On the Effects of Sensory Noise in ADHD

Akademisk avhandling

som för avläggande av farmacie doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Hörsal Arvid Carlsson, Medicinaregatan 3, fredagen den 21 september 2018, klockan 13:00

av Daniel Eckernäs

Fakultetsopponent: Rochellys Diaz Heijtz, Docent Karolinska Institutet

Avhandlingen baseras på följande delarbeten

- I. Göran Söderlund*, **Daniel Eckernäs***, Olof Holmblad and Filip Bergquist. *Acoustic noise improves motor learning in spontaneously hypertensive rats, a rat model of attention deficit hyperactivity.* Behavioural Brain Research 280 (2015) 84–91
- II. **Daniel Eckernäs**, Fredrik Hieronymus, Thomas Carlsson and Filip Bergquist. *Acoustic white noise ameliorates reduced regional brain expression of CaMKII and ΔFosB in the spontaneously hypertensive rat model of ADHD*. Submitted.
- III. **Daniel Eckernäs***, Ghazaleh Samoudi*, Göran Söderlund, Fredrik Hieronymus, Peik Gustafsson, Sebastian Lundström, Pia Tallberg, Aikaterini Trantou, Christopher Gillberg and Filip Bergquist. *Vestibular near threshold stochastic electric stimulation does not improve cognitive performance in ADHD A pilot study*. Submitted.

*) Contributed Equally

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Abstract

Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders amongst children of the developed world. The main symptoms of the disorder include hyperactivity, inattention and impulsivity. Psychotropic stimulants are considered the first line treatment option. Although effective, they are associated with negative side effects. A recently proposed non-pharmacological intervention for ADHD is loud (>70 dBA) acoustic white noise, a random signal with equal intensities across all included frequencies. Acoustic white noise has demonstrated positive effects on cognitive performance in children with ADHD. The aim of this thesis is to investigate possible neurobiological effects of sensory noise in experimental pre-clinical and clinical test paradigms and to evaluate possible mechanisms of action behind the positive effects of acoustic white noise in ADHD.

The pre-clinical studies were conducted using the spontaneously hypertensive (SH) rat, currently the best validated animal model of ADHD. Skilled reach in the Montoya staircase test and gross motor skill acquisition on the rotarod were assessed. Further, spontaneous motor behavior was evaluated in an open field activity box. The effect of acoustic white noise on neuronal brain activity was investigated using immunohistochemistry. Results indicate that the SH rat develops skilled reach more slowly and has lower plateau performance in rotarod running compared to a control strain. Additionally, the SH rat displays less habituation to an open field chamber and has significantly higher locomotion and rearing activity. Acoustic white noise exposure during training increased the skilled reach acquisition and performance on the rotarod to the same level as a control strain. Acoustic white noise had no attenuating effects on the increased locomotor activity or rearing activity of the SH rat. Compared to a control strain the expression of the two neuronal activity/plasticity markers ΔFosB and Ca2+/Calmodulin dependent protein kinase II (CaMKII) tended to be lower in several brain areas in the SH rat model of ADHD. Similarly (but not identically) to methylphenidate (MPH), acoustic white noise reduced the observed differences in neuronal activity/plasticity marker expression.

Possible beneficial effects of stochastic vestibular stimulation (SVS) on cognitive function were assessed in an ADHD population in a clinical trial. However, SVS did not benefit cognitive function in ADHD in any meaningful way.

Effects of acoustic white noise on acquisition of skill and neural brain activity were similar to the effects of MPH in SH rats. Unlike previously demonstrated effects of loud acoustic white noise, SVS did not improve situational cognitive function in ADHD. The increased performance in ADHD during acoustic white noise can probably be attributed to informational masking mechanisms, and possibly to altered cortical arousal.

Keywords: ADHD, attention, sensory noise, motor learning, behavior,

immunohistochemistry, image analysis

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