Motor Skill and Motor Learning Deficits in Children with Autism: Implications for Social Skill Development and Therapeutic Intervention

Stewart H. Mostofsky, M.D.

Associate Professor, Neurology and Psychiatry

Director, Laboratory for Neurocognitive and Imaging Research

Medical Director, Center for Autism and Related Disorders

Kennedy Krieger Institute

Johns Hopkins University School of Medicine
MOLECULAR EXPRESSIONS
Digital Microscopy

Amoeba
(Protozoan)

Through the Nikon Eclipse E600 Microscope with Apodized Phase Contrast
Internal Models of Action (Behavior)
Internal Action Models of Behavior

- Reward-based modulation
- Error-based modulation
Core Deficits in Autism

Motor Skill Deficits

Communication

Social Interaction

Stereotyped Behaviors
Why Study Motor Function in Autism?

- Motor signs can serve as markers for deficits in parallel brain systems important for development of socialization, communication, and other higher-order behaviors.
- Anatomic and physiologic basis of motor function well understood.
- Motor examination offers ease and precision not achievable in examination of complex behavior.
  - Reliable and valid measures of functional impairment.
  - Differences can be detected in infancy (e.g., Landa et al.).
  - Powerful approach for examining brain-behavior correlations.
- Motor examination can provide insight into:
  - nature of the behavioral impairments
  - brain basis
  - effective therapeutic interventions
Significance of Motor Models to Autism

• Motor theories of cognition and social development:
  – Embodied Cognition Theory (e.g., Williams 2008)
  – Embodied Simulation (e.g., Gallese 2001)
  – Enactive Mind (Klin et al 2003)
  – Motor theory of social cognition (e.g., Fecteau, Lepage & Théoret 2006)
Core Deficits in Autism

Motor Skill (Procedural) Learning

Motor Skill Deficits
Outline
Background: Motor abnormalities in Autism

• DSM feature: stereotypies
• Other frequently reported motor findings:
  – Impaired basic motor control: gait, posture, balance, speed, coordination
    (e.g., Ghaziuddin, 1998; Jansiewicz, 2006; Noterdaeme, 2002; Rinehart, 2006)
ROC curve using PANESS: Autism vs. Controls
(overflow, gait, balance, and movement speed)

Area under curve = .936
Motor Control Impairment in ADHD and Autism

Significant: ASD performed worse than TD (p < 0.001)
ADHD performed worse than TD (p < 0.001)

MacNeil et al., 2012; Neuropsychology
Motor Abnormalities in Autism

- DSM feature: stereotypies
- Other frequently reported motor findings:
  - Impaired basic motor control: gait, posture, balance, speed, coordination
    (e.g., Ghaziuddin, 1998; Jansiewicz, 2006; Noterdaeme, 2002; Rinehart, 2006)
  - Impaired skilled motor performance
    » Emphasis on motor imitation
    » Deficits also with pantomime and tool use on praxis testing
      highly robust and reproducible finding
      (e.g., Mostofsky, 2006; Dewey, 2007; Dziuk, 2007; Dowell, 2009; MacNeil, 2012)

  ➔ “developmental dyspraxia” in autism
Praxis - Definition

• *Ideomotor praxis*

• Ability to perform learned, skilled motor actions
  – Communicative gestures
    “intransitive”
  – Tool use
    “transitive”
Praxis – Gesture to Command
Chalkboard Eraser
Praxis – Gesture to Imitation
Arm Circles
Children with HFA show significant impairments in performance of:

- Gestures to Command (GTC)
- Gestures to Imitation (GTI)
- Gestures with Tool Use (TU)

*Mostofsky et al., 2006*  
*Jnl Intl Neuropsych Soc*
Praxis Impairment Is Specific to Autism

Significant: ASD performed worse than TD ($p < 0.001$)
ASD performed worse than ADHD ($p < 0.001$)

MacNeil et al., 2012; Neuropsychology
Autism and Praxis—Hypotheses

• Internal Action Models: Representations of motor plans and their sensory feed-back

1. The brain uses the same internal action models to perform skilled motor actions as skilled social/communicative actions.
Motor Skill (Praxis) Performance Predicts Defining Social, Communication, Behavioral Deficits in Autism

\[ R^2 = 0.34, \ p < 0.001 \]

Dziuk et al., 2007
Dev Med Child Neurol
Autism: Dyspraxia for Social Skills?

