

Future Directions in Cognitive Impairment Associated with Schizophrenia: Social Cognition

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Disclosures for Michael F. Green

Consultant

AbbVie, DSP, Forum, Mnemosyne (scientific board),
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Amgen

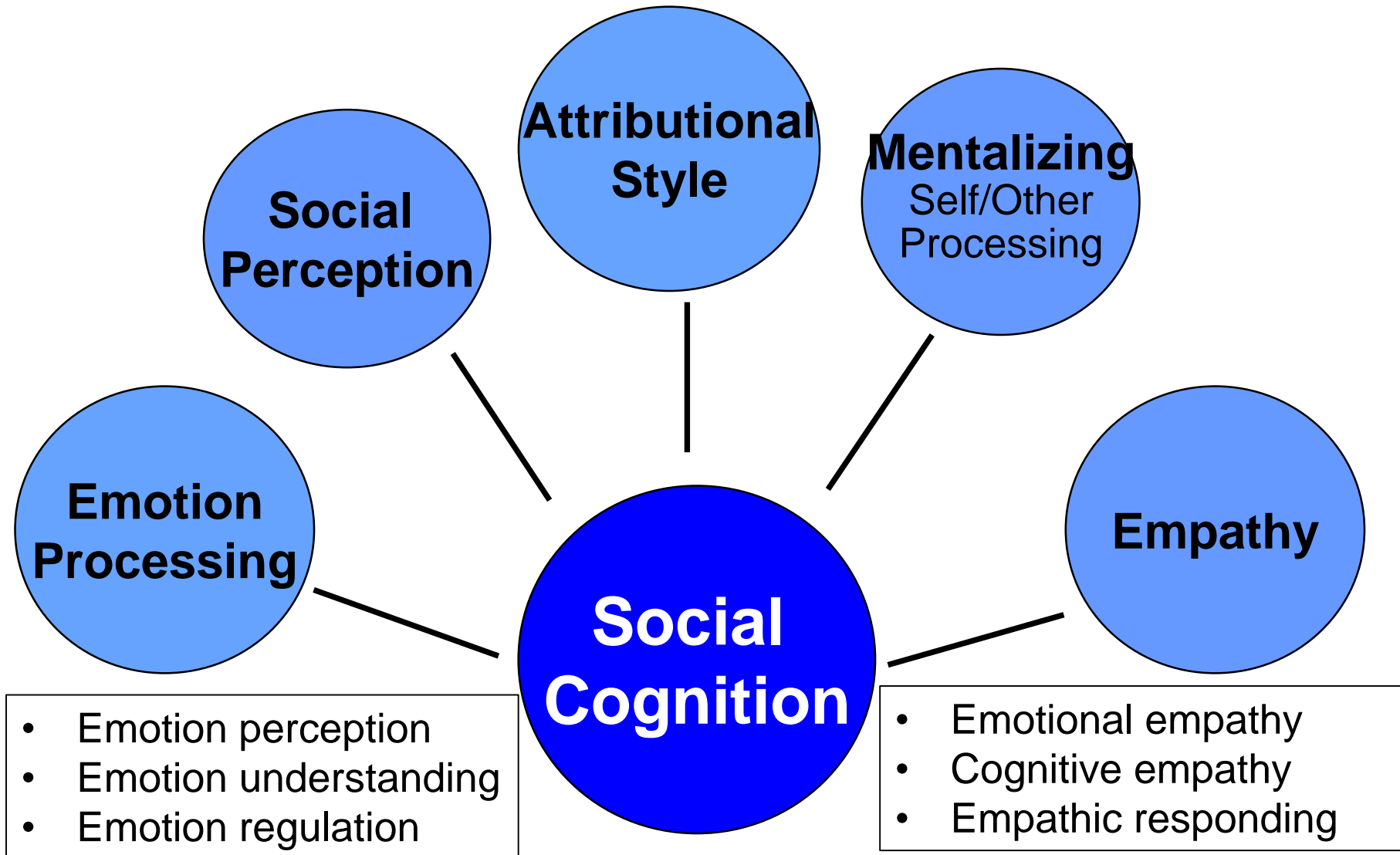
Officer in non-profit

MATRICS Assessment, Inc. – but receive no financial
compensation

Outline

- **Separability of social and non-social cognition**
- **Relationship to functional outcome**
- **Adapting measures from social neuroscience for schizophrenia clinical trials**

Social Cognition Research in Schizophrenia – At the moment



Evidence for the Distinction

- Is social intelligence just “general intelligence applied to social situations”? (David Wechsler).
- Most social processing involves brain regions distinct from non-social processing.
- Some regions are a “neural see-saw” with reciprocal activation with non-social processing regions (e.g., default mode, mentalizing).
- In MATRICS we did not appreciate distinction between social and non-social cognition. (*can influence the type of composite used*)

