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FUNCTIONAL REPRESENTATION OF SOMATOSENSORY, VISUAL, AND REINFORCEMENT PROCESSING ON THE CANINE BRAIN SURFACE

An early feasibility chronic use demonstration: BrainInterchange-BCI2000 ecosystem

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ABSTRACT

Implantable brain-computer interface (BCI) systems, promising for neurological disorder treatment, often encounter high technical barriers. Our fully-implanted CorTec BrainInterchange-BCI2000 ecosystem, aimed for widespread open-source adoption, demonstrates functionality through a year-post-implant canine study, using a brain surface electrocorticography (ECoG) construct. Broadband power-spectrum increases have been shown to track neural population activity in humans, and we find that they reveal distinct functional representation for processing of visual, somatosensory, and auditory reinforcement stimuli in the canine (captured at 65-150Hz). Canine visual and somatosensory rhythms resemble human alpha and beta rhythms but at different frequencies: a ∼15Hz visual rhythm in the occipital analog (marginal gyrus) suppresses with light exposure, and a ∼24Hz somatosensory rhythm diminishes upon petting. These findings indicate a unique canine neurophysiology and confirm the BCI2000-BrainInterchange ecosystem's robustness a year after the implantation. This ecosystem holds promise for developing open-source BCI devices to assist patients with neurological conditions.

INTRODUCTION

The technology behind practical brain computer interfacing has an exclusivity problem arising from a number of factors. Hardware that can record sufficient channels for the coding brain activity requires a large infrastructure to build, maintain, and troubleshoot. Engineers with the rare expertise needed to manage these devices typically professionally reside far from the clinical setting that patients with neurological disorders present to for therapy. The software skills and signal processing know-how needed to translate signals measured from the brain into closed-loop commands for external applications or internal recursive stimulation of the brain are similarly exclusive. For this and other clinical reasons, we have been developing a combined hardware-software open source ecosystem with the CorTec BrainInterchange (BIC) device [2] and the BCI2000 software environment [3] that will serve as a general purpose platform that can be easily applied for clinicians focused on a specific patient need.

Our development of this ecosystem has begun with canine (canis familiaris) implants. For chronic studies, dogs offer a viable model for cognitive and neurodegenerative studies, attributable to their trainability, cooperative nature, and neurophysiological similarities to humans [4, 5]. We are able to test the device on a daily basis without any restrain of the dog and upon the completion of the study the dogs can be adopted into homes. In this demonstration, a series of basic sensory input tasks are performed approximately a year after the time of implant. While the implanted neurophysiology of the canine brain is relatively unexplored, we expect that many aspects of well-described phenomena in the human brain will generalize.

Broadband changes in the brain surface electrical potential have been shown to be a robust correlate of local neural activity and an effective control signal in brain computer interfaces [6, 7]. However, these changes are often obscured at low frequencies by coincident oscillations, and so broadband changes must often be captured at frequencies above ∼50-60Hz, setting a performance threshold that BCI devices must rise to. In this manuscript, we demonstrate that the BrainInterchange-BCI2000 ecosystem has this capability and, in the process, uncover functional representation of somatosensory, visual, and social reinforcement in the canine brain.

