High Frequency Activity in the Orbital Frontal Cortex Modulates with Mismatched Expectations During Gambling in Humans

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***Abstract*—During gambling, humans often begin by making decisions based on expected rewards and expected risks. However, expectations may not match actual outcomes. As gamblers keep track of their performance, they may feel more or less lucky, which then influences future betting decisions. Studies have identified the orbitofrontal cortex (OFC) as a brain region that plays a significant role during risky decision making in humans. However, most human studies infer neural activation from functional magnetic resonance imaging (fMRI), which has a poor temporal resolution. In particular, fMRI cannot detect activity from neuronal populations in the OFC, which may encode specific information about how a subject reacts to mismatched outcomes. In this preliminary study, four human subjects participated in a gambling task while local field potentials (LFPs), captured at a millisecond resolution, were recorded from the OFC. We analyzed high-frequency activity (HFA: >70 Hz) in the LFPs, as HFA has been shown to correlate to activation of neuronal populations. In 3 out of 4 subjects, HFA in OFC modulated between matched and mismatched trials as soon as the outcome of each bet was revealed, with modulations occurring at different times and directions depending on the anatomical location within the OFC.**

I. INTRODUCTION

Gambling involves making decisions based on expected rewards and risks. However, expectations may not match actual outcomes as future betting decisions may be influenced by past performance and whether one feels more or less "lucky." Gambling behaviors and the role emotions play in biasing decisions have been extensively studied [1–3].

Several studies present physiological and anatomical evidence that the Orbitofrontal Cortex (OFC) is involved in both decision-making and emotional processing. The OFC is a prefrontal cortex region and has been associated with value encoding of choices [4,5], compulsive decision-making [6], and discrepancies between realized and expected results [7]. In addition, lesions of the OFC in humans have been shown to impair the ability to incorporate emotional cues into decisions [8]; while lesion of the OFC in macaques impair the ability to assign credit for outcomes to previously made decisions in [9].

Most studies, including the aforementioned studies, rely on (i) functional Magnetic Resonance Imaging (fMRI) or other noninvasive imaging modalities to study neural activity in the human OFC, or (ii) lesion studies in patients or lesion experiments in animal models, or (iii) electrophysiology in monkeys or rats during decision making. fMRI studies in humans have dominated decision-making neuroscience but have a poor temporal resolution (on the order of 1-2 seconds) and the blood oxygenation level-dependent signal is only a proxy for neural activity. Lesions studies can only *infer* neural function, not neural activation, by identifying deficits in behavior when a brain structure is damaged. To measure neural activity in the OFC directly during behavior, one must invasively implant electrodes in the OFC, and thus can only be done in animals and in experimental lab settings.

Recently, our investigative team consisting of bioengineers and clinicians has exploited a unique clinical setting wherein a state-of-the-art electrophysiological method, StereoElectro-EncephaloGraphy (SEEG), is applied to obtain activity in humans at millisecond temporal resolution across multiple brain structures [10]. This is accomplished by placing dozens of electrode contacts at all decision-making sources, including the OFC, which record the activities of populations of neurons at the local field potential (LFP) level. SEEG offers unprecedented access to the neuronal activity of superficial and subcortical brain structures (Fig. 1), and this complex wiring of cognitive circuits is being performed on epilepsy patients for treatment purposes.

Our recent experiment entailed capturing such LFP recordings across multiple brain structures from ten human subjects performing a gambling task [11,12,13]. In [12], we demonstrated that gamma band power (35-50Hz) in the OFC plays a role in encoding "luck" and thus biasing future bets when present at the beginning of a trial *before* options are shown. However, we hypothesize that OFC must modulate its activity *as soon as a mismatched outcome occurs*, thus updating the luck variable on a trial-by-trial basis. We test this hypothesis by analyzing the high-frequency activity (>70 Hz) in the OFC in four subjects time locked to when the outcome of each bet is made known to the subject. HFA gleaned from SEEG recordings has been shown to correlate directly with neuronal activity, thus describing how populations of neurons may be encoding mismatched expectations in our task [14].

We found that in 3 out of 4 subjects, HFA in OFC modulated between matched and mismatched trials as soon as the outcome of each bet was revealed, with modulations occurring at different times and directions depending on the anatomical location within the OFC.

