Abstracts | 33

Speaker 2: Yasumasa Okamoto
Title: The role of serotonin in waiting for future rewards in depression
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Abstract
Serotonin (5-HT) is a major neuromodulator implicated in a broad assortment of behavioral and physiological functions, including aggression, appetite, aversion, behavioral inhibition and impulsivity. The 5-HT system is one of the most important targets for the treatment of depression. It has been difficult, however, to explain the diverse effects of serotonin on adaptive behavior within a unified framework. Based on the review of experimental data and theoretical models, we previously proposed a model in which the function of serotonin is to modulate the value of waiting for a future reward. In this hypothesis, a higher level of 5-HT means a higher setting of the discount factor, which promotes waiting for longer delays. A low level of serotonin is often associated with impulsive behaviors (Doya, 2002). Here, we show a part of the results of a series of research carried out based on the hypothesis.

Human functional magnetic resonance imaging (fMRI) studies show differential involvement of brain areas in the prediction of immediate and delayed rewards, with the dorsal striatum and prefrontal cortex showing consistent activity for delayed rewards (Tanaka et al., 2004). To elucidate the role of serotonin in the evaluation of delayed rewards, we performed an fMRI experiment in which subjects chose either small-immediate or large-delayed rewards under dietary regulation of tryptophan, a precursor of serotonin. The study showed that the dorsal striatal activity correlated with long-term reward prediction was enhanced with the activation of the serotonergic system (Tanaka et al., 2007). From the behavioral data, we found an increase of proportion in small reward choices, together with an increase in the rate of discounting of delayed rewards in the low-serotonin condition compared with the control and high-serotonin conditions (Schweighofer et al., 2008). Recently, we found the attenuated activation in the dorsal striatum during waiting for delayed rewards in depressed patients (Okada et al., in preparation).

To examine any causal relationship between serotonergic activity and waiting behavior for delayed reward, we applied a 5-HT1A receptor agonist locally in the dorsal raphe nucleus (DRN) in rats; this treatment is known to suppress 5-HT neural activity through autoreceptors. Rats performed a sequential food-water navigation task in which they alternately visited food and water sites to acquire rewards after waiting periods. The rats performed the task under two reward conditions: a short delayed reward condition and a long delayed reward condition. We found that the suppression of 5-HT neural activity in the DRN by a 5-HT1A receptor agonist increased premature exit from reward sites before the delivery of delayed rewards, which indicated impaired patience for delayed rewards (Miyazaki et al., 2012).

From both human and animal studies, these results strongly supported our hypothesis that 5-HT promotes waiting for longer delays, and might explain not only impulsive behavior, but also certain aspects of depressive behavior.

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Speaker 3: Zaida Diaz-Cabiale
Title: Galanin and galanin fragment 1–15 modulate antidepressant responses by targeting 5-HT1A-GalR heteroreceptor complexes of the ascending midbrain serotonin pathways
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Abstract
Mood disorders, including depression and anxiety, are among the most prevalent mental illnesses with high socioeconomic impact. Although the underlying mechanisms have not yet been clearly defined in the last decade the importance of the role of neuropeptides, including Galanin (GAL), and/or their receptors in the treatment of stress-related mood disorders is becoming increasingly apparent.