A Conversation about Research on Sensorimotor Function and Autism

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A Conversation

- I am a neurobiologist who does research on autism to understand brain patterns that emerge across many ASD cases
- You have personal, real-life, direct experiences with autism
- We can learn from each other!
- How does my work interface with your experience, and how can it be shaped by your input?
- To facilitate this conversation...
Discuss!

What drew you to a talk about neurobiology research on autism?
A Conversation

I. Basic and translational research in autism spectrum disorders
II. Sensorimotor function and autism spectrum disorders
III. Researching on the cerebellum in autism spectrum disorders
As a neurobiologist, I’m interested in…

- Genes
- Development
- Experience
- Environment

- Personality
- Memory
- Identity
- Function
- Dysfunction
Three classes of question in the neurobiology of disease

- Basic Research
  - How does the brain work?
- Translational Research
  - How is brain function disrupted?
- Clinical Research
  - How does this knowledge help patients?
Neurobiology Research Questions for Autism Spectrum Disorders

• What factors lead to the presentation of autism-like symptoms?
Heterogeneous causes of autism

- Stress
- Infection
- Premature birth
- Environmental agents such as valproic acid, ethyl mercury, etc.

Genetic factors (50% for identical twins)

Environmental factors (2-35x)

Autism-related single-gene disorders, 8.50%

All other ASDs, 91.50% (500 known genes)
Neurobiology Research Questions for Autism Spectrum Disorders

• What factors lead to the presentation of autism-like symptoms?
• When during development do these factors have the most impact?
• How do these factors affect the typical function of the brain?
  – Behavioral, systems, neurons, molecules…
  – Knowing how the brain typically works…...
Neurobiology Research Questions for Autism Spectrum Disorders

• What may make a good early-life “biomarker” for detecting autism?
• Have we identified routes to treating autism?
• Are there time points for treatment that are particularly effective?
Discuss!

How has basic or translational scientific research interfaced with your experience with autism spectrum disorders?
Why study sensorimotor function?

1. Pervasive in cases of autism

B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive; see text):

1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases).

2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns or verbal nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat food every day).

4. Hyper- or hyporeactivity to sensory input or unusual interests in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).
Sensory Perception in ASDs

* Sensory sensitivity differences may account for sleep disturbances

(Tzichinsky et al., 2018, *Mol Autism*)
Motor Function in ASD

- Originally documented by Kanner and Asperger
- Affects >80% of patients
- Early and persistent dyspraxia
- Increased incidence in patients with known ASD-related mutations

(Teitelbaum et al.)  (Travers, 2018)  (YouTube, Spectrum)
Discuss!

• What experience do you have with the sensory, motor, or sensorimotor features of autism?
Why study sensorimotor function?

1. Pervasive in cases of autism
2. Potential as early biomarker for ASD diagnosis

(Hensch and Bilimoria, *Cerebrum*, 2012)
Sensorimotor disruption is highly predictive of ASD diagnosis

(Estes et al., *J. Neurodev. Disord.*, 2015)
Why study sensorimotor function?

1. Pervasive in cases of autism
2. Potential as early biomarker for ASD diagnosis
3. Window into how information is processed in the autistic brain
   • A few patterns prevail when you look at sensorimotor function…
Local rather than global

(Wang et al., *Neuron*, 2015)
Responses are highly variable

(Dinstein et al., Neuron, 2012)
Atypical control by inhibition

(Robertson and Baron-Cohen, Nat Rev Neurosci, 2017)

** There may be a role for time here...
Movements are not accurately timed

...leading to errors when pursuing targets and a high degree of variability

(Schmitt et al., 2016)
Disrupted sensorimotor integration underlying complex behaviors

(Wang et al., J Neurophysiol, 2015)

1. Magnitude
2. Timing
3. Use of sensory feedback to make adjustments
Why study sensorimotor function?

1. Pervasive in cases of autism
2. Potential as early biomarker for ASD diagnosis
3. Window into how information is processed in the autistic brain
   - Local, noisy processing over global processing and…
   - Disruption of brain areas that use integration and timing to shape and guide behavior
   - Opportunities for therapies using this information (e.g. ESDM)
4. Opens up questions for translational + basic neuroscience:
   - Do these features illustrate broad disruptions in the circuitry of the brain that apply to many features of autism?
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   - Do these features illustrate broad disruptions in the circuitry of the brain that apply to many features of autism?
   - Do these disruptions precede and lead to “core” features of autism?
Is sensorimotor function “primary” in autism?


