout the project, divided into the following sections:

- Training Activities
- Dissemination: Journal Publications
- Additional Dissemination
- Honors and Awards
- Patents and Tech Transfer
- Summaries

Within each of these sections, we:

1. Review accomplishments within each reporting period (adapted from Interim Reports);
2. Present any relevant accomplishments after the last reporting period; and
3. Summarize our accomplishments throughout the project.

Training Activities

Training Activities: August 1, 2014 to July 31, 2015

We did not report any training activities during this period. However, as shown in the dissemination summaries below, it was a particularly successful year for Mr. Coon in terms of peer-reviewed publications and his nomination for a BCI Research Award.

Training Activities: August 1, 2015 to July 31, 2016

Students have made good progress toward their degrees during this period.

Mr. William Coon: Four of the publications during this reporting period include Mr. Coon (two as first author). Mr. Coon is an author on another publication in PNAS that we expect will be published in thenext few months. He attended two conferences as an employee of GTEC neurotechnology in Albany, where he presented work on ECoG related to his thesis. Mr. Coon has met extensively with me, and other members of his thesis committee, and has been very active in responding to comments and finalizing his thesis. We anticipate that he will complete his PhD in the next reporting period.

Ms. Adriana De Pesters: In terms of publications, we have the same numbers to report as Mr. Coon. Four of the publications during this reporting period include Ms. De Pesters, two of which have her as first author. She also has other upcoming papers. She was also active with conferences during this period and meeting with me, and her committee, regarding her final responsibilities with her PhD. We also expect that she will complete her PhD in the next reporting period.

Training Activities: August 1, 2016 to July 31, 2017

This was our best reporting period in terms of student progress. Two of my students completed their PhDs during this period, and both have clear plans for the next step in their careers. Each of them also continued working on journal papers and earned co-authorship on a book chapter presenting our submission to the BCI Award that was nominated as a top project.

Mr. William Coon: He completed his PhD, and has decided to continue working a nearby company called GTEC Neurotechnology USA, with a promotion to manager. This company manufactures systems for both EEG and ECoG and supports some of our ongoing research collaborations, so I expect to report additional research with Dr. Coon and Dr. Guger from GTEC in the next progress summary.

Ms. Adriana De Pesters: She completed her PhD. Her PhD thesis was titled “Harnessing Electrocorticographic Signals for Neuroscience and Neurosurgery” and she has decided to return to the EU to continue her academic career in Switzerland. I am also continuing my collaboration with her.

Training Activities: August 1, 2017 to July 31, 2018

In the last reporting period, Drs. De Pesters and Coon finished their PhDs and successfully began good positions in academia and industry, respectively. In this period, a new student joined our team:

Ms. Ladan Moheimanian: Ms. Moheimanian is a new PhD student in our lab. During this period, she worked on a study characterizing oscillatory phase resetting in a reaction-time task. She does not yet have any publications with our lab, since she just joined, but we expect to have more to report soon.

Training Activities: August 1, 2018 to December 31, 2018

During this period, Ms. Moheimanian made good progress. We did not add any new students.

Training Activities Summary

We had three PhD students during this project. Two of these students, Ms. Adriana DePesters and Mr. William Coon, were very active for most of the project. During the project, both students completed their PhDs, earned authorship on several peer-reviewed journal papers (including first-author), and contributed to other accomplishments such as book chapters and BCI Research Award nominations. Both students found good jobs after finishing their PhDs.

The third student, Ms. Ladan Moheimanian, joined the team during the last reporting period. Hence, while she did contribute to the project, we do not yet have major accomplishments to report such as peer-reviewed papers.

Dissemination: Journal Papers

Dissemination: Journal Papers: August 1, 2014 to July 31, 2015

Imagined speech

Auditory reconstruction

Last year, we published work that explored auditory reconstruction based on ECoG data while patients read short stories presented on a monitor (Martin et al., 2014). In two different conditions, patients either read the stories out loud or covertly, and patients rested during a third (control) condition. We then developed two speech models (a spectrogram and a modulation-based feature space) based on high gamma activity in the 70-150 Hz range. Reconstruction accuracy for overt speech was based on the correlation between the actual speech features and predictions from our models. This reconstruction was significant in all subjects. We introduced dynamic time warping to transform the covert speech and align it with the matching overt speech. Our reconstruction of covert speech was also highly accurate. Our work also identified three gyri that contributed most strongly to effective speech reconstruction. These results demonstrate that the spectrogram of continuous actual and imagined speech can be reconstructed from electrocorticographic signals.

Brain-to-Text

A more recent publication (Herff et al., 2015) presented work toward decoding speech based on cortical activity. This article presented our Brain-to-Text system, which adapted techniques from automated speech recognition (ASR) to model single phones in continuous speech. We evaluated this approach on ECoG data collected from seven patients with epilepsy while they read text aloud. This system's error rate was as low as 25% with words and 50% with phones. Our approach could also identify cortical regions with the most relevant information about individual phones. These results demonstrate that full sentences of continuous actual and imagined speech can be reconstructed from electrocorticographic signals.

Network activity

Theoretical contribution

Neuroanatomy does not change substantially, especially over long distances and short time periods. Yet the brain's rigid structure can support a wide variety of tasks, performing specific functions that reflect effective coordination of rapidly changing dynamics. How? This is widely recognized as an important unanswered question in neuroscience, and previous publications have proposed explanatory frameworks such as the communication-through-coherence (CTC) and gating-by-inhibition (GBI) hypotheses. Despite the strong interest in this topic, these and other proposed frameworks have failed to provide a practical, frugal explanation of the underlying cortical phenomenon. In my recent paper (Schalk, 2015), I reviewed these two explanatory frameworks and relevant experimental evidence. I then introduced the function-through-biased-oscillations (FBO) hypothesis to provide an alternate explanation for cortical function. This FBO hypothesis provides a simple and highly testable framework to explain cortical dynamics and their connection to cortical information transmission.