Neurocognition and Social Cognition as Separate Factors in Schizophrenia

Studies with multiple social cognitive tasks

Study & year	Patients	Analysis	Support?
Sergi, et al. 2007, Sz Res	100 Sz and Sz-Aff	Structural equation modeling	Yes
Allen et al. 2007 Sz Res	169 Sz	Confirmatory Factor Analysis (CFA)	Yes
van Hooren et al. 2008, Sz Res	44 psychotic dx; 47 familial risk; 41 psychom. risk	Exploratory (EFA) groups separately and together	Yes
Williams et al. 2008, Sz Res	56 first episode Sz patients	Exploratory (PCA)	Yes
Bell et al. 2009, Sz Bulletin	151 Sz and Sz-Aff	CFA	Yes
Hoe et al. 2012, Psych Medicine	130 Sz at BL, 105 at 1 yr follow up	CFA	Yes

Social cognition and community functioning in schizophrenia

meta-analysis of 52 studies; 2692 subjects

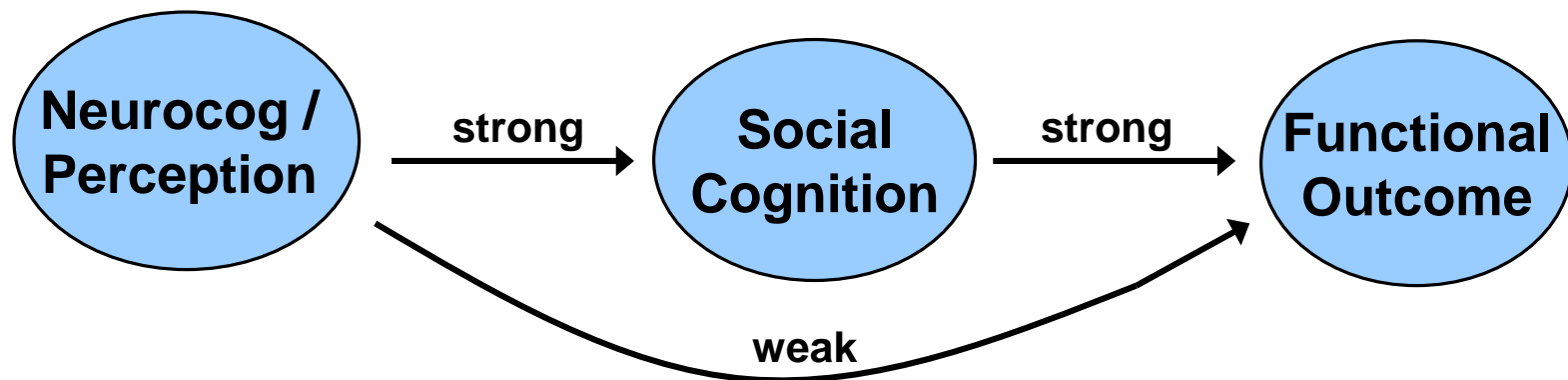
Estimated average correlation (and confidence interval) by social cognitive domain:

- **Mentalizing / Theory of Mind = .48 (.32 - .61)**
- **Social perception = .41 (.14 - .63)**
- **Emotion perception/processing = .31 (.21 - .40)**

Social cognition explained relatively more variance in community outcome (16%) than non-social neurocognition (6%)

Social cognition as a mediator for functional outcome

- At least 15 separate studies supported social cognition mediation between neurocognition or perception and functional outcome
- Average of 25% variance in functional outcome explained in the mediation model



Oxytocin (nasal spray) in Schizophrenia

At least 6 studies of oxytocin effects on social cognition performance in schizophrenia.

- Results are inconsistent / a couple studies are encouraging.

OT as augmentation for social cognitive skills training		Social cog results	
Davis et al. 2014	27 pts, parallel group design: 40 IU, 30 min before social cog skills training groups.	Between group effect on higher-level social cognition. Not on lower level	+/-
Cacciotti-Saija et al. in press	52 pts with early psychosis, parallel group design: 24 IU BID for 6 weeks	No improvement in social cognitive measures.	-

Many unknowns regarding OT studies:

- Target engagement
- Effective dose
- Single vs repeated administrations
- Outcome measures

Social Cognition and Functioning (NIMH SCAF Study) in Schizophrenia

Rationale

- **Social cognition is an core aspect of schizophrenia and has strong connections to functional outcome**
- **It is becoming a target for interventions (both pharmacological and training)**
- **There is a paucity of reliable, validated social cognitive endpoints for clinical trials**
- **This area is not well informed by the impressive developments in social neuroscience.**
- **Similar to the rationale for CNTRICS**

SCAF Project: Criteria for selection

Aim: To adapt and evaluate measures from social neuroscience for use in schizophrenia clinical trials

- Los Angeles and North Carolina
- 173 stable schizophrenia outpatients 88 controls; Patients retested at 4-weeks
- Data collection recently completed.

