Program#/Poster#: 259.11/Y42

Presentation Title: Infralimbic BDNF regulates extinction of active avoidance

Location: Hall A

Presentation time: Sunday, Oct 18, 2015, 1:00 PM - 5:00 PM

Presenter at Poster: Sun, Oct. 18, 2015, 3:00 PM - 4:00 PM

Topic: ++F.03.g. Motivation and emotions: Fear, anxiety, and pain

Authors: ***L. E. ROSAS-VIDAL**, W. A. RAMOS-GUASP, G. J. QUIRK; Psychiatry and Anat. & Neurobio., Univ. of Puerto Rico, San Juan, PR

Abstract: The infralimbic prefrontal cortex (IL) is necessary for fear extinction (Do-Monte et al., 2015) as well as the extinction of platform-mediated avoidance (Bravo-Rivera et al., 2014). Brain-derived neurotrophic factor (BDNF) is necessary for synaptic plasticity underlying learning and memory processes. We recently reported that blocking extracellular BDNF in IL during fear extinction training impairs its acquisition and recall (Rosas-Vidal et al., 2014). Here we show that blocking extracellular BDNF in IL during avoidance extinction training had no effect on the acquisition of extinction (Sal, n= 12; anti-BDNF, n= 13; p= 0.609), but impaired the recall of avoidance extinction the next day (p< 0.001). Using immunohistochemistry to measure neuronal BDNF, we found that avoidance extinction did not increase BDNF in IL neurons (p=0.61; No-Ext., n= 5; Ext., n= 8), suggesting that BDNF in IL may be released by inputs from the ventral hippocampus (vHPC) and/or the basal amygdala (BA), both of which show increased neuronal BDNF after fear extinction (Chhatwal et al., 2006; Rosas-Vidal et al., 2014). Accordingly, avoidance extinction increased neuronal BDNF in vHPC (p= 0.004) and mediodorsal thalamus (MD; p=0.049), but not BA (p=0.99). Our findings suggest that avoidance extinction may depend on BDNFergic inputs to IL from the vHPC and MD, rather than from BA.

Program#/Poster#: 259.12/Y43

Presentation Title: Optogenetic silencing of prelimbic cortex in active avoidance

Location: Hall A

Presentation time: Sunday, Oct 18, 2015, 1:00 PM - 5:00 PM

Presenter at Poster: Sun, Oct. 18, 2015, 4:00 PM - 5:00 PM

Topic: ++F.03.g. Motivation and emotions: Fear, anxiety, and pain

Authors: *M. M. DIEHL, J. RODRÍGUEZ-ROMAGUERA, P. A. PAGÁN-RIVERA, G. J. QUIRK;
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Abstract: We previously showed that pharmacological inactivation of prelimbic prefrontal cortex (PL) with muscimol impairs the expression of platform-mediated avoidance in response to a conditioned tone (Bravo-Rivera, et al., 2014). Here, we used an optogenetic approach to silence PL glutamatergic neurons only during the tone period, in rats trained in our avoidance task. Silencing PL somata with archaerhodopsin (CaMKIIα-eArchT3.0) during the entire 30 sec tone did not block avoidance, as most rats had moved to the platform by the final 2 sec (n=9/9 eYFP controls, n=12/15 Arch, p=0.27). However, PL silencing decreased the amount of time rats spent on the platform (eYFP=90%, Arch=49%, p=0.002), suggesting that silencing PL delayed platform mounting. In agreement with this, Arch increased the latency to mount the platform (eYFP=4.8s, Arch=11.6s, p=0.03). This delay in mounting was not due to a decrease in fear, as freezing (p=0.96) and bar press suppression (p=0.22) were unaffected. This suggests that PL glutamatergic activity accelerates, but may not be necessary for, avoidance responses. We next wanted to assess whether silencing PL during specific time periods within the tone presentation would also affect platform mounting. We have previously reported that PL neurons exhibit responses to both tone onset and platform mounting in this task (Bravo-Rivera, et al., 2014 SFN abstract). We therefore assessed if silencing PL during platform mounting (typically 3 to 20 sec after tone onset) would also delay mounting. Our preliminary data (Arch n=7, eYFP n=3) show that silencing 3-20 sec during the tone did not delay platform

mounting (eYFP=83%, Arch=79%, p=0.45), suggesting that the initial tone response (0-3 sec) may be important for accelerating avoidance, a hypothesis we are currently testing.

