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Understanding the Pathophysiology of Schizophrenia

Announcer Introduction:
Welcome to *NeuroFrontiers* on ReachMD. On this episode, supported by Sunovion Pharmaceuticals Inc. and Otsuka Pharmaceutical Co., we're joined by Dr. Jose Rubio, who's an Assistant Professor at the Institute for Behavioral Science at the Feinstein Institutes for Medical Research. Dr. Rubio is here to give us a better understanding of the underlying mechanisms of treatment response in schizophrenia. Let's hear from him now.

Dr. Rubio:
We are starting to understand more about the pathophysiology of the illness, and certainly, it's becoming very apparent that dopamine is at the core of the pathophysiology. However, we are also understanding that it's not just about subcortical dopamine transmission, and that also there are many other systems that are affected. So the more we understand about this, the more we understand about the therapeutic options. So far, all of the drugs that we have need to interact in one way or another with dopamine 2 receptor. But the more we understand about all of these other systems that are involved and all of these other aspects of dopamine transmission even that are involved, we are starting to understand that it's not just about blocking the B2 receptor, but that there might be other potential mechanisms that could be involved in the treatment of schizophrenia, as well.

Whenever individuals fail to respond to treatment, and unfortunately, that's something that happens more and more as the illness progresses, that's very challenging because typically, the failure to respond to one drug is a poor sign. Many of those patients won't respond to another trial, and then once you fail to trials, it's very unlikely that you're going to respond to a third one unless that's clozapine. So it's very critical because there are really not many options that we do have at that point, and that translates in a great burden to patients and families that are actually very limited by the symptoms that we cannot successfully treat.

We have two particular therapeutics that are very exciting in the pipeline. None of them seem to be directly engaging the dopamine 2 receptor, which is certainly a novelty of those two drugs, that I think are the most exciting. One of them is a TAAR1 agonist. The other one is a muscarinic agonist, and these two drugs again, do not interact with the dopamine 2 receptor, and probably affect the way dopamine is released presynaptically. They may have affects upstream, and that could be helpful; one because it could mean that these are better tolerated drugs but not just that there's a question as of whether these drugs affect mechanisms that other drugs don't affect, and therefore could be helpful when other drugs cannot help. For instance, do these drugs work for individuals who fail to respond to other drugs? I mean, I think that that's a critical question and one that we will see in the next few months or years, whether that is the case. And that could certainly be a very important moment in the field of psychopharmacology of schizophrenia.

We are starting to understand more about the pathophysiology of the illness, and certainly it's becoming very apparent that dopamine is at the core of the pathophysiology. However, we are also understanding that it's not just about subcortical dopamine transmission, that also there are many other systn – systems that are affected. So, the more we understand about this, the more we understand about the therapeutic options. So far, of all of the drugs that we have are – need to interact in one way or another with dopamine-2 receptor, but the more we understand about all of these other systems that are involved, and all of these other aspects of dopamine transmission even, that are involved, we are starting to understand that it's not just about blocking the B2 receptor, but that there might be other potential mechanisms that could be involved in – in the treatment of schizophrenia as well.

Announcer Close:
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