For social cognitive domains:

1. Performance metrics for use in clinical trials
2. Relevant to social functioning in schizophrenia.

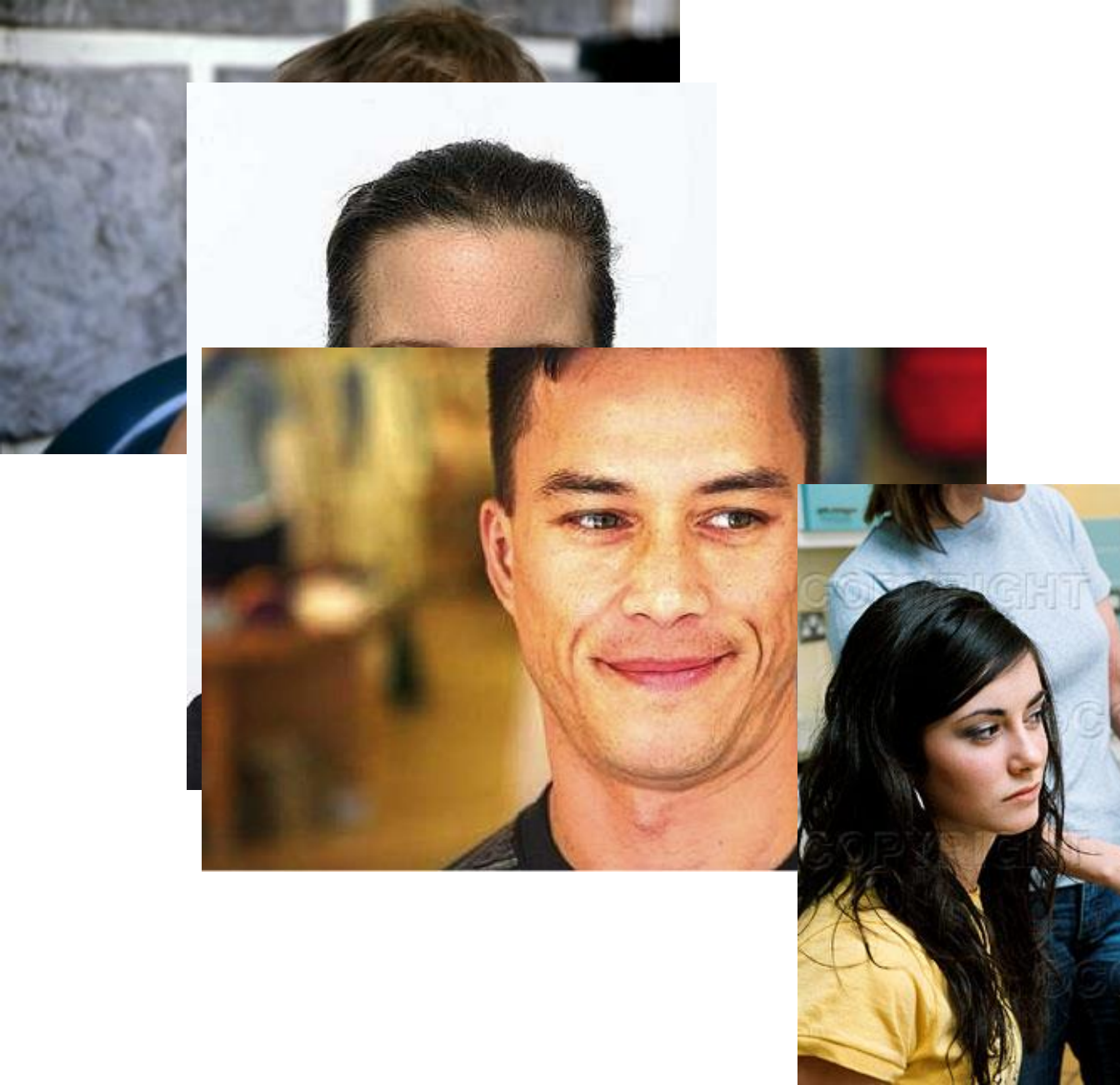
For social cognitive paradigms:

1. Can assess a large range of difficulty
2. Tolerable length of time (e.g. 30 min or less)
3. No complex or time consuming scoring
4. Equipment is practical for a clinical trial (no EEG/fMRI)
5. No excessive demands on reading / verbal intelligence

Lower-level Social Cognition: Social / Emotion Cue Identification



Higher level Social Cog: Mentalizing



SCAF Selected Domains / Paradigms

Domain 1: Nonverbal social cues:

1. Basic Biological Motion
2. Emotion in Biological Motion

Domain 2: High-level inferences:

1. Self-Referential Memory
2. Empathic Accuracy

Lower to higher levels



Biological Motion

Do you see human motion?

