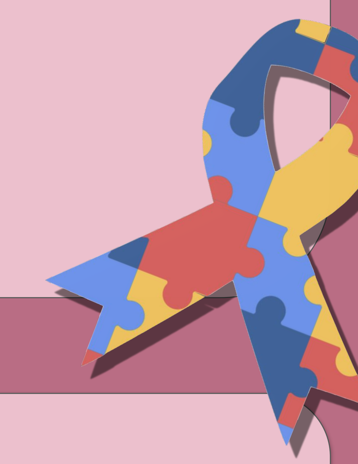
A Novel Association of Atypical Hemispheric Weighting and Differential Mirror Neuron System Dynamics in Autism Spectrum Disorder

Sydney Bock[1,5], Jacob Pena[2,5], Sarah Kovalev-Sheinberg[3,5], EmmaRose Zilla[4,5]

Walter Payton College Preparatory High School, Chicago, IL[1]; Joshua High School, Joshua, TX[2]; Sherman Oaks Center for Enriched Studies, Los Angeles, CA[3]; Milton Academy, Milton, MA[4]; Boston University, Boston, MA[5]

BOSTON UNIVERSITY



Introduction

- **Autism spectrum disorder (ASD)** involves atypical sensory-perceptual functions and socio-cognitive skills
- **Social mirroring,** a skill often impaired in ASD, is linked to the **mirror neuron system (MNS),** a network that activates during **action observation (AO)** and subsequent **action execution (AE)**
- On the macro-scale, individuals with ASD tend to have either **equal hemispheric weighting**, or **reverse asymmetry** (right weighting) patterns (*Fig. 1*)
- Non-autistic individuals (NAI), conversely, often have **left weighting** as a result of left-heavy cortical thickness (*Fig. 1*)
- **Atypical hemispheric weighting** & decreased **functional laterality** have been linked with socio-cognitive impairments, such as **response to social cues**
- However, sparse research has been conducted, if any, on the the effect of ASD-related atypical hemispheric weighting and laterality on the MNS
- To probe this limited field, we developed a modified **Wilson-Cowan Neural Mass Model (NMM)** to simulate MNS firing during AO vs AE with ASD-specific laterality and hemispheric weighting parameters

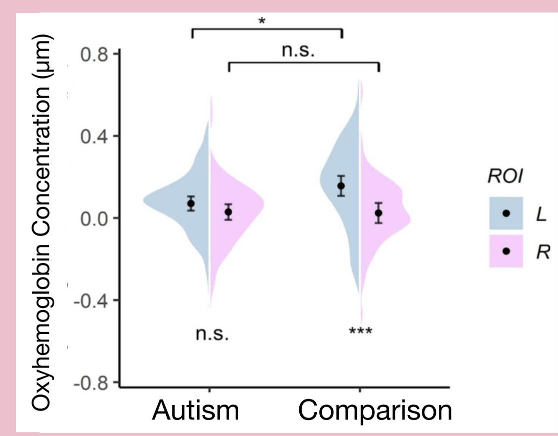


Fig. 1. Cohort x hemisphere weighting (Lai *et al*. 2024)

Methods

- We employed a **modified Wilson-Cowan Neural Mass Model (NMM)** to stimulate activity of excitatory and inhibitory neural populations together
  - Neural populations are simulated for the left and right hemispheres, stratified along ASD/NAI cohorts
- The Wilson-Cowan NMM utilizes parameters for **hemispheric weighting** and **interhemispheric communication** (representing corpus callosum connection) to reflect ASD and NAI-related differences in MNS functionality, particularly when receiving AO vs. AE stimuli

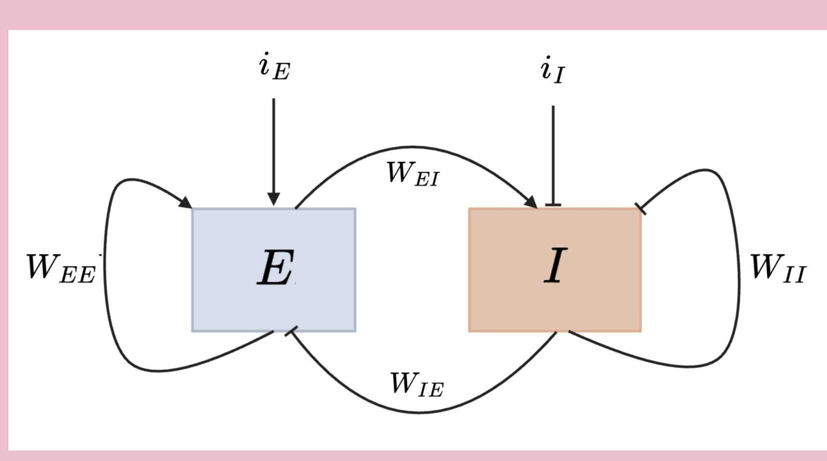


Fig. 2. Wilson-Cowan NMM schematic. ***E*** and ***I*** represent excitatory and inhibitory neural populations respectively. $\boldsymbol{i_E}$ and $\boldsymbol{i_I}$ represent the stimulation given to each neural population. The $\boldsymbol{W_{XY}}$ terms represent input from population $\boldsymbol{Y \rightarrow X}$