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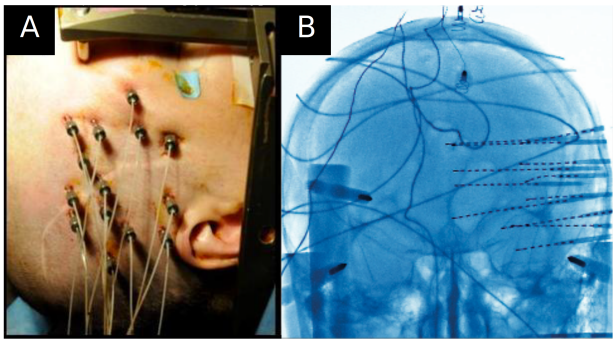

Figure 1. Imaging fusion and placement of multiple electrodes using the SEEG method. Fig. A is a photograph showing 14 electrodes at the skin surface. Fig. B is a fluoroscopy image of an SEEG-implanted subject (coronal view with eye forward). Note the precise parallel placement, with tips terminating at the midline or dural surface.

II. Methods

A. Subjects

Subjects at the Cleveland Clinic, patients with medically intractable epilepsy, routinely undergo SEEG recordings in order to localize the seizure focus. In this study, aside from the behavioral experiments, no alterations were made to the patient's clinical care, including the placement of the electrodes [10]. Subjects enrolled voluntarily and gave informed consent under criterion approved by the Cleveland Clinic Institutional Review Board. A total of ten subjects volunteered to perform the task, and the four subjects in this study has contacts in the OFC.

B. Neural Recordings - Stereoelectroencephalography

The innovative approach using SEEG methodology relies on its capability in accessing large-scale networks, providing precise human brain data, from cortical to subcortical areas, in a three-dimensional fashion. In the routine placement of depth electrodes, burr-holes that are each 15 mm in diameter are required for safe visualization of cortical vessels, and therefore only a small number of electrodes are placed. SEEG placement, however, uses several small drill holes (1.8 mm in diameter), allowing many electrodes to be inserted.

Since direct visualization of the cortical surface is not possible with small drills (Fig. 1A–B), the SEEG technique may require detailed pre-procedural vascular mapping using pre-operative imaging with magnetic resonance angiography (MRA) and cerebral angiography. Angiography is an X-ray examination of the blood vessels. The mapping procedure is performed under fluoroscopy using general anesthesia, and an expert neuro-anesthesiologist correctly titrates anesthesia to permit the measurement of intracranial EEG. The number and location of implanted electrodes are pre-operatively planned based on a hypothesis, which is formulated in accordance with non-invasive pre-implantation data such as seizure semiology, ictal and inter-ictal scalp EEG, MRI images, PET and ictal single-photon emission computed tomography (SPECT) scans. Thus, the implantation strategy has the goal of accepting or rejecting the pre-implantation hypothesis of the location of the epileptogenic zone (EZ).

Table 1. Subject Information

Patient ID	Gender	Age	# Contacts in OFC
2 (EFRI 7)	F	41	5
3 (EFRI 12)	F	53	7
6 (EFRI 18)	F	32	3
7 (EFRI 21)	M	28	5

SEEG provides complete coverage of the brain, from lateral, intermediate and/or deep structures in a three-dimensional arrangement recorded over hundreds of channels. Using strict techniques, this procedure is safe and minimally invasive [10], [11].

C. Gambling Task

Subjects performed the gambling task in their Epilepsy Monitoring Unit room for approximately 30 minutes. The task was displayed via a computer screen and the subject interacted with the task using an InMotion2 robotic manipulandum (Interactive Motion Technologies, USA). The manipulandum is controlled by the subject's hand and allows for 2D planar motion, which translated directly to the position of a cursor on the screen.

The gambling task (Fig. 2) is based on a simple game of high card where subjects would win virtual money if their card beat the computer's card. Specifically, at the beginning of each trial, the subject controlled a cursor via a planar manipulandum to a fixation target. Afterward, the subject is shown his card (2, 4, 6, 8, or 10) that is randomly chosen with uniform probability (subjects are given the distribution of cards a priori). The computer's card is initially hidden. The screen then shows their two choices: a high bet ($20) or a low bet ($5). The subject has 6 seconds to select one with his cursor. Following selection, the computer's card, which is also randomly chosen, is revealed. The final screen depicts the amount won or lost.

