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Deep Brain Stimulation for Obsessive Compulsive Disorder Reduces Symptoms of Irritable Bowel Syndrome in a Single Patient

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Abstract

Irritable bowel syndrome (IBS) is a frequent gastrointestinal disorder that is difficult to treat. We describe findings from evaluation of a woman (55 years old) with obsessive compulsive disorder, which was treated with bilateral deep brain stimulation in the anterior limb of the internal capsule, and IBS. After the brain stimulation treatment she reported substantial relief of her IBS symptoms. This reduction depended on specific stimulation parameters, was reproducible over time, and was not directly associated with improvements in obsessive compulsive disorder symptoms. These observations indicate a specific effect of deep brain stimulation on IBS. This observation confirms involvement of specific brain structures in the pathophysiology of IBS and shows that symptoms can be reduced through modulation of neuronal activity in the central nervous system. Further studies of the effects of brain stimulation on IBS are required.

Keywords

Deep Brain Stimulation; Irritable Bowel Syndrome; Brain Gut Axis; Neuroplasticity

Irritable bowel syndrome (IBS) is characterized by recurrent abdominal pain and discomfort associated with changes in bowel habits. In the absence of generally agreed biomarkers, this common syndrome remains defined by symptom criteria and the absence of organic disease.[1] Current therapy is based on treatment of individual symptoms, dietary

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Conflicts of interest

These authors disclose the following: Loes Gabriels and Juergen Schlaier have a consultancy agreement with Medtronic. The remaining authors disclose no conflicts.

Supplementary Material

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recommendations, and cognitive behavioral approaches.[2] Because of the high prevalence (about 10% of the American population[3]), the chronicity, and the lack of effective treatments, IBS represents an important health problem and causes a major socioeconomic and humanistic burden.[4]

There is general agreement that IBS symptoms result from a dysregulation of brain-gut interactions that result in enhanced perception of visceral sensations and altered autonomic modulation of intestinal motility and secretion.[1]

These concepts are supported by findings from neuroimaging studies indicating abnormal processing of visceral information,[5,6] altered autonomic output,[7] and alterations in cognitive and affective functioning in IBS patients.[8,9] Moreover, the recent observation of white matter changes in cortico-basal ganglia-thalamocortical loops[10] provides an increasingly detailed neuronal correlate for the long established interaction between IBS and psychological factors.[1]

Deep brain stimulation (DBS) is an innovative technique for the treatment of brain disorders. Bilateral DBS of the posterior part of the anterior limb of the internal capsule (ALIC) has been shown to be an effective treatment option for otherwise treatment-resistant obsessive compulsive disorder (OCD).[11] Similar to anterior capsulotomy, it normalizes pathologically increased activation in a cortico-striato-pallido-thalamocortical circuit.[12] Here we report the case of a patient who received DBS of the ALIC for the treatment of OCD and who was also suffering from comorbid IBS.

Case Report

The 55-year-old female patient developed first compulsive symptoms at age of 14, with partial remission of symptoms at age of 21. Four years later she developed recurrent abdominal pain, associated with alternating diarrhea and constipation. Initially accompanied by 6 kg of weight loss, the patient received extensive diagnostic assessment that did not reveal any organic cause to explain her symptoms, and she was diagnosed with mixed IBS on the basis of the Rome III criteria. At the age of 32 she developed full-blown OCD with severely impairing obsessive thoughts and compulsive rituals. Despite several months of inpatient treatment, cognitivebehavioral psychotherapy, and psychopharmacologic treatment with serotonin reuptake inhibitors and tricyclic antidepressants, the patient was preoccupied with OCD symptoms such as contamination fears and hand washing or taking showers for more than 8 hours/day. Moreover, she was obsessed with numbers and spent almost all her waking time with counting. Apart from a transient worsening of OCD symptoms after getting divorced from her husband at age of 36, both OCD and IBS symptoms were rather stable during more than 20 years before DBS treatment.

In June 2012 the patient presented at the interdisciplinary center for DBS of the University of Regensburg, Germany for evaluation of DBS therapy. In February 2013 she was implanted with deep brain leads that targeted the posterior aspects of the ALIC bilaterally in both hemispheres[11] (Figure 1). After 8 weeks of stimulation of contacts 2 and 10, which were localized directly at the lateral edge of the caudate, the patient reported a moderate

improvement of OCD symptoms that was accompanied by almost complete relief of her IBS symptoms. Abdominal pain almost completely disappeared, and stool habits normalized to about 1 bowel movement per day. In the further course, different stimulation settings were tested for periods of 6–8 weeks to identify optimal stimulation parameters. After 6 weeks of stimulation via contacts 3 and 11, further improvement of OCD symptoms was observed, whereas the effect on IBS diminished. The beneficial effect on IBS completely disappeared when stimulation contacts 1 and 9 were used, whereas a small improvement in OCD symptoms persisted. When stimulation of both contacts 2 and 10 and contacts 3 and 11 was reinstalled, the beneficial effects on both disorders first reappeared but diminished with reduction of voltage. When stimulation settings were changed to the initial contacts, both OCD symptoms and IBS symptoms improved again (Figure 2, Supplementary Table 1, Supplementary Material).