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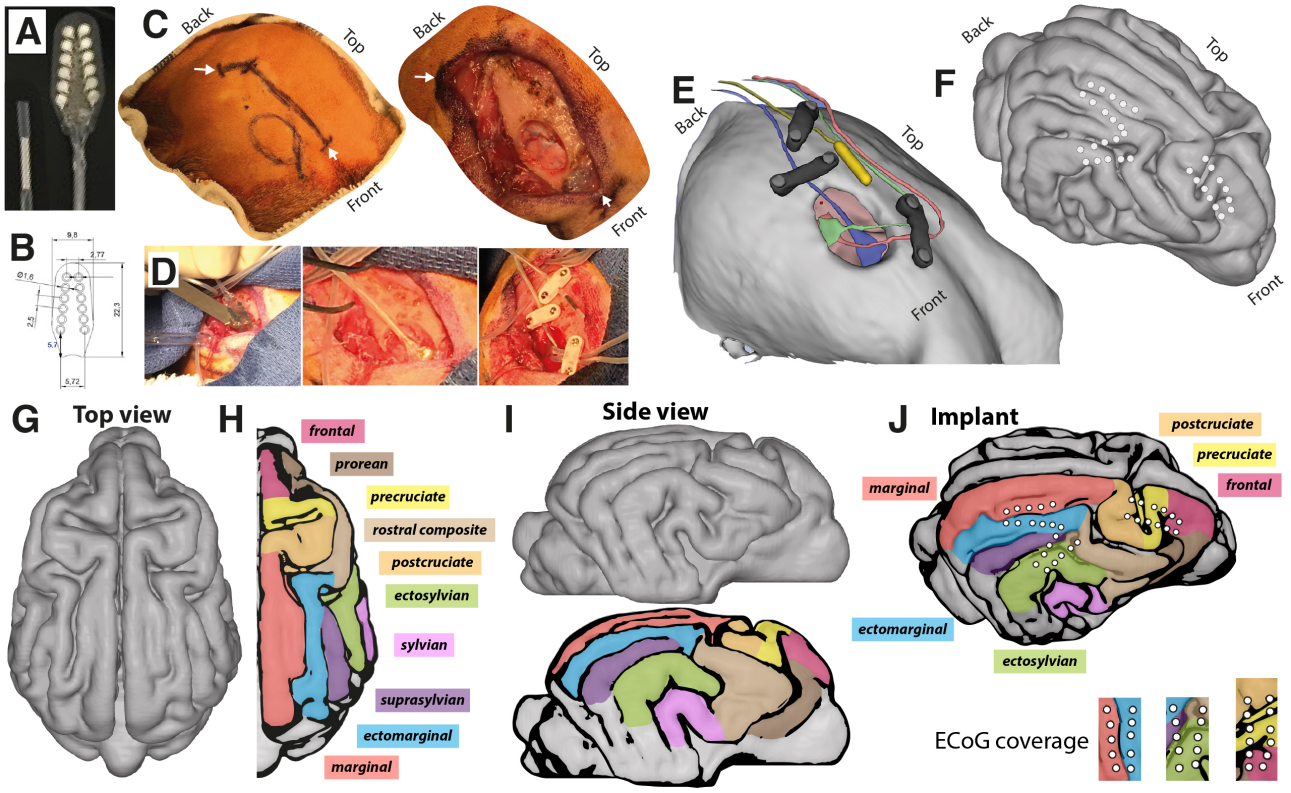

Figure 1: **Right hemisphere implant and anatomic segmentation** **(A)** Electrode grid and ground electrode. **(B)** Schematic with dimensions of grid (in mm). **(C)** Planned incision and craniotomy on scalp (left) with opening and craniotomy, showing epidural space (right). White arrows correspond to same location on left and right. **(D)** Insertion and anchoring of electrodes. **(E)** Rendering of skull and craniotomy with electrodes in situ, ground electrode in yellow. **(F)** Brain rendering showing three grids in situ, extracted from pre-implant MRI and post-implant CT. **(G)** Top view of the canine cortex. **(H)** Color-map representation of canine right hemisphere gyral anatomy [1]. **(I)** Sagittal view of canine right hemisphere and color-map representation of its gyral anatomy. **(J)** Schematic placement of electrode grids over the canine cortex.

MATERIALS AND METHODS

Surgical implant: A 2-year-old female beagle, "Belka", was implanted with the 32-channel sensing-and-stimulation Cortec BrainInterchange device as previously described [2], according to a public operative protocol [8]. Three arrays (32 ECoG channels) were implanted epidurally over the right hemispheric convexity with the FDA-approved AirRay electrodes [9] (Fig. 1).