Methodological contribution

Improved understanding of speech production, as well as many other neural phenomena, depends on effective characterization of large-scale neural dynamics. We need methods that can characterize interdependent activities and processes within and across different brain regions, including the progression of activity. Typical analysis approaches entail signal averaging, which can simplify analyses but also omits critical information from single-trial dynamics. We introduced a new method to explore population-level dynamics based on precise characterization of the times and locations of relevant neural activity in single trials. Our paper validated and explored this new method, and showed how it could reveal information that conventional methods ignore with two sets of results. Our results provided new insight about the progression of neural activity during sensorimotor task performance, including the changes in oscillatory activity that occurred with the task began. Thus, we introduced and validated a new method to understand how different brain areas communicate with each other during task performance (Coon and Schalk, 2015).

Neuroscientific contribution

These two contributions provided the foundations for a third publication focused on a neuroscientific contribution (Coon et al., 2015). We applied the concepts from our theoretical publication, and methods from our methodological contribution, to new data acquired while subjects performed a modified Posner paradigm. While hundreds of studies have explored electrophysiological and other changes resulting from different Posner paradigms and other visuo-spatial attention tasks, these studies have relied heavily on averaged data, without our innovative approach to explore single-trial dynamics. The variability in the delays in neural transmission, and concordant variability in task performance and other behaviors, remain poorly understood. We found several interesting results that involved oscillatory activity in the 8-12 Hz range. Activity within neuronal populations tends to begin during a trough of this alpha activity. We also found that the subsequent propagation of neural activity varied in speed and other characteristics that depended on the phase of oscillatory activity at task onset. These results further validate our theoretical and methodological contributions to network dynamics, and help introduce a badly needed explanation of why and how neural activity propagates at different rates.

Dissemination: Journal Papers: August 1, 2015 to July 31, 2016

Cortical Activity During Imagined Speech

Word pairs across three speech conditions

During the previous reporting period, we reported several activities focused on decoding imagined speech, including decoding imagined words. This year, we extended this work with new publications. We explored high gamma activity relating to word pairs across three different conditions: listening, overt speech, and covert speech. As expected, we attained the highest classification accuracy in the listening and overt speech conditions. Our classifier also performed well in the covert speech condition, corresponding to imagined speech, even though we have no way to know the precise onset of each word during an imagined speech condition (Martin et al., 2016).

Passive language mapping

We have substantial progress to report with an emerging direction: passive language mapping. “Passive mapping” refers to mapping areas of the cortex without requiring the active participation of the patient. Today, mapping expressive language (speech) typically requires the patient’s active participation. The neurosurgeon may ask the patient to generate a verb, repeat a word, or a similar speech task that is not reasonable if the patient cannot actively participate. However, many patients cannot actively participate for various reasons – young children or persons with some language deficits cannot understand task instructions, other patients may be unable to maintain attention or remember task instructions, and others cannot be awakened at all during neurosurgery for medical, psychiatric, or other reasons. This limits the options available to neurosurgeons, as well as researchers.

What if we could map speech areas and study expressive language without the patient’s active participation? We explored this question with three patients who passively listened to stories. Importantly, they were not instructed to speak, nor perform any task. We analyzed gamma activity from 70-170 Hz immediately after the onset of speech. Even though this was a passive listening task, we found activation in areas responsible for speech as well as listening. All three patients exhibited increases in broadband gamma activity within the inferior frontal cortex, superior temporal gyrus, and/or perisylvian areas. Two patients also showed increased activity in premotor and/or supplementary motor areas, both of which are important for speech. Thus, we can track activation of speech areas in patients who just passively listen to tasks. In addition to improving our understanding of how listening can influence imagined speech, these results support the new direction of passive language mapping for patients who are not able to actively participate (de Pesters et al., 2016a).

We produced another publication that supported rapid functional mapping during neurosurgery, as well as our results from the preceding paper. We present a case report from a single person who underwent neurosurgery to remove a tumor located very near expressive language areas. The patient performed a variety of active language tasks and a passive listening task, as well as other tasks. We again found activation of imagined speech areas during the passive listening task, and further explored neural activity during language and non-language tasks (Taplin et al., 2016).

This was also a landmark methodological paper, because it was the first instance of using a high-density subdural grid in the intraoperative environment for language mapping. This high-density grid provided spatial resolution that is impossible with conventional grids. We used this improved spatial resolution to create a highly refined boundary between the tumor and expressive language cortex and explore specific regions responsible for language. We also noted some questions for future study that emerge from the use of high-resolution ECoG grids. For example, how can improved spatial resolution best translate into improved patient outcomes? Could grid resolution someday exceed the operative resolution of available neurosurgical techniques?

Cortical Activity During Non-language Function

Perception

We studied seven subjects with subdural electrode grids that were implanted to localize seizure foci and provide extended clinical monitoring. We asked these subjects to view pictures of houses and faces presented in rapid succession. We explored the resulting ERP and ERBB activity and found that both measures provided complementary information to track the location and timing of the different subtasks of the subjects' visual processing. We also found that this information could be used to classify which image the subject had seen (a face or a house) and infer the timing of stimulus onset (Miller et al., 2016).

Movement

Eleven subjects performed a center-out task while ECoG signals were recorded. We analyzed HGA and local motor potentials (LMPs) to detail the timing and location of activity supporting both movement planning and execution. Consistent with prior work with lower frequencies, HGA activation supported a strong role of sensorimotor areas in execution, and modulations of LMPs in prefrontal cortices supported movement planning. We were able to identify directional tuning information within HGA and LMP information (Gunduz et al., 2016).

Movement and hearing

Prior work, based largely on lower-frequency signals measured via the EEG such as alpha, have suggested that the brain increases activation in task-relevant areas while decreasing activation in other areas. This is key to our ability to focus our attention on specific tasks without unnecessary distraction. However, this prior work faced the same limitations as other EEG studies: poor spatial resolution and frequency range. We used ECoG to study task-related activation and inhibition while participants (five persons and one macaque monkey) performed auditory and motor tasks. The results were similar for the people and macaque monkey. Interestingly, we found a suppression in alpha power that preceded population-level activity in the motor task, but followed it in the auditory task. We found, for the first time, that we could track and analyze alpha dynamics within regions, not just across regions. These results provide additional detail about how and when the brain activates and deactivates different areas to support task execution through modulation of alpha activity (de Pesters et al, 2016b).

