Behavioural and physiological effects of electrical stimulation in the nucleus accumbens: a review

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Summary

Electrical stimulation (ES) in the brain is becoming a new treatment option in patients with treatment-resistant obsessive-compulsive disorder (OCD). A possible brain target might be the nucleus accumbens (NACC). This review aims to summarise the behavioural and physiological effects of ES in the NACC in humans and in animals and to discuss these findings with regard to neuroanatomical, electrophysiological and behavioural insights. The results clearly demonstrate that ES in the NACC has an effect on reward, activity, fight-or-flight, exploratory behaviour and food intake, with evidence for only moderate physiological effects. Seizures were rarely observed. Finally, the results of ES studies in patients with treatment-resistant OCD and in animal models for OCD are promising.

Keywords: Neuromodulation; electrical stimulation; behaviour; nucleus accumbens; ventral striatum; review.

Introduction

Some patients with obsessive-compulsive disorder (OCD) are treatment-refractory to conventional behavioural therapy and/or pharmacological treatment. Part of these patients may benefit from a neurosurgical lesion in a specific brain target [36, 46]. In one of those brain targets, the anterior limbs of the internal capsule [60, 67], we demonstrated that high frequency ES was also therapeutically effective [77]. In contrast to neurosurgical lesions, electrical brain stimulation is a reversible technique, which is a major advantage in case severe side effects occur. Moreover, in Parkinson’s disease ES has a lower rate of side effects compared to lesioning with thermocoagulation [103].

Although the clinical outcome of ES in the anterior limbs of the internal capsule is satisfactory, high voltage levels are necessary. Hence, the battery lifetime is limited to 4–12 months requiring frequent exchange of the batteries under local anaesthetic, limiting the comfort of the patient. One of the strategies to surpass the high energy consumption is to search for other brain targets that yield the same or even better therapeutic results with a lower voltage.

A possible new target for ES in patients with treatment-refractory OCD might be the nucleus accumbens (NACC) [1, 117], which participates as the anteroventral part of the ventral striatum in the corticostriato-pallido-thalamo-cortical circuitry. Functional brain imaging studies indicate that this circuitry is involved in OCD [100]. Additional evidence for the involvement of the NACC in OCD comes from stereotactic lesioning studies in the anterior limbs of the internal capsule. Lesioning of the ventro-caudal part of the internal capsule was imperative for successful treatment. It is likely that such a lesion also affects the NACC [67, 110]. The
The current article reviews the reported behavioural and physiological effects of ES in the NACC of humans and different mammalian species.

Methods and results

We performed a computer-aided search of Pubmed using the keywords ‘nucleus accumbens’, ‘ventral striatum’ and ‘ES’ and selected articles dealing with the behavioural and physiological effects of ES in the NACC. In addition, we searched the reference lists of these selected relevant articles. Because we cannot read or comprehend Chinese language one article was rejected [53]. The results of our search are described in the following sections.

Anatomy of the NACC

Core and shell NACC

The NACC has been subdivided in a core and shell subregion based on cytoarchitectonic and neurotransmitter characteristics and differences in afferent and efferent connections [142]. The shell is situated in the medial

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Fig. 1. NACC core and shell: Graphical representation of coronal sections through the human NACC core (blue) and shell (green) and its surrounding structures (modified from the atlas of Mai et al. 63). The distance from the midpoint of the anterior commissure at the midline is denoted below each coronal section. ac Anterior commissure; acos anterior commissure, olfactory limb; aic anterior limb of internal capsule; aps anterior parolfactory nucleus; BSTC bed nucleus of the stria terminalis, central division; BSTLJ bed nucleus of the stria terminalis, lateral division, juxtacapsular part; BSTM bed nucleus of the stria terminalis, medial division; Cdl lateral caudate nucleus; CdM medial caudate nucleus; Cdv ventral caudate nucleus; CG cingulate gyrus; CSP cavity of septum pellucidum; db diagonal band; ec external capsule; EGP external globus pallidus; Fcd caudate fundus region; FLV frontal horn of the lateral ventricle; FPu putaminal fundus region; gcc genu of the corpus callosum; GTI great terminal island; lml external medullary lamina of the globus pallidus; LSD dorsolateral septal nucleus; LSJ intermediolateral septal nucleus; LSV ventrolateral septal nucleus; NACCc accumbens nucleus, central (subventricular) part (core); NACCt accumbens nucleus, lateral (subventricular) part (core); NACCm accumbens nucleus, medial (subventricular) part (shell); OTI olfactory trigone; pcfx precommissural fornix; PirF (pre-)piriform cortex, frontal area; PPCI (pre-) piriform claustrum; pps posterior parolfactory sulcus; PTG paratemporal gyrus; PuM medial putamen; rac radiation of corpus callosum; SB striatal cell bridges; SCA subcallosal area; SCGP supracapsular part of the globus pallidus; SFI septofimbrial nucleus; SGI substantia gliosa; SSTI substriatal terminal island; sv septal vein; Tu olfactory tubercle; TuITI tubercular terminal island(s); unc uncinate fasciculus; VDB vertical limb of the diagonal band