Neurocognitive Deficits in Schizophrenia

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Magnitude of Cognitive Deficits in Schizophrenia


Meta-Analysis: 204 studies, 7420 patients and 5865 controls

SD below mean of controls
- Dig Span
- Vocab
- Block Des
- WCST
- Trails B
- CPT
- Fluency
- Vis Mem
- Verb Mem

[Bar chart showing percentage of cognitive deficits for different tasks]
Trajectory of Cognitive Deficits

Cognitive Deficits Predict Functional Outcomes

Cognitive Deficits and Short-Term Clinical Outcome

Clinical outcome assessed at 6 months
Good outcome: > 2 on all global SAPS and > 3 on all global SANS (except attention)

Controls (n = 31)
Good Outcome (n = 73)
Poor Outcome (n = 78)

Domain specific vs. generalized deficits?

MATRICS Consensus Battery
- based on domain specific hypothesis
  - Speed of Processing
  - Attention/Vigilance
  - Working Memory
  - Verbal Learning and Memory
  - Visual Learning and Memory
  - Reasoning and Problem Solving

If generalized deficit, why engage in long neuropsych testing?
- Probably a combination
- Generalized deficits, with some domains affected more than others
- Variability in specific domains across individuals?
Hierarchical Clustering of Cognition in First Episode Psychosis

Above average cognition

Severe cognitive impairments
Why such a large deficit for Trails B?

Highly multi-factorial test

Scored by time, allowing “unlimited failure”
• Select, via consensus, specific tasks to evaluate different cognitive functions
• Emphasis on imaging
• “Domain specific” in approach
• Tasks intended to be highly specific to a particular cognitive domain or function
  • Avoids “multifactorial” problem of traditional neuropsychological tests
Verbal Memory and Encoding Strategies

Incidental encoding (supported ‘deep’ encoding) vs. Intentional encoding (instruction to memorize)

Meta analysis of fMRI studies of Memory Encoding

Memory deficits mainly related to prefrontal cortex

LTM effects (high subsequent memories)

Greater DLPFC activity for rehearse over reorder related to less negative symptoms
Patients with Schizophrenia have a Deficit in Source Monitoring

- Tendency to attribute internally generated stimuli to an external source
- Particularly in patients who hallucinate

Wang et al. Schizophrenia Research 125 (2011) 136–142
fMRI of Source Memory in Schizophrenia

- Encoding session with two tasks
- Source memory: identifying the task associated with a word
- 13 Patients and 13 controls


Green: Controls
Red: Schizophrenia
Source Memory in Schizophrenia: An fMRI VR Study

Recognition:
- Person
- Place
- Object
Controls       Schizophrenia

X = -45
X = -30
X = -15
X = 0
X = 15
X = 30
X = 45

Person > object
Place > object
Person AND place > object

Controls       Schizophrenia

X = -45
X = -30
X = -15
X = 0
X = 15
X = 30
X = 45

Object > person
Object > place
Object > person AND place
Cognitive insight in Schizophrenia

Regression, SRS vs. Beta (Place > Object) in SCZ
Current Project: TMS-fMRI during working memory in Schizophrenia

TMS-fMRI gives us a measure of temporally specific connectivity

Single TMS pulse at 500ms into delay
High TMS vs. Low TMS

500ms TMS to assess Maintenance vs. manipulation
4000ms as a control: Manipulation should have completed and now maintaining
Treating Cognitive Deficits

- Behavioural Interventions: Cognitive remediation
  - Transfer effects? Efficacy? Duration?
- Pharmaceutical Interventions: Aripiprazole
- Neural Modulation: rTMS, TDCS
  - Efficacy? Duration of effects?
- Combined approaches
  - Brain stimulation combined with cognitive remediation
Neurological effects of Cognitive Remediation

Ramsay and McDonald. Schiz Bulletin. 20015,

CRT Changes activity in the left prefrontal cortex, thalamus, caudate, and right anterior insula and parietal cortex

Some regions showing changes overlap areas where SCZ shows reduced activity during working memory.

There is some suggestions that CRT normalized brain function as opposed to compensatory patterns.
Future of Brain Stimulation: Targeting?
Summary

• Cognitive deficits are present throughout the lifespan and functionally important.

• While generalized deficits may be present, some domain specificity exits (e.g. worse verbal memory)

• Multi-factorial nature of neuropsychological test may affect results and interpretations
  • Cognitive neuroscience approach may better detect specific effects (but longer tests limit utility)

• Patients show deficits across a range of brain regions, often reduced activity.
  • Particularly in HUB regions (e.g. DLPFC).
  • Reduced activity related to less supporting cognitive processing?

• Understanding and treating these deficits may lead improved outcome and quality of life for these patients.
Merci!
Functional Connectivity and Cognition

AX-BX continuous performance task

Control > SCZ
BX-AX

Controls showed increased connectivity between DLPFC and these regions while patients did not.