Group Therapy: New approach to psychosis treatment could target multiple nervous system receptors

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Antipsychotic drugs, used in the treatment of psychotic disorders involving severe delusions and hallucinations, have been studied for more than 70 years. Currently available antipsychotic drugs, however, only alleviate certain symptoms, with results that vary greatly from patient to patient and frequently cause significant side effects.

A new understanding of how the brain's G-protein receptors work may soon enable a way to better customize and target antipsychotic drugs to treat specific symptoms. Researchers from Virginia Commonwealth University (VCU) will present their findings at the 57th Annual Meeting of the Biophysical Society (BPS), held Feb. 2-6, 2013, in Philadelphia, Pa.

G-protein coupled receptors (GPCRs) are responsible for activating so-called "G-proteins," internal signaling messengers that control the activity of many other internal proteins. The starring role of GPCRs in regulating a cell's activity makes them a leading pharmaceutical target: approximately 50 percent of the antipsychotic drugs produced are aimed at these important nervous system receptors.

A specific GPCR is integral to each of three key pathways for intercellular signaling, one for each of the chemical messengers dopamine, serotonin, and glutamate. But these individual GPCRs also form complexes with each other, altering their effects on signaling in the

brain. The VCU team has focused on how GPCR complexes influence signaling in a distinct way from how individual GPCRs operate.

"The realization that receptors in the brain that bind and interpret dopamine, serotonin, and glutamate neurotransmitters form complexes with one another that signal very differently than when these receptors are found in isolation, promises to change the way we approach treatment of psychosis," explains VCU Ph.D. candidate Jason Younkin, who will present the team's findings.

Instead of targeting one neurotransmitter pathway at a time, Younkin and colleagues plan to target two or more at the same time. Antipsychotic drugs that target the complexes formed by the individual GPCRs will allow use of the signaling differences and could lead to more effective therapies.

"By understanding how receptor complexes signal and learning how to control these signals, it should enable the development of specific antipsychotic drugs that lack the many side effects that exist today," says VCU professor Diomedes E. Logothetis, a co-author of the study.

More information: Presentation #595-Pos, "Functional signaling changes resulting from GPCR heteromerization: Relevance to psychosis," will take place at 1:45 p.m. on Sunday, Feb. 3, 2013, in the Pennsylvania Convention Center, Hall C. ABSTRACT: tinyurl.com/bhhsz7h

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