100% coherent



70% coherent



Emotion in Biological Motion

What emotion do you see:

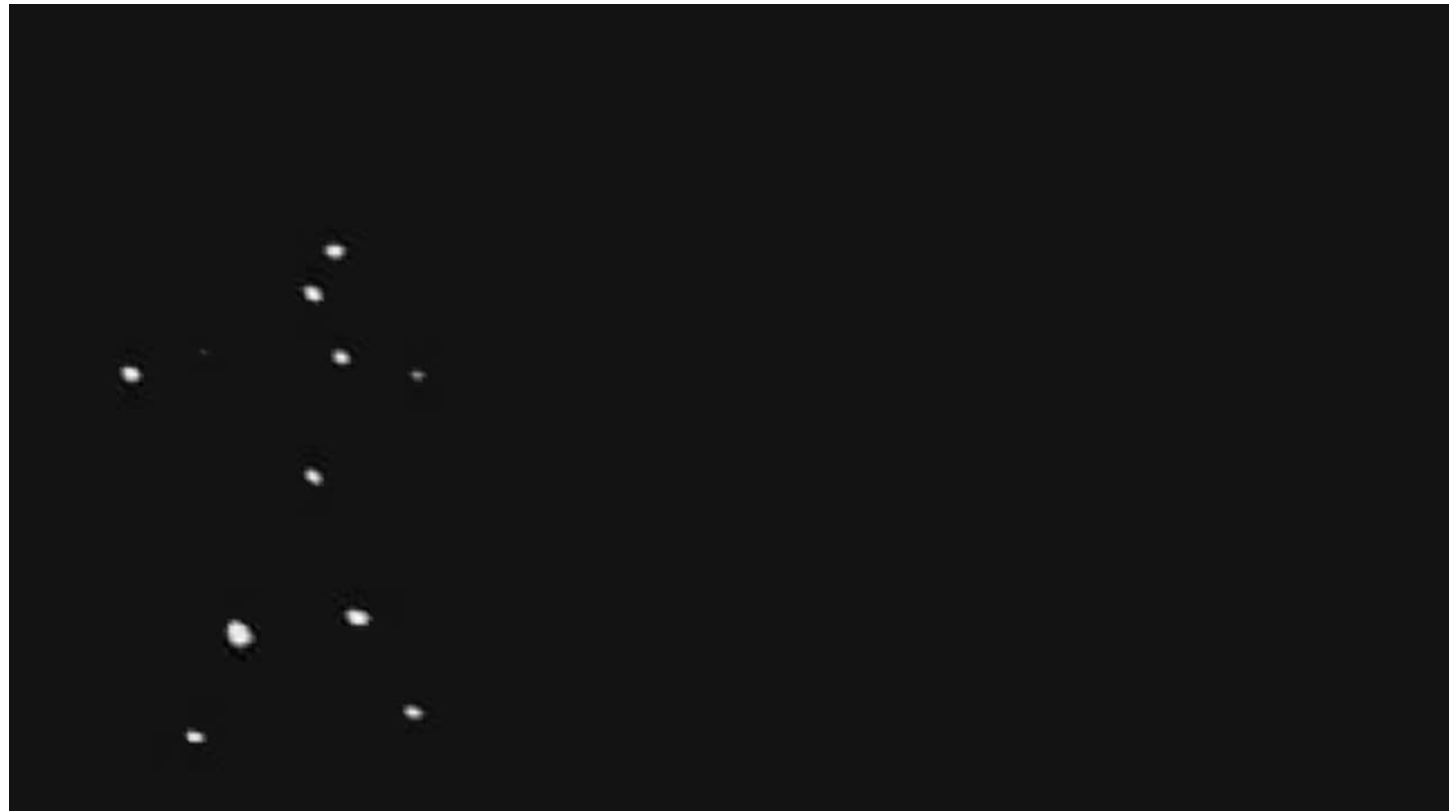
- Fear
- Anger
- Happiness
- Sadness
- Neutral



