5-17-2013

The Progression of a Disease: an Overview of Schizophrenia

Lucas Stone
University of Puget Sound, lastone@pugetsound.edu

Follow this and additional works at: http://soundideas.pugetsound.edu/soundneuroscience
Part of the Neuroscience and Neurobiology Commons

Recommended Citation
Available at: http://soundideas.pugetsound.edu/soundneuroscience/vol1/iss1/14

This Article is brought to you for free and open access by the Student Publications at Sound Ideas. It has been accepted for inclusion in Sound Neuroscience: An Undergraduate Neuroscience Journal by an authorized administrator of Sound Ideas. For more information, please contact soundideas@pugetsound.edu.
The Progression of a Disease: an Overview of Schizophrenia.
Lucas Stone

Schizophrenia is a psychotic disease that alters the way people perceive reality on a cognitive, social and or emotional level. First detection is often difficult because some of the patients have not had a history of psychosis before their first episode and to them; nothing is out of the ordinary. My aunt had adolescent onset schizophrenia which first was recognized when she was fourteen. She had recurring encounters with a man who was dressed in a rat suit and he became a familiar face to her. Unfortunately Melinda was the only person who could see the peculiar man in the rat suit. Adolescent onset is just one of the ways that schizophrenia can surface, often it does not surface until adulthood. On average men don’t have a psychotic episode until they are between 17 and 27 and women are even later, with the majority of them not showing signs of psychosis until they are between 25 and 35.[1] Despite how common and widespread schizophrenia is, not very much is known about the disease and researchers around the world are trying to better understand it. Like most of diseases involving psychosis, schizophrenia was poorly treated and even more poorly understood until recently.[2] There were not effective pharmacological treatments for schizophrenic patients until the 1950’s and those drugs had terrible side effects.[2] The aim of this paper is to provide an overview of schizophrenia, from what is known about the mechanism and the causes to the methods of treatment and detection. This information will then be used to propose possible future avenues of treatment, research and understanding.

The Mechanism

The mechanism for schizophrenia has only been hypothesized. The question that needs to be answered is how does schizophrenia convince the mind that the stimuli it is receiving are coming from the physical world and not just from within the body. In his article, Kunjumon Vadakkan proposes that to achieve this requires a link between postsynapses so a signal can travel laterally through the synapses instead of in the prototypical fashion from axon to synapse.[3] In a normal collection of synapses there are ones associated with external pathways (physical sensations), ones confined to internal pathways within the mind and they are all separated by their plasma membranes.[3] In schizophrenia there might be something that causes the plasma membranes of synapses from external pathways and internal pathways to become fused in a way that allows for the passage of a signal from one postsynapse to another.[3] In this way the brain can perceive that it sees something tangible when there is actually nothing there.[3] Delusions such as the chronic paranoia are another common among symptom of schizophrenia and can work by the same mechanism.[3]

Causes

The most intriguing research into the cause of schizophrenia revolves around the genetics component of the disease. Epidemiological studies have shown that schizophrenia is a heritable disease and this was confirmed by a concordance rate of 60-70% between monozygotic twins.[4] Later studies looking at the sequence of patients with schizophrenia showed a common mutation was present within most of their genomes. The COMT gene was deleted.[1] The COMT gene controls a catabolic
enzyme involved in the degradation of dopamine and molecules and when it is deleted a complex syndrome involving schizophrenia occurs.[1] While this mutation is common in many schizophrenic patients and it could be an important key in understanding the cause of this disease, there is conflicting data that shows that the COMT gene may have not have any role in schizophrenia.[1] The conflicting data as well as the 60-70% concordance rate between monozygotic twins suggests that there may be some form of epigenetic regulation as well occurring in schizophrenia.[4] Epigenetic regulation is a change in gene expression that is triggered by changes in the structure of the genome rather than changes to the actual sequence.[5] A frontal cortex tissue study to search for DNA methylation sites showed that there were highly active methylation sites next to regions involved in glutamatergic and GABAergic neurotransmission and brain development.[4] These factors have been linked with potential causes of schizophrenia; however, because the epigenetic component of schizophrenia is a recent idea, there has not been enough research yet to make concrete conclusions.[4]

