SESSION E7

Glutaminergic Aspects of Psychiatric Disorders and Psychopharmacology

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Session Description:

Our understanding of the complexities of the Glutamate system is rapidly expanding. This emerging knowledge is informing our understanding of the biological basis of serious mental illness and revealing new opportunities for psychopharmacological interventions.

Learning Objectives:
Following my presentation, participants will be able to:
1. Describe synaptic and neural projection components of the glutamate system.
2. Comprehend the implications of the glutamate system for the neural basis of schizophrenia.
3. Apply knowledge of glutamate system to emerging approaches to psychopharmacology.
Glutamate & Psychopharmacology
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Molecular, Cellular & Synaptic Perspectives

Glutamate: Essential Amino Acid

Glutamate Receptors
Ionotrophic Receptors: NonNMDA

Glutamate Receptors
Ionotrophic Receptor: NMDA

Fig. 6a. Non-NMDA receptors are selectively agonized by kainate, AMPA, and quinoxalines. The associated ion channels are more permeable to Na+ and K+ ions than Ca2+ (from Kandel et al., 1991).

Fig. 6b. NMDA receptors are structurally complex, with separate binding sites for glutamate, glycine M3+2, 2Na+2 and polyamines. NMDA-gated channels are more permeable to Ca2+ than Na+ ions (from Kandel et al., 1991).
**NMDA Receptors, Post Synaptic Response & Retrograde Transmission**

Carlson, 1998

**Glutamate & Long Term Potentiation (LPT)**


**Critical NMDA Receptor Subunits**


**Metabotrophic Receptors**

Acquired from https://www.chrisparsons.de/Chris/Metabotropic.htm, August 29, 2014

**NMDA Receptor Activation**

[YouTube Video](http://www.youtube.com/watch?v=Q_z5ZL9STMw)
Metabotropic Glutamate Receptors

8 Subtypes of mGlu Receptors
2 critical subgroups of mGlu Receptors

mGLU 2/3 Receptors
Presynaptic
Limit Glutamate Release
Postsynaptic ???

mGlu 5 Receptors
Post Synaptic
Modulate/Enhance NMDA Activity

Multi-Transmitter Neurocircuits & Mental Illness
Exemplar: Schizophrenia
From: Joshua A. Gordon

Testing the glutamate hypothesis of schizophrenia, 
Nature Neuroscience 13, 2–4 (2010),

Acquired September 3, 2014

Ketamine

PCP

GLU

GABA

Excitatory Input

Modulated Output From PFC

NMDA Hypofunction, Reduced GABA Input & Excitotoxicity

NMDA-R Hypofunction & Schizophrenia

NMDA-R Antagonists: Ion Channel Blockade

Prefrontal Cortex, GABA Interneurons & Neural Regulation
Where Do Current Antipsychotics Influence This System??

Psychopharmacological Efficacy & Neural Mechanisms of Mental Illness

Enhancing Glutamate Function

What Could Possibly Go Wrong??

Excitotoxicity

Acquired from http://jp.physoc.org/content/585/3/741/F8.expansion.html, September 2, 2014

Enhances D-Serine


The Future