This work, and the two preceding papers in this section on "Non-language function," extends issues that we describe elsewhere in this report from language to perception and movement. This work also provides further hope that new methods in neurosurgery could help patients with a broad range of conditions. These papers have implications for BCI systems that could provide patients with more accurate control of prosthetic limbs or, further in the future, identify stimuli that patients heard or saw. In addition to this clinical impact, we have further shown that ECoG signals, with our analysis methods, can elucidate the nature and timing of activation in different regions and thereby clarify how different regions work together to accomplish the different subtasks required. We also addressed major issues with oscillatory activity and its relationship with function through theoretical and methodological publications, detailed in the next section.

Cortical Oscillatory Activity

Theoretical publication

In the previous report, I reported work to present a new approach to explain oscillatory activity in the brain and its role in coordinating and managing information transmission and task coordination across large areas of the brain (Schalk, 2015). I showed that explanatory frameworks such as the communication-through-coherence (CTC) and gating-by-inhibition (GBI) hypotheses fail to adequately address this issue, and introduced the function-through-biased-oscillations (FBO) hypothesis.

During the present reporting period, we published another paper focused on the relationship between oscillatory activity, cortical excitability, and behavior (Coon et al., 2016). We explored this relationship within the context of a daunting question within neuroscience: why is response timing so variable? Variations in response timing have been extensively explained through cognitive and emotive factors, such as regional attention, general or task-specific arousal, confidence in cues, multi-task interference, etc. However, there is still no viable explanation for this variability at a neural level. We argued that response timing relates to the phase of oscillations, which relate to cortical excitability. As neural activity propagates through different regions, it encounters variable delays based on the phase of oscillatory activity. This work helps explain this variability in information transmission and task performance.

Methodological publications

In tandem with the preceding paper (Coon et al., 2016), we also published a methodological paper focused on how to explore oscillatory activity and its impact on information transmission and task performance as signals propagate through the brain. This approach relies on determining the precise timing and location of task-specific activation based on single-trial analysis of ECoG data. Our paper explored the impact of different parameters and validated the approach, including demonstrating how it can lead to a new interpretation of two existing data sets. This should encourage new work to explore how neuronal activity spreads on a single trial basis, and how it is affected by neuronal oscillations (Coon and Schalk, 2016).

In another study focused on methodology, I sought to explore spatial filters used with ECoG data. Many publications have used the common average reference (CAR) approach, which is often used in EEG, but there has been little work to explore the impact of CAR or other spatial filters on ECoG data. Also, authors often remove channels with artifact prior to CAR, and we wanted to explore the possible resulting loss of task-relevant information. We applied two types of unsupervised spatial filters and three methods of detecting signal artifacts with a large ECoG data set (20 subjects, four task conditions in each subject). Our results showed that spatial filtering does improve performance by reducing signal variance unrelated to the task, and that removing artifact can reduce potential contamination but does not provide greater task-relevant information. Finally, our new "median average reference" filter could allow the retention of more task-relevant information, since it does not require removing channels with artifact prior to spatial filtering (Liu et al., 2016).

ECoG review

We also contributed to a publication that reviewed recent scientific and clinical progress in ECoG. During the last reporting period, I presented a lecture at the Seventh International Workshop on Advances in Electrocorticography (ECoG), along with other presenters. This workshop occurred in Washington, DC, on November 13–14, 2014. I collaborated with the other workshop contributors toward a publication, in which we each summarized recent progress. The paper presented progress in functional brain mapping during neurosurgery, language, seizure termination, brain-computer interfaces, ECoG electrodes, analysis methods, and other topics (Ritaccio et al., 2016). The article notes that the keynote speaker, as well as other contributors (including me) addressed neural oscillations and its importance in language and other tasks. This is consistent with other work I presented above, and supports my view that there is rich opportunity for new clinical and scientific advances based on newly available ECoG data.

During the present reporting period, I again contributed to an ECoG workshop in tandem with clinical and scientific experts. We have begun developing a collaborative paper presenting the proceedings from this workshop. This workshop occurred in Chicago, IL in October 2015, and thus we have had ample time to develop the publication. As of Aug 2016, the article is "in press" and should be published in the next few months.

Dissemination: Journal Papers: August 1, 2016 to July 31, 2017

Cortical Activity During Language

Continuous speech

Many studies have explored EEG activity related to production of individual words, but the neural dynamics underlying continuous speech production have not been well explored, particularly with ECoG. In this study, we sought to explore the spatio-temporal evolution of population-level activity relating to continuous overt speech. We also aimed to identify common structures and processes in both overt and covert speech. Eight participants repeated sentences aloud (overt) or silently (covert). Our results consistently indicated a spatio-temporal progression of cortical engagement, in which speech begins in frontal motor areas and concludes in the superior temporal gyrus, where auditory feedback is monitored. We also found that both overt and covert speech shared a common network of regions and activities. These results are among the first to explore continuous speech in this detail with electrophysiological recordings, and could also support new paradigms and analysis methods for passive language mapping during neurosurgery (Brumberg et al., 2016).

Continuous listening

Similar to word production, word comprehension has often been studied in the context of individual trials – unlike natural comprehension, in which we usually must process a continuous stream of text or speech in which surrounding words matter. In this study, we showed that HGA increases steadily as people read sentences. This did not occur if people read and remembered information in which context was irrelevant, including lists of words and structurally meaningless or "Jabberwocky" sentences. This result suggests that the increased HGA activity reflects ongoing compositional processes that underpin our ability to understand sentences. Like the preceding paper, this work helps to detail the sequence of neural events that provide linguistic meaning, and could contribute to new passive language mapping and related procedures during neurosurgery (Fedorenko et al., 2016).