Anatomic co-registration: A pre-implantation 3T MRI and a post-implantation CT were obtained. The brain was manually segmented from the MRI using 3D Slicer [10], and the CT was co-registered with electrodes aligned to the anatomy using the CTMR package as previously described [11], which was also used for subsequent plotting. Anatomic segmentation of the brain surface was determined manually with reference to the *Stereotactic Cortical Atlas of the Domestic Canine Brain* [1] (Fig. 1). The 3 grids were localized to the 1) *frontal, precruciate* and *postcruciate* gyrus; 2) *ectosylvian gyrus* extending to the border of the *suprasylvian & ectomarginal* gyrus and the *rostral composite*; and 3) flanking the *marginal* and *ectomarginal* gyri.

Canine tasks: Three types of tasks were performed - somatosensory, visual, and reinforcement (auditory input with face touching). For each task, the four best runs (as determined by behavior, prior to data analysis) were selected for further analysis. Each run consisted of 15 repetitions of active & inactive task blocks.

Somatosensory - The dog was positioned unrestrained within the examination room with the room lights on, next to the examiner. 3-second blocks of tactile stimulation (petting along the left side of the dog, encompassing the whiskers, front and hind limbs, and torso) were interleaved with 5s blocks of rest (Fig.2A).

Visual - Examination took place in a closed room with all external sources of light blocked. The dog was placed on a leash in the middle of the room, allowing her to move within the reach of the leash. 5-second "lights OFF" blocks with the room lights turned off were interleaved with 5s "lights ON" blocks, where the rooms lights were turned on. A laptop was in the room, with monitor light exposed, cuing the examiner to turn the room lights on and off.

Reinforcement with auditory encouragement and & face touching - The dog was positioned unrestrained in the examination room next to the examiner with the room lights on and calming classical music playing at a low volume. 5-second reinforcement blocks where the examiner provided verbal reinforcement ("Good girl Belka!") & gently touched the left side of the face were interleaved with rest periods.

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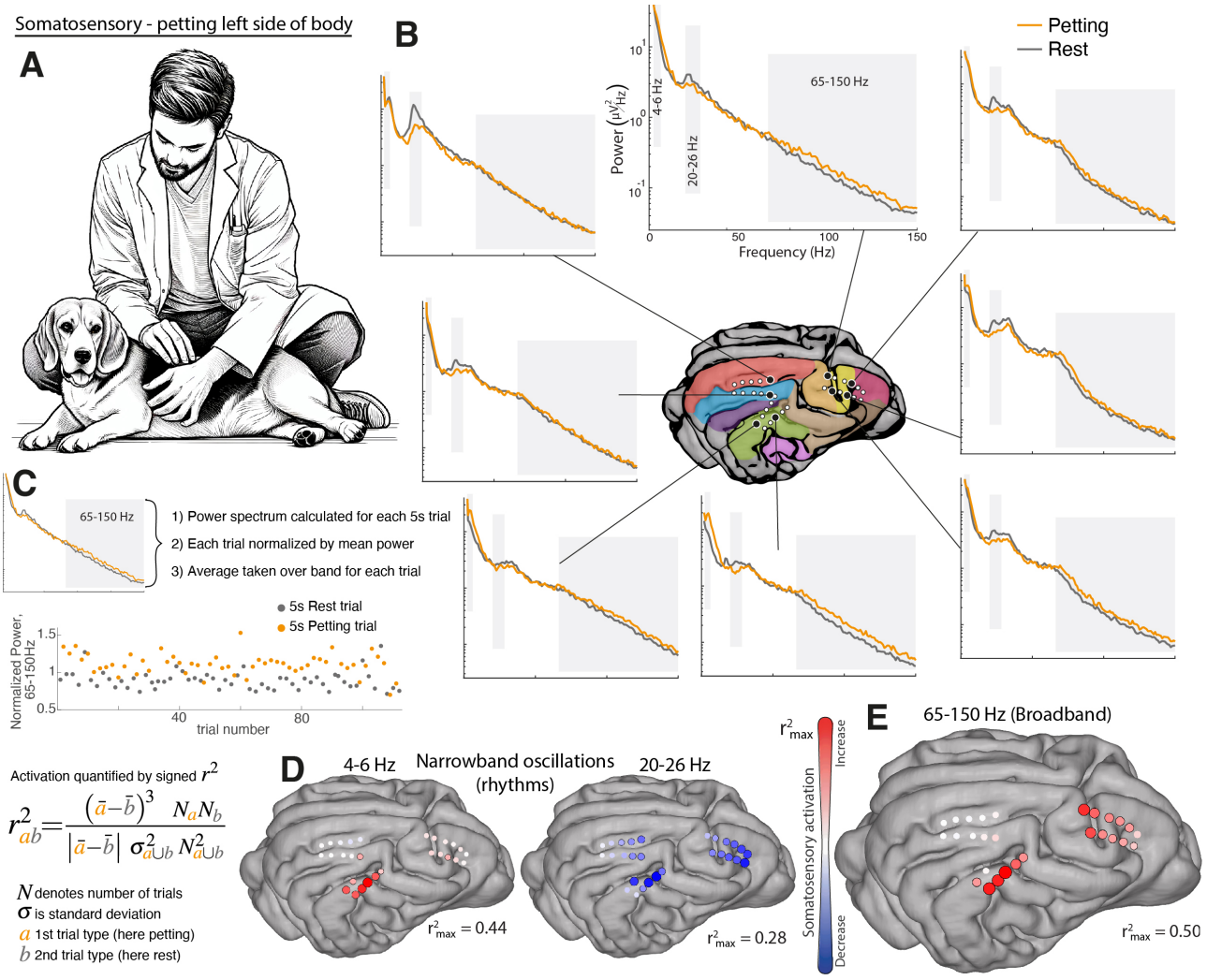