Discussion

In our patient who suffered from both OCD and IBS, we could observe substantial improvement of both disorders after DBS of the ALIC. Improvement depended critically on exact stimulation settings and was replicable, largely ruling out an unspecific or placebo effect.

This observation of substantial, replicable, and several months of long-lasting relief from IBS symptoms after DBS of the posterior ALIC indicates that specific modulation of central nervous activity can reduce IBS symptoms. Best effects on IBS symptoms were obtained after stimulation of contacts 2 and 10, which were located in the posterior ALIC at the lateral edge of the caudate nucleus (Supplementary Table 1, Supplementary Material). With stimulation of the neighboring contacts 3 and 11, which were localized in a similar region but targeted slightly different fibers within the ALIC, results were optimal for reducing OCD symptoms.

Our observations suggest specific fibers within the ALIC seem to be of critical relevance for influencing IBS symptoms. Positron emission tomography studies have revealed that DBS of the ALIC induces widespread metabolic network changes including cortico-striatopallido-thalamocortical connections.[12] In this circuit, white matter abnormalities have recently been identified in patients with IBS,[10] including increased mean diffusivity in the internal capsule, thalamus and corona radiata, and a higher degree of connectivity between the thalamus and prefrontal cortex, as well as between the medial dorsal thalamic nuclei and anterior cingulate cortex.[10] Even though other explanations are possible, interference of ALIC stimulation with the altered connectivity between the thalamus and the frontal lobe may provide a potential explanation for the observed reduction of IBS symptoms in the current case.

Cortico-striato-pallido-thalamocortical networks are involved in multisensory integration and corticothalamic modulation and seem to be involved in the pathophysiology of both OCD and IBS. Whether the stimulation effect influenced primarily brain circuits involved in altered sensory processing (normalizing visceral hypersensitivity) or also altered autonomic regulation of the gut (normalizing bowel function) could not be clinically differentiated

because the patient reported both relief of abdominal pain and normalization of bowel habits.

However, even if the stimulation effect is highly specific, it results in activity changes in different functionally connected areas. Thus, we are well aware that the effects of ALIC stimulation on IBS symptoms may also be mediated by other central or peripheral nervous structures. Further studies with high-resolution fiber tracking may provide more detailed information about the exact brain circuits by which the treatment effects are mediated.

Because the patient suffered from both OCD and IBS, one could argue that the observed effect on IBS symptoms may solely be a secondary effect of OCD improvement. However, this seems highly unlikely because the initial effect on IBS symptoms was clearly more pronounced than the effect on OCD symptoms. Moreover, the effects on both syndromes dissociated depending on the DBS contacts used for stimulation (Figure 2). Nevertheless, it seems likely that the effects on IBS symptoms and OCD symptoms are not completely independent. Imaging studies suggest an involvement of cortico-basal gangliathalamocortical loops in the pathophysiology of both OCD[13,14] and IBS,[10] and presumably the modulation of neuronal activity in this circuit has resulted in symptom improvement of both disorders in the presented case. Whether the co-occurrence of OCD is a prerequisite for the therapeutic effect of ALIC stimulation on IBS symptoms (limiting the current observation to such cases) or whether DBS of the ALIC may also have positive effects on IBS in patients without OCD symptoms can only be answered by further research.

Regardless of the limitations of the current case study, our observation of substantial improvement of IBS symptoms by focal modulation of central nervous system activity (1) underscores the relevance of central nervous system abnormalities in IBS, (2) confirms the involvement of cortico-basal ganglia-thalamocortical loops, (3) turns correlational evidence from imaging studies into a causal relationship, and (4) warrants further investigation of brain stimulation techniques for the treatment of patients with severe IBS symptoms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Figure 1 was produced by Medtronic, Inc (Minneapolis, Minnesota) with the program Optivise. The authors thank Medtronic for permission to use this figure.

