possible attenuating effect on the symptoms of OCD. The association of OCD-schizotypal comorbidity with the beneficial effect of memantine is noteworthy in view of a pertinence of glutamatergic dysfunction in both OCD and schizophrenia spectrum disorders (5). Our case suggests that memantine may be an option for treatment-resistant OCD, but controlled studies are needed to substantiate this observation.

References

1. Pallanti S, Hollander E, Goodman WK: A qualitative analysis of nonresponse: management of treatment-refractory obsessive-compulsive disorder. J Clin Psychiatry 2004; 65(suppl 14):6–10
2. Arnold PD, Rosenberg DR, Mundo E, Tharmalingam S, Kennedy JL, Richter MA: Association of a glutamate (NMDA) subunit receptor gene (GRIN2B) with obsessive-compulsive disorder: a preliminary study. Psychopharmacology (Berl) 2004; 174:530–538
3. Rosenberg DR, MacMaster FP, Keshavan MS, Fitzgerald KD, Stewart CM, Moore GJ: Decrease in caudate glutamatergic concentrations in pediatric obsessive-compulsive disorder patients taking paroxetine. J Am Acad Child Adolesc Psychiatry 2000; 39:1096–1103
4. Goodman WK, Price LH, Rasmussen SA, Mazure C, Delgado P, Heninger GR, Charney DS: The Yale-Brown Obsessive Compulsive Scale, II: validity. Arch Gen Psychiatry 1989; 46:1012–1016
5. Poyurovsky M, Koran LM: Obsessive-compulsive disorder (OCD) with schizotypy vs schizophrenia with OCD: diagnostic dilemmas and therapeutic implications. J Psychiatr Res 2005; 39: 399–408

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Deep Brain Stimulation for OCD and Major Depression

TO THE EDITOR: Deep brain stimulation has been proposed to alleviate treatment-resistant obsessive-compulsive disorder (OCD) (1). We examined the long-term efficacy of deep brain stimulation of the ventral caudate nucleus in a case of primary, severe, and intractable OCD with concomitant major depression.

We previously reported the case of Mr. A, a 56-year-old man suffering from a severely disabling and refractory form of OCD that began over 4 decades before (2). He mainly experienced somatic obsessions concerning potential disturbances in bodily functioning, especially regarding his arms, fingers, legs, and gastrointestinal tract, and his mental capacities, with compulsive verification of functioning, comprising repetitive voluntary movements, controlled intake of foods according to their purgative properties, and repeated mental acts of questioning. Aggressive obsessions with fear of embarrassing thoughts about his children occurred, although considerably less frequently. OCD coexisted only with a lifetime history of recurrent major depression. Mr. A's written informed consent had been obtained before his participation in the study. Psychiatric assessments included the Yale-Brown Obsessive Compulsive Scale, the Hamilton Depression Rating Scale, the Hamilton Anxiety Rating Scale, and the Global Assessment of Functioning (GAF) scale. Neuropsychological assessments consisted of a wide range of tests primarily exploring memory and executive functions (2). These evaluations were performed independently and blindly, regarding stimulation settings. No pharmacological and/or psychological treatment was administered postoperatively.

We previously reported that deep brain stimulation of the ventral caudate nucleus progressively improved Mr. A's depressive and anxiety symptoms until remission was achieved at 6 months (Hamilton depression scale score ≤7 and Hamilton anxiety scale score ≤10) (2). There was also a marked but delayed reduction in OCD symptom severity on the Yale-Brown Obsessive Compulsive Scale from a baseline score of 25 to 10 and 14 at 12 and 15 months after deep brain stimulation, respectively. His level of functioning on the GAF scale gradually increased from 35 to 60 over the first 15 months of the postoperative period (2). Failure of the pulse generator battery, which was discovered after a clinical impairment, did not affect depressive and anxiety symptom intensity but worsened his obsessive-compulsive manifestations, especially his somatic preoccupations and the related checking compulsions (Yale-Brown Obsessive Compulsive Scale score=21), with a slight deterioration of global functioning (GAF scale score= 55) at 18 months. A return to remission levels of OCD (Yale-Brown Obsessive Compulsive Scale score <16) was observed 3 months after replacement of the generator and remained stable until the end of the 27-month follow-up (final Yale-Brown Obsessive Compulsive Scale score= 12). This was paralleled by an improvement in psychosocial functioning (final GAF scale score=65). Of interest, no neuropsychological alteration or any adverse clinical effect was reported.

Thus, this finding strengthens our previous report, suggesting that deep brain stimulation of the ventral caudate nucleus could be a promising strategy for the treatment of refractory cases of both OCD and major depression.

References

1. Nuttin B, Cosyns P, Demeulemeester H, Gybels J, Meyerson B: Electrical stimulation in anterior limbs of internal capsules in patients with obsessive-compulsive disorder (letter). Lancet 1999; 354:1526
2. Aouizerate B, Cuny E, Martin-Guehl C, Guehl D, Amieva H, Benazzouz A, Fabrigoule C, Allard M, Rougier A, Bioulac B, Tignol J, Burbaud P: Deep brain stimulation of the ventral caudate nucleus in the treatment of obsessive-compulsive disorder and major depression: case report. J Neurosurg 2004; 101: 682–686

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Therapeutic Brain Stimulation and Cortical Excitability in Depressed Patients

TO THE EDITOR: Changes in central cortical inhibitory pathways, especially associated with γ-aminobutyric acid (GABA) neurotransmission, have been widely implicated in the pathogenesis of major depressive disorder. Furthermore, a

number of studies have supported the view that response to antidepressant interventions is accompanied by an increase in GABA-ergic neurotransmission. In accordance, there is evidence that antidepressant therapeutic brain stimulation techniques, such as vagus nerve stimulation and ECT may act via GABA-ergic pathways (1, 2). Transcranial magnetic stimulation is a noninvasive investigational tool that has been extensively used over recent years to assess human motor cortex excitability (3).