Word retrieval

Word selection is a key component of language, Priming can facilitate lexical and conceptual retrieval, while interference can impair it. By exploring these phenomena in more detail with ECoG, we hoped to address basic questions regarding how the brain recruits different areas to support word retrieval. We explored ECoG activity from 70-150 Hz over frontal and temporal cortical areas while patients performed word retrieval tasks. The results suggest that word retrieval in speech production is not a modular process. Instead, the brain recruits overlapping regions and processes to support word retrieval (Riès et al., 2017).

Cortical Activity During Movement

This article explored an EEG-based BCI to support motor rehabilitation training at home. We studied ten chronic hemiparetic stroke survivors with moderate to severe upper limb motor impairment, measured by the well-known Action Research Arm Test or ARAT. These ten patients used a BCI system in which spectral EEG measures were used to drive a powered exoskeleton. By imagining hand movement, the patients could drive the exoskeleton to move the affected hand to execute the movement.

Presumably, this approach should increase Hebbian learning by increasing the correlation between activation in damaged cortical motor areas (through motor imagery) and the downstream neurons that they control (through the hand movement driven by the exoskeleton). This is a fundamental challenge in stroke rehabilitation therapy. Therapists may ask a patient to imagine or attempt a movement, but have no objective way to confirm that the patient is complying if s/he cannot actually move the affected hand, such as in severe cases. Thus, the patient might receive rewarding feedback – such as through the action of an avatar on a monitor, an FES system, powered exoskeleton – even though the patient isn't actually performing the desired motor imagery. Therapists are very familiar with this problem of "non-compliance," which may result from low motivation (post-stroke depression is common), misunderstanding task instructions, fatigue, or "compensatory strategies" in which they imagine a shoulder or elbow movement instead of a hand movement. Hence, patients could benefit from a new way to assess compliance by confirming via EEG spectral activity that patients are indeed imagining movement as instructed by the therapist. This new approach also uses EEG-based measures of motor imagery to drive rewarding feedback. Hence, patients can see when they are not imagining movement correctly, which helps them learn to generate the EEG activity, and hence the required cortical activation.

Patients used the system at home for 12 weeks, and their scores in the ARAT and other tests of motor function improved significantly (Bundy et al., 2017). These results not only supported other growing work validating motor imagery EEG BCIs for stroke rehabilitation, but also extended this approach to the home environment. If motor imagery EEG BCIs for stroke rehab and/or home-based rehab continue to show promise, then clinical translation could provide new hope for stroke survivors without requiring extensive trips to a hospital or rehab center.

ECoG review

In the last reporting period, I was an author on a publication that reviewed work from the seventh international workshop on advances in ECoG, and presented work at the eighth workshop in this series, which was held in Chicago in October 2015. I also reported that we were developing a publication based on the eighth workshop, which was likely to be published in the next few months.

Concordantly, within three months after the end of the last reporting period, this paper was published (Ritaccio et al., 2016). It is broader than our preceding paper about the seventh workshop, with summaries of 16 presentations. The summaries were structured within sections addressing clinical, engineering, basic science, and translational issues. The paper presented new approaches that could help patients with epilepsy, Tourette's syndrome, and disorders of language, movement, memory, and attention. Like last year's article, the article included a summary of some of my recent work and concluded with a perspective and summary that I wrote.

Dissemination: Journal Papers: August 1, 2017 to July 31, 2018

Cortical Function in Vision

Facephenes

One of the most trenchant questions in neuroscience revolves around the specificity of function of different cortical regions. Can a specific region of the brain perform different functions? Or, are different regions devoted primarily to the execution of a specific task? Classic work from Lashley and others has been viewed as supporting a "mass action" view of cortical function, implying that one cortical region may perform a specific function about as well as any other cortical region. More recent neuroimaging work – often with low-resolution, non-invasive approaches – has also suggested that, at least on a broader scale, large cortical regions seem active across many tasks. However, some of our earlier work in this project has suggested otherwise. With the millimeter-scale resolution that we can explore with ECoG, we have often observed that cortical subregions appear to be active only for very specific subtasks involved with language, perception, and other activities.

The present study addressed this question with a single subject who underwent epilepsy surgery. During the surgery, we recorded activity while the subject viewed both color and black/white images of four stimuli presented sequentially. One of the stimuli was a face (of one of the experimenters), and we showed three nonface stimuli: a round object (an orange soccer ball), a rectangular object (achromatic box), and a word (a large kanji character printed on a piece of paper). HGA analysis identified a region within the FFA that only responded to faces, and a nearby region that responded only to colored stimuli. This initial result supported the view that different subregions were active only for specific tasks (processing faces and colors, respectively) and not other tasks.

Next, we again presented the same stimuli as before to the subject. However, during some stimulus presentations, we electrically stimulated the electrode pairs that we previously identified as subserving either face-specific or color-specific functions. When we stimulated the face area, the subject reported seeing face-like percepts superimposed on whatever stimulus was presented. Concordantly, the subject reported seeing colors when we stimulated the color area. These results further indicate that specific functional subregions are each responsible for a single, specific task. Furthermore, some prior neuroimaging data supporting the alternative view may have been misinterpreted, or at least failed to capture the task specificity of specific functional subregions that our ECoG-based methods can reveal (Schalk et al., 2017, PNAS).

Schalk, G., Kapeller, C., Guger, C., Ogawa, H., Hiroshima, S., Lafer-Sousa, R., Saygin, Z.M., Kamada, K., Kanwisher, N. Facephenes and Rainbows: Causal Evidence for Functional and Anatomical Specificity of Face and Color Processing in the Human Brain. Proceedings of the National Academy of Sciences (PNAS); doi: 10.1073/pnas.1713447114, 2017.

Classification and discrimination of visual responses

In this paper, participants viewed seven types of images (shown in both grayscale and color) while ECoG activity was recorded over ventral temporal areas. While these visual stimuli were similar to our preceding “facephenes” paper, our main goal was to develop and evaluate a sequence of automated processing stages to discriminate and classify the stimuli. Across three experiments reported in this paper, our processing stages attained modest to good accuracy, and always well above chance.