Subjects were given time to practice the task until they understood the rules and felt comfortable. Recorded sessions typically lasted about 30 minutes thereafter, with 142 trials completed on average (SD: 16). Since the cards were drawn uniformly, the number of trials for each card type were in roughly equal proportion. Each trial typically took 8-10 seconds to complete, with subjects occasionally taking short breaks. As all participants were adults, they were assumed to be familiar with the concept of gambling.

Labeling of Matched versus Mismatched Trials: Data for electrodes in the orbital frontal cortex and cingulate cortex were separated into trials where the subject's inferred expectation of the outcome was either matched or mismatched by the actual outcome. We defined a mismatched outcome as one in which the subject bet low ($5) but won or drew the bet or bet high ($20) but lost or drew the bet. For 6 card trials, we assume that the player expects a draw, thus any outcome other than a draw is classified as a mismatch. Otherwise, a trial is classified as one in which the player's expectations were matched.

D. Data Analysis

All electrophysiological and behavioral analyses were conducted offline using custom MATLAB ® scripts.

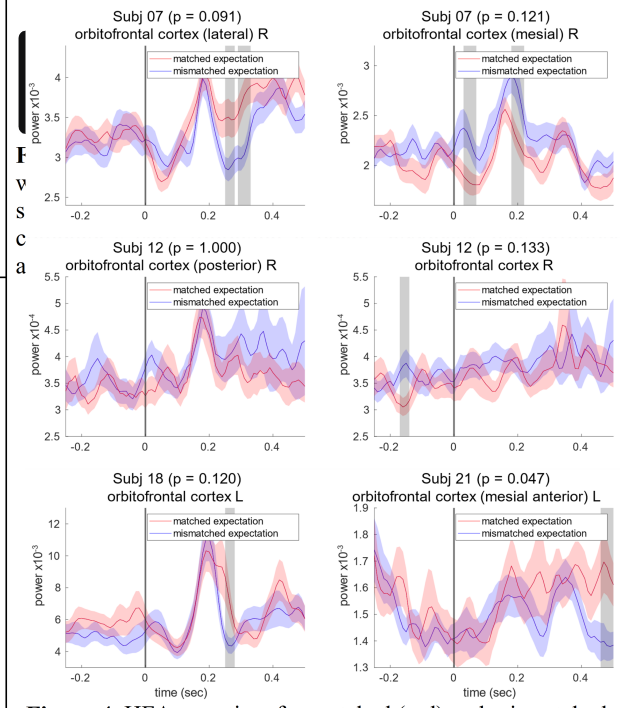

Figure 4. HFA over time for matched (red) and mismatched (blue) trial averages in OFC. Gray shaded regions indicate windows with $p < 0.2$. p-values shown are the lowest found in the window. Red and blue shaded regions indicate standard error.

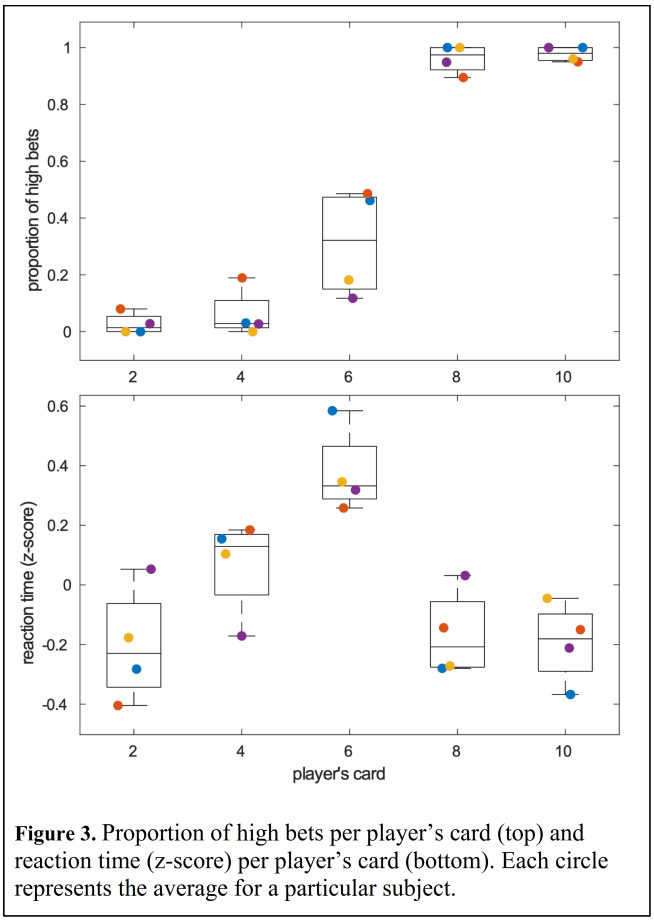

Figure 3. Proportion of high bets per player's card (top) and reaction time (z-score) per player's card (bottom). Each circle represents the average for a particular subject.