After approval by a local ethics committee and receipt of written informed consent, we tested the motor threshold, postexcitatory inhibition, and intracortical excitability to clarify the influence of vagus nerve stimulation and ECT on motor cortex excitability with transcranial magnetic stimulation in two female patients with unipolar major depressive disorder (40 and 65 years old); each received two different antidepressant stimulatory interventions. In the premenopausal patient, each of the three assessments was performed within the follicular phase of her menstrual cycle. Antidepressant medication (tranylcypromine, 40 mg/day, and venlafaxine, 150 mg/day) was kept constant at least 4 weeks before the first stimulation treatment and throughout the whole treatment. Response was defined as a 50% reduction in score on the 21-item Hamilton Depression Rating Scale.

Ms. A did not respond to 12 sessions of right unilateral ECT (her Hamilton depression scale score dropped only 1 point, from 27 to 26) and was then successfully treated with vagus nerve stimulation (her Hamilton depression scale score dropped from 26 to 12). Ms. B did not respond to 10 weeks of vagus nerve stimulation (her Hamilton depression scale score increased by 2 points, from 29 to 31) and was then successfully treated with 12 sessions of ECT (her Hamilton depression scale score dropped from 31 to 10). In both patients, measurements of motor cortical excitability were performed at baseline, after completion of the first unsuccessful intervention, and after the completion of the second (successful) intervention. Regardless of the type of intervention, all parameters remained unchanged after the first therapeutic trial. After the second therapeutic intervention (vagus nerve stimulation in Ms. A and ECT in Ms. B), both patients showed a treatment response and an increase in cortical silent-period duration and intracortical inhibition.

To our knowledge, this is the first report of an increase in motor cortical inhibition in depressed patients receiving vagus nerve stimulation and ECT. The data suggest that a common GABA-ergic pathway is activated in both vagus nerve stimulation and ECT responders. Furthermore, the data indicate that measurement of motor cortical excitability may be a useful tool for investigating and monitoring inhibitory brain effects of different antidepressant stimulation techniques. In the future, further studies with larger groups are needed.

References

1. Sanacora G, Mason GF, Rothman DL, Hyder F, Ciarcia JJ, Ostroff RB, Berman RM, Krystal JH: Increased cortical GABA concentrations in depressed patients receiving ECT. Am J Psychiatry 2003; 160:577–579
2. Bajbouj M, Gallinat J, Lang UE, Neu P, Niehaus L: Motorcortical excitability after electroconvulsive therapy in patients with major depressive disorder. Suppl Clin Neurophysiol 2003; 56:433–440
3. Siebner HR, Rothwell J: Transcranial magnetic stimulation: new insights into representational cortical plasticity. Exp Brain Res 2003; 148:1–16

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Understanding the Heterogeneity of OCD

TO THE EDITOR: I read with interest the excellent review of dimensional approaches to understanding obsessive-compulsive disorder (OCD) heterogeneity by David Mataix-Cols, Ph.D., and colleagues (1). I agree with the authors that OCD heterogeneity is an important issue and that failure to identify differences within the condition has significantly hindered advances in theory and treatment. My comments focus on the authors' contention that a dimensional approach to understanding OCD heterogeneity is an inherently superior method.

There have been three recent approaches to understanding OCD symptom heterogeneity. Some researchers have focused on patients' dominant compulsive behavior to form symptom subgroups (e.g., washers versus checkers). This approach is limited and fails to capture most cases in which patients are seen with multiple classes of symptoms. In recent investigations, the diversity and complex patterns of symptoms seen in clinical presentations have been characterized with multivariate statistical analyses. Factor analysis has been used to identify the latent dimensions of several comprehensive OCD symptom measures. Alternatively, symptom measures have been subjected to cluster analysis to form symptom-based subgroups of individuals. In cluster analysis, individuals are assigned to groups created by maximizing between-group differences and minimizing within-group variability on a set of measures (2).

Cluster analysis may offer several advantages over factor analysis in characterizing OCD heterogeneity, and this categorical approach is not limited in some of the ways Dr. Mataix-Cols et al. implied. In cluster analysis, individuals are unambiguously assigned to unique groups, whereas in factor analysis, each individual is assigned a score on all of the identified latent dimensions. Thus, the factor scores estimated for individuals may not connect the person to a specific dimension. As Dr. Mataix-Cols et al. pointed out, hoarding symptoms have emerged as a symptom dimension that predicts unresponsiveness to current pharmacotherapy and standard behavior therapy. Although there has been limited study, similar results have been reported with a cluster analysis approach in which the hoarding subgroup was less responsive to behavior treatment (3). The results of several recent cluster analyses (e.g., reference 4) suggest that complex symptom presentations can be captured with a cluster analysis approach and that resultant clusters are far from monosymptomatic.

The relative merits of categorical and dimensional approaches to psychiatric classification have long been debated. The use of each of these approaches to understanding OCD heterogeneity warrants further investigation.