Sensorimotor impairments in autism spectrum disorder (ASD): New targets for improving treatment

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Talk outline

• The candidate
• Research focused presentation
• Why am I the BEST fit for this advertised position?
• Why is the School of Kinesiology at the University of Minnesota the IDEAL home for me to be successful?
The candidate

Education

• Ph.D. training: Dr. Karl M Newell
• Postdoctoral training: Dr. Matthew W Mosconi

Academic Employment

• Research Assistant Professor
• Assistant Professor

Neurocognitive and behavioral development laboratory
Research projects and assessments

Autism spectrum disorder (ASD)

Lack of joint attention/eye contact

Insistence on sameness

“Spectrum” represents the broad range of different autism associated behavioral features and cognitive skills

- Intellectual disability
- Social interaction (i.e., Making Eye Contact, Joint Attention)
- Not interested in others
- Communication (i.e., Verbal, Non-verbal)
- Nonverbal
- Behavioral (i.e., Repetitive and Unusual Behaviors)
- Intense
- Sensory (i.e., Touch, Smell, Taste)
- Hyposensitive
- Less coordinated
- Motor (i.e., Gross, Fine Motor)
- Coordinated
- Gifted
- A variety of friendships
- Verbal
- Mild
- Hypersensitive

Image recreated according to Centers for Disease Control (CDC) webpage at: http://www.cdc.gov/ncbddd/autism/signs.html

Autism prevalence and annual cost

Estimated Autism Prevalence 2018

Projected cost to society by 2025 to reach $1 trillion annually
Sensorimotor impairments matter

- Sensorimotor abnormalities are common in ASD, they emerge early in infancy (Fournier et al. 2010), appear to be familial (Mosconi et al. 2010), and are associated with worse social, cognitive and functional outcomes (Travers et al. 2010).

- Defining sensorimotor deficits and their neural substrates hold promise for determining pathophysiological processes associated with core ASD symptoms (Mosconi et al. 2015).

Motor dyspraxia in ASD

Manual dexterity deficits in ASD

Fuentes et al. (2009)
Cerebellum and cerebellar circuitry alterations serve as targets in the pathophysiology of sensorimotor deficits in ASD

To quantify the extent to which children with ASD showed increased postural sway during static and dynamic stances

Study aims

➢ To quantify the extent to which children with ASD showed increased postural sway during static and dynamic stances
Study aims (cont.)

➢ To quantify the postural orientation processes in ASD by characterizing the spatial relations of individuals’ postural sway relative to their own postural sway limitation boundary

Demographic characteristics [range] of children with ASD and typically developing (TD) children

<table>
<thead>
<tr>
<th></th>
<th>ASD (n=22)</th>
<th>TD (n=21)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>7-18</td>
<td>4-18</td>
<td>0.719</td>
<td>0.401</td>
</tr>
<tr>
<td>% Male</td>
<td>86.4</td>
<td>85.7</td>
<td>0.004</td>
<td>0.951</td>
</tr>
<tr>
<td>FSIQ</td>
<td>70-131</td>
<td>80-141</td>
<td>3.766</td>
<td>0.059</td>
</tr>
<tr>
<td>PIQ</td>
<td>72-132</td>
<td>80-129</td>
<td>0.030</td>
<td>0.864</td>
</tr>
<tr>
<td>VIQ</td>
<td>64-129</td>
<td>85-129</td>
<td>9.006</td>
<td>0.005**</td>
</tr>
</tbody>
</table>

Wechsler abbreviated scale of intelligence was used for children >=6 yr (ASD=26; TD=19);
Wechsler preschool and primary scale of intelligence (ASD=4; TD=4) or
Differential abilities scales-II (ASD=1) were used for children < 6 yr.
**Task conditions**

1. Postural limitation boundary trial
2. Static stance: side-by-side
3. Dynamic stances
   - Anterior-posterior postural sway (AP sway)
   - Mediolateral postural sway (ML sway)

**Dependent measures**

- **Aim 1: Postural sway variability**
  - COP standard deviation
- **Aim 2: Postural orientation**
  - Spatial relation between COP time series and individuals’ postural limitation boundary

Children with ASD show increased postural sway variability during static and dynamic stances
Children with ASD show increased postural sway variability across all standing postures.