Detection

The invention of the MRI and specifically the fMRI (functional MRI) has remarkably helped diagnostic protocol for schizophrenic patients. By using fMRI, researchers have been able to study how the brains of schizophrenic patients respond differently to various stimuli in comparison to normal brains. Some studies have shown that abnormal frontotemporal system activity is integral to common cognitive problems in schizophrenia.[6] When stimulated with a more complex abnormal visual stimulation, schizophrenic brains have been shown to have a harder time processing the information.[6] The fMRI showed that the mid-frontal gyrus and the inferior frontal gyrus are more activated in schizophrenic patients than in the control subjects. In addition to impairing cognitive control, schizophrenia also affects the perception, interpretation, and processing of social information. Studies have shown that the overstimulation of the amygdala is a central part of the issue people with schizophrenia have with emotional processing.[6] While the right amygdala is stimulated in normal people when they see a positive or negative reaction on the faces of those around them, schizophrenic patients have bilateral amygdala stimulation when they perceive a negative reaction.[6] A similar occurrence is true when patients have a stimulus for fear.[6] The overstimulation of the amygdala is linked to the lack of social control that is common in many schizophrenic patients. Because of the hotspots of activity that are generated during these stimulation tests, they provide a way to see if a patient’s brain has schizophrenic tendencies. This display of brain function allows doctors to possibly identify schizophrenia before the first episode of psychosis.

Medication

The original psychosis drug was a dopamine receptor blocker called chlorpromazine and it was used because it was found to have calming activity on those with psychosis.[2] Similar dopamine inhibitors came out soon after but all of the first generation antipsychotics had the neurological side effects of parkinsonism (Parkinson’s disease like symptoms) or dyskinesia.[2] Second generation antipsychotics followed and were considered superior to first generation because they did not have the intense neurological side effects, but the second generation drugs had their own problem. When
taken over a long period of time like antipsychotics are prescribed for, the second
generation drugs were found to increase weight gain, increase prevalence for
cardiovascular risk factors and lead to metabolic abnormalities.[2] These are factors that
contribute to the average life span of severely mentally ill patients being 25 years
shorter than the rest of the population.[2] While antipsychotics are a good fill in, they are
far from perfect. The important step in antipsychotic medicine is going be when the drug
can attack the disease at its source, and not by blocking some of the body's natural
processes.

Conclusion and Future Treatment

Schizophrenia is a disease that mankind has been unable to figure out. For a
long time it was not understood, but that is beginning to change. If the mechanism
proposed in this paper is correct then it could potentially provide an explanation for why
fMRIs show overstimulation of the amygdala when schizophrenics are faced with
emotional distraught. If postsynapses become linked then a stimuli could move laterally
through a neuron and create bilateral amygdala stimulation when it is meant to be only
right amygdala stimulation. If this mechanism can be confirmed then the treatment for
schizophrenia would change dramatically. With fMRIs showing where there is abnormal
overstimulation in the brain, medicines could be created to target those plasma
membrane linkages and sever them from each other. If the mechanism is not confirmed
the potential of the epigenetic control of schizophrenia is another area that research
could investigate. By pairing fMRI and genetic screens, pre-episode diagnosis of
schizophrenia would be possible and would allow for preemptive treatment. Ideally
these strategies would push antipsychotic drugs out of schizophrenia treatment
altogether.

References

   & Epidemiology in Mental Health 8:52–66.
2) Kane JM, Correll CU. (2010) Past and Present Progress in the Pharmacologic
3) Vadakkan KI. (2012) A structure-function mechanism for schizophrenia. Front
   Psychiatry 3:108.
6) Gur RE, Gur RC. (2010) Functional magnetic resonance imaging in schizophrenia.