**Receptive language is associated with visual perception in typically developing children and sensorimotor skills in autism spectrum conditions.**

Hannant P.

**Author information**

**Abstract**
A number of studies have evidenced marked difficulties in language in autism spectrum conditions (ASC). Studies have also shown that language and word knowledge are associated with the same area of brain that is also responsible for visual perception in typically developing (TD) individuals. However, in ASC, research suggests word meaning is mapped differently, on to situational sensorimotor components within the brain. Furthermore, motor coordination is associated with communication skills. The current study explores whether motor coordination and visual perception are impaired in children with ASC, and whether difficulties in coordination and visual perception correlate with receptive language levels. 36 children took part: 18 with ASC and 18 TD children, matched on age and non-verbal reasoning. Both groups completed the Movement ABC, Beery-Buktenica Developmental Test of Visual-Motor Integration, British Picture Vocabulary Scale and Matrices (WASI). Results showed that ASC children scored significantly lower on receptive language, coordination and visual motor integration than the TD group. In the TD group receptive language significantly correlated with visual perception; in the ASC group receptive language significantly correlated with balance. These results imply that sensorimotor skills are associated with the understanding of language in ASC and thus the relationship between sensorimotor experiences and language warrants further investigation.
Why study sensorimotor function?

Does proper sensorimotor development precede higher cognitive/emotion development?

(Hensch and Bilimoria, *Cerebrum*, 2012)
Does sensorimotor disruption drive other autism behaviors?

(Piven et al., Mol Psychiatry, 2018)

(Amaral et al., TINS, 2008)
Outstanding questions

• How can we use our understanding of sensorimotor function to design effective therapies?
• Does sensorimotor disruption drive or parallel other autism-related behaviors?
• If it does, how does it work and what brain areas are involved?
Discuss!

• What questions do you still have about sensorimotor function in autism?
• How does this information fit into your experience and/or work with autism?
Cerebellum: A key sensorimotor brain area

(Wang, Kloth & Badura, Neuron, 2014)
What does cerebellar function have to do with autism?

The cerebellum integrates sensory information to:

• controls timing
• produce a response of the appropriate size
• learn the appropriate action through quick adjustments
• potentially applicable to motor as well as nonmotor function in autism...
What does cerebellar function have to do with autism?

(D'Mello and Stoodley, 2014, Front Neurosci)
Further evidence of cerebellar involvement in ASD

(Wang, Kloth & Badura, Neuron, 2014)

(D'Mello and Stoodley, Front Neurosci, 2015)

(Menashe et al., PLoS Comput Biol, 2013)
Cerebellar function disrupted in ASD mouse models

(Giovannucci et al., Nat Neurosci, 2017)

(Kloth et al., eLife, 2015)
Cerebellar function disrupted in ASD mouse models

(Tsai et al., Nature, 2012)
A causal role for the cerebellum?

- Stoodley et al., *Nat Neurosci* 2017
- When right Crus I connection weakened, social and repetitive phenotypes worsened
- When right Crus I connection restored in ASD mouse model, phenotypes rescued
- Demonstrated that this finding has direct human relevance...
A causal role for the cerebellum?

(Stoodley et al., Nat Neurosci, 2017)
What’s next?

• What exactly is the cerebellum doing in autism patients (and, for that matter, neurotypical individuals)?
• How does this work become relevant to patients?
• What types of sensorimotor environments would be best suited to cerebellum in ASD patients?
• Can eyeblink conditioning or another cerebellar task become a biomarker?
• Can we intervene at the cellular and molecular level and at what timepoint?
Final Words

• Continued basic and translational research on the brain is critical for understanding how autism arises.
• This research may uncover explanations and mechanisms for individual features of autism, or a larger overall mechanism that accounts for all autism features.
• Sensorimotor features may be one route to figuring this out.
• In the end, this information is intended to help individuals who work each day with autism patients, and needs to be tailored and delivered as such.
Thank you!

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