

## Concerns about the antidepressant-like effects of high-dose ketamine in mice

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We read with great interest the recent article *CD-1 and Balb/cJ mice do not show enduring antidepressant-like effects of ketamine in tests of acute antidepressant efficacy* by Bechtholt-Gompf et al. (in press). In that study, the tail suspension test (TST) and forced swimming test (FST) were not sensitive to long-lasting antidepressant-like effects of ketamine in mice. We appreciate this study and would like to discuss an issue relevant to this article.

The authors administered high-dose ketamine to observe the behavioral changes in the FST and TST. However, the administration of ketamine 25 mg/kg induces an immediate behavioral activation, characterized by hyperlocomotion, stereotypies, and ataxia in rats (Razoux et al. 2007), suggesting that ketamine exceeding 25 mg/kg tends to elicit schizophrenia-like manifestations. Similarly, in that study, the authors did not investigate the motor behavior before FST and TST. Although a citation was provided by the authors in the discussion that the effective dose (10, 50 mg/kg) of ketamine, instead of high dose, did not affect general locomotor activity, in either the plus-maze or the open field test (Engin et al. 2009). On the other hand, low-dose

ketamine was commonly used to investigate its antidepressant effect in experimental studies and was recommended to ameliorate the symptoms of patients with depression (Machado-Vieira et al. 2009). Thus, we assumed that high-dose ketamine may be not very suitable to investigate its antidepressant effect.

### References

- Bechtholt-Gompf AJ, Smith KL, John CS, Kang HH, Carlezon WA Jr, Cohen BM, Ongür D (2011) CD-1 and Balb/cJ mice do not show enduring antidepressant-like effects of ketamine in tests of acute antidepressant efficacy. *Psychopharmacology (Berl)* (in press)
- Engin E, Treit D, Dickson CT (2009) Anxiolytic- and antidepressant-like properties of ketamine in behavioral and neurophysiological animal models. *Neuroscience* 161:359–369
- Machado-Vieira R, Salvadore G, Diazgranados N, Zarate CA Jr (2009) Ketamine and the next generation of antidepressants with a rapid onset of action. *Pharmacol Ther* 123:143–150
- Razoux F, Garcia R, Léna I (2007) Ketamine, at a dose that disrupts motor behavior and latent inhibition, enhances prefrontal cortex synaptic efficacy and glutamate release in the nucleus accumbens. *Neuropsychopharmacology* 32:719–727

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