Can Psychopharmacology Do More for Our Patients With Anosognosia?

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I would like to draw the reader's attention to the commentary in this issue by Rachel Streiff, who discusses the perspective of a family member caring for a loved one suffering from anosognosia. The aim of Ms Streiff's Commentary and my editorial is to heighten awareness of the scant research on medication treatments for people with serious mental illness who also experience anosognosia.

The term anosognosia (a = without, noso = disease, gnosia = knowledge) was introduced in 1914 by the French neurologist Joseph Babinski[1] to describe the clinical condition of patients who presented with left hemiplegia following a right cerebral hemisphere stroke and "denied" that there was anything wrong with their left arm or leg. This phenomenon has been described in many neurological diseases including cortical blindness (Anton syndrome), aphasia, Huntington disease, Parkinson disease, Alzheimer disease, frontotemporal dementia, and postacute patients with severe traumatic brain injury.[2–8]

Anosognosia is seen in many psychiatric disorders. In schizophrenia, between 50% and 80% of patients have been shown to be partially or totally lacking insight into the presence of their mental disorder.[9,10] When Eugen Bleuler categorized the core symptoms of schizophrenia as the four "A's"—alogia, autism, ambivalence, and affect blunting,[11] he may have missed one of the most important "A's" of all—anosognosia.

Anosognosia has also been observed in patients with bipolar disorder,[9,12] major depression with psychotic features,[13] obsessive-compulsive disorder,[14] eating disorders,[15] and specific[16] and social phobias.[17] Some patients with psychiatric disorders may also exhibit anosodiaphoria or "lack of suffering from disease," an indifference to the impact of their deficits. Anosodiaphoria, observed in stroke patients,[18] is closely linked to anosognosia.[19]

According to the *Diagnostic and Statistical Manual of Mental Disorders*, *Fifth Edition*, *Text Revision*, "Some individuals with psychosis may lack insight or awareness of their disorder (ie, "anosognosia"). This "lack of insight" includes unawareness of the symptoms of schizophrenia and may be present throughout the entire course of the illness. Unawareness of illness is typically a symptom of schizophrenia itself rather than a coping strategy. It is comparable with the lack of awareness of neurological deficits after brain damage, termed anosognosia. This symptom is the most common predictor of nonadherence to treatment, and it predicts higher relapse rates, increased number of involuntary treatments, poorer psychosocial functioning, aggression, and poorer course of illness."(p116). Patients with anosognosia are the most severely ill, and unfortunately, the anosognosia may remain even after symptomatic improvement in the patient's psychiatric illness.

Insight in schizophrenia is a continuum involving multiple dimensions such as awareness of having a disorder, attribution of one's symptoms to the disorder, and acknowledging the need for treatment.[20] Detailed and valid measures of the assessment of insight in psychotic patients have been developed that encompass these different dimensions such as the Scale to Assess Unawareness of Mental Disorder.[21] But are clinical trials of new medications for the treatment of schizophrenia enrolling the severely ill people with anosognosia?

Anosognosia in psychiatric illness has a biological basis. There is considerable evidence that pathophysiologic changes in the prefrontal cortex, insular cortex, and the default mode network are associated with anosognosia and poor insight in people suffering from schizophrenia.[22,23] Despite research that indicates a biological basis for anosognosia and the independence of anosognosia and poor insight from other psychotic symptoms, insight is rarely the primary outcome measure in clinical trials[24] and is often not specifically measured in treatment studies at all.[22] Regrettably, there are no psychopharmacologic treatments with a Food and Drug Administration indication to treat anosognosia or improve insight in psychiatric illnesses and I am not aware of any in development.

Ms Streiff and I attended the 61st Annual Meeting of the American College of Neuropsychopharmacology in Phoenix, Arizona, this past December. Although there were numerous presentations and posters regarding trendy psilocybin and other psychedelic research there was not a single lecture or

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poster mentioning anosognosia at the conference. However, it is the single most devastating symptom of severe psychiatric illness that is responsible for the majority of deaths, violence, incarceration, homelessness, and disability.[25]

What should be done? Clearly, given the notable adverse effects on patient's recovery, the field of psychopharmacology needs to devote more investigations in medication treatments for patients with anosognosia. We need to know whether any medication that purportedly treats schizophrenia also treats anosognosia. To date, we do not have tangible evidence about the efficacy of current psychopharmacologic treatments on anosognosia. Assessment of anosognosia should be included in standard scales and systematic measurements of anosognosia to evaluate whether there is, or is not, improvement. In addition, efficacy in treating anosognosia should be stated in the drug label.

In her commentary, Ms Streiff raises an interesting question as to whether anosognosia deserves its own diagnosis. If anosognosia was a distinct diagnosis, it could lead to drug development specifically aimed at this symptom. Would the Food and Drug Administration be willing to consider it as a separate diagnosis? Is there evidence that anosognosia has a different target brain region/pathology/cell dysfunction/molecular target than other symptoms of schizophrenia? These are important questions to answer.

There are available techniques and tools to assess a patient's competence to participate in clinical research such as the MacArthur Competence Assessment Tool for Clinical Research.[26] This tool has been used to assess competency to participate in research in a variety of psychiatric disorders including schizophrenia[27] and Alzheimer disease.[28] If the patient can understand what is going to take place in the study and understands the research procedures, they could participate even though they may disagree that they have an illness. We could learn from Amador's Listen-Empathize-Agree-Partner® approach, agreeing on some areas with the patient, and agreeing to disagree on others, and then partnering with the patient on future goals.[29]

Although I believe that the strategy outlined above is preferred, what about patients who are not competent to consent to participation in a research protocol? Why cannot guardians, who may have legal authority to consent on behalf of the patient for treatment, not also have the authority to consent for participation in research? We must find a way to increase the enrollment of patients with anosognosia in clinical trials of new (and currently available) treatments following the example of neurologists.[19,30] Guardians commonly give consent for Alzheimer patients to participate in clinical research, without the guardianship specifically giving authority to consent to research. We should advocate for laws around the world that would allow a legal guardian to be able to consent on behalf of the patient with anosognosia for participation in research studies.

Patients who deny illness may never come to treatment, but people with severe schizophrenia almost always enter the healthcare system, including at clinics that conduct clinical trials. Psychopharmacology researchers must make a concerted effort to enroll people with anosognosia in clinical trials so we can learn what the optimal treatments are for our most severely ill patients.

AUTHOR DISCLOSURE INFORMATION

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