

Hypothesis: A Hypothetical Animal Model for Psychosis Based on the Silencing of GABAergic System



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ABSTRACT

Although many studies have highlighted the role of gamma-aminobutyric acid (GABA) in the pathophysiology of psychosis, there is no drug-induced animal model in which GABA is manipulated. In this article we propose a hypothetical animal model for psychosis based on the silencing GABAergic system. The presentation also suggest Pre-Pulse Inhibition test as a preferred approach towards proving this hypothesis.

1. Introduction

Pschosis is a generic psychiatric term for a mental state often described as “a loss of contact with reality”, during which hallucinations, delusions and impaired insight may develop [1]. Although disruption of several neurotransmitter systems, including dopaminergic, glutaminergic, GABAergic and serotonergic are proposed for the pathophysiology of psychosis [2], majority of the studies are focused on dopamine overactivity [3, 4] and glutamate hypoactivity [5, 6] in the brain as underlying causes. Moreover, it seems that the role of GABA in pathophysiology of psychosis is underestimated. Several lines of evidence have highlighted the role of GABA hypoactivity in the neurobiology of psychosis and its effect on modulating other transmitters [7-14]. Nowadays, drug-induced animal models, basically designed following the manipulation

of neurotransmitter systems, are widely used to resemble psychosis, mainly in basic and pre-clinical research. The majority of drug-induced animal models of psychosis are designed based on the application of dopamine agonists (e.g. apomorphine) and glutamate antagonists (e.g. ketamine) [15]. To the best of our knowledge, there is no drug-induced animal model via the application of GABA antagonists to induce psychosis.

2. Hypothesis

There are three types of GABA receptors in the brain, GABAA, GABAB, and GABAC receptors, which have different electrophysiological and biochemical properties and their own specific binding sites [16]. Therefore, to establish an animal model relying on the silencing of GABAergic system, we suggest different GABA antagonists of the three types of receptor antagonists to be tested. In addition, to achieve greater results, we pro-

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pose antagonists of all three types to be tested together. Furthermore, choosing different doses of each of antagonists are important.

It is known that in patients who suffer from psychosis, the process of gating or filtering irrelevant stimuli is compromised, inasmuch as such an issue is regarded as an important manifestation of the disease. The most reliable cross-species test to evaluate the compromised gating or filtering irrelevant stimuli is Pre-Pulse Inhibition (PPI) test. This test is based on the fact that a weaker prestimulus (prepulse) prevents the response to a subsequent strong startling stimulus (pulse). The stimuli can be acoustic, tactile, or visual [17]. Accordingly, after trying GABA antagonists, PPI can be considered a preferred approach towards proving this hypothesis.

3. Conclusion

Silencing of the GABAergic system could be a proposed animal model for psychosis. To establish this model, it is reasonable that antagonists of the three types of GABA receptors are tested with different doses in combination or by their own. Following the GABAergic antagonism, using PPI is proposed as a preferred approach prove the accuracy of this hypothesized model.

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Conflict of Interest

The authors declared no conflict of interests.

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