

CNTRICS



**Cognitive Neuroscience Treatment Research
to Improve Cognition in Schizophrenia**

Translational Neuroscience

Clinical trials targeting cognitive and emotional processing deficits

Behavioral and neuroimaging studies of normal and disordered cognitive and emotional processing in humans

Cognitive Neuroscience

Behavioral, non invasive and invasive studies of normal and disordered cognitive and emotional processing in animal models

Basic molecular, cellular and systems neuroscience and neuropharmacology





MATRICES

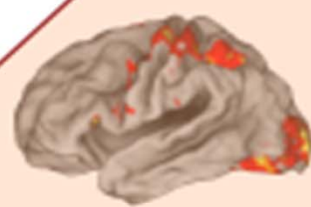
**Measurement And Treatment Research
to Improve Cognition in Schizophrenia**

Tools and Constructs of Cognitive Neuroscience: The Opportunities

- Measure specific deficits in discrete cognitive systems and component processes
- Linked to identifiable neural systems (at least in some cases)
- Functionally regulated by identifiable neuromodulatory systems (at least in some cases)
- Distinguish between specific deficits versus generalized deficits such as sedation, dysphoria, poor test taking skills, etc.
- Bridge human and animal models of cognition, facilitate translational research

Tools and Constructs of Cognitive Neuroscience: The Challenges

- No general consensus regarding constructs from cognitive psychology that should be measured
- Uncertain psychometric properties and practicalities of administration
- No generally agreed upon tasks for measuring specific mechanisms

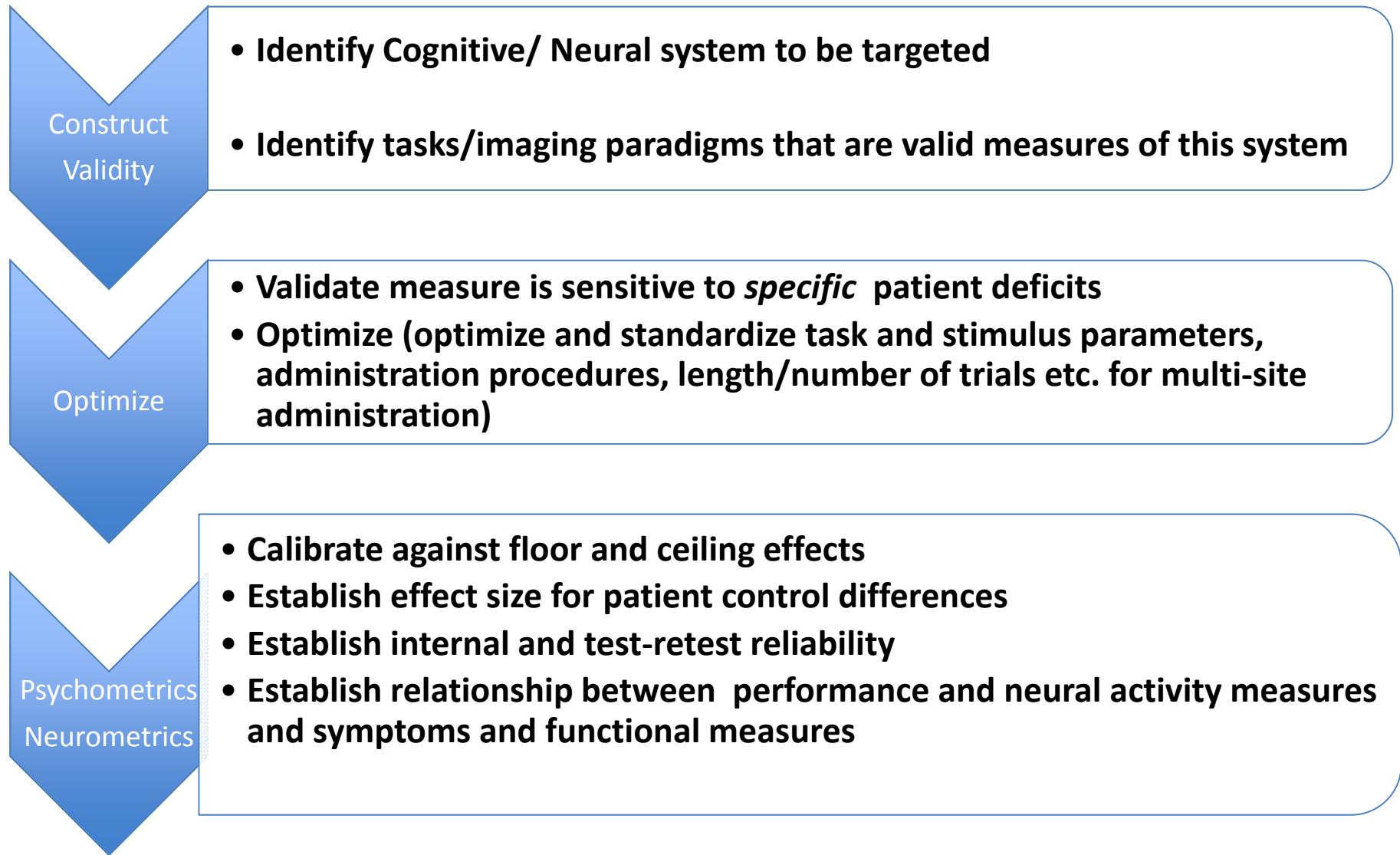


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**Cognitive Neuroscience Treatment Research
to Improve Cognition in Schizophrenia**

Development Path for Tasks and Imaging Biomarker Paradigms



CNTRICS PROCESS

- “consensus based” meetings
- Grounded in basic neuroscience of cognition and emotion with strong participation by prominent basic scientists (as well as clinicians, pharma)
- Pre meeting surveys developed criteria to constrain decision making (constructs, measures, paradigms)
- Emphasis on *validity* of measures
- Mechanisms first, then on to tasks

CNTRICS I

- 3 consensus building meetings over 2 years
- Identify cognitive systems and component processes with strong construct (and neural) validity *Biological Psychiatry July 2008 Vol 64 (1)*
- Identify measurement and pragmatic issues related to developing cognitive neuroscience measures into translational research tools *Schizophrenia Bulletin July 2008 34(4)*
- Identify a set of tasks for translation *Schizophrenia Bulletin 2009 35(1)*
- RFA MH-08-090 “Adapting Basic Cognitive Measures for Clinical Assessment in Schizophrenia” and ensuing RO1’s

CNTRICS II

- Imaging Biomarkers
 - Meeting 4 Baltimore 10/09 Biological Psychiatry *in press*
 - Meeting 6 Davis 10/10 Schizophrenia Bulletin *in submission*
- Animal Models
 - meeting 5 St Louis Conceptual 4/2010
 - Meeting 7 Dulles new paradigm selection 4/2011

CNTRICS II, Mtg 2: Developing Homologous Animal Models

Emphasis on Cognitive and Neural Construct Validity in Treatment Development Research

- **Defining and measuring CNTRICS I cognitive constructs in non-human primate and rodent models**
- **Cross-species homology in the neural substrates underlying key constructs**
- **Identifying challenges in implementing tasks with high construct validity while meeting standards for reliability and throughput in treatment-development research.**

CNTRICS II, Mtg 4: Selecting Translational Animal Model Paradigms

MEETING OBJECTIVES

- 1. To recommend up to 2 animal cognitive neuroscience paradigms per cognitive domain to be further developed for use in research aimed at developing treatments for cognitive impairments in schizophrenia.**
- 2. To identify mechanisms to foster collaborations among academia, industry and government to perform the work needed to move the recommended paradigms into treatment development settings.**