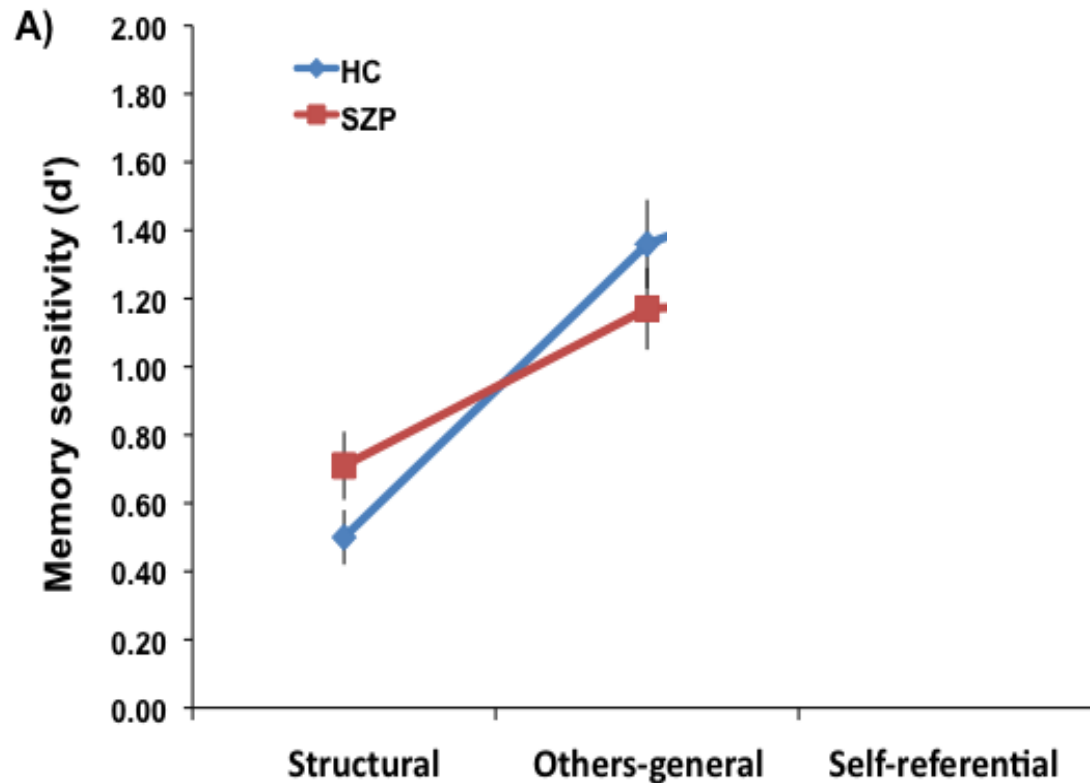
Emotion in Biological Motion

What emotion do you see:

- Fear
- Anger
- Happiness
- Sadness
- Neutral



Self-referential Memory in Patients and Controls



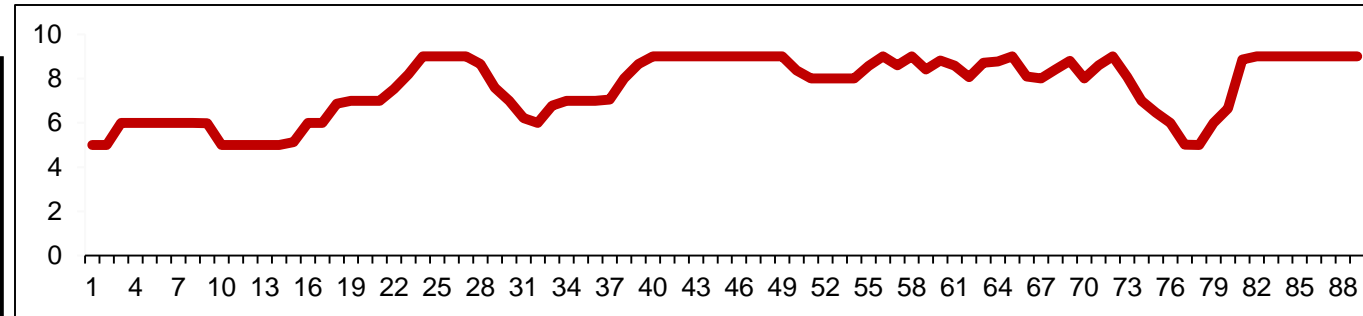
Memory sensitivity (d') for each group (HC = healthy controls; SZP = schizophrenia patients) for Structural, Others-general, and Self-referential.

Empathic Accuracy

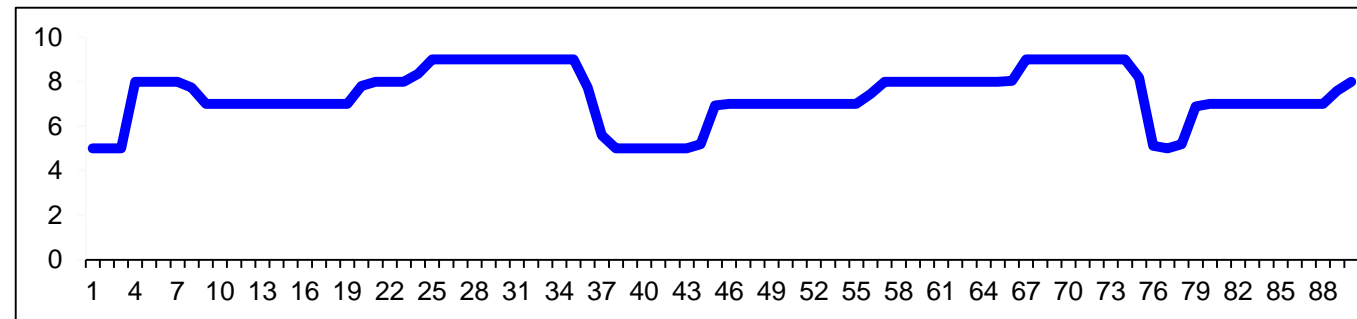
How to Create an Ecologically Valid Assessment