Abbreviations used in this paper

ALIC	anterior limb of the internal capsule
DBS	deep brain stimulation
IBS	irritable bowel syndrome
OCD	obsessive compulsive disorder

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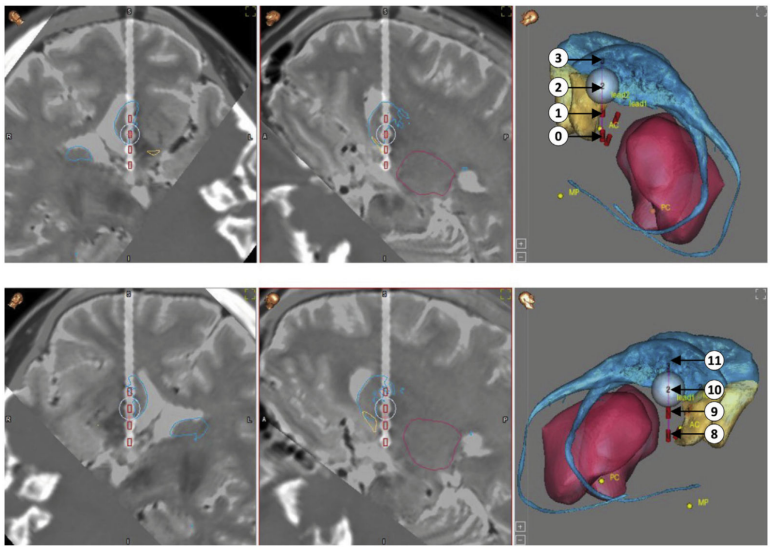

Figure 1.

Visualization of lead localization. Stimulation leads were localized in the posterior ALIC on left (*upper row*) and right sides (*lower row*) (thalamus, *red*; caudate nucleus, *blue*; nucleus accumbens, *yellow*). Each lead has 4 cylindrical electrodes at its tip (electrode length 3 mm, space between electrodes 4 mm; electrodes are named 0, 1, 2, 3 on the left lead and 8, 9, 10, 11 on the right lead). The sphere around electrode 2 illustrates the extent of the stimulated brain area during stimulation with 4 V. AC, anterior commissure; MP, midplane point; PC, posterior commissure.

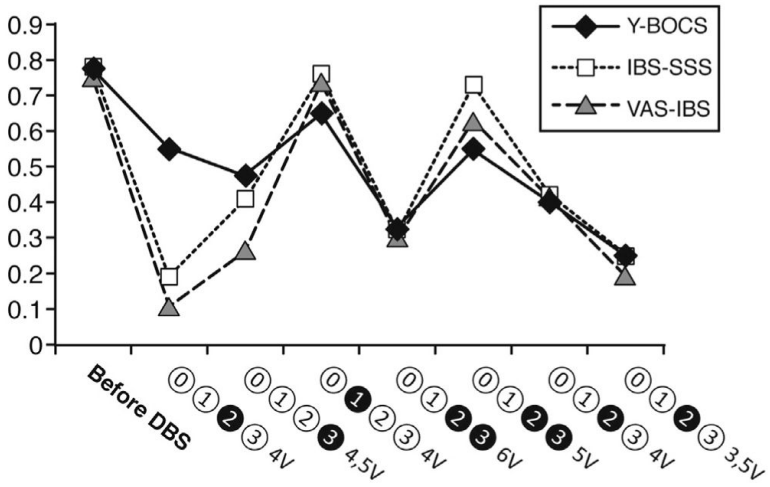

Figure 2.

Improvement of OCD (Yale–Brown Obsessive Compulsive Scale [Y-BOCS]) and IBS (Irritable Bowel Syndrome Severity Scoring System [IBS-SSS], Visual Analogue Scale for Irritable Bowel Syndrome [VAS-IBS]) symptoms depending on stimulation settings. For better comparability Y-BOCS, IBS-SSS, and VAS-IBS were normalized, with 0 representing no symptoms (Y-BOCS, 0; IBS-SSS, 0; VAS-IBS, 700) and 1 representing maximal symptoms (Y-BOCS, 40; IBS-SSS, 500; VAS-IBS, 0). On the x-axis the different stimulation settings are given. Negative charged electrodes are indicated by *black circles* (for better readability only electrodes on the left side are given; on the right side the corresponding electrodes were activated). In all stimulation settings the case of the stimulation generator was positively charged, and stimulation was performed with frequency of 130 Hz and pulse duration of 210 ms. There is almost no effect on either IBS or OCD symptoms with stimulation at the distal electrodes 1 and 9 (indicated as ⩽ on the x-axis). In contrast, stimulation at the more proximal electrodes 2 and 10 (indicated as ❷ on the x-axis) resulted in reproducible improvement of both ICD and OCD.