The first experiment explored offline classification. Accuracy was 72.9% when discriminating across the seven image types, 67.1% for separating grayscale vs. color images and 51.1% when discriminating across all types of fourteen visual stimuli. The second and third experiments involved a real-time decoder, which correctly detected 73.7% of responses to face, kanji and black computer stimuli and 74.8% of responses to presented natural scenes. This accuracy was possible with data from only 500 ms after stimulus onset.

In addition to further detailing the HGA activity associated with different types of image presentations and the specificity of color vs. face processing regions, our results could have practical benefit in the near future. Real-time feedback could facilitate neurosurgical mapping and BCI applications that could detect presented or even imagined stimuli (Kapeller et al., 2018).

Kapeller, C., Ogawa, H., Schalk, G., Kunii, N., Coon, W.G., Scharinger, J., Guger, C., Kamada K. Real-Time Detection and Discrimination of Visual Perception Using Electrocorticographic Signals. Journal of Neural Engineering, doi: 10.1088/1741-2552/aaa9f6, 2018.

Electrical stimulation mapping (ESM)

Electrical stimulation mapping (ESM) of the brain has been used clinically for about a century, and is likely to remain prominent in the foreseeable future. However, alternatives are emerging from the work in this project, along with outside work. In this article, we reviewed ESM and its clinical applications, noting the relatively sparse studies that objectively assessed the value of ESM. Newer approaches to electrical stimulation of cortical activity, as well as passive mapping techniques and improved non-invasive approaches, could supplement or even obviate ESM in some situations. This could in turn lead to improved neurosurgical protocols and systems that reduce the risk of accidental seizure and time required for mapping while providing the neurosurgeon with more detailed maps of neural function and connectivity. We expect that ongoing research with additional neurosurgery cases involving epilepsy and lesions will provide new options for doctors as well as new scientific results (Ritaccio et al., 2018).

Ritaccio, A.L., Brunner, P., Schalk, G. Electrical Stimulation Mapping of the Brain: Basic Principles and Emerging Alternatives. Journal of Clinical Neurophysiology, 35 (2), 86-97, 2018.

Instantaneous voltage

The interpretation of oscillatory brain activity has relied on power and phase for decades, even though we have little understanding of how either of these factors relate to cortical excitability. I presented the Function-through-Biased-Oscillations (FBO) hypothesis (Schalk, 2015), which noted that cortical excitability directly relates to instantaneous voltage and is influenced by oscillatory power and phase. If this is correct, then instantaneous voltage should provide a more direct and informative means of measuring cortical excitability than power and phase.

In the present study, we tested this hypothesis with ECoG data from 28 people. The results showed that instantaneous voltage explained 20% and 31% more of the variance in broadband gamma than power- and phase- based approaches. Furthermore, power and phase together did not produce better predictions than instantaneous voltage. Hence, instantaneous voltage is an appealing alternative to power and phase, and could lead to a better understanding of cortical excitability and information transmission (Schalk et al., 2017).

Schalk, G., Marple, J., Knight, R.T. and Coon, W.G., Instantaneous Voltage as an Alternative to Powerand Phase-Based Interpretation of Oscillatory Brain Activity. NeuroImage, 157: 545–554, http://dx.-doi.org/10.1016/j.neuroimage.2017.06.014, 2017.

Dissemination: Journal Papers: August 1, 2018 to December 31, 2018

We have four new peer-reviewed journal publications during this period. Consistent with earlier reporting periods, these papers address methodological, scientific, and clinical issues. The last paper in this list was published after the project ended, but was submitted and revised during the project and presents work from the project.

Ignacio Saez, Jack Lin, Arjen Stolk, Edward Chang, Josef Parvizi, Gerwin Schalk, Robert T Knight, Ming Hsu. Encoding of multiple reward-related computations in transient and sustained high-frequency activity in human OFC. Current Biology, 28:18, 2889, 10.1016/j.cub.2018.07.045, 2018.

Li, G., Jiang, S., Paraskevopoulou, S.E., Wang, M., Xu, Y., Wu, Z., Chen, L., Zhang, D., Schalk, G. Optimal Referencing for Stereo-Electroencephalographic (SEEG) Recordings. NeuroImage, 183, 327-335,2018.

Swift, J.R., Coon, W.G., Guger, C., Brunner, P., Bunch, M., Lynch, T., Frawley, B., Ritaccio, A.L., Schalk, G. Passive Functional Mapping of Receptive Language Areas Using Electrocorticographic Signals. Clinical Neurophysiology, 129:12, 2517-2524, 10.1016/j.clinph.2018.09.007, 2018.

Crowther, L.J., Brunner, P., Kapeller, C., Guger, C., Kamada, K., Bunch, M.E., Frawley, B.K., Lynch, T.M., Ritaccio, A.L., Schalk, G. A Quantitative Method for Evaluating Cortical Responses to Electrical Stimulation. Journal of Neuroscience Methods, 311, 67-75, 10.1016/j.jneumeth.2018.09.034, 2019.

Dissemination: Journal Papers Summary

We are extremely proud of our dissemination achievements, particularly peer-reviewed journal papers. Our copious publications present our accomplishments involving methodological, scientific, clinical and technical contributions, as well as review and commentary. We have successfully branched out beyond our original focus on imagined speech with applications in other cognitive and motor domains, including extensive work with patients. Our author lists often include our PhD students as well as top collaborators worldwide.

Additional Dissemination

Additional Dissemination: August 1, 2014 to July 31, 2015

We did not report any published book chapters during this period. We did report that two book chapters about our nominated BCI Research Award projects had been accepted for publication during this period, and would be published n the subsequent reporting period.

Additional Dissemination: August 1, 2015 to July 31, 2016

In the previous report, we noted that we submitted two projects to the prestigious annual BCI Research Award, and both projects were nominated as top submitted projects. We also stated that “Since nominated projects are included in an annual book by Springer publishing, we produced two book chapters that have passed peer review and are in press with Springer.”

