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

MALEK BAJBOUJ, M.D.
UNDINE E. LANG, M.D.
PETER NEU, M.D.
ISABELLA HEUSER, M.D., PH.D.
Berlin, Germany

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.

References

1. Mataix-Cols D, Conceição do Rosario-Campos M, Leckman JF: A multidimensional model of obsessive-compulsive disorder. Am J Psychiatry 2005; 162:228–238
2. Everitt BS, Landau S, Leese M: Cluster Analysis, 4th ed. New York, Oxford University Press, 2001
3. Abramowitz J, Franklin M, Schwartz S, Furr J: Symptom presentation and outcome of cognitive-behavior therapy for obsessive-compulsive disorder. J Consult Clin Psychol 2003; 71:1049–1057
4. Calamari JE, Wiegartz PS, Riemann BC, Cohen RJ, Greer A, Jacobi DM, Jahn SC, Carmin C: Obsessive-compulsive disorder subtypes: an attempted replication and extension of a symptom-based taxonomy. Behav Res Ther 2004; 42:647–670

JOHN E. CALAMARI, PH.D.
North Chicago, Ill.

Dr. Mataix-Cols and Colleagues Reply

TO THE EDITOR: We were pleased to read Dr. Calamari's letter in relation to our recently published review. It highlights methodological and conceptual issues that are unlikely to be easily resolved. Rather than diametrically opposite techniques, factor analysis and categorical approaches, such as cluster analysis, are likely to be complementary because they constitute different ways of looking at the same phenomenon—the heterogeneity of OCD (1). Both have demonstrated their usefulness. For example, tic-related OCD and early-onset OCD both appear to be overlapping and valid subtypes (2). Our preference for factor analytical techniques to address the *classic* symptoms of OCD is twofold.

First, our model hypothesizes that obsessive-compulsive phenomena are normally distributed in the general population (3, 4) and are not limited to the traditional diagnostic boundaries of OCD, i.e., they may be present in many other neurological and psychiatric conditions. Conceptually, a dimensional approach seems to reflect this more accurately. Second, if one adopts a strictly categorical approach, patients need to be unequivocally allocated to only one subtype: a patient is either in cluster X or in cluster Y but not both. We doubt that nature is so exact regarding these symptoms. This is one of the main limitations of the DSM-IV multiaxial system and has been heavily criticized. Along with other theoreticians (5, 6), we propose that a dimensional approach can better deal with the problem of comorbidity or the coexistence of various symptom types in OCD. In short, we reiterate the idea that different methods of analysis are probably likely to yield complementary results. We are glad that Dr. Calamari concurs that considering the heterogeneity of OCD is the direction to take in this important area of research.

References

1. McKay D, Abramowitz JS, Calamari JE, Kyrios M, Radomsky A, Sookman D, Taylor S, Wilhelm S: A critical evaluation of obsessive-compulsive disorder subtypes: symptoms versus mechanisms. Clin Psychol Rev 2004; 24:283–313
2. do Rosario-Campos MC, Leckman JF, Curi M, Quantrano S, Katsovich L, Miguel EC, Pauls DL: A family study of early-onset obsessive-compulsive disorder. Am J Med Genet B Neuropsychiatr Genet 2005; May 12. http://www3.interscience.wiley.com/cgi-bin/abstract/110493822/ABSTRACT
3. Rachman S, de Silva P: Abnormal and normal obsessions. Behav Res Ther 1978; 16:233–248
4. Mataix-Cols D, Cullen S, Lange K, Zelaya F, Andrew C, Amaro E, Brammer MJ, Williams SCR, Speckens A, Phillips ML: Neural correlates of anxiety associated with obsessive-compulsive symptom dimensions in normal volunteers. Biol Psychiatry 2003; 53:482–493
5. Krueger RF, Piasecki TM: Toward a dimensional and psychometrically informed approach to conceptualizing psychopathology. Behav Res Ther 2002; 40:485–499
6. Maser JD, Patterson T: Spectrum and nosology: implications for DSM-V. Psychiatr Clin North Am 2002; 25:855–885

DAVID MATAIX-COLS, PH.D.
London, England
MARIA CONCEIÇÃO DO ROSARIO-CAMPOS, M.D.
San Paulo, Brazil
JAMES F. LECKMAN, M.D.
New Haven, Conn.

Heart Transplantation in a Schizophrenia Patient

TO THE EDITOR: Mr. A, in the clinical case conference by Stephanie M. Le Melle, M.D., M.S., and Charles Entelis, M.D. (1), is one of many patients with schizophrenia, schizoaffective disorder, and bipolar disorder who have undergone heart transplantation at New York Presbyterian Hospital–Columbia University Medical Center. The case conference provided an opportunity to reflect on what psychiatric consultants to heart transplant programs have learned about helping patients with severe mental illness and other psychosocial risk factors achieve successful heart transplant outcomes.

First, some psychiatric disorders and psychosocial variables do have an effect on transplant outcomes. Recent substance abuse, severe personality disorders, poor global function, and an avoidant coping style predict worse outcomes (2, 3). Second, in some cases, even high-risk patients can do well with expert management. Third, especially in such cases, good family support is invaluable. Fourth, a longitudinal relationship with the transplant team provides an opportunity to assess and modify psychosocial risks much better than evaluation at a single moment in time. Mr. A was undoubtedly a high-risk patient, but he had the benefit of devoted and expert psychiatric care, time to develop a relationship with his transplant cardiologist, and superb support from his family.

I would demur on one point made in the report. There has been no shortage of previous experiences with the development or exacerbation of psychosis in patients after transplantation who were receiving a high dose of corticosteroid immunosuppressant therapy. The role of steroids in precipitating psychosis and mood disorders in heart transplant recipients has been described repeatedly since the late 1960s (4–6).

As we noted previously (2), the presence of psychosocial risk factors should not be reason to prejudicially deny care; rather, it should stimulate efforts to mitigate these risks to provide the best possible care and outcome.

References

1. Le Melle SM, Entelis C: Heart transplant in a young man with schizophrenia (clin case conf). Am J Psychiatry 2005; 162:453–457
2. Shapiro PA, Williams DL, Foray AT, Gelman IS, Wukich N, Sciacca R: Psychosocial evaluation and prediction of compliance problems and morbidity after heart transplantation. Transplantation 1995; 60:1462–1466