During dynamic sways, children with ASD showed reduced spatial perception of body sway relative to postural limitation boundary in target directions.
Summary

- Children with ASD showed increased postural sway variability during both static and dynamic stances relative to typically developing children.
- Children with ASD demonstrated reduced spatial perception of their postural limitation boundary towards target directions during dynamic postural sways.

Individuals with autism spectrum disorder show abnormalities during initial and subsequent phases of precision gripping.
Study aims

- Quantifying precision grip force variability during sustained force production as a function of target force level in children with ASD to examine the effect of visual feedback to precision motor output
- Quantifying the type of initial force pulse during the rise phase of grip force production in children with ASD to examine children’s predictive force production prior to receiving visual feedback

Demographic characteristics [mean (SD)] of children with ASD and typically developing (TD) children

<table>
<thead>
<tr>
<th></th>
<th>ASD (n=34)</th>
<th>TD (n=25)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>8.77 (2.64)</td>
<td>8.76 (3.11)</td>
<td>0.00</td>
<td>0.99</td>
</tr>
<tr>
<td>% Male</td>
<td>82.8</td>
<td>72.0</td>
<td>1.01</td>
<td>0.31</td>
</tr>
<tr>
<td>FSIQ</td>
<td>95.66 (15.58)</td>
<td>110.40 (15.15)</td>
<td>13.36</td>
<td>0.00**</td>
</tr>
<tr>
<td>PIQ</td>
<td>99.94 (17.43)</td>
<td>106.60 (16.76)</td>
<td>2.20</td>
<td>0.14</td>
</tr>
<tr>
<td>VIQ</td>
<td>92.60 (16.23)</td>
<td>111.32 (16.03)</td>
<td>19.60</td>
<td>0.00**</td>
</tr>
</tbody>
</table>

Wechsler abbreviated scale of intelligence was used for all children except for 4-yr old participant who completed the Wechsler preschool and primary scale of intelligence (4th ed.)
Task conditions
1. Two-sec trial: two blocks of 5 trials; force trial was 2-sec in duration and alternated with 2-sec rest period (10 trials in total)
2. Eight-sec trial: two blocks of 3 trials, force trial was 8-sec in duration and alternated with 8-sec rest period (6 trials in total)
3. Target force levels: 15%, 45% and 85% maximum voluntary contraction (MVC)

Dependent measures
- Aim 1: Sustained phase force variability (8-sec test)
  - Coefficient of variation (CoV)
- Aim 2: Rise phase (2- and 8-sec tests)
  - Types of initial force pulse
  - Initial force pulse ratio

Grip force profiles during the 2-sec test for representative children with ASD and TD controls

Increased initial pulse overshooting (*) in children with ASD at 15% MVC target force level
Grip force profiles during the 8-sec test for representative children with ASD and TD controls

Increased initial pulse overshooting (*) and force variability (→) during sustained phase of force production in children with ASD at 15% MVC target force level

Reduced sustained mean force and increased force coefficient of variation (CoV) in children with ASD during 8-sec precision gripping
Three different types of initial pulse during rise phase of precision gripping

Individuals with ASD show delayed transition from Type 1 to Type 2 primary pulse
Summary

➢ Sustained phase (feedback control):
  • Children with ASD showed an overall weakness during precision gripping with this effect more pronounced at the medium and high target force levels (mean force: 45% and 85% MVC)
  • Children with ASD showed increased force variability (CoV) at all target force levels suggesting they have a reduced ability to accurately adjust motor output according to visual feedback

