Plenary session speech

Neuronal discharges and network oscillations in ictogenesis

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Date: 9/2(Fri) 13:40~14:25
Ph.D. Harvard University
M.D. National Taiwan University

Abstract

The nervous system is a complicated network functionally connected by electric discharges, which could lead to oscillating waves in local field potential (LFP) recordings such as electroencephalography (EEG). Epileptic seizures are brain disorders characterized by distinctive temporospatial patterns of LFP or EEG waves, and exploration of epileptogenesis may provide imperative mechanistic insight into the genesis and consequences of oscillating neural codes. With a basolateral amygdala (BLA) kindling model, we found that the dominant or "natural" frequency of oscillations is in the delta range (1–5 Hz) in BLA in both normal and seizure conditions. Interestingly, multi- and single-unit discharges are clustered into "bursts", more abundant at higher stages of seizures but remain phase-locked to delta oscillations, with the changes in synchrony preceding and outlasting that in discharging units and behaviors. In the cellular level, the rhythmic discharges are collaborating performances of a set of pyramidal and inhibitory neurons (PN and IN), and the rhythmogenic currents are provided by glutamatergic rather than intrinsic cellular pacemaking conductances (e.g. the h currents). In other words, the glutamatergic output of PNs starts a network-based "relay burst mode" of discharges especially in INs, which in turn precondition PNs into a state prone to subsequent burst discharges. PNs and INs could be grouped by synchronized discharges, respectively, and then have alternating activities as well as discernible LFP oscillations if the masses are large enough. Under such circumstances, the burst and interburst intervals will set the basic wavelength for the oscillations in the PN-IN networks, which may entrain one another to make different temporospatial patterns of resonating activities in the system. Seizures thus are erroneous continuums to normal oscillating activities in a network with a built-in synchronizing and resonating nature for information relay.

Selected recent publications:

1. Lo, Y.-T., and Kuo, C.-C. (2019) Temperature dependence of the biophysical mechanisms underlying the inhibition and enhancement effect of amiodarone on hERG channels. Molecular Pharmacology 96:330-344
2. Chou, P, Wang, G-H, Hsieh, S-W, Yang, Y-C, and Kuo, C-C (2020) Delta-frequency augmentation and synchronization in seizure discharges and telencephalic transmission. iScience 23(11):101666
3. Wang, G-H, Chou, P, Hsueh S-W, Yang, Y-C, and Kuo, C-C (2020) Glutamate transmission rather than cellular pacemaking propels excitatory-inhibitory resonance for ictogenesis in amygdala. Neurobiology of Disease 148:105188
4. Lin, Y-C, Lai, Y-C, Chou, P, Hsueh, S-W, Lin, T-H, Huang, C-S, Wang, R-W, Yang, Y-C, and Kuo, C-C (2021) How can a Na+ channel inhibitor ameliorate seizures in Lennox-Gastaut syndrome? Annals of Neurology doi:10.1002/ana.26068
5. Lee, L-N, Huang, C-S, Chuang, H-H, Lai, H-J, Yang, C-K, Yang, Y-C, and Kuo, C-C (2021) An electrophysiological perspective on Parkinson's disease: symptomatic pathogenesis and therapeutic approaches. Journal of Biomedical Science 28:85

Plenary session speech

Piecing together the SLEEP puzzle: from genes to circuitries

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Date: 9/2(Fri) 13:40~14:25
Ph.D.Ohio State University

Abstract

Sleep of sufficient duration, continuity, and intensity is necessary to promote high levels of cognitive performance during the wake period and prevent physiological changes that may predispose individuals to many adverse health outcomes. Sleep insufficiency is prevalent in our society due to the high demand for work, school, and many environmental factors, thus significantly contributing to many health conditions that we are facing. However, the full impact of sleep disruption on our health is certain to be much broader than recognized so far. Interestingly, the biological need for sleep varies dramatically among humans. We have identified a group of humans who require fewer hours of sleep each night and remain healthy for life, and we call them familial natural short sleepers. We have been using human genetics approach to identify genes/mutations that give them this unusual sleep behavior. Mouse models recapitulating human condition, coupled with in vitro molecular and neurocircuitry studies, offer new insight into the underlying mechanisms. Because of the fundamental role that sleep plays in our health, the pathways regulating sleep are intertwined with those regulating other functions. Thus, our method also offers opportunities to investigate how sleep can impact other conditions, including mood, pain, and other disease pathology. Some of these genes/mutations and the mechanistic insight learned from our studies will be presented.

