Brain Development of Schizophrenic Patients

Bailey S. Zinger

In the distant past, the symptoms and characteristics of schizophrenia were considered the behavior of other worldly spirits or beasts dwelling within a host's mind ("History Cooperative"). Although this idea is captivating, the symptoms of schizophrenia can be explained through scientific investigation. In 1910, Swiss psychiatrist Paul Eugen Bleuler coined the term "schizophrenia", derived from the Greek words "schizo", meaning split, and "phren", meaning mind (National Institute of Mental Health, 2016). Consequently, many people mistake schizophrenia for a form of dissociative identity disorder. A person who suffers from schizophrenia, however, does not change from one personality to another unrecognizable personality (National Institute of Mental Health, 2016). Schizophrenia is not a split personality disorder, nor is it the work of unseen spirits. Although the disorder is enigmatic, studies have been conducted to elucidate some of its symptoms and characteristics.

Schizophrenia is a chronic and severe mental disorder that affects how an individual feels, thinks, behaves, and perceives reality (A Brief History of Schizophrenia, 2012). Delusions and hallucinations are among the most common positive symptoms of the disorder, often resulting in experiences of derealization or depersonalization (Cannon, T.D., 2015). Derealization is a phenomenon in which the external world becomes seemingly unreal, for instance, a person experiencing derealization may describe it as a dream-like state in which sights and sounds are fuzzy and muted. Depersonalization, one of the most common symptoms associated with schizophrenia, is a state in which one's thoughts and feelings do not seem like his or her own (Cannon, T.D., 2015).

The onset of schizophrenia is typically progressive and presents itself between the ages of 12 and 35 (Cannon, T.D., 2015). A young individual demonstrating stark changes in thought or perception that manifest into delusions is considered a prodromal or high-risk clinical case. Schizophrenia is a disconnection between functional neural networks in the brain; since different psychotic symptoms of schizophrenia may involve different interactions amongst networks, high-risk clinical cases are of extraordinary importance to scientists as they can be marked and traced through the progression of the disorder (Cannon, T.D., 2015). The complexity of schizophrenia is what makes the disorder so difficult to diagnose. The root causes of schizophrenia vary widely and may include genetic variants, social stress, and neurological complications during childbirth or early development (Cannon, T.D.). Due to the complex nature of the disorder, two leading theories of schizophrenia onset have been considered, but there is not yet one sure method to diagnose and treat individuals with the disorder. The two theories discussed in this article include the neurodevelopmental model and the excitation-inhibition imbalance model. Brain disconnectivity due to *axonal pathology, such as disrupted myelination, and deficits in dendritic spines is thought to be the neurodevelopmental feature of schizophrenia (Cannon, T.D., 2015). One condition includes disrupted myelin, the sheath of protective plasma membrane extensions along axons of the nervous system (Snaidero, 2014). Disrupted myelin prevents high specificity of nerve impulses along axons, indicating the possibility of miscommunication amongst cells in regards to perception and memory. This condition is likely to have been expressed at birth in schizophrenic patients, but in some cases, this disruption may progress above a threshold of exposed psychotic symptoms despite normal neurological developments (Cannon, T.D., 2015). In other words, the neurological symptoms of schizophrenia are always present but are expressed later in life.

The notion of postponed symptom expression means that the disorder may be progressive and a method of mapping the brain over time is pertinent to discovering the patterns of the disorder. Thus, neuroimaging of high-risk clinical cases that did convert to the full psychosis of schizophrenia showed significantly greater thinning of the gray matter in the prefrontal cortex of the brain in comparison to healthy controls and those that did not convert (Cannon, T.D., 2015). These tests included subjects that had not previously been exposed to antipsychotic medications, ensuring that the medications themselves were not stimulating the acceleration of gray matter loss (Cannon, T.D., 2015). Networks that involve the medial prefrontal cortex play critical roles in memory formation and retrieval. These networks also indicate whether a person experienced their own memory or imagined the experience of another person (Cannon, T.D., 2015). This memory discrepancy can now be much better identified through the tracking of the thinning of gray matter in this region. "Reality monitoring" is defined as the ability to assess the characteristics of memory representations. The characteristics of the memory representations may reflect the neurological processing activity that occurs when a memory becomes encoded. This includes the marking of perceptual or actual details about an event and/or the associated thoughts and feelings at the time (Brandt, 2013).

