Local Field Potential – A Link Between Behavior and Physiology

Marta U. Wołoszynowska-Fraser[1], Gernot Riedel[1]

[1]Institute of Medical Sciences, University of Aberdeen, Aberdeen, Scotland, United Kingdom. [1]r01muw11@abdn.ac.uk

Introduction

Cognitive events bind ensembles of neurons together to bring about a uniform behavioral response. The elements of these ensembles are typically neurons with their own individual properties encoding/retrieving specific task parameters so that an overall appropriate response pattern can be observed. Yet, the same neurons may exhibit differential neuronal activity in a spatial versus a non-spatial task, or a short-term relative to a long-term memory task. Characteristic firing patterns have been recorded from extracellular electrodes and, at least for hippocampus, theta oscillations can be demodulated and reveal the spatial location through feature-tuned field potentials [1]. More globally, theta oscillations are associated with the complex behaviors, including processing of memory and decision making, and working memory and navigation in rodents and humans [2] and their propagation from hippocampus to prefrontal cortex can entrain prefrontal gamma oscillations to activate attentional processes, cognition and working memory [3,4]. These rhythms are typically recorded in animals by multi-electrode arrays recording several dozens of cells and are locally restricted to the few neurons in the proximity of the electrode.

This is in stark contrast to human studies, in which brain activity is readily accessed through scalp electrodes placed in the outside of the scalp in regular rows on predetermined spaces in a high density of sometimes 256 probes constituting the EEG. At the same time, the human test subject is required to perform specific tasks so much so that the EEG can be fragmented to carry trial-specific information relative to stimulus onset, inter-trial interval, or recall phase. Such an approach is widely lacking in animals, particularly mice given the size and fragility of the skull, and the finesse required to align behavioral stimuli and responses with EEG measures with high fidelity. Here we describe the development and implementation of such an approach using a light-weight wireless EEG device connected to the head of the mouse in a working memory paradigm.

Methods

All experiments were performed under the United Kingdom Animals (Scientific Procedures) Act 1986 and EU directive 63/2010EC and approved by the local Ethical Review Committee. Mice (C57BL/6, locally bred, both genders, 8-10 weeks old, no water or food restrictions) were stereotaxically implanted with bilateral gold electrodes placed into prefrontal cortex and hippocampus. For recording of continuous local field potentials, NeuroLoggers (NewBehaviour, Zurich, Switzerland) were attached to the head-stage before mice entered the behavioral apparatus. To measure working memory we recorded spontaneous alternation in the Y-maze. Using EthoVision 3.1 (Noldus Information Technology, Netherlands) we defined zones in the Y-maze: distal zones (A1, B1 and C1) and proximal zones (A2, B2 and C2). Entry into these zones generated TTL pulses, which were transmitted via a buffer to the infrared (IR) pattern generator (Fig.1). Each zone entry was identified by a different IR pattern and recognized by the IR sensor on the NeuroLogger. IR signals were aligned to LFPs, downloaded and processed with MatLab® together with the neuronal activity and analyzed using BrainVision Analyzer 2.0 (Brain Products GmbH, Germany). Recording were segmented according to the IR stamps with the view to determine neuronal differences when animals pass through or explore different zones of the maze (spatial sorting). Extracted episodes of brain activity were then Fourier transformed and compared for absolute and normalized power. Statistical comparison used parametric tests with alpha set to 5%.

Results

The ability to pinpoint the brain activity in the regions of interest to a particular place in the maze helps to understand alterations in oscillatory activity in response to different cognitive demands. In theory, one could argue that the distal zones are regions of pure exploration with very little valence; at the same time, all distal zones are proposed to be of equal relevance. In contrast, the proximal zones carry higher cognitive load as a decision has to be rendered whether to turn left or right (or re-enter the same arm). Subjects displayed lower prefrontal power (normalized) in the decision (proximal) zone compared with the distal zone in the all frequency bands analyzed including theta, alpha, beta and gamma (low, high) (F's>5; p's<0.02). The hippocampal normalized power in the proximal zones was lower only in 20-50Hz range ($p=0.0009$, $Df=1$, $F=11.28$) compared with the distal zones.

Conclusion

We here present a novel means for the alignment of behavioural observations and wireless recordings of oscillatory activity in the brain. This was established in a Y-maze paradigms with the particular view to recording of working memory, but we have also utilised the method in other behavioral settings (open field, Barnes maze, etc...). In this experiment, animals readily modulated their neuronal activity depending on cognitive load. Overall, they lowered the power of LFPs when passing through the decision zones/heightened their activity when exploring the distal zones. This ability to pinpoint the activity of neuronal ensembles in brain regions of interest to specific cognitive functions thus allows a translational approach matching the measurment of EEG changes during cognitive testiing in human controls and patients.