Selected recent publications:

1. Hirano A, Hsu P-K, Zhang L, Xing L, McMahon T, Yamazaki M, Ptacek LJ, Fu Y-H*. DEC2 modulates orexin expression and regulates sleep. Proc Natl Acad Sci USA. 2018 Mar 12.

2. Shi G, Xing L, Wu D, Jones CR, McMahon T, Chong C, Chen J, Coppola, Geschwind D, Krystal A, Ptáček LJ, Fu Y-H*. A rare mutation of β1¬-adrenergic receptor affects sleep/wake behaviors.Neuron 2019 Sep 25;103(6):1044-1055..

3. Xing L, Shi G, Mostovoy Y, Gentry NW, Fan Z, Mcmahon TB, Kwok P-Y, Jones CR, Ptáček LJ, Fu Y-H*. Mutant Neuropeptide S receptor reduces sleep duration with preserved memory consolidation. Sci Transl Med 2019 Oct 16;11(514).

4. Shi G, Yin C, Fan Z, Xing L, Mostovoy Y, Kowk P-Y, Ashbrook LH, Krystal AD, Ptáček LJ, Fu Y-H. Mutations in metabortopic glutamate receptor 1 contribute to natural short sleep trait. Curr Biol 2021 Jan 11;31(1):13-24.

5. Dong Q, GentryNW, McMahonT, YamazakiM, Benitez-RiveraL, WangT, GanL, PtáčekLJ, FuY-H. Familial Natural Short Sleep mutations reduce Alzheimer pathology in mice. iScience 2022 March 15.

Plenary session speech

Gastric vagal afferent signaling to the basolateral amygdala mediates anxiety-like behaviors in mice with experimental colitis

Kuei-Sen Hsu(許桂森)
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Date: 9/2 (Fri.) 13:40~14:25
Ph.D. National Taiwan University

Abstract

Inflammatory bowel disease (IBD) is a relapsing-remitting disorder characterized by chronic inflammation of the gastrointestinal (GI) tract. Anxiety symptoms are commonly observed in IBD patients, but the mechanistic link between IBD and anxiety still remains elusive. In this study, we sought to characterize gut-to-brain signaling and brain circuitry responsible for the pathological expression of anxiety-like behaviors in male dextran sulfate sodium (DSS)-induced experimental colitis mice. We found that DSS-treated mice displayed increased anxiety-like behaviors, which were prevented by the GI vagal afferent ablation. The locus coeruleus (LC) is a relay center connecting the nucleus tractus solitarius to the basolateral amygdala (BLA) in controlling anxiety-like behaviors. Chemogenetic silencing of noradrenergic LC projections to the BLA reduced anxiety-like behaviors in DSS-treated mice. This work expands our understanding of the neural mechanisms by which IBD leads to comorbid anxiety and emphasizes a critical role of gastric vagal afferent signaling in gut-to-brain regulation of emotional states.

Selected recent publications:

1. Lin YT, Chen CC, Huang CC, Nishimori K, Hus KS (2017) Oxytocin stimulates hippocampal neurogenesis via oxytocin receptor expressed in CA3 pyramidal neurons. Nat. Commun. 8:537.

2. LinYT, Hsieh TY, Tsai TC, Chen CC, Huang CC, Hsu KS (2018) Conditional deletion of hippocampal CA2/CA3a oxytocin receptor impairs the persistence of long-term social recognition memory in mice. J. Neurosci. 38(5):1218-1231.

3. YangCY, Yu TH, Wen WL, Lin P, Hus KS (2019) Conditional deletion of CC2D1A reduces hippocampal synaptic plasticity and impairs cognitive function through Rac1 hyperactivation. J. Neurosci. 39(25):4959-4975.

4. LeeIC, Yu TS, Liu WH, Hsu KS (2021) Social transmission and buffering of stress-induced hippocampal metaplasticity in mice. J. Neurosci. 41(6):1317-1330.

5. TsaiTC, Yu TH, Hung YC, Fong LI, Hsu KS (2022) Distinct contribution of granular and agranular divisions of the retrosplenial cortex to remote contextual fear memory retrieval. J. Neurosci. 42(5):877-893.

