

Effects of chronic administration of the glutamate NMDA receptor antagonist memantine on food intake and body weight

RS Bains, D Cheung, IS Ebenezer. University of Portsmouth, Portsmouth, UK

It has been previously reported that chronic administration of the glutamate (glu) NMDA receptor antagonist 2-amino-5-phosphonovalerate (D-APV5) into the lateral hypothalamus (LH) suppresses daily food intake and decreases body weight in rats (see Stanley et al., 2011). In the present study we investigate the effects of chronic systemic administration of the NMDA receptor antagonist memantine (mem) on 24 h food consumption and body weight in rats.

Adult male Wistar rats (n = 16; starting body weights: 300 – 360 g) were divided into 2 equal groups and injected i.p. with either saline (Group 1) or mem (4 mg kg⁻¹; Group 2) on a daily basis for 30 days. The dose of mem used in this study was previously found to reduce acute food intake in rats (Bains et al., unpublished results). Following the 1st, 8th and 15th injection, the rats were placed separately into experimental cages with free access to food and water and cumulative food intake measured at 24h. Daily body weight for each rat was also recorded and expressed as the percentage change relative to body weight on treatment Day 1. The body weight data were analysed by ANOVA and the 24h food intake data by the Student's t-test. The results show that mem (4 mg / kg, i.p.) had no significant effects on (i) body weight gain (see Fig. 1) and (ii) 24h food consumption. Thus, for example, the mean \pm s.e. mean 24h food intake after the 15th injection was as follows: saline 23.9 \pm 1.3g, mem 20.0 \pm 3.4g, n.s).

Mem is used clinically in the treatment of Alzheimer's disease and it was of interest to examine the effects on chronic administration of the drug on food intake and body weight, given that hypophagia and weight loss is characteristic of this condition as it progresses. The present results indicate that chronic administration of mem does not affect daily food consumption and body weight. However, given the possible differences in the pharmacokinetic profile of the drug in rat and man, it may be prudent to carry out further experiments in rats using daily multiple dosing schedules before reaching any potential translational conclusions about the effects of the drug on long term food intake and body weight.

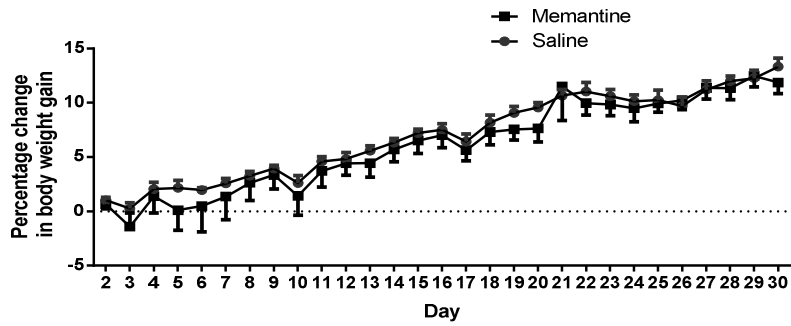


Fig. 1 Effects of memantine on body weight gain.
Vertical Line rep +/- s.e.mean.

Stanley, B.G et al. (2011) *Physiol. Behav.* 104, 40 – 46.

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