Figure 2: **Somatosensory activation (A)** Cartoon representation of the somatosensory stimulation task, where 3s blocks of tactile stimulation (petting left whiskers, front and hind limbs, and torso) were interleaved with 5s blocks of rest. **(B)** Power spectral densities (PSDs) of petting and rest blocks. Gray shaded regions highlight 4-6Hz, 20-26Hz and 65-150Hz frequency ranges. **(C)** For analysis, PSDs for each task block were normalized by the average PSD over the whole experiment, and averaged normalized power was quantified for each frequency range. Task-associated changes were quantified using a signed r^2 metric (which can range from -1 to 1). **(D)** Scaled activation maps (by signed r^2) shows domains of change for the low frequency brain rhythms. Black circle outline indicates task-induced significant change at p<0.05 (after Bonferroni correction, unpaired t-test in mean normalized power in band for each trial). **(E)** Maps of local brain activity, reflected by broadband spectral change, is captured at (65-150Hz), showing engagement of the pre- and post-cruciate, ectosylvian, and rostral composite gyri.

Electrophysiological measurements: Data were measured using BCI2000 general-purpose software [12], which provides a graphical user interface for data acquisition, online processing for closed-loop application (though not used in this study), and stimulus presentation. Data were sampled at 1000 Hz, with an amplification gain of 57.5 dB / 1 μV, and initially referenced to the channel 1 (Fig. 3). Missing samples due to the packet loss were replaced with the first valid sample preceding the packet loss. This is a default setting for handling missing data packages in Cortec's BIC device (see the work of *Ayyoubi et al.* [13] for further packet loss discussion).

Signal processing: Data were examined by raw trace as well as relative signal power to identify bad channels, which were discarded prior to common-average re-referencing of the data. Power spectral densities (PSDs) up to 150Hz were calculated for each task block using Welch's averaged periodogram method [14] with 1s Hann windowing [15] and 50% window overlap. Several data blocks were rejected (across all channels) due to significant transient artifact (4/6/0 blocks for somatosensory/visual/reinforcement). Individual block PSDs were normalized by the mean power at each frequency (mean calculated over each full task). Signed r^2 cross-correlations comparing task conditions (Fig. 2C) were calculated across all the channels at each frequency, and plotted on featuremaps (Fig. 3) to characterize the spatial and frequency-specific structure of neurophysiological changes associated with each task. Based on the visual examination of the raw PSDs and the featuremaps, three low-frequency narrow-band ranges (4-6Hz, 14-16Hz [visual only], & 20-26 Hz) were cho-