➢ Rise phase (feedforward control):
  • Children with ASD showed a persistent bias toward using a pulse-release (type 1) initial pulse pattern at higher target force levels and during longer trials suggesting they show difficulty generating predictive models to accommodate different task demands

Functional MRI studies of visuomotor control
Visual-motor processing in the brain

- **Motor Cortex (Motor commander)**
- **Parietal Cortex (Spatial processor)**
- **Visual Cortex (Visual processor)**
- **Cerebellum (Translator)**

Ungerleider & Mishkin (1982)
Glickstein (2000)
Stein (1986)

Low gain

High gain
Visuomotor behavioral deficits in individuals with ASD were associated with atypical modulation of parietal-cerebellar processes that included both hypo- and hyper-activation relative to controls across different levels of visual feedback gain.

Visuomotor- Rest
ASD-TD

Summary

- We provide new evidence that parietal-cerebellar networks involved in translating sensory feedback information into reactive motor adjustments are compromised in ASD.
- Studying behavior and brain function across different visual gains, we also demonstrate both reduced and increased activation in ASD relative to controls suggesting atypical regulation of neural processes involved in encoding and translating sensory information during motor performance.
- Increases in parietal-cerebellar activity in ASD relative to controls despite intact behavior at medium gain suggests reduced efficiency in processing feedback even when motor behavior appears unaffected.
Why am I the BEST fit for this advertised position?

• 4 approved IRB protocols
• 2 independent lines of research
  ➢ Neuromotor degeneration in mid- and older-aged adults with ASD
Behavioral
- Cortical-cerebellar tract (Romberg stances, reaching)
- Cortical-basal ganglia tract (Step initiation, sit-to-stand)

Brain
- Structural scan (T1, T2)
- Free-water diffusion MRI
- Functional MRI (pulse vs. sustained trials)

Clinical
- MDS-Unified Parkinson’s Disease Rating Scale (MDS-UPDRS)
- International Cooperative Ataxia Rating Scale (ICARS)

Diagnostic
- Autism Diagnostic Observation Schedule (ADOS)
- Repetitive Behavioral Scale Revised (RBS-R)
- Wechsler Abbreviated Scale of Intelligence (WASI-II)

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Submitted grant proposals to:
- UF Opportunity Seed Fund
  - (Two of the 3 reviewers recommended for funding)
- UF Claude D. Pepper Center Junior Scholar Award
- DOD Autism Research Program Idea Development Award
  - (Overall Evaluation Score: 2.3 (1.0- highest merit to 5.0- lowest merit)
- NIH-NIA R21
  - (1st submission scored 38 on the 33rd percentile)

Next step:
- NIH-NIA R01 (2020-2021)
2 independent lines of research (cont.)

- Oromotor impairments in children with ASD

Maladaptive feeding behaviors (i.e., feeding difficulties with no identifiable medical condition) are common in ASD with the prevalence varying from 70% to 90% of individuals. They lead to nutritional inadequacy and obesity in school-aged children as well as anxiety and distress of caregivers in managing patients' behaviors.

Sensory-based assessment (e.g., textural, taste, and odor aversions to specific food choices)

Submitted grant proposals to:
- UF CTSI Pilot Award
- Organization for Autism Research
- Brain & Behavioral Science Foundation

Fig. 2 A 6-yr old control participant made 5, 10 and 20 chews on the gums during two-color chewing gum mixing ability test. Figures show qualitative color changes of the gums across three conditions. Variance of hue (VH) is 0.871, 0.644 and 0.440 for the 5, 10, and 20 chews respectively.