“Shake-Hand Diagnosis”
Neurobiological Basis of Praxis and Imitation

Internal Models of Action (Behavior)
Autism and Praxis – “Mirror Neuron” Hypothesis

• Internal Action Models: Representations of motor plans and their sensory feed-back

1. The brain uses internal action models to perform skilled motor actions, including those actions necessary to social and communicative behavior.

2. The brain uses internal action models in a feed-forward manner to understand the intents of others.

   – The same internal models that are the basis of learning skilled movements are also the basis with which our brain understands the actions of others (“action understanding”).

   – Anomalous formation of action models, including those important for social interaction, may therefore contribute to impaired development of “theory of mind.”
Internal Models of Action (Behavior)
Performing Actions
Understanding Others’ Actions
Do children with autism show abnormalities in the stored representations of motor skills?

Do children with autism show impairment in their ability to identify and recognize correct gestures in others (impaired postural knowledge)?
Postural Knowledge Test (PKT)

Mozaz et al., 2002
Children with ASD show worse performance on the PKT than TD children

\( F = 4.63; \ p = .03 \)

Dowell et al., 2009; *Neuropsychology*
Postural Knowledge Impairment is Specific to Autism

Significant: ASD performed worse than TD ($p = 0.003$)
ASD performed worse than ADHD ($p = 0.024$)

MacNeil et al., 2012; Neuropsychology
Children with ASD show impaired ability to identify and recognize correct gestures in others

Postural Knowledge ↔ Praxis
Children with ASD show impaired ability to identify and recognize correct gestures in others.
Core Deficits in Autism

Motor Skill (Procedural) Learning

Motor Skill Deficits

Communication

Social Interaction

Stereotyped Behaviors
“Dyspraxia” in Autism – Developmental Perspective

- Adult lesion-based model (loss of skill after focal lesion) may not be appropriate
- “Dyspraxia” in autism unlikely due to loss of already acquired skills
- Consider lesion resulting in impaired acquisition (learning) of motor skills
  - help identify neural mechanisms
  - guide therapeutic intervention
Learning/Memory

- Declarative
  - (“Conscious” explicit learning of facts/events)

- Procedural
  - (“Unconscious” implicit learning of skills)
Procedural Learning and Social Skills

• Development of social skills involves learning to execute a series of complex movements.

• Individuals with autism often report inability to “automatically” perform social gestures; compensate by using “declarative” scripts.

• “Enactive Minds” (Klin, 2003)
  • Impaired formation of action models beginning in infancy may also explain impaired social cognition (e.g., theory of mind) in autism.
Motor Learning: Reaching Adaptation
Significant effect of group on adaptation rate (p<0.005).

Post-hoc analysis:
ASD significantly slower rate than TD (p<0.001) and ADHD (p<0.01)

Izawa et al., 2012; Autism Research
Proprioceptive vs. Visual Sensitivity

- Single trial proprioceptive perturbations given by three different field magnitudes
  - Experiment balanced with both leftward and rightward errors
- Visual perturbations were caused by three different gains applied to the hand path
  - Displayed with cursor
- Error trials given between two channel trials (C1 and C2)
  - Adaptation resulting from the perturbation measured as the change in force from C1 to C2
Results: Proprioceptive vs. Visual Sensitivity

- The ASD group showed increased adaptation to a proprioceptive error alone, of three different sizes
  - 6.5, 13 and 19.5 $\frac{N}{m/s}$
Greater Intrinsic Generalization Predicts Impairments in Imitation and Praxis

Intrinsic generalization predicted performance of:
Gestures to Imitation
\( R = -0.57, \ p = 0.006 \)

Also predicted performance of:
Gestures to Command
\( R = -0.544, \ p = 0.009 \)
Gesture with Tool Use
\( R = -0.551, \ p = 0.008 \)

Haswell et al., 2009 *Nature Neuroscience*
Intrinsic Generalization Predicts Social Impairment

Haswell et al., 2009 Nature Neuroscience
Interim Conclusions – Motor Control/Learning

• Autism is associated with anomalous patterns of motor development: “dyspraxia”

• Children with ASD show a bias towards reliance on proprioceptive (intrinsic), rather than visual (extrinsic), feedback to guide formation of internal models of action (i.e., to guide motor learning).