This book was published during the present reporting period, in November 2015. In addition to publishing our two chapters (Miller et al., 2015 and Brunner et al., 2015), the editors commented favorably on our work in their concluding chapter with their analysis and review of the submissions that year. Consistent with the guidelines from Springer, our chapters presented material aimed at students and other people who are not established experts. We reduced technical detail, presented longer explanations of why this work is important for both scientific questions and improved neurosurgery, and included some additional details of related work. I have several publications with each of the three book editors (Drs. Christoph Guger, Brendan Allison, and Gernot Mueller-Putz), and hence the editing and interaction with editors was brief. Hopefully, these two chapters will supplement our journal publications and share our results with broader groups of readers.

Additional Dissemination: August 1, 2016 to July 31, 2017

We submitted two projects to the Annual BCI Research Award in 2015. As before, an international jury nominated the top ten projects. Both of our projects were nominated for an award, and so we were asked to write a chapter based on each of these two projects. This book, titled "Brain-Computer Interface Research: A State-of-the-Art Summary 5," was published in Apr 2017. Both chapters presented work to characterize cortical activity with respect to language processing. One of our chapters presented our work on continuous speech recognition, extending our text-to-speech work (Herff et al., 2017), and another chapter presented an ECoG BCI based on auditory attention to natural speech (Brunner et al., 2017). In addition to our two chapters, eight chapters presented work from the other eight nominated projects, the editors wrote introductory and discussion chapters.

Additional Dissemination: August 1, 2017 to July 31, 2018

We published four book chapters in this period. Three book chapters are within a new textbook on BCIs published through Taylor and Francis, and the fourth is in a book on neuromodulation from Elsevier.

ECoG-Based BCIs

This chapter reviewed recent progress with ECoG-Based BCIs, addressing:

1) Clinical settings and signal acquisition, including grids;
2) ECoG signal physiology and features, highlighting information that non-invasive methods cannot provide and its relevance to BCIs;
3) ECoG BCIs in the literature for communication, control, and therapeutic neuromodulation;
4) Implantable ECoG devices that are approved for human use (including investigational use);
5) Open questions and future directions, including translation to clinical practice (Gunduz and Schalk, 2018).

Gunduz, A., Schalk, G. ECoG-Based BCIs. In: Brain-Computer Interfaces Handbook: Technological and Theoretical Advances. Eds: Chang Soo Nam, Anton Nijholt, and Fabien Lotte, Taylor & Francis, ISBN: 978-1498773430, 2018.

BCI Software

This chapter reviewed different BCI software platforms. We first presented the technical demands for a BCI software system and the scope. Next, we explored different implementations of BCI Software, including high-level software (Matlab, Simulink, and LabView) and self-contained BCI applications (BCI2000 and OpenVibe). We discussed the impact of BCI software and concluded with the observation that the increasing attention to BCIs will place greater demands on BCI software while increasing the impact that improved BCI software could have (Brunner and Schalk, 2018).

Brunner, P., Schalk, G. BCI Software. In: Brain-Computer Interfaces Handbook: Technological and Theoretical Advances. Eds: Chang Soo Nam, Anton Nijholt, and Fabien Lotte, Taylor & Francis, ISBN: 978-1498773430, 2018.

Perspectives on BCIs

This chapter addresses a question that keeps coming up during discussions at conferences and in papers. Why haven't BCIs been more clinically or commercially successful, amidst so many new publications and other (incremental) improvements? This chapter reviews prior answers to this problem and proposed solutions, such as increased bit-rate and reduced demand for expert help, and presents other issues impeding more widespread clinical translation of BCI technology (Schalk, 2018).

Schalk, G. Perspectives on Brain-Computer Interfaces. In: Brain-Computer Interfaces Handbook: Technological and Theoretical Advances. Eds: Chang Soo Nam, Anton Nijholt, and Fabien Lotte, Taylor & Francis, ISBN: 978-1498773430, 2018.

Non-invasive BCIs

This chapter summarizes different types of non-invasive BCIs. We adopted the framework presented in Wolpaw and Wolpaw (2012) to structure most of the paper, which grouped BCIs in terms of the function they were meant to serve (replace, restore, improve, enhance, and supplement). Our chapter presented a myriad of established and emerging directions, ranging from basic spelling and orthosis control to stroke rehab, immersive gaming and exoskeleton control. While we focused mainly on EEG-based BCIs, consistent with most work in non-invasive BCIs, we addressed metabolic approaches for non-invasive BCIs (Schalk and Allison, 2018).

Schalk, G., Allison, B.Z. Noninvasive Brain–Computer Interfaces. In: Neuromodulation: Comprehensive Textbook of Principles, Technologies, and Therapies. Eds: Elliot Krames, Hunter Peckham, and Ali Rezai, Elsevier, ISBN: 978-0128053539, 2018.

Unlike previous reporting periods, we presented additional dissemination – that is, accomplishments that disseminated project achievements and were neither journal papers nor book chapters. We reported that:

In addition to the journal publications and book chapters, we conducted numerous other dissemination activities during this reporting period. Prof. Schalk gave over a dozen talks at institutes and conferences in New York, California, Florida, Pennsylvania, Japan, China, Israel, and elsewhere. Notable examples include:

• Prof. Schalk gave the keynote address on the Real-Time Functional Imaging and Neurofeedback Conference in Nara, Japan in December 2017. The talk was titled "Real-time Passive Functional Mapping of Eloquent Cortex Using Electrocorticography."

• In May 2018, Prof. Schalk gave a lecture in Prof. Robert Knight's lab at UC Berkeley about his new ECoG work.

• Prof. Schalk led a workshop titled "ECoG based BCIs" at the Eighth International BCI Meeting in May 2018 in Asilomar, California. The audience saw talks from Prof. Schalk, Drs. Kai Miller and Dora Hermes from Stanford University, and Prof. Aysegul Gunduz from the University of Florida.

• Prof. Schalk delivered three lectures on ECoG research in Shanghai in June 2018. Two talks were at Jiao Tong University, and the third was at Huashan Hospital.