Designing The Model

- Our model was developed using Python with NumPy, Matplotlib, and SciPy
- Each timestep (1ms) calculates excitatory/inhibitory interneuronal activity through differential equations, with AO stimuli felt at timesteps 5s, 15s, and 25s, and AE stimuli felt at timesteps 10s, 20s, and 30s
- Equations show **filtering of synaptic inputs → observable signals** (*Fig. 2*)

Simulation Parameters:

- Left hemispherical weighting: **w_XY_L** (Models left cortical thickness)
- Right hemispherical weighting: **w_XY_R** (Models right cortical thickness)
  - where **XY** are placeholders for either **E** for excitatory or **I** for inhibitory
- Corpus callosum strength: **'inter'** (2 floats from 0.0 to 2.0,) multiplied by previous value generated by opposite hemisphere

Analysis:

- Output activity analysed by comparing **amplitude** and timing of neural oscillations in response to AO vs AE stimuli
- Leveraged **2-tailed, unpaired *t-test* statistical analyses** on generated signals to assess cohort-wise differences in MNS functioning

References

- Wan B, Hong SJ, Bethlehem RAI, Floris DL, Bernhardt BC, Valk SL. Diverging asymmetry of intrinsic functional organization in autism. Mol Psychiatry. 2023 Oct;28(10):4331-4341. doi: 10.1038/s41380-023-02220-x. Epub 2023 Aug 16. PMID: 37587246; PMCID: PMC10827663.
- Oberman, L. M., Hubbard, E. M., McCleery, J. P., Altschuler, E. L., Ramachandran, V. S., & Pineda, J. A. (2005). EEG evidence for mirror neuron dysfunction in autism spectrum disorders. Cognitive Brain Research, 24(2), 190–198. https://doi.org/10.1016/j.cogbrainres.2005.01.014
- Aziz-Zadeh, L., Koski, L., Zaidel, E., Mazziotta, J., & Iacoboni, M. (2006). Lateralization of the Human Mirror Neuron System. Journal of Neuroscience, 26(11), 2964–2970. https://doi.org/10.1523/jneurosci.2921-05.2006
- Saffin, J. M., & Hassaan Tohid. (2016). Walk like me, talk like me. Neurosciences, 21(2), 108–119. https://doi.org/10.17712/nsj.2016.2.20150472
- Bonaiuto, J., & Arbib, M. A. (2010). Extending the mirror neuron system model, II: what did I just do? A new role for mirror neurons. Biological Cybernetics, 102(4), 341–359. https://doi.org/10.1007/s00422-010-0371-0