• This bias towards proprioceptive-based learning is strongly associated with autism-associated impairment in:
  – motor function (dyspraxia, imitation, basic motor skill)
  – social function
These neural mechanisms underlying abnormal development of motor skills in autism (e.g., dyspraxia) may be directly relevant to the neural basis of impaired development of social and communicative skills.

Feedforward hypothesis:
Impaired development of “social awareness” and difficulty understanding social cues (“theory of mind”) may result from anomalous formation of internal models of action necessary to social behavior.
Next Steps

- **Behavior:** Further define dyspraxic impairment and associated anomalous patterns in motor learning.
- **Neural Basis:** Is this anomalous pattern of motor learning associated with abnormal patterns of sensory-motor connectivity?
- **Treatment Implications:** How can we use these observations of anomalous patterns of learning in autism to guide therapeutic intervention?
Next Steps

- **Behavior**: Further define dyspraxic impairment and associated anomalous patterns in motor learning.
- **Neural Basis**: Is this anomalous pattern of motor learning associated with abnormal patterns of sensory-motor connectivity?
- **Treatment Implications**: How can we use these observations of anomalous patterns of learning in autism to guide therapeutic intervention?
Autism: local overconnectivity & long-range underconnectivity

Belmonte et al., JNeurosci, 2004
Sensory-Motor Connectivity

Proprioceptive-Motor (Intrinsic)

Visual-motor (Extrinsic)
Total Brain Volume: Autism vs. Control

Courchesne et al., UCSD
Autism – enlargement of radiate (outer zone) white matter in all lobes

Herbert et al, 2004
Increased Motor Cortex White Matter Volume Predicts Basic Motor Skill Impairment in Children with Autism (but not TD or ADHD Children)

Mostofsky et al., 2007; Brain

Typically Developing Children

![Graph showing the relationship between Total PANESS score and Left Motor White Volume (cubic cm) for Typically Developing Children. The R² value is 0.23, and p = 0.04.]

Children with Autism

![Graph showing the relationship between Total PANESS score and Left Motor White Volume (cubic cm) for Children with Autism. The R² value is 0.72, and p = 0.0001.]
Autism: Differences in Functional Connectivity

Functional Connectivity
Motor Networks

Dorsal Motor

BA 6

BA 4

AC

I-V
Motor Networks

Dorsal Motor

BA 6
AC
BA 4
BA 3
Put

Ventral Motor

z = 62
z = 46
z = 36
z = -6
z = -14

Scans

BA 4
BA 6
AC
Put
VI
I-V
Visual Networks

Visual 1

Visual 2
Visual Networks

Visual 1

Visual 2

Visual 3

BA 17
BA 18
BA 17
BA 18

V3
V4

ITG
Ling

Hip
Visual – Motor Connectivity

* p < .05 (corrected)
Brain – Behavior Correlation: Social Responsiveness Scale

Visual 3 – Dorsal Motor Connectivity

R = .390, p = .02

Visual 3 – Ventral Motor Connectivity

R = -.496, p = .003
Brain – Behavior Correlation: Social Awareness

Visual 3 – Dorsal Motor Connectivity

R = .503, p = .002

Visual 3 – Ventral Motor Connectivity

R = -.477, p = .004
Social Awareness Items

- Facial expressions do not match spoken word
- Aware of others thoughts and feelings
- Does not seem to mind being out of step with or not on the same wavelength as others
- Has good personal hygiene
- Focuses his/her attention to where others are looking or listening
- Knows when he/she is talking to loud or making too much noise
- Seems to react to people as if they are objects
- Walks in between two people who are talking
Brain – Behavior Correlation: Imitation and Praxis

Praxis - % Correct Imitation

Visual 3 – Ventral Motor Connectivity

Praxis - Total % Correct

Visual 3 – Ventral Motor Connectivity

R = .402, p = .02

R = .496, p = .004
Conclusions - Neuroimaging

- Is anomalous pattern of motor control and learning in autism associated with abnormal patterns of neural connectivity?
  - Disorganized overgrowth of localized connections within primary sensory-motor cortex (SM1) is associated with motor impairments.
  - DTI reveals a generalized pattern consistent with increased local connectivity
  - fcMRI (using ICA) reveals differences in visual-motor connectivity, predictive of:
    - core social-communicative impairments in children with ASD
    - imitation and praxis in TD children, and perhaps subset of children with ASD
Therapeutic Implications: Teaching Skills to Children with Autism

