IN BRIEF…

Integration of stimuli from across the primate hand

JL Reed, P Pouget, HX Qi, Z Zhou, MR Bernard, **MJ Burish**, J Haitas, AB Bonds and JH Kaas (2008). Widespread spatial integration in primary somatosensory cortex. *PNAS USA*. **105** (29): 10233-10237.

Tactile sensation and discrimination are critical functions of the primate hand, yet the integration of signals from the many sensory neurons in the hand is not well understood. Here, the authors provided evidence for widespread sensory input integration in the brain of the owl monkey, *Aotus trivirgatus*. While small minimal receptive fields in monkey primary somatosensory cortex area 3b are important for stimulus localization, the results in this study indicate that integration in area 3b can also span beyond these small receptive fields. Information is integrated not only within digits, but across the hand in a type of global stimulus processing.

Addiction, extinction and not the α_2-adrenergic receptor

AR Davis, AD Shields, JL Brigman, M Norcross, **ZA McElligott**, A Holmes and DG Winder (2008). Yohimbine impairs extinction of cocaine-conditioned place preference in an α2-adrenergic receptor independent process. *Learning Memory*. **15**: 667-676.

Extinction of learned place preference and drug addiction is poorly understood. In this study, the authors investigated the role of the α_2-adrenergic receptor (α_2-AR) in extinction of cocaine-conditioned place preference (CPP) using the α_2-AR antagonist yohimbine in behavioral and electrophysiological tests. The authors reported that yohimbine impaired cocaine CPP similarly in α_2-AR knockout mice and wildtype mice. Because these effects of yohimbine, a relatively dirty drug, were not seen with a more selective α_2-AR antagonist, atipamezole, and because yohimbine produced an electrophysiological depression of glutamatergic signaling in the bed nucleus of the stria terminalis that was also not seen with atipamezole, the authors suggest that the effects of yohimbine on cocaine CPP are independent of α_2-AR.

Getting the Dopamine Rush

DH Zald, RL Cowan, P Riccardi, RM Baldwin, MS Ansari, R Li, ES Shelby, CE Smith, **M McHugo** and RM Kessler (2008). Midbrain Dopamine Receptor Availability Is Inversely Associated with Novelty-Seeking Traits in Humans. *J. Neurosci*. **28** (53): 14372-14378.

Novelty-seeking behaviors are a great predictor for tendency towards drug abuse in that both novelty-seeking and addiction involve dopamine stimulation of reward centers in the brain. In this study, the authors correlated D_2-like (D_2 and D_3) dopamine autoreceptor availability in the midbrain of human subjects using [^{18}F]fallypride, a specific radiolabeled agonist. Human subjects were given a novelty-seeking questionnaire, and then scanned using positron emission tomography. The authors found an inverse relationship between D_2-like receptor availability in the midbrain of subjects and their tendency towards novelty-seeking behavior, leading the authors to speculate that novelty-seekers may be self-medicating by causing the release of dopamine in response to thrills and novel environments.

DAT Leak: A link to ADHD?

The dopaminergic system has long been thought to be involved in the etiology of attention-deficit hyperactivity disorder (ADHD). The dopamine transporter (DAT), as a target for ADHD medication, has been characterized for common genetic variants, and yielded several interesting targets for further study. In a paper published recently in the *Journal of Neuroscience* (and later featured as an "Editor's Choice" in *Science*), a team of neuroscientists at Vanderbilt University characterized the human dopamine transporter (hDAT; *SLC6A3*) containing an A559V mutation.

Mazei-Robison *et al*. expressed the hDAT A559V mutation in HEK-293T and found that overall protein expression and cell-surface expression were similar to wildtype hDAT. Using amperometry, the authors found that while levels of dopamine uptake in these cells was comparable to wildtype hDAT, efflux of dopamine was 300% normal. Combining amperometry with whole-cell patch-clamp recording, the authors also found that hDAT A559V exhibited increased sensitivity to intracellular Na^+ which contributed to greater dopamine efflux when depolarized.

Perhaps the most intriguing result from this study was the author's finding that dopamine efflux through hDAT A559V could be blocked by amphetamine (AMPH), which normally enhances dopamine efflux in wildtype hDAT. Because this mutation was originally identified in two male probands with ADHD that were treated with AMPH, this unexpected result suggests a possible mechanism for the efficacy of AMPH as a treatment. Furthermore, the authors found that baseline dopamine efflux in hDAT A559V mimicked the level of efflux seen in AMPH-treated wildtype hDAT. These data strongly suggest that dopamine efflux may be linked to ADHD in a heritable manner, and provide a specific target for further research into therapeutics for the disorder.

Original Research Article:
MS Mazei-Robison, **E Bowton**, M Holy, M Schmudermaier, M Freissmuth, HH Sitte, A Galli and RD Blakely (2008). Anomalous Dopamine Release Associated with a Human Dopamine Transporter Coding Variant. *J. Neurosci*. **28** (28): 7040-7046.