Alzheimer’s disease is a neurodegenerative disorder representing the leading cause of dementia in the elderly. There is some evidence that acetylcholinesterase (AChE) inhibitors improve symptoms in mild to moderate Alzheimer’s disease and specific cognitive deficits in patients with schizophrenia when given as adjunctive therapy (Racchi et al., 2004; Ribeiz et al., 2010).

We have recently shown that the AChE inhibitor, donepezil, can reverse a delay-induced deficit in object recognition memory in the rat (McLean et al., 2011).

Aim: To investigate the efficacy of the AChE inhibitor, tacrine, and the NMDA receptor antagonist, memantine to reverse the delay-induced cognitive deficit in object recognition memory.

Materials & Methods

• Adult female hooded-Lister rats received tacrine (2.5 mg/kg; i.p.), memantine (0.5 and 5.0 mg/kg) or vehicle and were tested in the novel object recognition (NOR) task using a 6 and 24 hour inter-trial interval (ITI).

• The NOR task involves a 3-min acquisition phase in which rats explore 2 identical objects (figure 1A), followed by an ITI of 6 and 24 hours, followed by a 3-min retention phase in which rats explore a familiar and a novel object (figure 1B).

• All drugs were administered only once, 30 min before the acquisition trial. The 6 and 24 hour ITI experiments were carried out one week apart.

• The NOR data are expressed as the mean exploration time ± SEM and were analysed using Student’s paired t-tests.

Results

• In all treatment groups and in both the 6 and 24 hour ITI experiments there was no preference for the left or right identical objects in the acquisition trial (figures 2A and 3A).

• In the retention trial, vehicle and memantine (5.0 mg/kg) treated rats were unable to distinguish between the novel and familiar objects following a 6 hour ITI (figure 2B).

• Tacrine and memantine (0.5 mg/kg) treated rats spent significantly (P<0.05) more time exploring the novel object compared to the familiar object following a 6 hour ITI (figure 2B).

• Following a 24 hour ITI, only the memantine (5.0 mg/kg) treated group spent significantly (P<0.05) more time exploring the novel object compared to the familiar object (figure 3B).

• Total object exploration time was significantly reduced in the acquisition trial of the 6 and 24 hour ITI experiments in the memantine (5.0 mg/kg) and tacrine treated groups (P<0.01 and P<0.001 respectively, compared with the vehicle control). Total object exploration time was significantly increased in the retention trial of the 6 hour ITI experiment in the memantine (5.0 mg/kg) and tacrine treated groups (P<0.05, compared with the vehicle control).

Materials & Methods

• Adult female hooded-Lister rats received tacrine (2.5 mg/kg; i.p.), memantine (0.5 and 5.0 mg/kg) or vehicle and were tested in the novel object recognition (NOR) task using a 6 and 24 hour inter-trial interval (ITI). The NOR task involves a 3-min acquisition phase in which rats explore 2 identical objects (figure 1A), followed by an ITI of 6 and 24 hours, followed by a 3-min retention phase in which rats explore a familiar and a novel object (figure 1B).

• All drugs were administered only once, 30 min before the acquisition trial. The 6 and 24 hour ITI experiments were carried out one week apart.

• The NOR data are expressed as the mean exploration time ± SEM and were analysed using Student’s paired t-tests.

Results

• In all treatment groups and in both the 6 and 24 hour ITI experiments there was no preference for the left or right identical objects in the acquisition trial (figures 2A and 3A).

• In the retention trial, vehicle and memantine (5.0 mg/kg) treated rats were unable to distinguish between the novel and familiar objects following a 6 hour ITI (figure 2B).

• Tacrine and memantine (0.5 mg/kg) treated rats spent significantly (P<0.05) more time exploring the novel object compared to the familiar object following a 6 hour ITI (figure 2B).

• Following a 24 hour ITI, only the memantine (5.0 mg/kg) treated group spent significantly (P<0.05) more time exploring the novel object compared to the familiar object (figure 3B).

• Total object exploration time was significantly reduced in the acquisition trial of the 6 and 24 hour ITI experiments in the memantine (5.0 mg/kg) and tacrine treated groups (P<0.01 and P<0.001 respectively, compared with the vehicle control). Total object exploration time was significantly increased in the retention trial of the 6 hour ITI experiment in the memantine (5.0 mg/kg) and tacrine treated groups (P<0.05, compared with the vehicle control).

References