Differences in the neural responses between the task conditions during the 0.5 seconds after the computer's card is shown were examined by means of a non-parametric cluster statistic. Specifically, the high-gamma power over time for each trial was obtained, time-locked to when the computer's card was shown. Then the power over time for matched trials was compared to those for mismatched trials. To see if the signals for each group were significantly different, we used a nonparametric cluster-based test. Clusters are defined as a set of adjacent time windows whose activity is statistically different at a given level between the two trial types.

1) Spectral analysis: Data were preprocessed by first subtracting off a 10-second moving average to eliminate voltage drift. 60 Hz electrical noise and higher harmonics were then filtered out. Finally, trials with likely movement artifacts during the window of interest after the computer's card was shown were removed. This was done by projecting the signal for each trial into a 5-dimensional principal component space and estimating the mean and covariance of the data. The 10% of trials that were least likely under this distribution were removed. We calculated the power between 70-150 Hz using the MATLAB *bandpower* function (Signal Processing Toolbox) applied to a moving window of width 100 ms. The window was shifted by 10 ms for each estimate. Signals from contacts within each subregion (e.g. posterior OFC or lateral OFC) were averaged.

2) *Non-parametric cluster statistical test:* Significant differences between the neural response data in the orbitofrontal cortex and cingulate cortex regions are defined by a non-parametric cluster statistic run on data aggregated

from trials by all relevant subjects [15]. This test takes into account the correlation between adjacent time windows in order to avoid over-penalizing with multiple comparison corrections. For each time window in the high-gamma-power time series, a null distribution was created by shuffling these matched and mismatched labels 1000 times between trials within each subject. Within each shuffle, the average difference between the newly labeled matched and mismatched high-gamma power signal was calculated. A p-value was assigned for each window by comparing the difference acquired from the true labels with the distribution of differences acquired from the shuffled labels. Clusters were formed by grouping windows with p-values below a desired threshold that were adjacent in time.

3) High-frequency activity: The high-frequency activity (HFA) metric captures high-gamma activity and reflects previous work in SEEG [14] and other invasive recordings.

III. Results & Discussion

We first examined the overall behavior in the four subjects. Fig. 3 shows the mean responses to player's cards during 30 min sessions. Specifically, we plot the proportion of high bets per player's card and reaction time (z-score) per player's card. As seen in Fig. 3, all subjects almost always bet low on 2 and 4 cards and high on 8 and 10 cards. For 6 cards, some subjects consistently bet low, while others have a mix of high and low bets. The bottom figure shows that reaction time (time taken to choose a high or low bet) is longer for cards where the odds of winning or losing are closer to 50/50, with the longest reaction time seen on 6 card trials. This clearly indicates that subjects form some notion of how likely they are to win or lose given their card.

Preliminary results suggest that the HFA in the OFC correlates with mismatched expectations. These results align with previous studies, mentioned above, that the OFC is one region involved in both decision-making and risky behavior during gambling. After analyzing the nonparametric cluster-based test results for each subject, it was found that small differences in the signal may exist in OFC in 4 out of 6 cases. Fig. 4 highlights these differences in power for matched (red) and mismatched (blue) expectations. In 3 of these, higher gamma power appears to correspond to matched expectations. The increase in activity seen roughly 200 ms after the computer card is shown is likely due to visual processing of the image.

Our findings are preliminary and based on a small sample. We had relatively few patients performing our decision-making task. This is because not all patients consented and/or met the criteria of our study. The small sample size of the study population is further limited by the fact that each patient had electrodes implanted in different brain regions. However, future work entails capturing more recordings from the OFC while subjects perform our gambling task, and identifying more regions involved in encoding mismatched expectations.

IV. Acknowledgments

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