

Schizophrenia and the Sexual Differences

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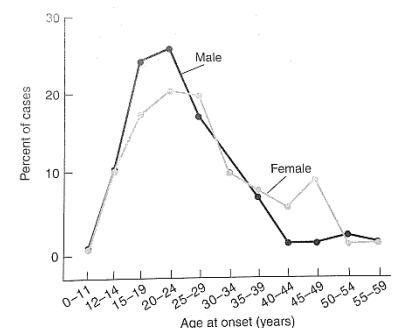
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GENERAL BACKGROUND

All of the information that will be told in this section will be from the textbook *Physiology of Behavior*, from chapter 16, which is all about schizophrenia and the other affective disorders. Schizophrenia, something that people misuse quite often when referring to psychological disabilities. The literal meaning of this is “split brain”, but this does not mean that the person diagnosed with schizophrenia has multiple personalities. Eugen Bleuler was the man behind this word, his intention was for schizophrenia “to refer to a break with reality caused by disorganization of the various functions of the mind, such that thoughts and feelings no longer worked together in a typical fashion” (). This mental disorder only affects one percent of the world’s population.

Diagnosing schizophrenia is not the easiest, symptoms can start as early as childhood, and as late as early adulthood. Symptoms of this disorder cross paths with other mental disorders, so when someone is getting diagnosed, clinicians have certain symptoms that they look for. There are three different categories of symptoms, each having characteristics; the first category is positive symptoms characterized by hallucinations, delusions, and thought disorder; followed by negative symptoms; social withdrawal, lack of initiative and persistence, and just overall absence of typical behaviors. The last of the three categories is cognitive symptoms, these symptoms may be caused by some abnormalities in the brain mixing with the negative symptoms which causes the person to experience poor problem solving, difficulty paying attention, etc. The order in which these symptoms appear can vary among people, the usual order is depression followed by the negative symptoms leading to the cognitive symptoms, having the

Figure 16.1 Age at First Sign of Psychotic Symptoms in Patients with Schizophrenia
(Based on data from Häfner et al., 1993.)



positive symptoms be the last to come to the surface (). To the right is Figure 16.1 showing the age that symptoms first start to appear in both male and females.

There is no single gene mutation that causes schizophrenia, instead it is a combination of multiple gene mutations. Studies have shown that schizophrenia is inherited, but there is no evidence showing whether or not these mutations are recessive or dominant. From these studies scientists have found that either there are multiple genes involved or having these genes increases the susceptibility of schizophrenia, meaning that the disease can be triggered by other factors. These factors could be genetic or environmental. There is not a definite answer to who gets this and who doesn't.

SUMMARY FOR SCIENTIFIC CONTEXT FROM REVIEW PAPER

Here is a little bit of background research from a review article written by Medrek and Mancini-Marie, throughout this review article they explain why male and females experience different symptoms for schizophrenia. Knowing that there is an abundance of research on males, and the affects schizophrenia has on their bodies, the research on females is less. So there are people out there that are trying to find ways in which schizophrenia differs among genders.

To start off, research has shown that men start to show symptoms sooner, and that men also experience more of the negative symptoms. One of the major differences that was seen among male and female subjects was the enlargement of ventricles. "Men diagnosed with schizophrenia had significantly larger ventricles relative to the same-sex controls, while in women patients the ventricular enlargement was significantly less pronounced or non-existent," (Mendrek & Mancini-Marie, 2016, p. 60).

Besides the enlargement of ventricles in men, women had an increased volume of the amygdala and the men had a decrease of volume. This leading to an increase in the orbitofrontal cortex amygdala ratio (OAR) in men, usually higher levels of OAR are seen in healthier women. The reasoning behind this is because the men have a decrease in the amygdala volume where women had decreased OAR because of reduced orbitofrontal volumes (Mendrek & Mancini-Marie, 2016, p. 61).

Researchers have also studied the effects schizophrenia has on the hippocampal volume of the brain. What they found was that only men have a reduction in the hippocampal volume when compared to the same-sex controls, but women that had a longer illness duration showed similar hippocampal reduction as the men (Mendrek & Mancini-Marie, 2016, p. 62). Further research has indicated that there may not be a definitive answer for who experiences the symptoms of schizophrenia first, or even who experiences them at all. A few studies have shown that there were little to no differences in male and female cognitive performance, but the flaw to these studies is they didn't use any control subjects. By not having control subjects, it is hard to tell whether or not the results that are coming from these studies are normal for the typical person of that gender. The results of these studies may not be completely accurate because of the doses of medications that the subjects are on. One subject may be on a higher dose of a medication, skewing the results of the study. To have accurate results from any type of study, there needs to be a control group, in this schizophrenia study these are typical people that do not have and psychiatric disorder. The control group needs to be compared to the experimental group, which would be the subjects diagnosed with schizophrenia. By comparing the control to the experimental one could get more accurate results.

