Effects of mGlu1 antagonism on processes of acquisition and retention in the water maze task

Prickaerts J, Oliveira AFM, Van Dyck C, Van Craenendonck H, Lesage ASJ*, Steckler T
CNS-Affective Spectrum Disorders, *CNS-Psychiatry 1, Johnson & Johnson PRD, Beerse, Belgium

There is increasing evidence that the $mGlu_1$ receptor is involved in the modulation of learning and memory. Effects of the selective $mGlu_1$ antagonist JNJ 16259685 on spatial and non-spatial memory processes were tested in the water maze task. C57BL/6 mice had to find a submerged platform hidden in a circular water tank on the basis of spatial cues surrounding the maze. Mice were trained with 10 trials per daily session.
In the first experiment treatment was given 30 min before the five daily sessions. Only the vehicle-treated group learned to locate the platform, while the $mGlu_1$ antagonist impaired spatial acquisition (LAD ≥ 0.63 mg/kg, s.c.).
In the second experiment, the experimental design was the same, except that animals were always started from the same position in the maze. This makes the task conceptually easier to perform and animals can use both spatial and non-spatial strategies. Likewise, JNJ 16259685 impaired performance (LAD ≥ 0.63 mg/kg, s.c.).
In a third experiment mice were treated 30 min before the probe trial which was given 24 h after all animals had learned the spatial task (6 sessions). A mild retrieval deficit was seen following mGlu1 blockade and only the vehicle-treated mice showed a clear preference for the former platform position (LAD ≥ 0.63 mg/kg, s.c.). Subsequently, spatial reversal learning was tested in the following two days. Treatment with the $mGlu_1$ antagonist 30 min before the daily sessions was found to affect spatial re-acquisition (LAD ≥ 1.25 mg/kg, s.c.).
Swim speed remained unaffected in all experiments, indicating that the behavioural impairments were not due to locomotor effects.
These data suggest that blockade of the $mGlu_1$ receptor primarily affects spatial and non-spatial acquisition, while having less pronounced, although significant effects on retrieval.

Jos Prickaerts, CNS-Affective Spectrum Disorders, Johnson & Johnson PRD, Turnhoutseweg 30, B-2340 Beerse, Belgium, t +32 14 607925, e-mail jprickae@prdbe.jnj.com

Poster Session Neuroscience 2