Program#/Poster#: 538.06/BB80

Presentation Title: Low-frequency deep brain stimulation of the ventral striatum facilitates the extinction of morphine place preference

Location: Hall A

Presentation time: Tuesday, Oct 20, 2015, 8:00 AM -12:00 PM

Presenter at Poster: Tue, Oct. 20, 2015, 9:00 AM - 10:00 AM

Topic: ++F.03.h. Motivation and emotions: Reward

Authors: ***F. J. MARTINEZ**[1], J. RODRIGUEZ-ROMAGUERA[1,2], M. E. LLORET-TORRES[1], J. M. MIRANDA-FAJARDO[1], F. H. DO MONTE[1,2], G. J. QUIRK[1,2], J. L. BARRETO-ESTRADA[1]; [1]Anat. and Neurobio., Univ. of Puerto Rico, Med. Sci. Campus, San Juan, PR; [2]Psychiatry, Univ. of Puerto Rico, Med. Sci. Campus, San Juan, Puerto Rico

Abstract: Recently, research in humans and rodents has indicated that DBS of the ventral striatum (VS) may be an effective treatment for drug addiction (Luigjes et al., 2012). However, we recently found in rats that high-frequency DBS (HF-DBS) of the VS impaired extinction of morphine-induced conditioned place preference (CPP; Martinez-Rivera et al., SFN 2013). Furthermore, low-frequency DBS (LF-DBS) has also been suggested as a treatment of neuropsychiatric disorders in humans (Hernando et al., 2008). In rats, LF-DBS of the VS attenuated cocaine sensitization (Creed et al., 2015) and relapse (Hamilton et al., 2014). However, no studies have applied LF-DBS of the VS during the extinction of drug-associated memories. In this study, we examined whether LF-DBS of the VS facilitates the extinction of morphine-CPP. Rats were implanted with DBS electrodes in the VS and conditioned to prefer a side paired with morphine. Subsequently, rats expressing morphine-CPP received extinction sessions, together with 60 min of LF-DBS (20 Hz) or sham stimulation. Our results showed that

LF-DBS of the VS had no effect during extinction training, but strengthened extinction memory when tested 2 days (p=0.005) or 9 days (p=0.04) after stimulation was turned off. In addition, LF-DBS increased c-Fos immunolabeling in the infralimbic cortex (p=0.03) and medial portion of central amygdala (p=0.04), key regions in the extinction of drug seeking behaviors (Gass and Chandler, 2013). Our results support the idea that LF-DBS (rather than HF-DBS) of the VS represents a possible therapy for treatment-resistant opioid addicted patients, who undergo extinction-based therapies.

Program#/Poster#: 723.20/AA31

Presentation Title: The paraventricular nucleus of the thalamus regulates cued food-seeking during reward omission

Location: Hall A

Presentation time: Wednesday, Oct 21, 2015, 8:00 AM -12:00 PM

Presenter at Poster: Wed, Oct. 21, 2015, 11:00 AM - 12:00 PM

Topic: ++F.02.c. Appetitive and incentive learning and memory

Authors: ***F. H. DO MONTE**, A. M. MINIER-TORIBIO, G. J. QUIRK; Psychiatry and Anat. & Neurobio., Univ. of Puerto Rico, San Juan, PR

Abstract: Recent studies have shown that the paraventricular nucleus of the thalamus (PVT) is a key region for retrieval of well-consolidated fear memories. Particularly, silencing of PVT projections to the central nucleus of the amygdala (CeA) impairs both retrieval and maintenance of cue-associated fear memories (Do Monte et al, 2015; Penzo et al 2015). Studies have also implicated PVT in cue-associated reward memories (Haight and Flagel, 2014; Matzeu et al., 2014). Here, we sought to understand the role of PVT and its projections in cued food-seeking. We used a reward conditioning task in which rats learned that each bar press in the presence of a light cue delivered a sugar pellet into a nearby dish. We therefore

manipulated PVT activity under two conditions: 1) when food was available during the cue (positive outcome), or 2) when food was omitted during the cue (negative outcome). Inactivation of the anterior PVT, but not the posterior PVT, with fluorescently labeled muscimol increased pressing when food was omitted (aPVT Sal: 26.6 presses/min, n= 9, aPVT Mus: 40.8 presses/min, n= 5; p= 0.015). To assess the role of PVT projections to CeA during positive vs. negative outcomes, we used an optogenetic approach (halorhodopsin, AAV5:CaMKIIa::eNpHR3.0-eYFP) to specifically silence PVT terminals in CeA during the cue presentation. Silencing of PVT-CeA projections reduced pressing during the cue when the food was omitted (eYFP-Control: 21 presses/min, n= 8, NpHR-eYFP: 13.1 presses/min, n= 8; p< 0.001), but not when the food was available (p= 0.88). Our findings suggest that distinct antero-posterior subregions of PVT regulate food-seeking during negative states induced by food omission. We are currently examining PVT projections to nucleus accumbens, a region involved in reward.