Additional Dissemination: August 1, 2018 to December 31, 2018

We do not have any new published book chapters during this period. However, one book chapter that we developed during the project was accepted for publication during this period:

Ritaccio, A.L., Brunner, P., Schalk, G. **Cortical and Subcortical Mapping.** In: Functional Neurosurgery: The Essentials. Eds: Brown, Pilitsis, and Schulder, in press.

Otherwise, we do not have any additional dissemination to report during this period.

Additional Dissemination Summary

Peer-reviewed journal publications are the most prominent way to disseminate results through projects such as these, and the preceding section focused on these publications. However, we also have extensive outcomes to report with other dissemination mechanisms, primarily book chapters. We published eight book chapters throughout this project. The first four book chapters presented projects that were nominated for an Annual BCI Research Award, one of which won second place in during an annual awards competition. The remaining four book chapters were all published during the last reporting period (August 1, 2017 to July 31, 2018). Three of these four book chapters were published in a major textbook published by Taylor and Francis, which has since become a prominent resource for students and BCI practitioners. We also have one book chapter in press that presents methodological guidelines and details for cortical and subcortical mapping that we developed during this project.

During the last reporting period, we also reported over a dozen other dissemination activities, with some detail about five of them. We didn't report other additional dissemination in previous interim reports. This does not reflect that we had no such activities. We just focused on our journal papers and book chapters.

Honors and Awards

Honors and Awards: August 1, 2014 to July 31, 2015

We submitted two projects based on this project to the Annual BCI Research Award competition in 2014. Both projects were nominated for an award. Since nominated projects are included in an annual book by Springer Publishing, we produced two book chapters that have passed peer review and are in press with Springer.

Award description:

The Annual Brain-Computer Interface (BCI) Research Award is widely recognized as the top honor in the BCI community. While the number of submissions for the 2014 BCI Award are not publicly available, there were 169 submissions to the BCI Award in 2013 (Guger and Allison, 2014, Springer Publishing). An independent jury of six top BCI experts chose ten nominees and one winner. While neither of our submissions won the top prize, being nominated is still noteworthy.

In addition to earning authorship on two upcoming chapters with a major publisher, our work was also recognized in a major public ceremony attached to the Sixth Intl. BCI Conference in Graz, Austria from Sep 16-19, 2014. Drs. Schalk and Brunner attended the ceremony and publicly received an award certificate, along with the other nominees.

Nominated projects:

P. Brunner, K. Dijkstra, W. Coon, J. Mellinger, A. L. Ritaccio, G. Schalk (Wadsworth Center and AlbanyMedical College, US).

"Towards an Auditory Attention BCI."

This nominated project presented work using gamma band activity (70-170 Hz) from ECoG data to infer the identity of auditory speech stimuli. We developed real-time software tools through BCI2000 and identified key areas that were active during our auditory attention task: the superior and medial temporal gyri.

K. J. Miller, G. Schalk, D. Hermes, J. G. Ojemann, R. P.N. Rao (Department of Neurosurgery, Stanford University, Wadsworth Center and Albany Medical College, Department of Psychology, Stanford University, Department of Neurological Surgery, University of Washington, Department of Computer Science and Engineering, University of Washington, US).

"Unsupervised decoding the onset and type of visual stimuli using electrocorticographic (ECoG) signals in humans."

We presented images of faces or houses to subjects and recorded the resulting ECoG data. We developed classification algorithms for when the stimulus onset time was known, and when it was unknown. Our classifiers were 96% accurate with a known onset time, and 94% accurate without it. We could predict stimulus onset time within about 20 ms.

Honors and Awards: August 1, 2015 to July 31, 2016

We did not report any new Honors nor Awards during this period.

Honors and Awards: August 1, 2016 to July 31, 2017

We did not report any new Honors nor Awards during this period.

Honors and Awards: August 1, 2017 to July 31, 2018

We won second place in the 2017 BCI Research Awards for our project titled "Individual Word Classification During Imagined Speech." During this reporting period, we publicly received our certificates and a trophy during the awards ceremony on Sep. 20, 2017, which was part of the Seventh International BCI Conference.

We also extended our relationship with the BCI Research Award infrastructure. In late 2017, Prof. Schalk became the co-chair of the BCI Award Foundation, along with Dr. Christoph Guger. The BCI Award Foundation is a non-profit entity that administers the Annual BCI Research Award.

In November 2017, Prof. Schalk was awarded the Albert Nelson Marquis Lifetime Achievement Award and was announced for recognition in Who's Who in the World 2018.

Honors and Awards: August 1, 2018 to December 31, 2018

We have no new Honors nor Awards to report during this period.

Honors and Awards Summary

The Annual BCI Research Awards are presented each year to top projects in BCI research. Each year, an international jury of BCI experts reviews submitted BCI projects based on novelty, benefit to patients, real-time functionality, and other factors. The competition for these awards is considerable, and the substantial majority of projects that are submitted each year are not nominated.

Throughout the project, we submitted three projects to the Annual BCI Research Award competition. All three of these projects were nominated for an award, and one project won second place. Prof. Schalk joined the non-profit BCI Foundation as co-chair in late 2017. He will influence this growing annual award by attracting top jury members and submissions.

In addition to the Annual BCI Research Awards, Prof. Schalk was awarded the Albert Nelson Marquis Lifetime Achievement Award and was announced for recognition in Who's Who in the World 2018.

Tech Transfer

Tech Transfer: August 1, 2014 to July 31, 2015

We did not report any patents nor other tech transfer during this reporting period.

Tech Transfer: August 1, 2015 to July 31, 2016

We filed a patent application on March 17, 2016; please see the US15/558,780 patent application in the section beginning August 1, 2017.

