ATTENTION DEFICIT DISORDERS: PT544 – PT558

PT544
The effect of acoustic white noise on motor learning and correlation with neural activity in an animal model of ADHD.

Overview
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Abstract
Objective: In addition to attention deficits and hyperactivity it is common for children with ADHD to display impaired fine and gross motor skills. The spontaneously hypertensive (SH) rat model of ADHD displays impaired motor learning [1]. We used this characteristic to study if the recently described acoustic noise benefit in learning in children with ADHD [2, 3] is also observed in the SH rat model using the Montoya staircase and Rotarod motor learning paradigms. In addition immunohistochemistry was used to assess differences in neuronal activity in animals treated with 75dBA white noise or ambient silence.

Methods: Effects of acoustic white noise (75 dBA) compared to ambient silence (45 dBA) on skilled reach and Rotarod running were investigated in male SH and Wistar controls. In parallel experiments the effect of methylphenidate compared to NaCl was investigated using the same motor learning paradigms. Antibodies for Fos B and Ca2+/calmodulin-dependent protein kinase II was used to investigate neuronal activity.

Results: We confirm impaired motor learning in the SH rat compared to Wistar controls. Acoustic noise restored motor learning in SH rats learning the Montoya reach test and the rotarod test, but had no influence on learning in Wistar rats. Methylphenidate completely restored rotarod learning and performance but did not improve skilled reach in the SH rat.

Conclusion: Our data suggests that the acoustic noise benefit previously reported in children with ADHD is also shared by the SH rat model of ADHD, and the effect is in the same range as that of methylphenidate treatment. Acoustic noise may be useful as an alternative treatment to stimulant medication in the management of ADHD. These results also strengthens the face validity of the SH rat as an animal model of ADHD.

References
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PT545
The Direct Protein-Protein Interaction between Dopamine Transporter and Dopamine D2 Receptor: A Novel Target Site to Modulate Synaptic Dopamine
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**Abstract**

**Background:** Dopamine level is strictly regulated at the synaptic level because a slight alteration can lead to severe neurological and neuropsychiatric consequences. Dopamine transporter (DAT), which facilitates the reuptake of extracellular dopamine, is used to be the sole component of regulating synaptic dopamine level. However, our previous discovery of a direct protein-protein interaction between DAT and presynaptic dopamine D2 receptor (D2R) revealed that this protein complex enables D2R to recruit extra intracellular DAT to the membrane surface and enhance dopamine reuptake. Despite we uncovered this novel target for modulating dopaminergic tone, its effects at the behavioural level remain elusive.

**Methods:** Male Sprague-Dawley rats were used in all three experiments. To examine the effects of D2R-DAT disruption on locomotion, normal rats and dopamine-depleted rats were injected intra-cranially (i.c.v.) with an interfering peptide to disrupt the interaction, and were subsequently placed in 43 x 43 x 30 cm open-field chambers to record their voluntary movements. Acute dopamine depletion was induced by two intra-peritoneal injections of α-methyl-p-tyrosine.

**Results:** The elevation in locomotion and increase in extracellular DAT observed in vivo micro-dialysis indicated that the disruption of DAT-D2R interaction increased the extracellular dopamine level by approximately 30% compared to baseline.

**Conclusion:** The results suggest that low-dose MPH causes changes in wild-type mouse reward system to increase response rate to the same level as naive DAT-KO mice via DAT inhibition. Meanwhile, high-dose MPH could decrease ICSS behaviors via not only DAT inhibition but also by other mechanisms. Although the role of DAT in AD/HD is still controversial, it might be thought there is less risk of drug dependence to occur in AD/HD patients treated with MPH.

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**PT547**

17α-estradiol prevents gamma-aminobutyric signaling dysfunction induced by repeated stress in the hippocampus associated with behavioral abnormalities via G-protein-coupled estrogen receptor in ovariectomized mice

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**Abstract**

In our previous study, we reported that repeated stress (RS) of forced gastric insertion in ovariectomized (OVX) mice induced less attention, impaired cognition associated with GABAergic functional deficit via the expression alterations of K+-Cl- co-transporter 2 (KCC2) and Na+-K+-2Cl- co-transporter 1 (NKCC1) in the hippocampus. In this study, we aimed to investigate the effect of 17α-estradiol (alfaE2) as an anti-psychotic medicine and the involvement of G-protein-coupled estrogen receptor (GPR30) using immunohistochemical and behavioral analysis.

8-week-old C57BL/6J mice were OVX and/or RS were conducted for 21 days followed by several behavior tests. We found that GPR30 were overexpressed in the hippocampus of RS-OVX mice. Therefore, to prevent the overexpression of GPR30, we administered alfaE2 and G1, a GPR30 agonist, in RS-OVX mice. The administration prevented all the behavioral abnormalities and the expression alteration of KCC2, NKCC1 and GPR30. Additionally, the efficacy of alfaE2 was completely diminished by co-administration of G15, an antagonist of GPR30. Subsequently, we evaluated the expressions of phosphorylated STE20-related...