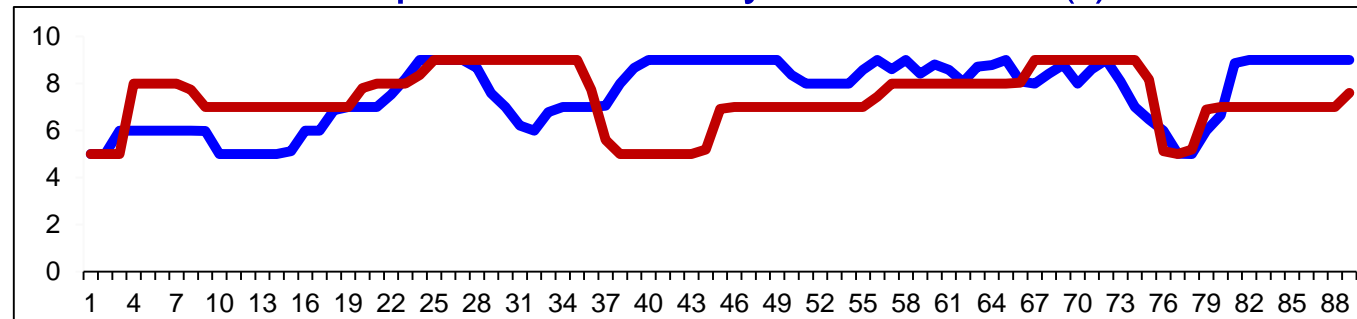
Ratings from a target



Ratings from a subject



Empathic Accuracy Correlation (r)



SCAF Measure Evaluation

For each measure we examined:

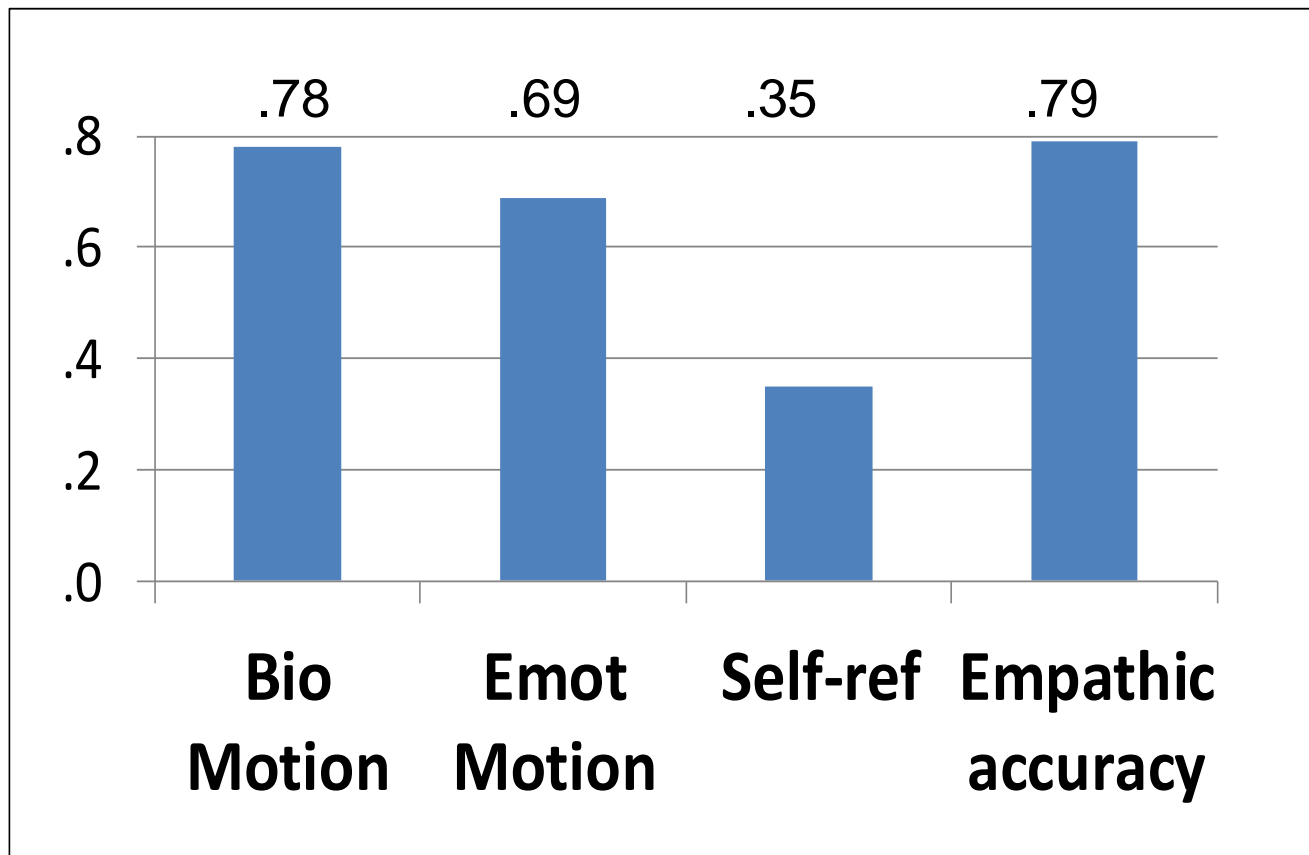
- patient – control group differences
- test-retest reliability
- utility as a repeated measure (e.g., practice effects, ceiling or floor effects)
- tolerability (patients' perspective), admin. time

