Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia
What Criteria Should We Use For Cognitive Biomarkers?

- Tied to the needs of clinical trials
- Relevant for treatment development
- Relevant for understanding cognitive function
## Possible Criteria for Cognitive Biomarkers

<table>
<thead>
<tr>
<th>Criteria</th>
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<tbody>
<tr>
<td>Demonstrated sensitivity to pharmacological manipulations</td>
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<tr>
<td>Demonstrated sensitivity to manipulations of cognitive/affective processing</td>
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<tr>
<td>Test-retest reliability</td>
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<tr>
<td>Openness to pharmacological confounds</td>
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<tr>
<td>Directness of interpretation</td>
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<tr>
<td>Standardization of administration protocols</td>
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<tr>
<td>Clear quality assurance protocols</td>
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<tr>
<td>Standardization of analysis approaches</td>
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<tr>
<td>Ability to assess both cortical and subcortical signals</td>
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<tr>
<td>Easy accessibility</td>
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<td>Patient tolerance</td>
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<tr>
<td>Practicality and ease of use</td>
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<tr>
<td>Spatial Resolution</td>
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<tr>
<td>Temporal Resolution</td>
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<tr>
<td>Feasibility of application in multi-center trials</td>
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</tbody>
</table>
## Rating Scale

<table>
<thead>
<tr>
<th>Not Necessary</th>
<th>Somewhat Helpful</th>
<th>Very Helpful But Not Essential</th>
<th>Somewhat Essential</th>
<th>Very Essential</th>
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Results of Survey Criteria

Please rate how important each of the following is for choosing a biomarker method for assessing brain function during cognitive performance for use in pro-cognitive treatment development.

N=121

- Demonstrated sensitivity to manipulations of cognitive and/or emotional states
- Test-retest reliability
- Clear Quality Assurance protocols
- Patient tolerance
- Standardization of administration protocols
- Standardization of analysis approaches
- Directness of interpretation (known source of signals, ability to locate)
- Ability to assess both cortical and subcortical signals
- Demonstrated sensitivity to pharmacological manipulations
- Practicality and ease of use
- Feasibility of application in multi-center studies
- Easy accessibility
- Temporal resolution
- Spatial resolution
- Openness to pharmacological confounds (e.g., confounds associated with...
Results of Survey Criteria

Academia

- Test-retest reliability
- Standardization of administration protocols
- Ability to assess both cortical and subcortical signals
- Temporal resolution
- Spatial resolution
- Standardization of analysis approaches
- Clear Quality Assurance protocols
- Openness to pharmacological confounds (e.g., confounds associated with)
- Directness of interpretation (known source of signals, ability to locate)
- Easy accessibility
- Practicality and ease of use
- Patient tolerance
- Demonstrated sensitivity to pharmacological manipulations
- Demonstrated sensitivity to manipulations of cognitive and/or emotional
  Feasibility of application in multi-center studies

Industry

Not Important | Somewhat Helpful | Helpful, But Not Essential | Somewhat Essential | Very Essential

- Test-retest reliability
- Standardization of administration protocols
- Ability to assess both cortical and subcortical signals
- Temporal resolution
- Spatial resolution
- Standardization of analysis approaches
- Clear Quality Assurance protocols
- Openness to pharmacological confounds (e.g., confounds associated with)
- Directness of interpretation (known source of signals, ability to locate)
- Easy accessibility
- Practicality and ease of use
- Patient tolerance
- Demonstrated sensitivity to pharmacological manipulations
- Demonstrated sensitivity to manipulations of cognitive and/or emotional
  Feasibility of application in multi-center studies
Initial fMRI Ratings

Functional Magnetic Resonance Imaging (fMRI)

- Good Test-retest reliability
- Good standardization of administration protocols
- Able assess both cortical and subcortical signals
- Good Temporal resolution
- Good Spatial resolution
- Good Standardization of analysis approaches
- Clear Quality Assurance protocols
- Pharmacological confounds easily dealt with (e.g.,...)
- Results are clearly interpretable (known source...)
- Practical and easy to use
- Tolerated well by patients
- Demonstrated sensitivity to pharmacological...
- Demonstrated sensitivity to manipulations of...
- Feasible to use in multi-center studies

Legend:
- Orange: Does not meet this criteria
- Blue: Meets this criteria somewhat
- Purple: Meets this criteria moderately
- Red: Meets this criteria very well
- Green: Meets this criteria extremely well
- Brown: Not enough research to judge
- Light blue: I do not have enough information to judge
Initial EEG Ratings

