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The Cube

PSYCHOSIS

Schizophrenia Today: What's New and What's Coming

Experts in schizophrenia research and treatment offer glimpses of the future.

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THE BASICS

- What Is Psychosis?
- Find a therapist to treat psychosis

KEY POINTS

- **"Who's Who in Schizophrenia?" refines and replaces older conceptualizations of this mental disorder.**
- **Treatment of negative symptoms, particularly anosognosia and avolition, may be the key to long term prognosis.**
- **A new drug in clinical trials, Roluperidone, has shown success in treating negative symptoms.**
- **New data suggest that positive symptoms of schizophrenia may result from compensatory brain miscalculations.**

Source: Robert Francis / used with permission

Think of any literary work or film in which a character with schizophrenia is featured — Russell Crowe's portrayal of Dr. John Nash in *A Beautiful Mind* comes to mind first for many — and the most prominent symptoms portrayed are usually the condition's "positive symptoms," especially hallucinations and delusions. But for countless people who actually suffer from schizophrenia, including Robert Francis, LCSW, author of a new book on the subject — *Who's Who in Schizophrenia? The Legends and Icons Among Us* — it's the negative symptoms that are often the most debilitating.

Sometimes referred to as "the "A's of schizophrenia," these negative symptoms include **avolition** (limited desire for goal-directed activities), **asociality** (lack of desire for social contact), **anhedonia** (reduced pleasure or anticipated pleasure related to previously enjoyed activities), **alogia** (reduction in the quantity of speech and elaboration), and **attenuated affect** (i.e., reduced emotional expression in the face, voice, and body gestures).

Unfortunately, though existing medications in various drug classes have been able to reduce the intensity and frequency of schizophrenia's positive symptoms, with clozapine being the gold standard, few drugs have been able to treat schizophrenia's negative symptoms successfully. But this may be about to change.

In *Who's Who in Schizophrenia*, Robert Francis interviews several prominent researchers in the field, with some offering hope for a new drug to treat schizophrenia's negative symptoms. Gregory P. Strauss, PhD is a schizophrenia researcher who also founded the Clinical Affective Neuroscience (CAN) lab at the University of Georgia. Dr. Strauss is optimistic that a new drug, Roluperidone, can be a game changer in that it blocks the action of serotonin (at sigma and α-adrenergic receptors) rather than acting on dopamine, like most older medications.

Currently in phase 3 trials, Roluperidone has shown efficacy in improving global functioning in schizophrenia, and based on the data, Dr. Strauss reported that these global improvements were mediated by Roluperidone's ability to reduce avolition. According to Strauss, *"I believe that because the drug improved motivation, an improvement in all other domains was possible. Low motivation might underlie why individuals have reductions in social activity, goal-directed activity, recreational activity, speaking, and expressing emotion."* As such, Strauss feels that *"avolition may be the key negative symptom"* in schizophrenia.

Anosognosia

It is often said that the first step in solving a problem is to admit that you have one, and if you can acknowledge what that problem is you're halfway to resolving it. But what if the problem itself prevents you from admitting that you have a problem? Such is the dilemma with anosognosia. Anosognosia, which refers to a lack of insight into one's illness, is often included as the sixth "A" in the contemporary grouping of schizophrenia's negative symptoms. Though not part of Eugen Bleuler's original list of negative symptoms in 1908, some researchers, including Xavier Amador, PhD, author of *I Am Not Sick, I Don't Need Help*, consider anosognisa to be a hallmark feature.

In *Who's Who in Schizophrenia?*, Dr. Amador notes that anosognosia involves dysfunction of the pre-frontal and frontal brain regions, and it is observed in about half of those diagnosed with schizophrenia. More importantly, anosognosia is the top predictor of who will refuse medication, and, for those who are already taking medication, who will discontinue. Anosognosia is also a predictor of the frequency of involuntary hospitalizations and it's correlated with psychosocial functioning, as well as overall prognosis.

As with aikido, Dr. Amador recommends redirecting the energy of one with anosognosia instead of confronting it directly.