Prefrontal cortex regions are primarily involved in memory recollection. To verify this, a study was performed focusing on the inhibition of memory retrieval. In this study, subjects suppressed retrieval of some items from a study list, showing that the ability to retrieve those items was impaired and the medial prefrontal cortex was active during retrieval suppression (Peters, 1970). Therefore, reality monitoring of action memories is predicted to provoke activity in medial prefrontal cortex regions (Brandt, 2013) in specific structural variations, which correlate with differences in performance on reality monitoring tasks (Cannon, T.D., 2015). Schizophrenic patients are more likely to rely on familiarity-based mental processes, meaning activities and memories that are repetitive and easy to replicate due to prolonged exposure come more easily to them. This is due to the deficit in absolute or relational neural encoding, which reduces the ability to reference memories in context (Cannon, T.D., 2015). Considering this, disturbances in source monitoring during learning and memory encoding may cause disrupted belief evaluation (Cannon, T.D., 2015), the sensation of having difficulty discerning a belief from a fact or actual circumstance. Gray matter loss leading to disrupted belief in schizophrenia patients may explain why those with the disease become confused about what is real versus imaginary, and that the familiar begins to feel strange in the effect of derealization

*Axonal pathology refers to the laboratory tests conducted on samples of neural tissue including axons, the part of the nerve cell along which impulses are conducted. Samples are tested for various conditions such as disrupted myelination. The myelin sheath is an insulating cover over the axons in the brain that increase the speed of nerve impulses.

or depersonalization.

Another theory of schizophrenia onset is the excitation-inhibition imbalance model. The basis of this model is derived from the neurological developments of drug abusers, particularly in phencyclidine and ketamine abusers. These drug abusers experience similar symptoms to schizophrenia sufferers; the abusers' brains can be mapped and the findings applied to brains with schizophrenia. The effects of the drugs are driven by excitation of N-methyl-D-aspartate (NMDA) receptors in the brain, and these receptors in turn are activated by the excited state of the amino acid transmitter glutamate (Cannon, T.D., 2015). Cells associated with glutamine, glutamatergic pyramidal cells, converge, or synapse, onto some neurons that express the inhibitory gamma-aminobutyric acid (GABA) transmitter. These cells in turn project back to the pyramidal cells, completing a set of regional neurological circuits (Cannon, T.D., 2015). Pyramidal cells function by transforming synaptic inputs into a patterned output of action potentials. They are special due to their abundance in the brain and that they are able to send their axons long distances throughout the brain (Bekkers, n.d.). Since some pyramidal cells ultimately activate NMDA receptors, NMDA receptor hypofunction may result in an imbalance of excitation and inhibition that could contribute to some symptoms of schizophrenia (Cannon, T.D., 2015). For example, as NMDA receptor function continues to weaken, the previously learned memory interpretations show a directly correlating positive linear relationship. This process creates an altered environment for the development of new explanations of experience and phenomena (Cannon, T.D., 2015), such that an alien is controlling the patient's thoughts or beliefs.

Another interesting aspect of the excitation-inhibition imbalance theory is that mismatch negativity (MMN) potential is dependent on NMDA receptors. MMN is an electrophysiological potential generated when a stimulus occurs out of a series of standard stimuli that is different from the rest (a black dot amongst a series of white dots, for example) (National Institute of Mental Health, 2016). Since MMN is dependent on NMDA receptors, reduced MMN in all stages of schizophrenia is consistent with the inhibition of NMDA-mediated synaptic activity, and in turn these deficits in NMDA activity may drive the accelerated gray matter loss thought to be associated with schizophrenic cases (Cannon, T.D., 2015).

In all, the two theories discussed in this article describe some of the leading scientific evidence and speculation in the development of schizophrenia. However, many questions are still unanswered due to the complex nature of the disorder. What causes the process of gray matter deterioration? How does the inhibition-excitation imbalance come to be? Scientists and researchers are working toward answering these questions so that schizophrenics will receive more effective medical treatment.

References

A Brief History of Schizophrenia. (2012, September 08). Retrieved January 04, 2019, from https://www.psychologytoday.com/us/blog/hide-and- seek/201209/brief-history-schizophrenia

Bekkers, J. M. (n.d.). Pyramidal Neurons. Retrieved February 15, 2019, from https://www.cell.com/current-biology/pdf/S0960-9822(11)01198-5.pdf

Brandt, V. C., Bergstrom, Z. M., Buda, M., Henson, R. N., & Simons, J. S. (2013, August 6). Did I turn off the gas? Reality monitoring of everyday actions. Retrieved January 6, 2019, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3969513/

Cannon, T. D. (2015, October 19). How schizophrenia develops: Cognitive and brain mechanisms underlying onset of psychosis. Retrieved January 5, 2019, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4673025/

History Cooperative. (2016, September 19). Divine Madness – a History of Schizophrenia. Retrieved January 4, 2019, from https://historycooperative.org/divine-madness-a-history-of-schizophrenia/

National Institute of Mental Health (2016). Schizophrenia. Retrieved January 4, 2019, from https://www.nimh.nih.gov/health/topics/schizophrenia/index.shtml

Peters, G. J., David, C. N., & Marcus, M. D. (1970, January 01). Gregory J. Peters. Retrieved from http://learnmem.cshlp.org/content/20/4/201.full.html

Snaidero, N., & Simons, M. (2014, July 15). Myelination at a glance. Retrieved from http://jcs.biologists.org/content/127/14/2999