Selected a representative dependent measure

- Biological Motion (85%)
- Emotion in Biological Motion (accuracy)
- Self-referential memory (self condition)
- Empathic Accuracy (9 clip version)

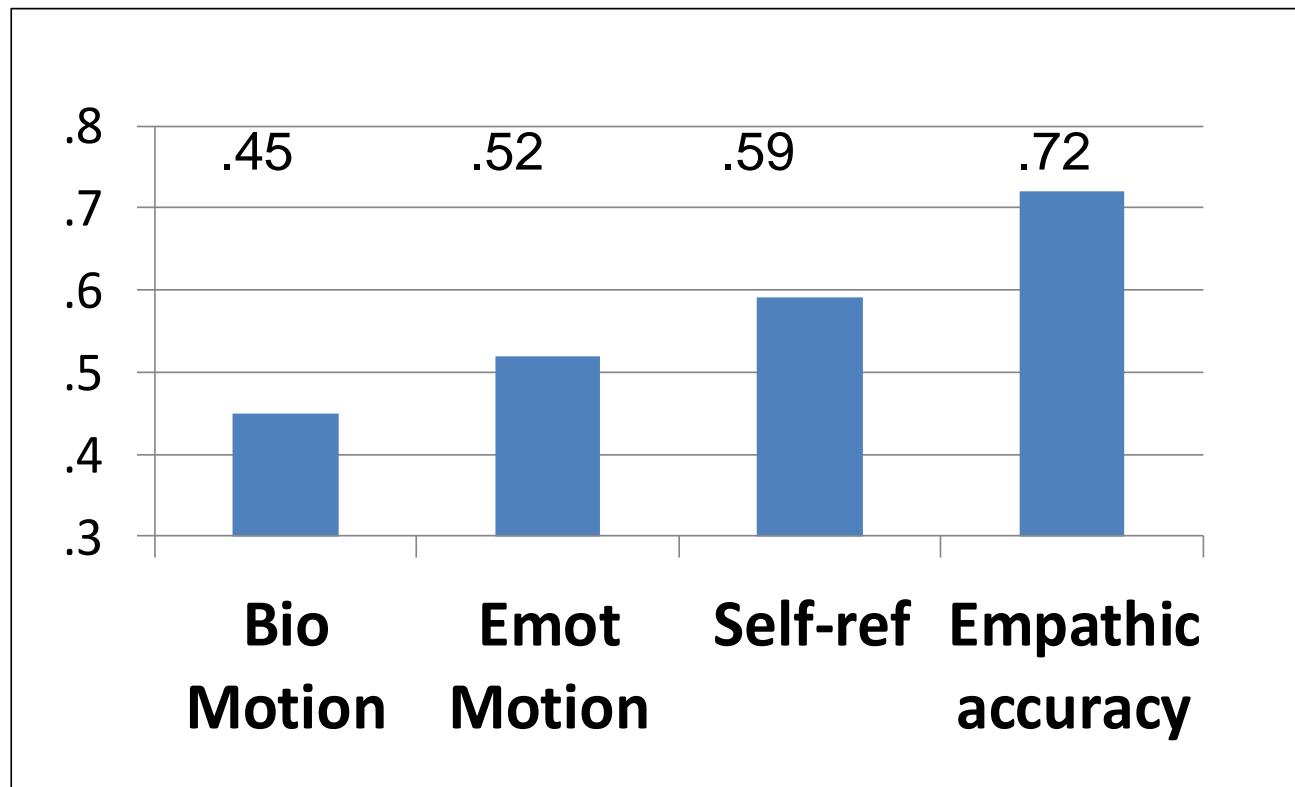
SCAF Study Results

Group Differences (d')