Another factor that may contribute to the differences of symptoms between male and female is the sexual hormones. In one of the studies that is talked about, researchers are focusing directly on females, specifically their menstrual cycle. The levels of estrogen in the female body correlate to the symptoms that they may be experiencing. Researchers used emotional stimuli on these females to see the affect it has on the brain, they found out that schizophrenic patients experienced less activation in the luteal phase when compared to the controls. The study that will be discussed in this next section focuses in on the affects that the estrous cycle can have on females, so keep in mind that during the cycle females have different hormonal levels which can affect how one might react.

PRIMARY ARTICLE SUMMARY

The study that will be summarized in this section is conducted by Perez, Donegan, and Lodge. They were testing to see the effects of the estrous cycle on schizophrenia like behavior in female rats exposed to MAM. Here is what they found, and why they decided to do this on female rats.

The rats that were tested were obtained on gestational day 16, there were multiple litters that these tests were conducted upon. There were two groups, the control group injected with saline and the experimental group injected with MAM (methylazoxymethanol acetate). These rats were then put through multiple tests, each one being recorded. The tests were as followed amphetamine-induced locomotor, pre-pulse inhibition of startle, latent inhibition, social interaction, elevated plus maze, western blot, immunohistochemistry, electrophysiology: local field potentials. Each of these tests were performed on all of the rats, they did these tests to get a

better understanding of the female brain. Since there is more research on males than females, these researches wanted to see what differences were actually there and what weren't.

Throughout this study the researchers were evaluating specific behavioral, electrophysiological, and molecular alterations that were caused by MAM in the female rats during their reproductive cycle. The overall results of these tests are as followed. For the amphetamine-induced locomotor response, both the saline and MAM-treated rats displayed an increased activity to amphetamine during proestrus/estrus compared to the rats that were in the metestrus/diestrus phase of their cycle. Figure 1 Amphetamine-Induced Locomotor Response shown below suggests that hormonal increases enhance the locomotive-inducing effects of amphetamine. The next test that was performed was the pre-pulse inhibition of startle, there were no differences between the pro/est and the met/di groups, which suggests that the PPI differences are driven more by prenatal treatment rather than hormonal. Figure 2. Pre-Pulse Inhibition to Startle is shown below with the results that came from this test. The next few tests that were run had similar results with hormones not having the greatest effect on the rat.

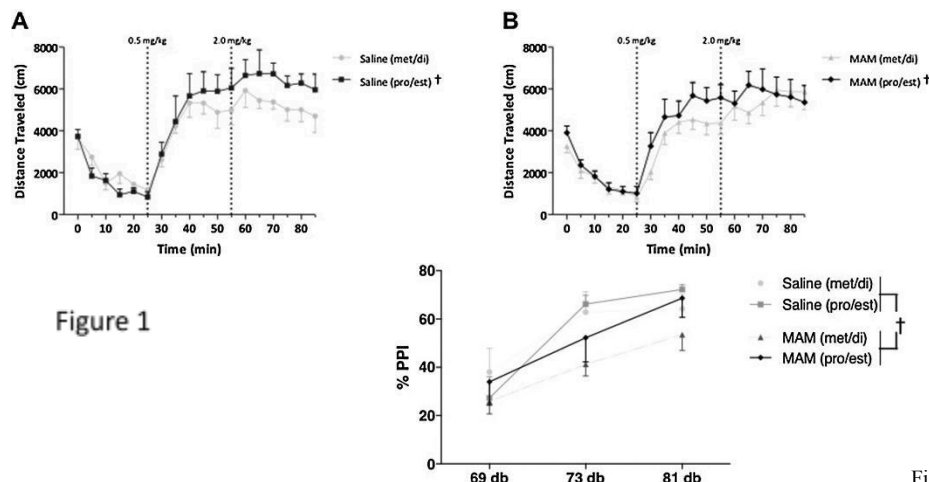


Figure 2

One test that was performed called the Western Blot test had been used to show the PV protein expression. MAM-treated animals had a decrease in PV expression compared to the control group. These results suggested that both prenatal and hormonal treatment have an effect on PV expression. Figure 5 Western Blot and Immunohistochemistry is shown below. The immunohistochemistry results showed that the MAM-treated animals had fewer PV-positive cells in the vHipp when compared to the controls. This suggests that prenatal treatment can influence cell number whereas the hormonal fluctuations show a more dynamic regulation of protein expression. All of the results listed above can be found in the study titled *Effects of estrous cycle on schizophrenia like behaviors in MAM exposed rats*. Some of the results that are listed above are word for word on what they suggest for females and schizophrenia. All of the graphs can also

