PhD Research Proposal Form
China Scholarship Council (CSC)
2024

A remplir en français ou en anglais en fonction de la langue qui sera utilisée pour la thèse

Si la proposition de thèse fait l'objet d'un autre financement chinois que le CSC, préciser ici:…..

FIELD

NEUROSCIENCE

Thesis subject title:
Plasticity of ocular dominance in the primary visual cortex of the adult ferret

Name of the French doctoral school/Ecole doctorale: ED3C

Name of the Research team/Equipe de recherche:
Neuro team, Laboratoire des Systèmes Perceptifs
Websites:
https://sites.google.com/view/yves-boubenec/home
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Lab Language/ Langue de travail: English

Research Proposal Abstract/Présentation du sujet:

Neuroplasticity is the ability of the brain to change over different timescales in response to ongoing sensory experiences. The visual system has been historically used as a gold standard system to investigate neuroplasticity, with the paradigm of monocular deprivation (MD) and its impact on ocular dominance (OD). In animal models, OD plasticity has been observed during development and after long-term (days to months) monocular deprivation, which induces a permanent OD shift in favor of the open eye[1]. More recently, studies in humans have found that a particular form of OD plasticity is preserved after development: short-term (2-2.5 h) monocular deprivation counterintuitively shifts OD in favor of the *deprived eye*, both at the perceptual[2], and at the neural level[3,4], reflecting visual homeostatic plasticity. Homeostatic plasticity is thought to play a key role in balancing responses to both eyes in primary visual cortex (V1), and as a consequence enhancing neural processing of the deprived eye. This homeostatic boost of the deprived eye is transitory (2-3h after MD), but can become permanent in patients with amblyopia[5], opening the way to new treatments for this widespread neurodevelopmental disease. Understanding the neural underpinnings of short-term OD plasticity is therefore instrumental for potentially important clinical applications.

While short-term OD plasticity has been investigated in adult humans, the underlying neural mechanisms are still unclear, because of the limited spatio-temporal resolution of the non-invasive neuroimaging techniques available. Here we propose to investigate the neuronal mechanisms of short-term monocular deprivation in the primary visual cortex of the adult ferret with a combination of high-resolution neuroimaging and electrophysiological recordings.

In a set of preliminary experiments, we set to map functional responses to monocular stimuli over the surface of ferret visual cortex. For this, we used functional UltraSound (fUS) neuroimaging[6], a new neuroimaging modality that provides high spatiotemporal resolution hemodynamic brain responses (100-µm side voxels, 2.5 Hz sampling rate) over extended spatial dimensions (3.6 mm x 15 mm in surface, and 2 cm in depth). Notably, it is the first use of fUS for this purpose in the ferret, following up previous characterizations with optical imaging. However, this imaging modality offers distinct advantages, including its unique capabilities in capturing high-resolution hemodynamic responses.

Our laboratory is expert in the use of fUS imaging in the awake ferrets[7,8]. Using the technique, we demonstrated the presence of bands of ocular dominance in the V1 of adult ferrets[9]. We also identified cortical patches responding to both eyes, at locations matching the center of the retinotopic field. Preliminary experiments with MD suggest a boost of responses to the deprived eye in a subset of recordings, consistent with the human literature[3,4].

Work package 1: Mapping functional properties of ferret V1 at multiple spatial scales
We aim to comprehensively map the functional properties of the primary visual cortex (V1) in adult ferrets across multiple spatial scales. To achieve this goal, we will couple functional UltraSound (fUS) neuroimaging, a cutting-edge technology known for its exceptional spatiotemporal resolution in capturing hemodynamic brain responses, with chronic electrophysiological recordings in the targeted region.

Task 1.1. **Defining retinotopic responses with fUS imaging:** We will perform fUS imaging to precisely delineate retinotopic responses within the ferret V1. This step is crucial for establishing a foundational understanding of how the visual cortex processes spatial information.

