Name: Marta Pratelli
PI Name: Nicholas Spitzer

Email: mpratelli@ucsd.edu
PI Email: nspitzer@ucsd.edu

Methamphetamine Induces Switching Neurotransmitter in Multiple Brain Regions

Marta Pratelli[1,2], Celia Fredman[1,2], Milana Withee[1,2], Lucia Wu[1,2], David Alvarez[1,2], Nicholas C. Spitzer[1,2]

[1]Neurobiology Department, University of California San Diego;
[2]Kavli Institute for Brain and Mind; University of California San Diego

Methamphetamine (METH) is one of the most commonly misused stimulants worldwide. Understanding the breath and relevance of METH-induced maladaptive neuroplasticity is essential to addressing the consequences of this misuse. We recently found that repeated exposure to METH induces ~600 neurons in the prelimbic cortex to switch from a glutamatergic to a GABAergic transmitter phenotype, in an activity-dependent manner, generating cognitive deficits. Since METH causes a widespread increase in neuronal activity, we hypothesized that it could induce neurotransmitter switching in other regions of the brain.

To explore this hypothesis, we generated a VGATFLP::VGLUT2CRE::TdTomatocON/fON reporter mouse line in which neurons that express or have expressed both the GABAergic marker VGAT and the glutamatergic marker VGLUT2, even if not necessarily at the same time, are permanently labeled with TdTomato. We found that a 10-day treatment with METH increased the number of TdTomato-labelled neurons, as compared to control, by more than 10,000 in each of 4 brain regions, and to a lesser extent in other regions. This result suggests that multiple changes in transmitter expression have occurred as a result of METH exposure. We are now using in situ hybridization and morphological analysis to determine the transmitter phenotype expressed by TdTomato+ neurons and identify the cell-type to which they originally belonged.

These ongoing studies are enabling an unprecedented understanding of the extent to which the use of METH can affect the neuron's transmitter phenotype and will provide the basis for future investigations into the behavioral effects of these changes.