This Week in The Journal

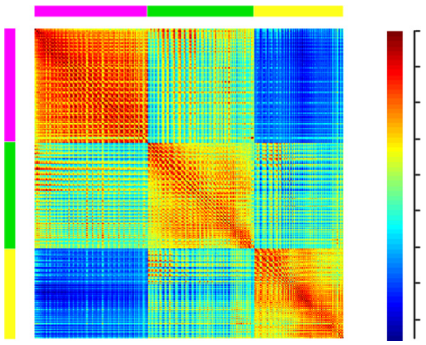
Mapping Motor Cortical Control of Ethological Movements

Riichiro Hira, Shin-Ichiro Terada, Masashi Kondo, and Masanori Matsuzaki

(see pages 13311–13322)

The ability to execute complex movement patterns has allowed animals to acquire critical skills such as tool manipulation. Movements in mammals are characterized as either discrete, in which a limb moves continuously to an endpoint, or rhythmic, like the repetitive movements of locomotion. Spinal subcircuits control these unlearned, so-called ethological movements, which are thought to be modulated by the motor cortex. A question remains in the field: If the motor cortex has zones that emphasize a small repertoire of ethologically relevant movements, then how does the motor cortex handle new, learned movements that don't have an obvious ethological basis?

Hira et al. set out to answer that question by mapping the cortical areas that control both types of movements and determining how they interact with one another. Using transgenic mice that express the light-sensitive protein channelrhodopsin-2 (ChR2) in neurons of the motor cortex, the researchers used prolonged transcranial optogenetic stimulation (pTOS) to activate cortical ChR2 neurons in awake, active mice. Depending on the site of stimulation, pTOS evoked different ethological movements. For example, stimulation of the anterior lateral part of the motor cortex caused mice to reach with the forepaw, which the authors categorized as a discrete movement. Stimulation of the caudal forelimb motor area, in contrast, evoked a circular rhythmic limb movement. When the researchers mapped the movements evoked by stimulation across the motor cortex, they found that the topography devoted to rhythmic movements was sandwiched between areas that control discrete forward and backward movements. Remarkably, when mice were presented with a lever, stimulation of cortex dedicated to rhythmic movement evoked nonrhythmic lever-pulling—a learned behavior that depends on a lever. This finding hints at how the brain uses existing modules for specific ethological movements and adapts them to environmental stimuli to learn new behaviors.



Unsupervised clustering analysis suggests cortical domains that induce forward discrete movement and rhythmic movement were functionally and anatomically distinct. See Hira et al. for details.

Sleep Bidirectionally Regulates Cocaine Craving in Rats

Bo Chen, Yao Wang, Xiaodong Liu, Zheng Liu, Yan Dong, et al.

(see pages 13300–13310)

Cocaine use disrupts sleep time and quality long after drug withdrawal in recovering addicts. After drug is withdrawn from cocaine-exposed rodents, animals intensify their efforts over time to obtain drug; this is called incubation of cocaine craving, and it serves as a model for human craving. Sleep disruption has long been suspected to contribute to drug craving and relapse, but how remains unknown.

Unlike humans, rodents are active in the dark and sleep during the light part of the cycle, but both species experience rapid eye movement (REM) and non-REM (NREM) sleep. To investigate the link between sleep and drug craving, Chen et al. allowed rats to self-administer cocaine for 5 d; 21 d after drug withdrawal, the rats displayed reduced total, REM, and NREM sleep. In humans and rats, preventing sleep during the active cycle—or limiting napping—increases sleep time and quality during the rest cycle. When the authors restricted dark-cycle sleep in the rats, total sleep time and NREM sleep were unaffected, but REM sleep increased significantly, and individual REM episodes lasted longer.

Forty-five days after withdrawal, cocaine-exposed control rats without nap limitation made 60% more attempts to obtain drug than on the first day, indicative of craving incubation. Nap-limited rats, in contrast, were protected from incubation: they showed no significant difference in drug seeking compared to day one.

Previous studies have shown that calcium-permeable AMPA-type glutamate receptors (CP-AMPARs) accumulate in nucleus accumbens (NAc) synapses following cocaine withdrawal and are necessary for incubation of craving (Conrad et al., 2008, Nature 454:118). Accordingly, electrophysiological recordings in control rats from the NAc contained significant currents through CP-AMPARs following cocaine exposure, but not in the rats that were nap-limited, demonstrating a correlation between sleep and accumulation of the calcium channels.

Conversely, another group of rats in which sleep was disrupted around the clock displayed craving incubation about 3 weeks earlier than control rats, suggesting that sleep disruption accelerates incubation (though craving behavior was similar in the two groups at 45 d). Similarly, CP-AMPAR currents were detectable sooner (day 22) in the sleep-disrupted rats than in control rats, but were comparable once incubation had developed in control rats (day 45).

Thus, sleep appears to regulate behavioral and molecular aspects of cocaine craving bidirectionally in rats. The findings hint that sleep-based therapies might aid addiction recovery.

This Week in The Journal is written by Stephani Sutherland, Ph.D.