Long-term effects of olfactory bulbectomy on open field hyperactivity in rats *Breuer ME*, Groenink L, Westenberg HW*, Olivier B Department of Psychopharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht *Rudolf Magnus Institute for Neurosciences, Utrecht

There are currently several animal models in existence that are useful for depression and anxiety testing. However, the olfactory bulbectomy (OBX) model in rats is one of the most valid models for both of these disorders. Removal of the olfactory bulbs results in several physiological and behavioral alterations that are favorable in depression/anxiety paradigms as the lesion often results in hyper-reactivity as well as neuroendocrine and immunological changes, reminiscent of those observed in anxiety and depression. Serotonin turnover in the hippocampus of bulbectomized rats is significantly reduced after 2 weeks as well as after 6 months. It can therefore be hypothesized that olfactory bulbectomy is not only an acute depression/anxiety animal model but also has implications as a chronic model for affective disorders. This paradigm allows us to study the effects of long-term alterations in the central nervous system, which is essential when studying pathophysiology of affective disorders. One of the most striking results of the olfactory bulbectomy is hyperactivity in the open field, perhaps due to increased striatal glutamate release in response to stress in the OBX rat brain. Increased activity has long been shown to be an acute symptom after olfactory bulbectomy, but the present study also shows that hyperactivity is a chronic symptom We tested a total of 29 rats in the open field (N= 15 sham, N= 14 OBX) one week prior to surgery to establish baseline activity levels. A second open field was performed two weeks after the surgery, and again 10 and 16 weeks later. Contrary to prior findings, OBX rats were significantly more active than shams not only during the first ten minutes, but also twenty and thirty minutes later. Future experiments will further examine the effects of long-term alterations in the central nervous system to improve the knowledge of the mechanisms of psychoactive drugs, using the open field paradigm among other tests.

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Preferred poster session: Cognition and Behavioral Neuroscience on Friday 4 June.