Results

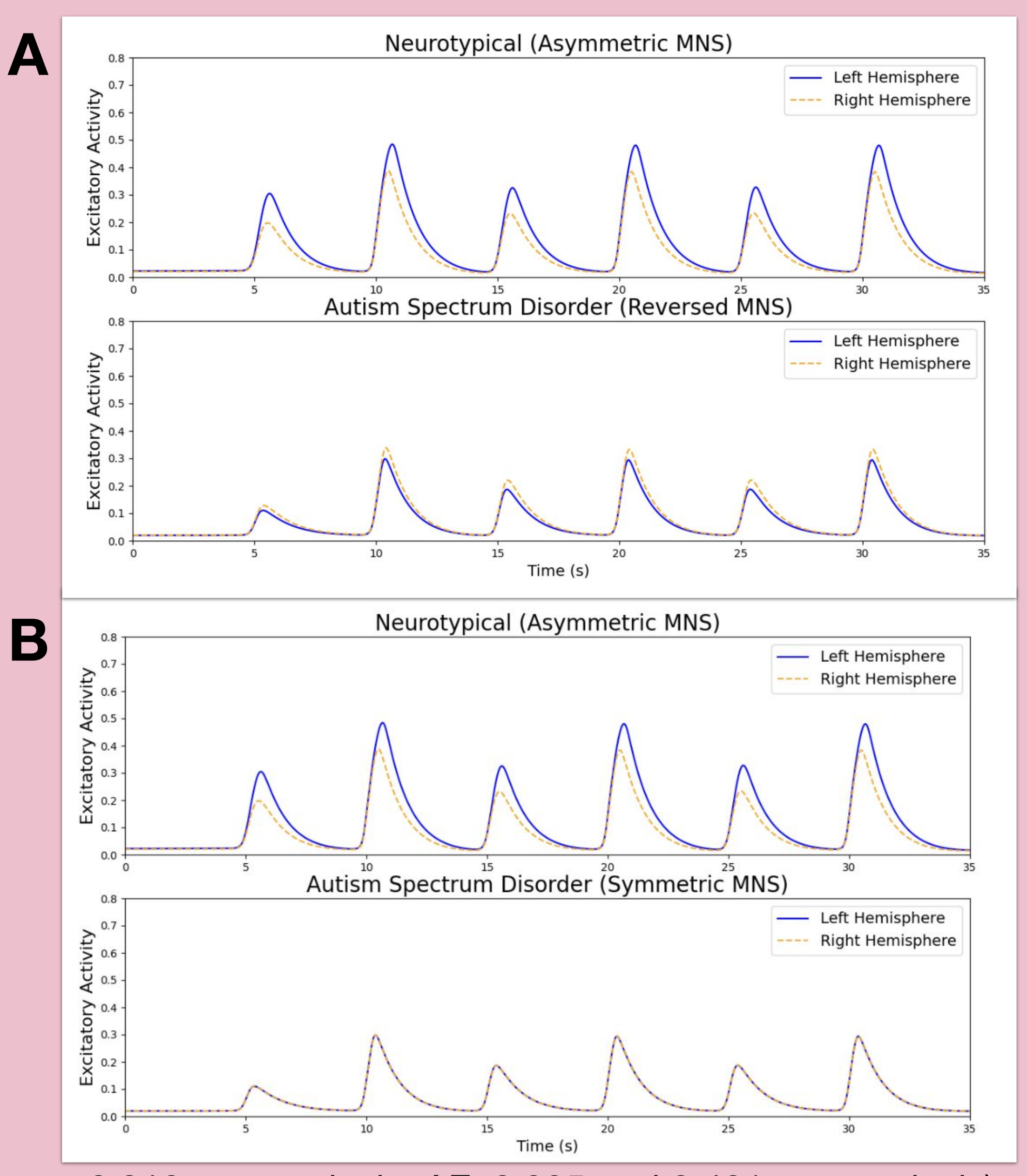


Fig. 3. Visualisation of neuronal excitation stratified along ASD/NAI cohorts

(A) NMM for ASD displays equal hemispheric weighting during AO (5, 15, 25s) vs AE (10, 20, 30s) Curve fitted to simulation.

(B) NMM for ASD represents right-preferential weighting during AO/AE. Fitted curve.

- In the NAI simulation, we observed **greater excitatory activity** in hemisphere in both observation and execution (Fig. 3A, 3B)
- However, in the ASD model, the cortical thickness between hemispheres was either **equal-weighted** (Fig. 3A) or reverse asymmetric (Fig. 3B).
- In both models, **mean action observation** was lower for ASD than NAI (AO: 0.161 and 0.319, respectively; AE: 0.295 and 0.481, respectively)
- This confirms and suggests a an **inhibition in intention understanding**
- Our data suggests atypical functional laterality and hemispheric weighting has a greater effect on **observation than execution**
- Furthermore, our data seems to negate the Hebbian postulate of **spike-timing-dependent plasticity** (**STDP,** fire together, wire together)
- dysfunctional cortical symmetry and weighting is shown here to disrupt correlation codes, likely **mistiming STDP learning processes** (Fig. 3)

Discussion

Limitations

- **Generalisability and presumed homogeneity of ASD phenotypes**
  - ASD is highly **heterogeneous**, and other individual differences in phenotype may influence laterality
  - Thus renders our study **less scalable** to differing degrees of ASD severity
- **Randomised cortical thickness input**
  - Our NMM leveraged **user-inputted data** for cortical thickness/hemisphere weighting parameters rather than culling from ASD repositories (i.e. ABIDE) to obtain empirical preprocessed (s/f)MRI data; we thus **cannot assess predictive utility** for **real life** patients quite yet

Applications

- **Development of Catered Pedagogical Models**
  - Findings warrant a push toward curriculum structures and varied ASD-education approaches that are catered toward **non-associative learning,** given that the MNS is most impaired during stimulus observation
- **Understanding of Socio-Cognitive Processes**
  - Recognizing macro-level differences in thickness and weighting may enable predictive algorithms for socio-cognitive deficits.
  - Findings enable us to best understand inhibitory imitative abilities in ASD, which may decrease ASD-related stigma, and allow us to continue probing **the gap between social knowledge and social performance**

Future Experimentation

A future study could perhaps **isolate firing populations in MNS regions of interest** to more accurately depict dynamics across distributed networks. Additionally, as mentioned above, a logical follow-up coul**d leverage empirical BOLD MRI data** to obtain ASD weighting/ cortical thickness data as a means to simulate MNS firing with real-life empirical parametres.

Acknowledgements

We would like to thank **Karla Montejo, Becky Belisle, Shankar Ramachandran,** and all of the **teaching fellows** for their continued support and guidance during our research. We would also like to thank **our families** for affording us the opportunity to attend BU RISE, and **Boston University Summer Term** for coordinating this invaluable experience.