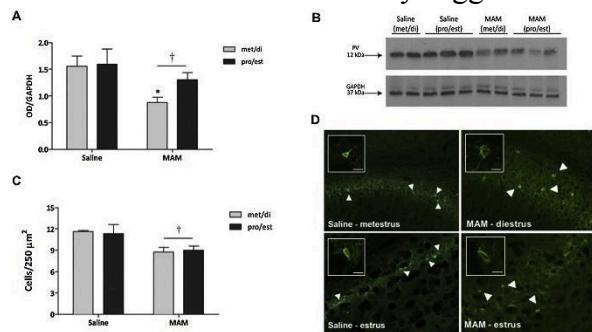


Figure 5

be found in that same study.

The findings from this study show that females may need different treatment options for schizophrenia when compared to males. The

female brain is different from that of a male in

many different ways. This study gave a greater insight into what differences there truly are. One of the last statements in the discussion section of this study states; “These findings have important implications for the treatment of schizophrenia in female patients, as fluctuating hormone levels may affect the efficacy of pharmacological therapies in female patients with schizophrenia.” Overall the study was done to see what affects the menstrual cycle has on hormonal levels in females, and how it might affect the way schizophrenia behaviors are shown during that cycle. Rats however do not have the 28-day menstrual cycle that human females go

through, they instead go through a four-day estrous cycle. With the stage of the estrous cycle being determined by the levels of hormones present at that time.

REFLECTION ON ANIMAL MODELS IN RESEARCH

The use of female rats in this study showed the effects that hormones can have on certain behaviors associated with some mental illnesses. This specific study was able to give researchers a better look into what differences there are between both male and female brains. And just how they should start to treat schizophrenia in females that are on their menstrual cycle. Using rats, knowing that they also have a “menstrual” cycle let researchers examine brains of living things that can mimic human behaviors. With there already being a study like this done on male rats, the researchers had something to compare the female behaviors to. We already knew that male and female brains show schizophrenia in different ways, but with this we can show and explain what is truly going on inside of the brain. Using the western blot test to determine the PV protein opened up a new door for researchers to go down. Proteins in human brains vary by gender and now there is proof to show what schizophrenia can do to the brain of that gender. We may want to think that male and female brains are not much different at all, but science proves otherwise. With what was showed during this study opened a door for researchers to go down on what pharmaceuticals should be used to treat schizophrenia.

SUGGESTIONS FOR FUTURE RESEARCH

One thing that I would suggest for furthering this research would be the reasoning behind the hallucinations. Are the hallucinations there for a specific reason, do they mean something to that person, are they always the same hallucinations? From being in Prairie St. Johns and having

seen a schizophrenic hallucinate, it made me question if they were having a hallucination for a deeper meaning. We know that hormonal levels and pharmaceuticals can change what a person sees but why, is there that deeper meaning that is still being found? I feel that this research should be done on actual schizophrenics, and have them draw or describe what they are hallucinating at that time. Once they have that hallucination written out on paper, see if there is a deeper meaning to the hallucination, for instance if it is something that happened to them. And then maybe to figure out what parts of the brain are firing when a hallucination is happening. I mean different parts of the brain do different things, what firings between neurons are causing these hallucinations, and why do they get them. From researching the symptoms of schizophrenia, the hallucinations are part of the positive symptoms. Schizophrenics at the hospital made me realize that we are not all the same. There are some things that schizophrenics cannot comprehend, and now with this study it could all be the hormonal changes. So overall my question for future research would be; why do schizophrenics hallucinate, is there a deeper meaning to these hallucinations, and what part of the brain is having the most activity causing these hallucinations.

REFLECTION ON THE SOCIETAL/SCIENTIFIC IMPACT OF THE RESEARCH

Honestly before I dug deeper into schizophrenia I always thought that they were just crazy people. But after finding studies on what is actually going on in the brain opened up a whole new world. Schizophrenics may seem crazy, but there is a deeper scientific explanation for all of their symptoms. And it all starts with the brain, what part of the brain is active and what symptoms they are experiencing. Society may like to think that hallucinations are not real and that those people are just crazy, but those hallucinations cause those people to stop and think.

Sometimes these thoughts that are nonstop going through their mind force them to get put into a hospital for help. So next time before we say that they are crazy, think about the research that is being done on schizophrenia to try and understand this disease. Those people did not choose to be schizophrenic, it just happened and we need to realize that they are no different than we are.

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