Tech Transfer: August 1, 2016 to July 31, 2017

We filed a US patent application titled "EEG Headsets with Precise and Consistent Electrode Positioning." The application number is 15/351045, and it was filed on November 16, 2016. This application extends our collaboration with Dr. Leuthardt involving a practical EEG system for stroke rehabilitation in home environments. The application covers a variety of ways to design a headset, position electrodes within the headset, align the electrodes across key landmarks (such as the anterior-posterior axis from the nasion to inion), analyze data, and configure a BCI system. As noted when reviewing our publication on home EEG stroke rehab with Dr. Leuthardt, this appears to be a promising direction, and we hope to secure intellectual property in this field as well as publications.

Tech Transfer: August 1, 2017 to July 31, 2018

The patent application that we mentioned earlier (US15/558,780) is proceeding:

Schalk, G., Brunner, P., Coon, W.G., dePesters, A. Improved Measurement of Cortical Excitability.

This application presents a new way to measure the activation of different brain areas, which has long been a challenge in neuroscience. Across different brain imaging techniques, including EEG, ECoG and LFP, there have been numerous papers that try to infer activation based on direct functional neuroimaging (typically based on electrical measures). By providing a new means to measure cortical excitability, we can better understand underlying neural processes as well as more effectively provide neurofeedback and other forms of treatment. The patent does cover neurofeedback applications.

Tech Transfer: August 1, 2018 to December 31, 2018

We do not have any additional patents nor tech transfer activity to report during this period.

Tech Transfer summary

We filed two US patent applications during this project.

Summaries

Summary: August 1, 2014 to July 31, 2015

Overall, we have made excellent progress. We were able to use funds to complete ongoing work with imagined speech, and successfully adapted our goals and activities to address network activity as well. These achievements have provided both knowledge and research flexibility to support our newer work with ECoG network analyses. In addition to moving us closer to our goal of recognizing imagined sentences, we have also advanced scientific and technical methods and bolstered our understanding of network dynamics underlying speech. Aside from theoretical implications, our progress could lead to new speech therapy opportunities and revolutionary brain-computer interface systems that can provide wholly new communication options that do not require muscle activity.

Summary: August 1, 2015 to July 31, 2016

Overall, this was an extremely successful reporting period. We were able to use funds to continue and extend our work with imagined speech. Moreover, we have effectively begun work to extend our ideas and methods to characterize ECoG-based assessment of cortical activity during movement and perception (visual and auditory). In addition to several papers with new data from humans and one non-human primate subject, we also published papers addressing theoretical and methodological issues, a review article, two book chapters, and several conference papers. Our publications included a wide range of top co-authors in scientific and clinical domains, across a wide range of disciplines. We submitted a patent application. We are beginning to generate impact well beyond imagined speech. Our activities during this period will also impact non-language function, ECoG analysis approaches, neurosurgical mapping procedures (notably passive mapping), high-resolution ECoG, and fundamental issues in how the brain manages the coordinated activity across different brain regions to perform a range of tasks. Furthermore, emerging trends such as high-resolution ECoG grids and passive mapping could make neurosurgery practical, and possible, for a broader range of patients. If so, our progress with ECoG-based procedures, analysis methods and underlying theory could have a greater clinical and scientific impact than we previously expected.

Summary: August 1, 2016 to July 31, 2017

This was a good reporting period. We produced a broad range of publications and continued our effort to characterize cortical activity, exploring imagined speech while branching into related disciplines. While our work focused heavily on ECoG, we also utilized other imaging approaches, which (among other benefits) could facilitate translating our work with cortical activity into non-invasive applications for stroke rehabilitation or other goals. Our publications included very well-established co-authors such as Nancy Kanwisher, Robert Knight, Nathan Crone, Dan Moran, Christoph Guger, Dean Krusienski, and Eric Leuthardt. Two students completed their PhDs.

During this period, some of the trends we reported in the previous period have continued. Both our team and outside groups have continued to produce publications supporting the use of high-resolution ECoG grids, passive mapping, and HGA analyses for both clinical and research applications. All of these three directions are consistent with our belief that ECoG is a powerful tool for recording and analyzing cortical activity. In addition to remaining active with these directions, we also worked on an emerging new direction, which is stroke rehabilitation using EEG-based measures of motor imagery. We expect that this direction will also gain attention and clinical translation. Entities such as Neurolutions, GTEC, and A*STAR have recently announced or released products designed to provide this capability, and several papers have validated them, or prototypes of them, with stroke patients.

Summary: August 1, 2017 to July 31, 2018

This reporting period went well. We produced four peer-reviewed papers and four book chapters, as well as other dissemination. The “facephenes” paper gained some outside attention, including articles in Discover Blogs, Nature Insight, The National Post, and at least 20 other external websites. Like previous periods, our papers focused primarily on original clinical and scientific research, and we also published methodological and review/commentary work. We have a new patent application, new honors and awards, and a new PhD student.

In our papers addressing ESM mapping and visual function, as well as other clinical and scientific applications, our approaches to characterizing cortical activity show clear advantages over state-of-the-art methods. In some cases, these new approaches could be applied in clinical practice relatively quickly. Clinical protocols and software upgrades may not require the extensive clinical approval procedures as hardware. We are already active in new work that is implementing some of our new outcomes in clinical research.

Summary: August 1, 2018 to December 31, 2018

During the last five months of the project, we reported three additional peer-reviewed journal publications, with another in press.

Overall Summary

During each of the summaries in our Interim Reports, we consistently reported good (or better) progress. Concordantly, we are proud of our accomplishments throughout this project. Across major reporting categories (training, dissemination, honors/awards, and tech transfer), we met or exceeded expectations for this project, and indeed any reasonable expectations for any project of this scope. In particular:

- Two PhD students completed their PhDs. While active in the project, they earned authorship on several publications (including first-author pubs) and finished their PhDs.
- We have extremely extensive dissemination activities, including over two dozen peer-reviewed papers in top journals and eight book chapters.
- Four of our project achievements were nominated for the prestigious BCI Research Award.
- We developed two patent applications.

We are grateful for the opportunity to work on this project, which we expect will continue to have a strong impact even though the project has ended. New work involving ECoG methods, systems, and applications should become much more prominent over the next several years, including clinical applications that could provide new options for patients.