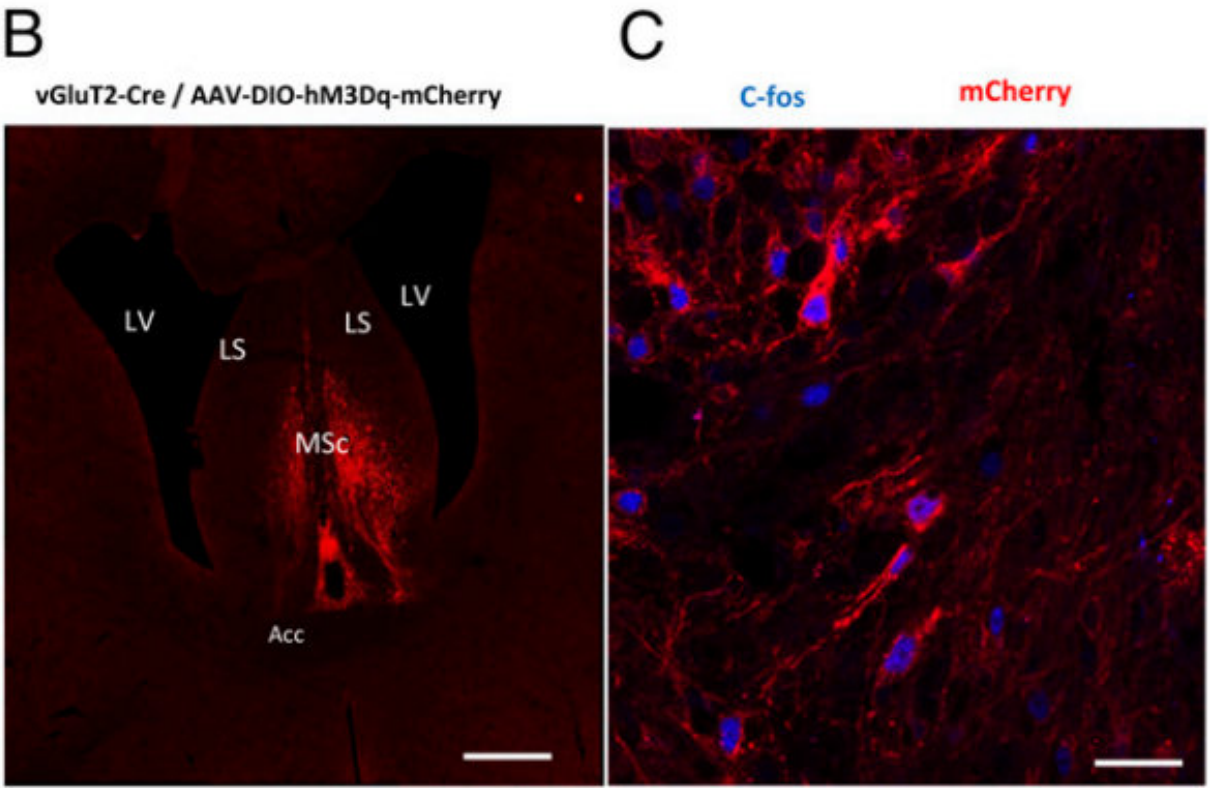
Activating MSc glutamatergic neurons found to cause mice to eat less

December 13 2017, by Bob Yirka



DREADD-based activation of MSc vGluT2 neurons. (B) Representative image of Cre-dependent expression of hM3Dq in MSc vGluT2 neurons. (C) Sample image showing overlap of hM3Dq-mCherry and c-fos in MSc vGluT2 neurons. I.p. injections of CNO were administered before perfusion to selectively activate MSc vGluT2 neurons. Credit: (c) *Proceedings of the National Academy of Sciences* (2017). DOI: 10.1073/pnas.1707228114

(Medical Xpress)—A trio of researchers working at the State University of New York has found that artificially stimulating neurons that exist in the medial septal complex in mouse brains caused test mice to eat less. In their paper published in *Proceedings of the National Academy of Sciences*, Patrick Sweeney, Changhong Li and Yunlei Yang describe experiments they carried out with mice and what their findings may represent for future studies aimed at controlling overeating in humans.

As the researchers note, humans and other animals eat even when they are not hungry—other factors besides hunger pangs cause us to reach for that mid-afternoon snack. Prior research has found evidence that suggests such actions are emotionally based. Prior research has also found that the septal nucleus, a limbic brain structure, plays a role in processing stress-related events, including those associated with aggression. In this new effort, the researchers sought to determine if there might be a link between firing nerve cells in this region and the urge to eat. To learn more, they studied lab mice, which are known to overeat when stressed.

The experiments consisted of injecting test mice with a designer drug known as agonist clozapine-N-oxide to activate the targeted neurons—prior research showed that such drugs cause some of the nerve cells in the medial septal complex to express glutamate when they fire. A control group was injected with saline solution.

The researchers report that giving the mice drugs to stimulate production of glutamate in their brains caused them to eat less than half as much food as the control group. Further testing showed that the reduction in eating occurred during both day and night cycles, suggesting that the drug had reduced eating related to non-hunger events. Intrigued by their findings, the trio gave the mice loss-of-function tests to determine if giving them the drugs had caused any obvious physical side effects. They report that they found no sign of such side effects. Then, to figure out if

the reduction in eating was indirectly due to changes in locomotion or levels of anxiety, the researchers conducted multiple behavioral tests. They report no significant differences between the test and control mice.

More research will have to be done, of course, before it can be shown that giving similar drugs to humans might help reduce overeating.

More information: Patrick Sweeney et al. Appetite suppressive role of medial septal glutamatergic neurons, *Proceedings of the National Academy of Sciences* (2017). DOI: 10.1073/pnas.1707228114

Abstract
Feeding behavior is controlled by diverse neurons and neural circuits primarily concentrated in the hypothalamus and hindbrain in mammals. In this study, by using chemo/optogenetic techniques along with feeding assays, we investigate how neurons within the medial septal complex (MSc), a brain area implicated in emotion and cognition, contribute to food intake. We find that chemo/optogenetic activation of MSc glutamatergic neurons profoundly reduces food intake during both light and dark periods of the rodent light cycle. Furthermore, we find that selective activation of MSc glutamatergic projections in paraventricular hypothalamus (PVH) reduces food intake, suggesting that MSc glutamatergic neurons suppress feeding by activating downstream neurons in the PVH. Open-field behavioral assays reveal that these neurons do not overtly affect anxiety levels and locomotion. Collectively, our findings demonstrate that septal glutamatergic neurons exert anorexigenic effects by projecting to the PVH without affecting anxiety and physical activities.