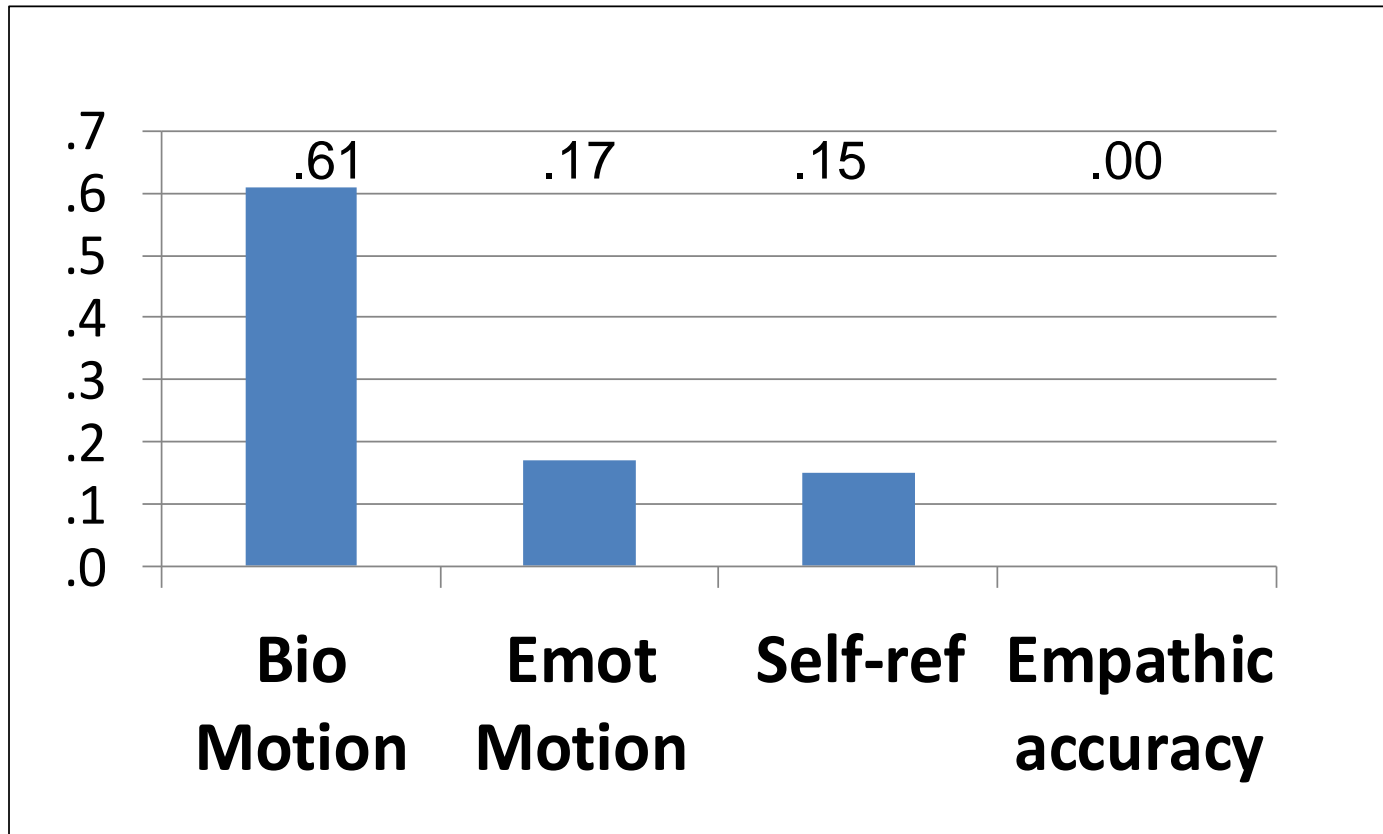
SCAF Study Results

Test-retest reliability (r)



SCAF Study Results

Utility as a repeated measure (Time 1 – Time 2 effect size)



Within-group effect sizes calculated by dividing mean difference score by its SD.

SCAF Study Results

Practicality and Tolerability

	Tolerability	Duration (min)
Bio Motion	5.2	7.5
Emotion Bio	5.4	8.0
Self-referential	5.3	11.7
Empathic accuracy (6-9 clips)	5.4	20-27*

Tolerability on 1-7 scale where 7 = best; 4 = midpoint

* Estimate -- we administered a beta version with more clips. We estimate 20 min for 6 clips and 27 min for 9 clips.

SCAF Study Results Summary

	Group Diff.	Test- retest reliability	Utility as repeated measure	Tolera- bility	Duration
Biological Motion					
Emotion Bio Mot					
Self- reference					
Empathic accuracy					

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The
GREEN LAB
UCLA/VA Greater Los Angeles



Dedicated to understanding cognition in Schizophrenia