169.06 / BBB4 - A modification of the platform-mediated avoidance task to study food-avoidance conflict.

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Abstract

Previous work from our group has shown that rats learn to avoid foot-shocks by stepping onto a platform when they are exposed to a 30s tone that co-terminates with a 2s shock (Bravo-Rivera C et al., 2014). In this platform-mediated avoidance task, rats continually press a lever to receive a sucrose pellet delivered on a variable interval schedule. Avoidance comes at a cost because the lever cannot be reached from the platform. This cost is minimal, however, because food is also available during the inter-tone intervals. In our modified task, we increased the food-avoidance conflict by limiting food availability to the tone period only. Food availability was signaled by a light co-occurring with the 30s tone. After 16 training sessions, most rats (44/60, 73%) learned to divided their time between pressing for food (avg 24% of time) and avoiding (avg 51% of time). Moreover, we observed two additional subgroups: an avoidance preferring group (6/60, 10%) showing virtually no pressing for food (<5% time) coupled with excessive avoidance (avg 96%), and a food-preferring group (10/60, 17%) that spent excessive time pressing (>50%) coupled with minimal avoidance (avg 28%). Thus, increasing the conflict in the platform-mediated avoidance task reveals three subgroups showing different motivational drives. We are analyzing neural activity with cFos to reveal structures that could mediate these behavioral strategies.

455.03 / JJJ19 - Opposing inhibition in prelimbic prefrontal neurons impairs active avoidance

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Abstract

It has been previously demonstrated that pharmacological inactivation of prelimbic prefrontal cortex (PL) with muscimol prevents the expression of platform-mediated avoidance in response to a conditioned tone (Bravo-Rivera, et al., 2014). Last year, we reported that optogenetically silencing PL using Archaerhodopsin (Arch) during the tone delayed but did not prevent avoidance (Diehl et al., 2015 SFN abstract). A possible reason for this discrepancy is that muscimol inactivates all cell types, whereas Arch containing the CaMKIIa promoter preferentially targets glutamatergic neurons. PL neurons recorded during this task showed both excitatory and inhibitory responses to the tone, but only inhibitory responses were correlated with avoidance (Bravo-Rivera, et al., 2014 SFN abstract). PL neurons exhibiting inhibitory tone responses in avoidance were classified as excitatory neurons, based on low baseline firing rate (<15 Hz) and broad spike width (>225 μs; Sotres-Bayon, et al, 2012). This suggests that inhibition of PL glutamatergic neurons may be key for avoidance responses. To test this hypothesis, we used channelrhodopsin (AAV-CaMkII-hChR2(H134R)-eYFP) to prevent tone-induced inhibition of glutamatergic neurons in PL. We stimulated during the tone at a rate of 4Hz, which is the average spontaneous firing rate of PL neurons (Burgos-Robles, et al., 2009). Photoactivation of rostral PL neurons blocked avoidance throughout the tone compared to eYFP controls (rPL-ChR2=17.5% time on platform n=5, eYFP=89.9% n=6, $p<0.01$). In contrast, photoactivation of caudal PL neurons had no effect on avoidance (cPL-ChR2=86.5% n=3, eYFP=89.9% n=6, $p=0.38$). The present findings suggest that inhibitory tone responses in rostral PL are essential for the expression of platform-mediated avoidance. Inhibition of PL glutamatergic neurons could serve to disinhibit neurons in striatum to drive avoidance, similar to disinhibition of basolateral amygdala SOM+ cells during fear conditioning (Wolff et al, 2014).

564.03 - Prefrontal-striatal control of active avoidance

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Abstract

In order to compare Pavlovian fear conditioning and active avoidance, we made a minor modification to our auditory fear conditioning task in which rats pressing a bar for food learn to freeze to a 30-sec tone that co-terminates with footshock. In the modification, rats can avoid the shock by stepping onto a platform located on the opposite side of chamber to wait out the tone. In platform-mediated avoidance, pharmacological inactivation of the BLA blocks both avoidance and freezing, consistent with a loss of tone-shock association. In contrast, inactivation of the prelimbic (PL) cortex or ventral striatum impairs avoidance but leaves freezing intact, suggesting a loss of the avoidance "option". This differs from fear conditioning in which PL inactivation reduces freezing and VS inactivation has no effect. Silencing PL neurons during the tone with archaerhodopsin delays, but does not prevent, avoidance, suggesting that lower circuits are recruited as the tone progresses. Extinction of platform-mediated avoidance depends on infralimbic (IL) cortex, and requires BDNFergic input to IL from the ventral hippocampus, but not from BLA. Rats exhibiting persistent avoidance outlasting extinction show excessive activity in PL and VS, and reduced activity in IL, resembling the profile of human homologues in PTSD. Persistent avoidance can be reversed with either inactivation of lateral orbital cortex, or deep brain stimulation of VS, resembling the profile observed in OCD.