Task 1.2. **Delineating a region exhibiting binocular responses with fUS imaging:** Our next objective is to identify cortical regions that exhibit binocular responses using fUS imaging. Once identified, we will perform electrophysiological recordings with chronic arrays (floating microelectrode arrays, in use in the laboratory) to validate the findings obtained through fUS imaging. This approach will allow us to gain a deeper insight into the neuronal activity within the identified binocular regions of the ferret V1.

Work package 2: Tracking plastic changes in visual cortex after monocular deprivation

We will then focus on understanding the plastic changes that occur in the visual cortex of adult ferrets following monocular deprivation. We will combine fUS imaging in one hemisphere and electrophysiological recordings in the other hemisphere to investigate the neural mechanisms underlying ocular dominance (OD) plasticity at multiple scales.

Task 2.1. **Mapping the neural correlates of OD plasticity:** We will map the neural correlates associated with OD plasticity at the microscale (electrophysiology) and mesoscale (fUS imaging). In addition, we will track the timecourse of OD plasticity, both during monocular deprivation and after patch removal. This will provide insights into the evolution of neural changes in the visual cortex over time.

Task 2.2. **Exploring the influence of arousal states during OD:** Arousal states is a key player in modulating OD plasticity[10,11]. We will investigate how changes in arousal levels affect neural responses during monocular deprivation. Arousal state will be monitored through different measurements (LFP recordings in olfactory bulb for sleep scoring, heart and breathing recordings, eye tracking).

Work package 3: Linking cortical changes to perceptual sensitivity after monocular deprivation

We will aim at establishing a connection between the observed cortical changes in the ferret V1 and the resulting perceptual effects of monocular deprivation.

Task 3.1. **Probing perceptual sensitivity after OD:** We will probe perceptual sensitivity in both eyes of the ferrets after OD. We will develop a simple detection task in which the stimulus contrast will be adjusted to assess the perceptual threshold in each eye (deprived and non-deprived).

Task 3.2. **Testing whether neural changes explain perceptual reports:** We will conduct experiments to determine if the neural changes observed in V1 can explain and account for the perceptual reports and sensitivities experienced by the ferrets following monocular deprivation. This step aims to bridge the gap between neural mechanisms and perceptual outcomes.

References:

1. Wiesel T. & Hubel, D. H. Single-cell responses in striate cortex of kittens deprived of vision in one eye. J. Neurophysiol. 26, 1003–17 (1963).
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3. Lunghi, C., Berchicci, M., Morrone, M. C. & Russo, F. Di. Short-term monocular deprivation alters early components of visual evoked potentials. J. Physiol. 593, (2015).
4. Binda, P. et al. Response to short-term deprivation of the human adult visual cortex measured with 7T BOLD. Elife 7, (2018).
5. Lunghi, C. et al. A new counterintuitive training for adult amblyopia. Ann. Clin. Transl. Neurol. 6, 274–284 (2019).
6. MacÉ, E. et al. Functional ultrasound imaging of the brain. Nat. Methods 2011 88 8, 662–664 (2011).
7. Landemard, A. et al. Distinct higher-order representations of natural sounds in human and ferret auditory cortex. Elife 10, (2021).
8. Bimbard, C. et al. Multi-scale mapping along the auditory hierarchy using high-resolution functional UltraSound in the awake ferret. Elife 7, (2018).
9. Issa, N. P., Trachtenberg, J. T., Chapman, B., Zahs, K. R. & Stryker, M. P. The critical period for ocular dominance plasticity in the Ferret's visual cortex. J Neurosci 19, 6965–6978 (1999).
10. Lunghi, C. & Sale, A. A cycling lane for brain rewiring. Curr Biol 25, R1122-3 (2015).
11. Wang, M., McGraw, P. & Ledgeway, T. Attentional eye selection modulates sensory eye dominance. Vision Res. 188, 10–25 (2021).

Type of PhD :

1.Full PhD

- Joint PhD/cotutelle (leading to a double diploma) : NO
- Regular PhD (leading to a single French diploma) : YES

2. Visiting PhD (students enrolled at a Chinese institution who come to ENS for mobility period) : NO

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