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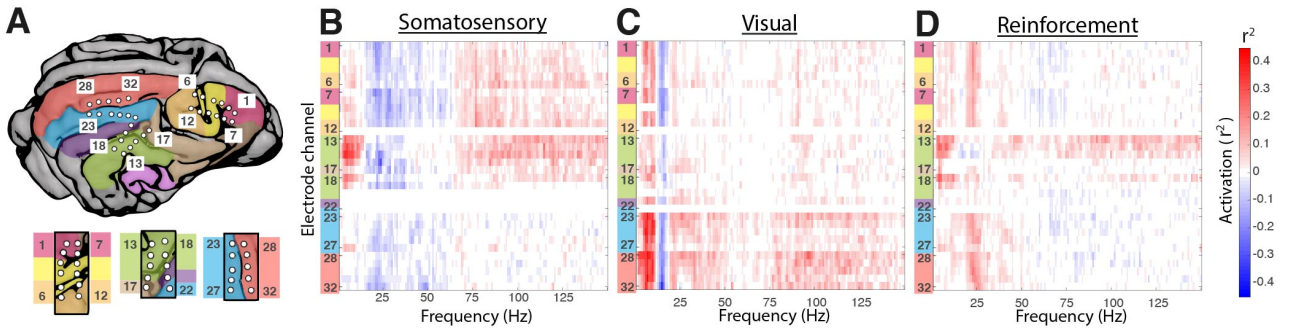

Figure 3: **Task featuremaps (A)** Segmentation of the canine right hemisphere gyral anatomy and electrode placement locations, with channel numbering that is referenced in (B-D). **(B-D)** r^2 feature-maps for the somatosensory, visual, and reinforcement tasks.

sen for statistical analysis. Separately, a high-frequency broadband range was chosen *a priori* at 65-150Hz to capture the 1/f structure that has been shown in humans to be a correlate of local population activity [6, 16]. Averaged power (after normalizing by the mean PSD) was calculated across each frequency range for each block. Blocks of each type within each task were then compared with one another using a signed r^2 metric and an unpaired (2-sample) t-test (mean normalized power in band for trials of petting vs. rest, lights on vs. lights off, and reinforcement vs. rest). Maps of r^2 values were projected onto the rendered brain to show task-associated brain activity (Figs. 2,4), with channels that reached threshold significance ($p<0.05$ after Bonferroni correction), were marked with a black outline.

Ethics statement: This research is conducted under Mayo Clinic IACUC protocol A00001713-16-R19. We maintain our canines in an IACUC-approved environment. In addition, according to State of Minnesota statute 135A.191, the canines will be made available for adoption at the conclusion of research. In the event of serious illness or decline, the animals may be humanely euthanized by the veterinary team according to an IACUC mandated protocol. The canine subject, Belka, is a 3 year old female (implanted at 2 years old). She is housed in a communal environment, and receives daily social interactions with veterinary staff as well as open time with other canines. The intent of this animal research is to test and develop a platform for novel human therapeutics.

RESULTS

Somatosensory - Somatosensory petting stimulation contralateral to the side of implantation showed robust activation (as revealed by broadband spectral power increase) over the pre- and post-cruciate gyri, as well as the ectosylvian / rostral composite gyri (Figs.2–4). A narrowband rhythm (oscillation) that was observed with a peak of ∼24Hz (20-26Hz) decreased in power over these same regions during petting.

Visual - Visual task stimulation showed a significant activation (as revealed by broadband spectral power increase) over the marginal and ectomarginal gyri (Fig. 3C, 4A). There was a very prominent oscillation, peaked at ∼15Hz, that emerged over most of the sampled sites during the lights off period, and diminished when the room lights were turned on (Fig. 3C, 4B).