Source: Opkangas / Wikimedia Commons

In terms of helping those for whom anosognosia is a problem, Dr. Amador developed a system of strategies summarized by the acronym LEAP: Listen, Empathize, Agree, and Partner. Here, the emphasis is on building a relationship, not combatively confronting the afflicted individual and trying to convince them that their beliefs are erroneous. To make a metaphor, this is a strategy reminiscent of how, in certain martial arts like aikido and jiu-jitsu, the aim is to redirect an opponent's energy rather than confront it head-on.

Schizophrenia is a Syndrome, Not a Specific Disease

In 1974, William T. Carpenter, MD, was among the first to recognize that schizophrenia better fit the model of a syndrome than a specific disease entity. Dr. Carpenter is co-founder of the Brain and Behavior Research Foundation (formerly the National Association for Research on Schizophrenia and Depression) and a former chair of the NIMH committee on schizophrenia treatment research.

In *Who's Who in Schizophrenia?*, Dr. Carpenter reports that it wasn't until the publication of DSM-5 in 2013 that his formulation of schizophrenia as a syndrome (rather than a specific disease) gained traction. According to Dr. Carpenter, the syndrome of schizophrenia encompasses at least six separable aspects of psychopathology, and none of them is necessarily unique to schizophrenia. As such, schizophrenia shares transdiagnostic similarities with other mental disorders, like depression, with each aspect of psychopathology manifesting on a continuum, not in an *all-or-none* way. Dr. Carpenter laments, however, that many aspects of his alternative conceptualization of schizophrenia were relegated to Section 3 of the DSM-5, not included in the main text of schizophrenia's diagnostic criteria.

Additional Insights and Perspectives

One of the methodological problems encountered in all areas of science is that, as we try to study more sophisticated phenomena, we need more sophisticated equipment — computers and software in particular — which removes us further and further from direct observation of the natural phenomena we hope to study. Although these more sophisticated computers give us the chance to investigate increasingly subtle, complex phenomena, there's a catch: sometimes there are errors in the software code (or the equipment itself) which can distort our observations, but we may never discover these errors or may only find them years later. Such was the conclusion of Swedish researchers in 2016 (Ecklund et al., 2016) who discovered a statistical software anomaly that likely invalidated 40,000 fMRI studies of neurology over a 15-year period.

In a related way, the brain is often compared to a computer, with the anatomical structures serving as the computer's hardware and the brain's physiology as the computer's software. Like a computer, the brain makes predictive calculations with its own form of adaptive software to interact successfully with all stimuli of the natural world. Most of the time, the brain's software works perfectly well, but according to Karl Friston, FMedSci FRSB, FRS, problems arise when the calculations of the brain's adaptive software are imprecise, and these problems can produce the symptoms of schizophrenia.

Dr. Friston is a British neuroscientist who has combined the use of neuroimaging techniques with advanced statistical methods to create models of how the brain might work in both typical and pathological ways. In *Who's Who in Schizophrenia?*, Dr. Friston explains that the positive symptoms of schizophrenia can be viewed as a "functional compensation" for some of the soft neurological symptoms of the disorder, like mild difficulties with eye movements, among others.

According to Dr. Friston, various neurological anomalies among those with schizophrenia may prohibit their brains from being able to process the sensory data they receive in an efficient way. As a result, their brains may create what computer programmers call a "work-around" (i.e., a quick fix for the problem that doesn't eradicate its underlying cause) to compensate for being overloaded. Problems then arise because these compensatory work-arounds make miscalculations about how the natural world matches up to the brain's representation of it. Interestingly, these miscalculations seem to produce a result similar to the miscalculations of the fMRI software referenced in the Ecklund and colleagues (2016) study above: the generation of faulty data, images, and conclusions. As it relates specifically to schizophrenia, Dr. Friston believes that these compensatory miscalculations are at the root of the disorder's positive symptoms (e.g., hallucinations and delusions).

In closing, *Who's Who in Schizophrenia?* is an informative primer on the recent developments in schizophrenia — whether they're related to new drugs currently in clinical trials, or more contemporary conceptualizations of this often debilitating syndrome. It is a valuable resource, not only for clinicians and researchers who work in this area, but for patients and their families as well.

About the Author

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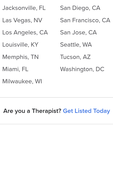

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