Tourette’s syndrome (TS) is a childhood-onset chronic neuro-psychiatric disorder that presents with multiple motoric tics combined with one or more phonemic tics. Inappropriate and sometimes even obscene movements and vocalisations entail affected quality of life and stigmatisation. Therapy of TS is challenging, often ineffective or plagued by side effects severe enough to discontinue it (Ludolph et al. 2012).

Still, it is underrepresented in preclinical studies with only very few animal models which allow insights into its pathophysiology and consequently contribute to the development of novel treatments (Bronfeld, Israelashvili & Bar-Gad, 2013).

Amounting evidence suggests an overactive dopamine transporter (DAT) as one important mechanism underlying TS pathophysiology. On this basis we further establish a recently generated transgenic rat model overexpressing the dopamine transporter (DAT). These rats exhibit multiple TS-related neurobiological effects exceeding expected alterations in the corticostriatal dopamine system. Transgenic rats further show behavioural and pharmaco-therapeutic profiles phenotypic of TS (Hadar et al., 2015).

We will further use the DAT rat model to investigate the applicability of certain brain stimulation techniques. Conventional drug treatments lack both spatial and temporal specificity. To approach this shortcoming, different brain stimulation techniques have been employed to improve spatial precision, by only modulating brain areas involved in the pathology. While deep brain stimulation constitutes an invasive procedure and consequently is restricted in its application, TMS (transcranial magnetic stimulation) and tDCS (transcranial direct current stimulation) offer a non-invasive approach. Repetitive transcranial magnetic stimulation of the supplementary motor cortex...
in humans has been shown to reduce tics significantly for months (Kwon et al. 2011, Le et al. 2013).
Here we want to test the effectiveness of tDCS.

The efficiency of tDCS has been shown successfully for various psychiatric disorders including depression, addictive disorders, schizophrenia, obsessive compulsive disorder and Alzheimer’s disease (Kuo, Paulus & Nitsche, 2014). However, only two cases have been reported that were treated against Tourette’s syndrome with tDCS. In each case, tDCS induced a significant reduction of motor and phonetic tics suggesting that tDCS might be a promising novel tool in treatment of TS (Mragic-Sposta et al. 2008).

In our experimental setup we will apply currents transcranially through a wet stimulation electrode directly placed on the rat cranium at the frontal cortex in a surgical procedure (Liebetanz et al. 2009). For stimulation, a reference electrode with electrode cream is positioned onto the breast using a corset. Repetitive behaviour is induced by low dosages of amphetamine ineffective in wildtype rats. Animals are placed into individual Plexiglas boxes and tDCS will be applied for 30 min. Then, we remove corset and stimulation electrode from the rats to allow free movement for further 90 min. All along, the animal behaviour will be video recorded. For analysis of stereotypic behaviour, the 120 min total recording time will be divided into intervals of 5 min and the most dominant behaviour for each interval is assessed using a scoring protocol adapted from Kelly, Seviour & Iversen (1975).

With this experimental setup we aim at testing how cathodal and anodal tDCS of different doses will affect amphetamine-induced stereotypy in the DAT rats. Based on previous findings, we hypothesise, that cathodal stimulation will reduce and anodal stimulation will enhance stereotypy.
Literatur


