Göteborg, 2017

Stochastic Vestibular Stimulation in Dopamine Related Disorders

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska Akademin, Göteborgs Universitet kommer att offentligen försvaras i hörsal Karl Isaksson, Medicinaregatan 16, den 7 april 2017, klockan 9.00

av Ghazaleh Samoudi

Fakultetsopponent:
Professor Peter Valkovič
Comenius University, Slovakia

Avhandlingen baseras på följande delarbeten

I. Ghazaleh Samoudi, Hans Nissbrandt, Mayank B. Dutia and Filip Bergquist. Noisy galvanic vestibular stimulation promotes GABA release in the substantia nigra and improves locomotion in hemiparkinsonian rats. 2012. *PLoS ONE. 7(1) e29308.*

II. Ghazaleh Samoudi, Andrea Nilsson, Thomas Carlsson and Filip Bergquist. Expression of c-Fos after stochastic vestibular stimulation and Levodopa in 6-OHDA hemilesioned rats. *Manuscript*

III. Ghazaleh Samoudi, Maria Jivegård, Ajitkumar P. Mulavara and Filip Bergquist. Effects of Stochastic Vestibular Galvanic Stimulation and LDOPA on Balance and Motor Symptoms in Patients with Parkinson's Disease. 2015. *Brain Stimulation, vol. 8, no. 3, pp. 474–80.*

IV. Ghazaleh Samoudi*, Daniel Eckernäs*, Göran Söderlund and Filip Bergquist. Does stochastic vestibular galvanic stimulation improve cognitive performance in ADHD? A pilot study. *Manuscript*
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SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR FARMAKOLOGI

GÖTEBORGS UNIVERSITET

Göteborg, 2017

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ABSTRACT

Dopamine related disorders usually respond to dopaminergic drugs, but not all symptoms are equally responsive. In Parkinson's disease (PD) in particular, axial symptoms resulting in impaired gait and postural control are difficult to treat. Stochastic vestibular stimulation (SVS) has been put forward as a method to improve CNS function in dopamine related disorders, but the mechanisms of action are not well understood.

This thesis aimed to investigate the effects of SVS on neuronal brain activity and to evaluate the possible enhancing effect of SVS on motor control in PD and on cognitive functions and motor learning in Attention deficit hyperactivity disorder (ADHD).

Behavioural tests were conducted in the 6-OHDA rat model of PD using the accelerating Rotarod and the Montoya skilled reach test to evaluate the effect of SVS on motor control. The effect of SVS on brain activity was assessed using in vivo microdialysis and immunohistochemistry. We evaluated the effect of SVS on postural control and Parkinsonism in patients with PD and the effect of SVS on cognitive function in people with ADHD.

The behavioural animal studies indicate that SVS may have an enhancing effect on locomotion, but not skilled forepaw function. SVS increased GABA transmission in the ipsilesional substantia nigra (SN) and may have a rebalancing effect on dysfunctional brain activity. SVS increased c-Fos activity more than levodopa and saline in the vestibular nucleus of all animals. c-Fos expression was also higher in this region in the 6-OHDA lesioned than in shamlesioned animals, supporting the theory that SVS may have larger effects in the dopamine depleted brain. SVS increased c-Fos expression in the habenula nucleus substantially more than levodopa did. Furthermore, SVS and levodopa had similar effects on many brain regions, including the striatum, where saline had no effect. The clinical studies revealed improvement of postural control in PD during SVS. There was a trend towards reduced Parkinsonism during SVS when off levodopa. No substantial effects were found on cognitive performance in ADHD.

In PD, SVS may improve motor control by inhibiting the overactive SN, possibly through a non-dopaminergic modulatory pathway involving increased neurotransmission in the habenula nucleus. SVS could be trialled in larger studies to evaluate long-term effects on treatment resistant axial symptoms associated with PD.

Keywords: Vestibular stimulation, Microdialysis, GABA, Substantia nigra, c-Fos, Habenula nucleus

ISBN: 978-91-629-0093-9 (TRYCK) http://hdl.handle.net/2077/50869
ISBN: 978-91-629-0094-6 (PDF)