SPEAKER NOTES

Targeting Sensory Processing Abnormalities in Schizophrenia with Cognitive Training

Summarized by Thomas T. Thomas

Research into the schizophrenia-spectrum disorders is proceeding on many fronts. The speaker at our January 28 meeting, Bruno Biagianti, MD, is a Post Doctoral Fellow in the Vinogradov Schizophrenia Laboratory at the University of California - San Francisco, where he coordinates a series of neuroimaging experiments to investigate the effects of cognitive training and oxytocin on key brain regions. He also investigates the use of mobile devices to disseminate cutting-edge treatments for schizophrenia, including cognitive training, automated cognitive behavioral therapy (CBT), computerized neuropsychological assessments, and virtual group therapy, to individuals with schizophrenia who live in community settings around the Bay Area.

BRUNO BIAGIANTI, MD

Dr. Biagianti trained as a psychiatrist at the University of Milan, Italy, and has worked with patients with schizophrenia. His long-term goal has been to improve their quality of life. He believes that, by treating sensory processing, we can improve their cognition, symptoms, and real-world functioning.

"Schizophrenia is a highly prevalent disorder," he said, twice as prevalent as Alzheimer's and five times the incidence of multiple sclerosis. "It's also a costly disease to treat," several thousands of dollars more annually than cancer, stroke, or heart disease. The hallmarks of schizophrenia are positive symptoms like delusions and hallucinations; disorganization in thinking and speech; negative symptoms like affect flattening and loss of volition or pleasure; and social or occupational dysfunction. "Medication works quite well on most of these symptoms," Biagianti said, "and psychotherapy can help with a person's coping skills, but neither addresses the cognitive impairments that may be present."

These impairments are common and stable features of the schizophrenia-spectrum disorders, even with individuals who are young, taking medications, and are clinically stable. They include problems with focusing, sustaining attention, learning and memorizing, retrieving information, and planning.

For the past 100 years, medical science has been deconstructing schizophrenia. From an empirical observation of patient behaviors and experiences (or phenomenology), it's a mental disorder. From the study of symptoms

(psychopathology), it's a thought and perception disorder. From the viewpoint of cognitive impairments (neuropsychology), it's a cognitive disorder. And from the viewpoint of neural system imbalances (psychophysiology), schizophrenia is a sensory processing disorder.[1]

Several parts of the brain are involved in sensory processing. Say you're walking down the street and a friend comes up and says, "Hi!" The sensory cortex processes both the auditory signal ("Hi!") and the visual signal (her face). The prefrontal cortex limits your attention, filtering out extraneous details, so you can focus on her voice and face. And the hippocampus retrieves information, so you can identify her voice and features as a particular person known to you, with associated emotional representation.

"In schizophrenia," Biagianti said, "every part of this process is disrupted. The system is 'noisy,' so you can't interpret the signals, can't filter the flow, can't retrieve the information." The usual processing time in the brain is 200 milliseconds, but a person with these sensory disturbances may take 600 or 700 milliseconds to make these connections.

Aberrations in neurochemical and neurophysiological processing can cause disturbances in sensory perception and representation, leading to faulty cognitive processes and experiences. Reverberations from these disturbed processes can then rupture an individual's sense of ownership of an experience, his or her sense of presence, corporeality, self-demarcation, and existential orientation. And that can ultimately lead to psychotic hallucinations and delusions.

Conversely, rehabilitation of sensory processing—in both its speed and its accuracy—should improve brain function and translate into an improved quality of life. Rehabilitation is possible because the brain exhibits "neural plasticity." That is, it is like a muscle and it responds to exercises.

Targeted training of early sensory processing uses computerized tasks that are carefully controlled and constrained. The subject undergoes a highly intensive training schedule—usually an hour a day, five days a week—for 20 to 40 hours total. The tasks are customized, based on psychological assessment. They are designed never to be too difficult, and therefore frustrate the subject, but never too easy, either. As the subject performs the training, he or she enters a learning curve, and the tasks become progressively harder.

For example, training the auditory system might play two "chirps," or sweeps up or down, from a low pitch to high, or vice versa. The subject identifies the direction of each chirp on screen with an arrow. As the training progresses, the chirps become shorter and closer together. Then the subject might be presented with four cards, two each associated with a spoken word like "fig" and "mat." The subject must match the cards to the words he or she hears. As training progresses, the subject is presented with closer-sounding words like "chuck" and "rug," and more cards are shown with more words to match.

[1] Other ways of looking at this disease are from molecular biology, the study of neurotransmitters and receptors, as a neurochemical disorder, and from the study of genetic polymorphisms and epigenetic modifications as a genetic vulnerability.

For visual training, the task might show a circle of eight birds all alike, except that one has different plumage. The circle disappears, and the subject must indicate the position of the unique bird. As the training progresses, more birds are shown in different patterns. Another task will show a human face, followed by two more, and the subject is asked to match the emotion shown on the first face with that on either of the second faces. This task can help with the subject's interpretation of facial expressions and social functioning.

To test whether this training improves cognition in people with schizophrenia, Biagianti's group ran tests between subjects with chronic schizophrenia—people in their 40s with a diagnosis for more than five years—and a set of healthy controls. The schizophrenia group was randomized to avoid contaminating results with effects of particular medications or other conditions. One group took 50 hours of auditory training; the other, 50 hours of computer games. Those with the training showed significant improvement in global cognition, speed of processing, memory, verbal learning, visual learning, and problem solving. Similar testing with younger people who had a diagnosis for less than five years showed even greater results.

Neural scans with magnetic resonance imaging (MRI) compared brain activity in the healthy controls with the schizophrenic test subjects both before and after training. After training, their brains showed areas activated in ways comparable with the controls. The improvements are real-world and lasting, because test subjects were followed for 24 months, and their improvements remained constant after the initial 50 hours of training. Biagianti attributed this lasting effect to the subjects being able to function better and exercise their cognitive faculties. Test subjects themselves reported sensing a 30% to 40% improvement in their abilities.

"The training has no negative side effects," he said. "But it does take time, hours of training—at least an hour each day." Biagianti also noted that the results apply only to individuals with schizophrenia, schizo-affective disorder, and bipolar with psychosis, but not to other forms of bipolar or other mental disorders like depression.

The cognitive training project is now in its fifth year. In the Bay Area, training started at the San Francisco Veterans Administration Medical Center and is also offered at Prevention and Recovery in Early Psychosis (PREP, https://askprep.org) facilities in San Francisco, San Mateo, and Alameda counties; at Putnam Clubhouse in Concord; Lakehurst Hotel, Oakland; and Alameda County Hospital. This training is not commercially available and is used for research purposes only, as it requires a battery of tests to develop an individual's capabilities and customize the tasks for his or her progression.

Biagianti is now developing a version available for the Apple iPad that can be delivered unsupervised, with weekly check-ins, for people in areas poorly served by mental health clinics. A future direction is use of cognitive training to prevent the onset of psychosis in youths at risk for schizophrenia.

Anyone interested in taking part in further work on cognitive training at UCSF should contact the study coordinator at (415) 221-4810 extension 3077, or contact bruno.biagianti@ucsf.edu.