Reinforcement with auditory encouragement & face touching - During reinforcement with coincident verbal praising and stroking of the left cheek, we found robust activation (broadband spectral increase) of the anterior measurement sites of the ectosylvian gyrus. Additionally, there was an increase in the rhythm centered around ∼24Hz, present over the pre- and post-cruciate, marginal, and ectomarginal gyri (Fig. 3D, 4).

Comparison across tasks Comparison of local representation, as reflected by 65-150Hz broadband spectral change, shows clear functional representation in the canine brain, with visual representation in the marginal gyrus, somatosensory representation in the pre- and post-cruciate gyri, and reinforcement (both tactile and auditory) in the ectosylvian gyrus. Notably, there was also: **1)** An oscillation/rhythm peaked at ∼5Hz (4-6Hz) that increased in power at all measured sites when lights were turned on in the visual task (with r^2_{max}=0.43), and selectively increased in the ectosylvian sites during the somatosensory (r^2_{max}=0.44) and reinforcement (r^2_{max}=0.28) tasks. **2)** A ∼15Hz rhythm was only seen with the lights off blocks of the visual task and was not seen during any other tasks. **3)** Although not modulated in the visual task, an oscillation peaked at ∼24Hz was present over much of the brain surface - it was selectively depressed during somatosensory input and augmented during reinforcement input (Figs. 3A&C, 4C).

DISCUSSION

These simple sensory tasks demonstrate for the first time that, as in humans [6, 16], local neural activity can be captured by broadband spectral change from the surface of the canine brain (here captured at 65-150Hz, Fig. 4). In agreement with emerging canine fMRI studies [17], clear functional representation for somatosensory processing was found most robustly surrounding the cruciate sulcus, which is the canine homolog of the human central sulcus, and also the ectosylvian & rostral composite gyri. The ectosylvian gyrus has previously been implicated in canine somatosensory function using peripheral-stimulation evoked brain potentials (SSEPs) [18]. Com-

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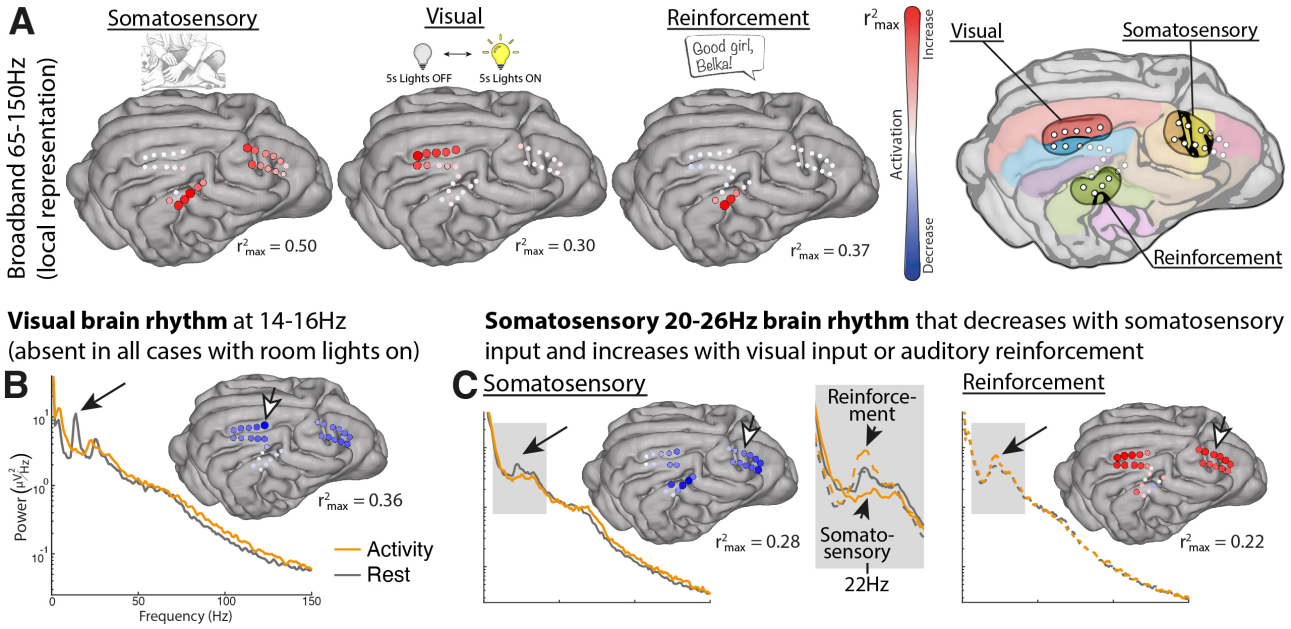

