

Remission of alcohol dependency following deep brain stimulation of the nucleus accumbens: valuable therapeutic implications?

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Chronic consumption of alcohol represents one of the greatest health and socioeconomic problems worldwide. We report on a 54-year-old patient with a severe anxiety disorder and secondary depressive disorder in whom bilateral deep brain stimulation (DBS) of the nucleus accumbens was carried out. Despite the absence of desired improvement in his primary disorder, we observed a remarkable although not primarily intended alleviation of the patient's comorbid alcohol dependency. Our case report demonstrates the extremely effective treatment of alcohol dependency by means of DBS of the nucleus accumbens and may reveal new prospects in overcoming therapy resistance in dependencies in general.

Together with its ensuing complications, chronic consumption of alcohol represents one of the greatest health and socioeconomic problems worldwide. According to the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), approximately 10% of the population can be classified as alcohol dependent.¹ The treatment of alcohol dependency rests on pharmacological, psychological and social therapeutic interventions. To date, however, a therapeutic breakthrough in terms of a reliably and permanently effective treatment has remained out of reach. This is underscored by high recidivism rates of 40–70%.² In attempting to treat a 54-year-old patient with a severe anxiety disorder and secondary depressive disorder by bilateral deep brain stimulation (DBS) of the nucleus accumbens, we observed a remarkable, although not primarily intended, alleviation of the patient's comorbid alcohol dependency.

CASE REPORT

Since early adolescence, the patient had suffered from agoraphobia with panic attacks (STAI-State 54; STAI-Trait 48), resulting in considerable impairment of psychosocial level of functioning.³ A series of previous stays in psychiatric hospitals had failed to bring adequate alleviation of symptoms. Various medicinal and psychotherapeutic treatment concepts, including two administrations of electroconvulsive therapy 20 years earlier, had been applied. In addition, an accompanying depressive disorder (BDI: 24) and, in particular, a pattern of alcohol consumption spanning across more than 10 years and fulfilling the DSM-IV diagnostic criteria for an alcohol dependency were found to exist. The WHO Alcohol Use Disorder Identification Test (AUDIT) further revealed a highly pathological score of 28 points.⁴ Prior to the stereotactic intervention, the patient consumed alcohol almost daily, often beginning in the morning, drinking in part excessively and on average more than 10 drinks per day. Moreover, hospital stays had been complicated by withdrawal states with delirium

resulting from an abstinence from alcohol. As objective parameters of the patient's chronic alcohol consumption, a carbohydrate deficient transferrin value of 5.2% and a gamma-glutamyl transferase value of 185 U/l were found.

On account of the severe as well as refractory psychiatric disorder, the express desire of the patient and our positive experiences in the context of treating obsessive-compulsive and anxiety patients,⁵ we considered carrying out a therapeutic trial of DBS to reduce anxiety symptoms. Selection of the nucleus accumbens as the primary target point of DBS in our patient was based on the above mentioned beneficial results gained in a pilot series of patients with intractable obsessive-compulsive and anxiety disorders.⁵ Furthermore, because of its central position within the amygdaloid complex, basal ganglia, mediodorsal thalamic nucleus and prefrontal cortex, the nucleus accumbens is well established in the pathophysiology of anxiety disorders.⁶

The quadripolar electrodes (Medtronic 3387; Medtronic, Inc., Minneapolis, Minnesota, USA) were bilaterally implanted using a deep frontolateral approach from 4.5 cm rostral of the coronal suture and 4.5 cm lateral left and right of the mid-sagittal suture, respectively. Access and electrode trajectories were determined by a computer supported image fusion of MRI and intraoperative CT. Three dimensional coordinates for localisation of the target site were as follows: 1 mm rostral anterior border of AC, 7 mm lateral of midline, 4 mm ventral AC. The correct positioning of the electrodes was confirmed postoperatively by cranial CT and conventional x ray procedures (pole 0,1: fundus subventricularis medialis of the nucleus accumbens; pole 2,3: anterior limb of the internal capsule). A pulse generator (Kinetra, Medtronic, Inc.) connected to the electrodes was implanted infraclavicularly.