Plenary session speech

Inflammation in depression: The new frontier of personalised psychiatry

CARMINE MARIA PARIANTE
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NIHR Senior Investigator
Consultant in the Perinatal Psychiatry Liaison Services, King's College Hospital & South London and Maudsley NHS Trust

Date: 9/2 (Fri.) 13:40~14:25
PhD, University of London

Abstract

We will review the recent scientific production in immune-psychiatry from our laboratory and collaborating research groups, spanning from clinical trials to in vitro research. We will discuss what it means to be an "inflamed depressed patients" and what are the best biomarkers to use in order to make clinically relevant decisions.

Selected recent publications:

- Sforzini L, Worrell C, Kose M, Anderson IM, Aouizerate B, Arolt V, Bauer M, Baune BT, Blier P, Cleare AJ, Cowen PJ, Dinan TG, Fagiolini A, Ferrier IN, Hegerl U, Krystal AD, Leboyer M, (…), Pariante CM. A Delphi-method-based consensus guideline for definition of treatment-resistant depression for clinical trials. Mol Psychiatry. 2021 Dec 15. doi: 10.1038/s41380-021-01381-x.
-Pitharouli MC, Hagenaars SP, Glanville KP, …, Pariante CM. Elevated C-Reactive Protein in Patients With Depression, Independent of Genetic, Health, and Psychosocial Factors: Results From the UK Biobank. Am J Psychiatry. 2021 May 14:appiajp202020060947.
- Chang JP, Su KP, Mondelli V, Pariante CM. Cortisol and inflammatory biomarker levels in youths with attention deficit hyperactivity disorder (ADHD): evidence from a systematic review with meta-analysis. Transl Psychiatry. 2021 Aug 19;11(1):430. doi: 10.1038/s41398-021-01550-0.
- Borsini A, Nicolaou A, Camacho-Muñoz D, Pariante CM. Omega-3 polyunsaturated fatty acids protect against inflammation through production of LOX and CYP450 lipid mediators: relevance for major depression and for human hippocampal neurogenesis. Mol Psychiatry. 2021 Jun 16.
-Bind RH, Biaggi A, Bairead A, Du Preez A, Hazelgrove K, Waites F, Conroy S, Dazzan P, Osborne S, Pawlby S, Sethna V, Pariante CM. Mother-infant interaction in women with depression in pregnancy and in women with a history of depression: the Psychiatry Research and Motherhood

Plenary session speech

Data-Driven and Theory-Driven Approaches in Neuroscience

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Okinawa Institute of Science and Technology Graduate University

Date: 9/2(Fri) 13:40~14:25
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Abstract

With the progresses in molecular probe, imaging, sequencing and other technologies, unprecedented amounts of neural data are being produced. Data-driven approaches utilizing statistical machine learning are expected to deliver novel discoveries about how brains are organized and working. However, a data-driven approach alone may not be sufficient for understanding a complex system like the brain; even if we have a complete circuit diagram of a computer chip, understanding its functioning requires the knowledge of arithmetic units, instruction codes, error correction, temperature compensation, and so forth. Theory-driven approaches important in providing possible candidates of computing architectures and the approaches from both directions eventually need to converge for a coherent understanding.

This talk highlights the approaches in both directions in brain science initiatives around the world, including Japan's Brain/MINDS Project, as well as those from my own lab. Topics include utilizing connectome data for brain network modeling, analyzing animal behavior data for understanding the algorithms of decision making, and analyzing two-photon imaging data to address the circuit mechanisms of mental simulation.

Selected recent publications:

1. Doya K (2021). Canonical cortical circuits and the duality of Bayesianinference and optimal control. Current Opinion in Behavioral Sciences, 41, 160-167.
2. Miyazaki K, Miyazaki KW, Sivori G, Yamanaka A, Tanaka KF, Doya K (2020). Serotonergic projections to the orbitofrontal and medial prefrontal cortices differentially modulate waiting for future rewards. Science Advances, 6, eabc7246.
3. Fermin AS, Yoshida T, Yoshimoto J, Ito M, Tanaka SC, Doya K (2016). Model-based action planning involves cortico-cerebellar and basal ganglia networks. Scientific Reports, 6, 31378.
4. Funamizu A, Kuhn B, Doya K (2016). Neural substrate of dynamic Bayesian inference in the cerebral cortex. Nature Neuroscience, 19, 1682–1689.
5. Ito M, Doya K (2015). Distinct neural representation in the dorsolateral, dorsomedial, and ventral parts of the striatum during fixed- and free-choice tasks. Journal of Neuroscience 35:3499-3514.