Figure 4: **Graphical summary of the obtained results. (A)** The functional representation of the canine brain, revealed by broadband increase in the power spectrum (65-150 Hz), shows distinct representation for each modality. **(B)** A clear ∼15Hz brain rhythm emerges in the dark that is suppressed when the lights are turned on (r^2_{max}=0.36), and is not seen in either of the other 2 tasks. **(C)** Interestingly, there is an oscillation with peak at ∼24Hz was present over much of the brain surface that is selectively depressed during somatosensory input and augmented during reinforcement input. Note that rest condition PSDs are approximately equal at this frequency range for both tasks (solid and dashed black lines in middle gray square), but that petting/reinforcement selectively suppresses/augments it. White arrows in (B)&(C) show sites where PSDs are from.

parison of lights-on to lights-off brain activity localized visual processing to the marginal gyrus, which agrees with fMRI localization [19], and the removal of which has been shown to blind dogs [20]. Combined light tactile and auditory reinforcement selectively activated only at sites in the ectosylvian gyrus and nowhere else, loosely agreeing with fMRI measurement [21].

Alongside broadband power spectral changes, we also observed a number of prominent oscillatory rhythms below 50Hz (Figs. 2-4). For example, a canine analog of the human occipital "alpha" rhythm emerged when the dog was in the dark, with a peak at ∼15Hz that is most prominent in the marginal gyrus, and is slightly higher in frequency than the 8-13Hz range reported by *Lopes da Silva, et. al.* [22]. Oddly, there was an increase in power at an ∼5Hz oscillation where *Kujala et al.* found a visually-induced decrease from the scalp [23]. The ∼24Hz rhythm that is selectively suppressed with somatosensory stimulus and augmented during reinforcement (Fig. 4C) appears to be a novel observation.

Importantly, human ECoG studies have shown that behaviorally-induced oscillatory brain rhythms are generally not functionally specific in the same way that the broadband changes are [6, 7, 24]. For this reason, it is important that chronically implanted hardware can be able to capture the broadband spectral changes. However, two factors make this technically non-trivial: 1) large power changes in oscillations/rhythms obscure smaller amplitude broadband power changes below ∼50Hz; 2) the broadband phenomena falls off in power at higher frequencies as $P \sim 1/f^4$ [16]. Implanted hardware must therefore have a sufficiently low noise floor such that behaviorally-associated broadband power increases can be resolved at higher frequencies. These canine behavioral results demonstrate, empirically, that the BrainInterchange-BCI2000 ecosystem accomplishes this, even after the device has been implanted for a year.

The BrainInterchange-BCI2000 ecosystem is undergoing continuous development and optimization [2]. All software, data, resources, & protocols for this initiative are fully open-source, with a vast documentation to teach the community how to use it without having extensive technical expertise. When fully developed, this ecosystem may enable clinical teams to create personalized BCI therapies tailored specifically to the needs of their patient population.

CONCLUSION

Our work demonstrates the utility of the BrainInterchange-BCI2000 platform in the setting of ECoG recordings during three sensory experiments almost a year after implantation. Captured local neural activity, revealed by broadband spectral changes, show robust sensorimotor, visual, and reinforcement functional organization in the brain of a canine. This represents an important step towards the development of an open source platform for clinical use, capable of closed-loop stimulation and applicable in personalized BCI therapies for patients suffering from neurological disorders.

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