During a postoperative phase of adjustment lasting a few weeks, the following stimulation parameters appeared most effective and were not accompanied by adverse reactions: (bilateral 0, off; 1, –; 2, –; 3, off; case +; pulse width 90 µs, 130 Hz, 3 V). Following application of DBS with the aforementioned parameters, the patient reported an acute feeling of "inner appeasement" which he described as pleasant. Within the 12 month period of treatment, the applied voltage was increased on three occasions and is currently set at 4.5 V.

Nevertheless, the patient showed no or at best a slight reduction of his anxiety disorder following application of DBS. The accompanying moderately pronounced depressive mood also proved almost intractable. Despite the absence of the desired improvement in his primary disorder, the patient showed a remarkable change with respect to his substance

Abbreviations: AUDIT, Alcohol Use Disorder Identification Test; DBS, deep brain stimulation; DSM, Diagnostic and Statistical Manual of Mental Disorders

abuse behaviour and alcohol dependency. Without any form of particular motivation, he proceeded to rapidly and drastically reduce his alcohol consumption. Twelve months after commencement of DBS, the patient only occasionally consumes alcohol. Within a month of treatment, alcohol free days prevailed, excessive drinking no longer occurred and the amount of alcohol consumed ranged from 1 to 2 drinks per day (AUDIT score 1 point). Subjectively speaking, the patient claims to have lost the desire to drink and further professes that the pressing need to consume alcohol had almost completely disappeared under stimulation. The gamma-glutamyl transferase value normalised to 43 U/l and the carbohydrate deficient transferrin value to 1.5%, correlating with these assertions.

DISCUSSION

In addition to environmental influences and social factors, the development of alcohol dependency is promoted by hereditary characteristics. The exact mechanisms which finally lead to the dependency of a predisposed patient have, however, not yet been completely identified. It is assumed that long term effects such as the development of tolerance, craving, dependency and withdrawal symptoms are induced at the cellular level, through for example modified gene expression and receptor down-regulation. In those functional circles affected, these modulations result in modified or pathological neurotransmission and signal transduction, and finally lead to a modification of neuronal architecture. Based on findings in neuroimaging and cellular studies in animal models, a relatively general consensus prevails that the mesocorticolimbic system, consisting of the ventral tectum, nucleus accumbens, amygdala, septum and orbitofrontal cortex, is to be viewed as the primary area impaired by psychotropic substances and consequently as the neural substrate for substance dependencies.^{7,8} Among these neural circuits, the nucleus accumbens is attributed a central role. Only recently, alcohol dependent changes, possibly leading to deficient synaptic transmission, were demonstrated at the cellular level explicitly for the nucleus accumbens.⁹ DBS targeting the nucleus accumbens could thus have a modulating effect provoking a normalising change in synaptic transmission.

At the level of the neurotransmitter, alcohol dependent impairments are particularly postulated to arise in connection with the dopaminergic and glutaminergic systems.^{10,11} Here too, the nucleus accumbens assumes a key position with its dopaminergic and glutaminergic portions. It is therefore possible that DBS directly interferes with the two named neurotransmitter systems, secondarily and indirectly influences the synaptic efficiency of the dopaminergic system and in so doing finally contributes to normalisation of neurotransmission.

Our observations demonstrate the effective treatment of alcohol dependency by means of DBS of the nucleus accumbens. Confirmation of this incidental finding in further cases

and empirical studies would underline the impact of the nucleus accumbens in neural mechanism of addiction. It could even reveal new prospects for therapy in the case of severe and otherwise refractory alcohol dependency and potential dependencies in general, although the ethical aspects of neurosurgery in addiction have to be discussed extremely conscientiously.^{12,13}

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