References

1. Agarwal, G., Stevenson, I.H., Berenyi, A., Mizuseki, K., Buzsaki, G., Sommer, F.T. (2014) Spatially distributed local fields in the hippocampus encode rat position, *Science,* **344**, 626-630.
2. Benchenane, K., Tiesinga, P.H., Battaglia, F.P. (2011) Oscillations in the prefrontal cortex: a gateway to memory and attention. *Current Opinion in Neurobiology,* **21**, 475-485.
3. Howard, M.W., Rizzuto, D.S., Caplan, J.B., Madsen, J.R., Lisman, J., Aschenbrenner-Scheibe, R., Schulze-Bonhage, A., Kahana, M.J. (2003) Gamma oscillations correlate with working memory load in humans. *Cerebral cortex*, **13**, 1369-1374.
4. Povysheva, N.V., Zaitsev, A.V., Rotaru, D.C., Gonzalez-Burgos, G., Lewis, D.A., Krimer, L.S. (2008) Parvalbumin-positive basket interneurons in monkey and rat prefrontal cortex. *Journal of Neurophysiology,* **100**, 2348-2360.

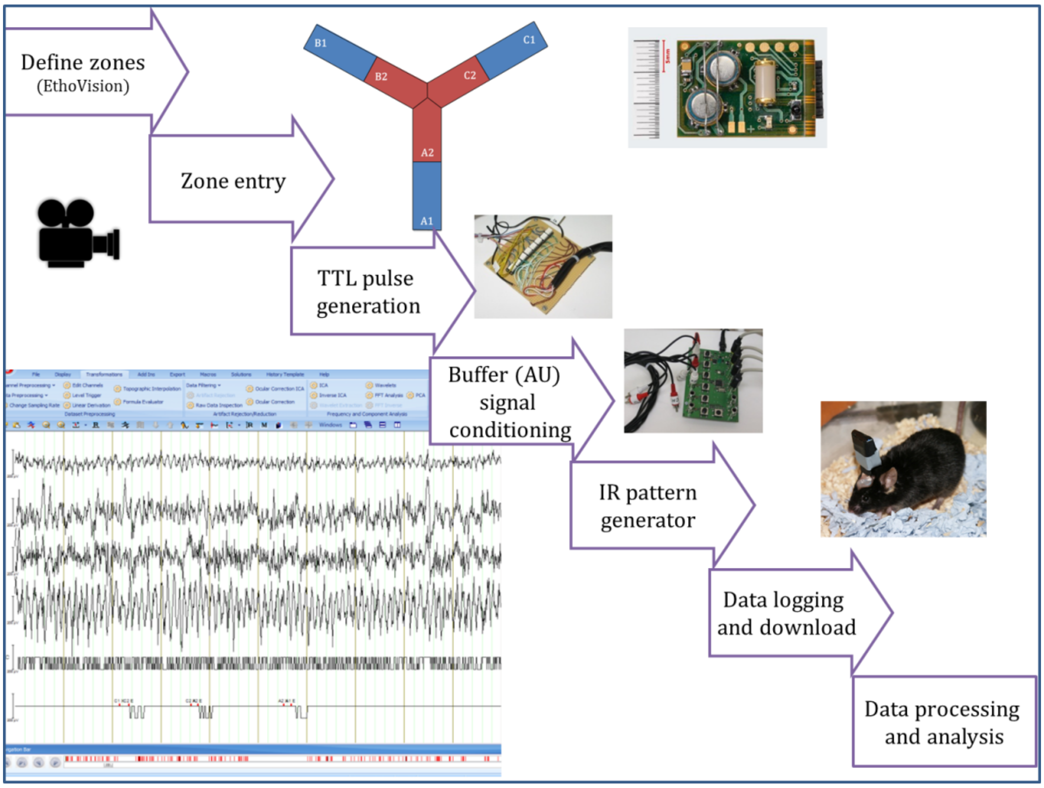

Figure 1. **Behavioral and EEG setup and analysis**.

Outline of stepwise alignment between spatial behavior and physiological observation using a zonal arrangement in the Y-maze (A1-C2) combined with wireless NeuroLogger recording in freely moving mice. For details see text.