Electro Electroencephalography (EEG)

- Good Test-retest reliability
- Good standardization of administration protocols
- Able to assess both cortical and subcortical signals
- Good Temporal resolution
- Good Spatial resolution
- Good Standardization of analysis approaches
- Clear Quality Assurance protocols
- Pharmacological confounds easily dealt with (e.g.,...)
- Results are clearly interpretable (known source, etc.,...)
- Practical and easy to use
- Tolerated well by patients
- Demonstrated sensitivity to pharmacological...
- Demonstrated sensitivity to manipulations of...
- Feasible to use in multi-center studies

Legend:
- Does not meet this criteria
- Meets this criteria somewhat
- Meets this criteria moderately
- Meets this criteria very well
- Meets this criteria extremely well
- Not enough research to judge
- I do not have enough information to judge
Initial Dynamic Ligand Ratings

High scores on some important criteria, but more information needed

Receptor Based Cognitive Imaging (PET)

- Good Test-retest reliability
- Good standardization of administration protocols
- Able to assess both cortical and subcortical signals
- Good Temporal resolution
- Good Spatial resolution
- Good Standardization of analysis approaches
- Clear Quality Assurance protocols
- Pharmacological confounds easily dealt with (e.g.,...)
- Results are clearly interpretable (known source...)
- Practical and easy to use
- Tolerated well by patients
- Demonstrated sensitivity to pharmacological...
- Demonstrated sensitivity to manipulations of...
- Feasible to use in multi-center studies

Legend:
- Orange: Does not meet this criteria
- Blue: Meets this criteria somewhat
- Purple: Meets this criteria moderately
- Green: Meets this criteria very well
- Pink: Meets this criteria extremely well
- Brown: Not enough research to judge
- Cyan: I do not have enough information to judge
Initial MEG Ratings

Magneto Electro Encephalography (MEG)

- Good Test-retest reliability
- Good standardization of administration protocols
- Able assess both cortical and subcortical signals
- Good Temporal resolution
- Good Spatial resolution
- Good Standardization of analysis approaches
- Clear Quality Assurance protocols
- Pharmacological confounds easily dealt with (e.g.,...)
- Results are clearly interpretable (known source...)
- Practical and easy to use
- Tolerated well by patients
- Demonstrated sensitivity to pharmacological...
- Demonstrated sensitivity to manipulations of...
- Feasible to use in multi-center studies

Need more Information!

Legend:
- Orange: Does not meet this criteria
- Blue: Meets this criteria somewhat
- Dark Green: Meets this criteria moderately
- Light Green: Meets this criteria very well
- Light Purple: Meets this criteria extremely well
- Brown: Not enough research to judge
- Cyan: I do not have enough information to judge
Initial NIR Ratings

Near Infrared Spectroscopy (NIRS)

- Good Test-retest reliability
- Good standardization of administration protocols
- Able to assess both cortical and subcortical signals
- Good Temporal resolution
- Good Spatial resolution
- Good Standardization of analysis approaches
- Clear Quality Assurance protocols
- Pharmacological confounds easily dealt with (e.g.,...)
- Results are clearly interpretable (known source...)
- Practical and easy to use
- Tolerated well by patients
- Demonstrated sensitivity to pharmacological...
- Demonstrated sensitivity to manipulations of...
- Feasible to use in multi-center studies

Need more Information!

Legend:
- Orange: Does not meet this criteria
- Blue: Meets this criteria somewhat
- Purple: Meets this criteria moderately
- Green: Meets this criteria very well
- Red: Meets this criteria extremely well
- Brown: Not enough research to judge
- Cyan: I do not have enough information to judge
Initial TMS Ratings

Transcranial Magnetic Stimulation (TMS)

- Good Test-retest reliability
- Good standardization of administration protocols
- Able to assess both cortical and subcortical signals
- Good Temporal resolution
- Good Spatial resolution
- Good Standardization of analysis approaches
- Clear Quality Assurance protocols
- Pharmacological confounds easily dealt with (e.g.,...)
- Results are clearly interpretable (known sources...)
- Practical and easy to use
- Tolerated well by patients
- Demonstrated sensitivity to pharmacological...
- Demonstrated sensitivity to manipulations of...
- Feasible to use in multi-center studies

Need more Information!
Initial sMRI Ratings

Low scores on some important criteria