Animal model of cognitive dysfunction responding to ADHD therapies

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Introduction

Over 90% of adults and children living with and seeking treatment for Attention Deficit Hyperactivity Disorder (ADHD) manifest cognitive dysfunction, particularly impairments in attention, working memory and executive function which provides support for a cognitive rather than psychomotor basis of ADHD pathology. The existing animal models for ADHD feature psychomotor behavior impairments (impulsivity and hyperactivity) but do not always favorably respond to the psychostimulant drugs used for the treatment of ADHD.

Objectives

To study the potential of ADHD medications (methylphenidate, amphetamine and atomoxetine) to restore the cognitive performance (spontaneous and continuous alternation in the T-maze) in mice with impaired cholinergic system via administration of scopolamine. The impact of treatment duration (single or repeated) as well as the pretreatment time before the T-maze test (short or longer) is studied.

Experimental design

Subjects: Male CD-1 mice (25-35 g) receiving 1 mg/kg scopolamine 0.5 h before the assessment of cognitive function in the T-maze. The experimental plan follows a stepwise approach, i.e., the protocol implemented for the next experiment depends on the outcome of the preceding one.

Figure 1: Methylphenidate (dopamine transporter inhibitor)

Single administration, 0.5 h pretreatment. Single administration, 10 h pretreatment. Repeated administration, 16 h pretreatment.

Step 1
Step 2
Step 4

Figure 2: Amphetamine (monoamine releasing agent)

Single administration, 0.5 h pretreatment. Single administration, 16 h pretreatment. Repeated administration, 16 h pretreatment.

Step 1
Step 2
Step 4

Figure 3: Atomoxetine (norepinephrine transporter inhibitor)

Single administration, 0.5 h pretreatment. Repeated administration, (3 days) 0.5 h pretreatment.

Step 1
Step 3

Key points

- Cognitive enhancing effect of ADHD medication can be evidenced in a mouse model of cognitive deficit caused by impairment of the cholinergic system.
- The pretreatment time as well as the treatment regime influence the appearance cognitive enhancing effect of ADHD drugs. Whilst the treatment regime is assumed to affect the exposure the pretreatment time potentially conditions the presence or not of side effect (confounding factor) at the time of cognitive assessment.