Fig. 3 iTero quantification of inter-molar width (purple), arch depth (red) and arch circumference (green) of maxillary (A) and mandibular (B) arch of a 9-yr old control.
• Data collection
  - Neuromotor degeneration in mid- and older-aged adults with ASD
    16 patients and 18 controls (8 months)
  - Oromotor impairments in children with ASD
    1 patients and 2 controls (1 month)

• Establishing an active and independent research program
• Seeking and securing external research funding

• 2 Co-I lines of research

  ➢ **Neural substrates of behavioral issues in ASD**

  R01 MH12734-01 Mosconi, M (PI) 07/01/2017– 05/31/2022
  NIMH

  Motor Abnormalities and Functional Brain Mechanisms in ASD
  This five-year R01 study identifies the distinct neural processes underlying rapid, repetitive sensorimotor abnormalities and deficits in controlling continuous motor output. Novel functional magnetic resonance imaging (fMRI) and motor physiology tests will be conducted to examine cerebellar-cortical and striatal-cortical brain function and their relation to sensorimotor abnormalities in ASD from late childhood to adulthood.

  • 5 peer-reviewed articles
  • 2 under reviewed manuscripts
  • Renewal in 2021
Establishing an active and independent research program
Seeking and securing external research funding

2 Co-I lines of research

- Neurophysiological mechanisms of the neurodegenerative process in older adults with fragile X mental retardation 1 (FMR1) gene premutation

R01AG066699 Mosconi (PI) Submitted 6/5/2019
NIH/NIA
Sensorimotor and cortical-cerebellar markers of Fragile X-associated tremor/ataxia syndrome (FXTAS)

This five-year, multi-site R01 proposal aims to identify new biobehavioral markers of core symptom traits of FXTAS using novel tests of sensorimotor physiology, cortical-cerebellar anatomy, and cortical-cerebellar function. Studying aging, asymptomatic premutation carriers and individuals with FXTAS, we will determine the power of our sensorimotor and cortical-cerebellar markers for reliably identifying FXTAS patients and tracking disease risk and progression.

(1st submission scored 38 on the 33rd percentile)

Disseminating research findings through publication and presentation

- Symposia presentation (1)
- Oral presentations (2)
- Poster presentations (9)
- Peer-reviewed articles (4)
- Under reviewed manuscripts (2)
- Manuscript in preparation (2)
- Facebook online streaming (1)
• Teaching undergraduate and graduate courses in Human Movement Science.
• Mentoring and advising masters and doctoral students for thesis and dissertation research

• OTH 5770 Research in Occupational Therapy
• RSD 6710 Motor control: Translating from fundamental research to rehabilitation practice
• RSD 6930 Matlab Basics for Rehabilitation Science
• 2019 UF University Scholar Award to Emily In

Courses I am interested in developing and teaching:
• Motor Control
• Neuroscience
• Motor Development
Why is the School of Kinesiology at the University of Minnesota the IDEAL home for me to be successful?

- Neuromotor degeneration in mid- and older-aged adults with ASD

  - **Recruitment & Diagnosis:**

  - Collaboration, Data Collection and analysis:

- Oromotor impairments in children with ASD

  - **Recruitment & Diagnosis:**

  - Collaboration, Data Collection and analysis:
Why is the School of Kinesiology at the University of Minnesota the IDEAL home for me to be successful?

Acknowledgement

**Collaborators**
- David Vaillancourt, Ph.D.
- Evangelos Christou, Ph.D.
- Christopher Hess, M.D.
- Mark Lewis, Ph.D.
- Greg Valcante, Ph.D.
- Ann-Marie Orlando, Ph.D.
- Paul Davenport, Ph.D.
- Tim Vollmer, Ph.D.
- Calogero Dolce, D.D.S., Ph.D.
- Leda Mugayar, D.D.S.
- Matthew Mosconi, Ph.D. (KU)
- Craig M. Powell, M.D., Ph.D (UArk)

**Current Lab member**
- Stefanie Perez, B.S.

**Current recruitment centers**

- UF Center for Autism and Related Disabilities
- FSU Center for Autism and Related Disabilities (CARD)
- Center for Autism and Related Disabilities (CARD)
- CARD + CENTER FOR AUTISM & RELATED DISABILITIES AT UF

**Undergraduate Student**
- Emily In
Thank you !!!