• Increased reliance on somatosensory feedback
  • Therapy that “Plays to the Strength” of children with ASD
  • “Hands on” instruction as a “way in” for improving skill acquisition in children with autism
    • Motor Skills
      • e.g., Handwriting
    • Social and Communicative Gestures
      • e.g., Sign Language
Handwriting and ASD

• Good handwriting crucial for academic progress, social and communicative development, and self-esteem (Feder & Majnemer, 2007)

• Only study in ASD assessed letter size in adults (Beversdorf et al., 2001)

➢ No study had explored handwriting in children or adolescents with ASD
➢ No study had assessed the multiple aspects of handwriting that may differentially contribute to impairments
Minnesota Handwriting Assessment

• Scoring: legibility, form, alignment, size, spacing, rate

• 14 ASD (10.2 ± 1.9 yrs)
• 14 CTL (11.1 ± 1.3 yrs)

(Fuentes, Mostofsky, & Bastian, 2009; *Neurology*)
Handwriting in Children with Autism: worse overall and form quality

(Fuentes, Mostofsky, & Bastian, 2009; *Neurology*)
Improving Letter Formation Through Proprioceptive Feedback
Therapeutic Implications: Improving Social Skills in Children with Autism

- Declarative “work around”
  - Teach social/communicative actions (gestures, eye contact) using explicit instruction
- HFA
  - “excellent memorization” commonly observed
  - often compensate for inability to “automatically” perform social gestures by using “declarative” scripts
- ABA
  - Repeated explicit instruction with contingency reinforcement
- Problems
  - Teaching specific actions; lack of context
  - Poor generalizability
Therapeutic Implications: Improving Social Skills in Children with Autism

• Remodel procedural learning – Hebbian approaches
• Can we alter the way the autistic brain learns skills, so that children with ASD are better able to form action models that are based on visual feedback from the external world (as this is critical to social learning)?
  • Increase frontal-parietal (MNS) connectivity
    • “External” stimulation to up-regulate visual-premotor connections
      • transcranial direct current stimulation (tDCS)
    • “Internal” remodeling using behavioral approaches
Therapeutic Implications: Improving Social Skills in Children with Autism

• “Internal” (behavioral) approaches for increasing frontal-parietal (MNS) connectivity
  • Imitation activation
    • Behavioral (video from Portia Iversen)
      • engender general concepts of Floor Time – “getting into child’s world”
Imitation
Therapeutic Implications: Improving Social Skills in Children with Autism

• “Internal” (behavioral) approaches for increasing frontal-parietal (MNS) connectivity
  • Imitation activation
    • Behavioral (video from Portia Iversen)
• Other methods that enhance reliance on external (visual) stimuli for the formation of action models
  • “Sticky mittens”
“Sticky Mittens”

Results: Face-Preference

- At 4-months, reliable preference for faces ($p<0.01$).
- Object-dance training does not increase face-preference

5/7/2013
• Clear face-preference in 3-month-old infants following simulated reaching experience ($p=0.017$).

• **Self-produced actions jump-start face-preference.**
Acknowledgments

Laboratory for Neurocognitive and Imaging Research (LNIR) / KKI
Mary Beth Nebel  Anita Barber  Jennifer Gidley-Larson  Lauren Dowell  Carrie Nettles  Kristie Sweeney  Deana Crocetti  Katarina Ament  Lindsey MacNeil  Dan Peterson  Ben Dirlikov  Mark Mahone  Martha Denckla

Ctr for Autism and Related Disorders
Rebecca Landa  Klaus Libertus

KKI Motion Analysis Laboratory
Amy Bastian  Christina Fuentes  Pablo Celnik

JHU Lab for Computational Motor Control
Reza Shadmehr, Mollie Marko, Jun Izawa, Courtney Haswell, Sarah Pekny

F.M. Kirby Imaging Center
James Pekar  Brian Caffo  Suresh Joel  Susumu Mori  Michael Miller

Support: Autism Speaks Foundation, NIH (NINDS) R01 NS048527, K02 NS044850, JHU Institute for Clinical and Translational Research (UL1 RR025005)