Dose-related effects of intraperitoneal administration of memantine on food intake in non-deprived and fasted rats

Alzheimer's disease (AD) is associated with hypophagia and weight loss. The non-competitive NMDA receptor antagonist memantine (mem) is used clinically in the treatment of AD. However, there is a paucity of information on how this agent may affect food intake. It has been previously shown that NMDA receptor antagonists given centrally suppress food consumption in rats (1) The present study was undertaken to investigate the effects of ip administration of mem on food intake in free-feeding and fasted rats.

Expt. 1. Non-deprived adult male Wistar rats (n=8; b.wt. 340 - 430g) were injected with either physiological saline solution or mem (2 – 8 mg kg^{-1}; i.p.) in a repeated measured design and placed separately in experimental cages with free access to food and water for 2h. Food intake was measured, as described previously (2); 2 – 3 days separated successive trials. Expt. 2. Male Wistar rats (n=8; b.wt. 320 – 420g) that were fasted in their home cages for 22h each day were injected with either saline or mem (1 – 8 mg kg^{-1}, i.p.) in a repeated measures design and food intake measured as described for Expt. 1. Food intake data for each experiment were analysed by ANOVA and the *post-hoc* Tukey test.

The results for Expt. 1 (see Fig.1A) show that mem reduced food intake in non-deprived rats in a dose-related manner, with the 4 and 8 mg kg^{-1} doses producing significant reductions in consumption. Fig. 1B illustrates the results for Expt. 2. Mem also reduced intake in fasted rats, with the 4 and 8 $mgkg^{-1}$doses producing significant reductions in food consumption. The results of this study show that mem decreases food intake in both free-feeding (non-deprived) and fasted rats in a dose-dependent manner. The doses that suppressed feeding are similar to those used clinically for the treatment of AD. The data thus indicate that the time when memis taken may be an important factor to consider when treating AD. Thus, for example, taking mem just prior to eating a meal may exacerbate the hypophagia associated with the condition. Thus, clinical trials to investigate such scenarios appear to be warranted, although it is noteworthy that chronic administration of mem does not affect daily (24h) food consumption and body weight in free-feeding rats (Bains and Ebenezer, this meeting).

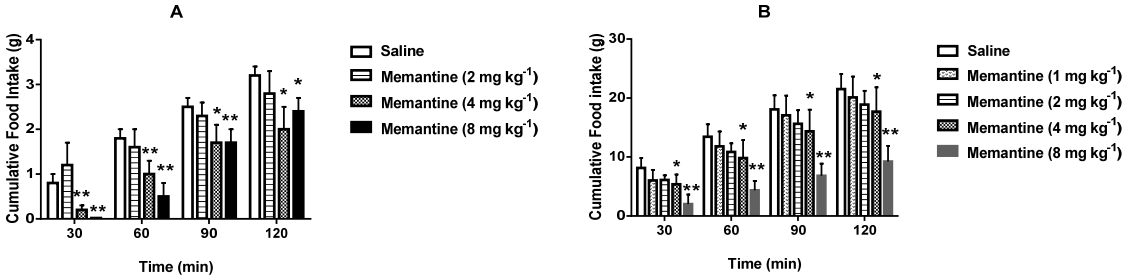

Figure 1. The effects of memantine on food intake in (A) non-deprived and (B) fasted rats. Vertical line rep. + s.e.mean. *P<0.05, **P<0.01

(1) Stanley, B.G. *et al.* (2011) PhysiolBehav **104**: 40 – 46

(2) Ebenezer, I.S. and Pringle, A.K. (1992) Neuropharmacol **31**: 39 – 42