Practical and scientific challenges in biomarker development for ASD

James C. McPartland, Ph.D.

Associate Professor of Child Psychiatry and Psychology
McPartland Lab (www.mcp-lab.org)
Yale Developmental Disabilities Clinic (www.autism.fm)
Autism Biomarkers Consortium for Clinical Trials (www.asdbiomarkers.org)
Overview

• Biomarkers
  • Definition
  • Objectives

• Challenges in ASD

• Progress and shortcomings

• Needs for future research
  • More rigorous studies
  • More sensitive biomarkers
  • Practical biomarkers
Biomarker definition

Any characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.

No clinically practicable biomarkers in ASD

Biomarkers Definition Working Group, 2001
Biomarker objectives

- Diagnosis/screening
- Stratification
  - Treatment selection
  - Prognosis
- Treatment response

Walsh, Elsabbagh, Bolton, Singh, 2011; Loth et al., 2015; McPartland, 2016
Challenges in ASD

- Behavioral diagnosis
  - Social-communicative impairment
  - Rigid, repetitive behaviors and atypical sensory responses

Developmental change

Multiple etiologies

Heterogeneity
ASD biomarkers: Progress

- Numerous promising biomarkers
- Neural response to faces
  - fMRI: Fusiform gyrus activation
  - Event-related potential: N170

Schultz et al., 2000
McPartland et al., 2004; O'Connor et al., 2005, 2007 McPartland et al., 2011; Dawson et al., 2012
ASD biomarkers: Shortcomings

- Inconsistent reproducibility
- True heterogeneity in ASD
- Underpowered studies
- Methodological variability
- No frame of reference in typical development

McPartland et al., 2004, 2011; Grice et al., 2005; O’Connor et al., 2005, 2007; Dawson et al., 2005; Senju et al., 2005; Valdizan, 2005; Kemner et al., 2006; Webb et al., 2006, 2009, 2012; Boeschoten et al., 2007; Gunji et al., 2009; Magnee et al., 2008; Wong et al., 2008; McCleery et al., 2009; Akechi et al., 2010; Churches et al., 2010, 2012; Hileman et al., 2011; Batty et al., 2011; Apicella et al., 2013; Khorammi et al., 2013; Wagner et al., 2013; Tye et al., 2013, 2014; Cygan et al., 2014; Key et al., 2014
Needs: More rigorous studies

- Larger samples to understand variability
- Tightly controlled methods
- Longitudinal design
- Development of normative “atlas”
Needs: More sensitive biomarkers

• Questionable ecological validity of social neuroscience methods

• Interactive social neuroscience

Schilbach et al., 2013; Rolison et al., 2015; Naples et al., in press; Hirsch et al., under review
Needs: Practical biomarkers

- Practicality limits ultimate utility
  - Cost
  - Accessibility
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