Identifying the cognitive locus of deficits in connectivity during lexico-semantic processing in autism

Emily Coderre[1], Barry Gordon[1,2], & Kerry Ledoux[1]

[1]Cognitive Neurology/Neuropsychology, Department of Neurology, The Johns Hopkins University School of Medicine, Baltimore, MD

[2]Department of Cognitive Science, The Johns Hopkins University, Baltimore, MD

Introduction

Language deficits in autism

Autism spectrum disorders (ASDs) are characterized by widespread language impairments, especially in higher-level linguistic functions (Tager-Flusberg et al. 2005). Such functions require the assimilation of different types of information and thus draw heavily on *semantic integration*: the ability to integrate the meanings of pieces of information and arrive at a holistic understanding. Impairments in semantic integration may underlie many of the observable cognitive deficits in ASD (Brock & Brown, 2002; Frith, 1989).

Semantic processing can be assessed using the N400 event-related potential (ERP) component: N400 amplitude is reduced when stimuli are easier to integrate with their preceding context (as in semantically related stimuli), compared to stimuli that are difficult to integrate (as in semantically unrelated stimuli; Kutas & Federmeier, 2011). In individuals with ASD, the *N400 effect* (i.e., the modulation of N400 amplitude by semantic relatedness) is reduced or absent compared to normal controls (NCs) when processing linguistic stimuli (McCleery et al., 2010; Pijnacker et al. 2010), suggesting impairments in semantic integration during language processing.

Lexico-semantic vs. visuo-semantic processing

Despite the observed deficits in lexico-semantic integration, visuo-semantic processing of non-verbal stimuli is not impaired (Kamio & Toichi, 2000; McCleery et al., 2010; Sahyoun et al., 2009). That the deficit in semantic integration is language-specific suggests that general semantic processing is intrinsically intact, but that lexico-semantic connections are selectively disrupted in ASD. Furthermore, compared to NCs, individuals with ASD show underconnectivity between left frontal and parietal brain regions (Just et al., 2004; Kana et al., 2006), a connection which is critical for language. This suggests that difficulties with lexico-semantic integration may arise from poor neural communication.

The current study

We examine neural connectivity via *EEG coherence* during semantic processing of pictures and words in high-functioning individuals with ASD (HFAs) and NCs. In particular, we focus on the theta frequency band (3-7.5 Hz), which has been associated with semantic processing and integration (Maguire & Abel, 2013). Reduced fronto-parietal theta connectivity is predicted in HFAs for word stimuli, but no group differences are predicted during semantic processing of pictures.

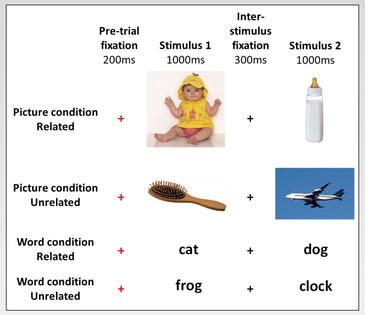
Methods

Participants

- 10 HFAs; mean age 33 years (range 18-68); 9 males, 1 female; 9 males, 1 female; 8 Caucasian; 1 African American, 1 mixed race
- 10 NCs matched on age and sex; mean age 37 years (range 22-68); 9 males, 1 female; 8 Caucasian; 2 African American
- All right-handed native English speakers

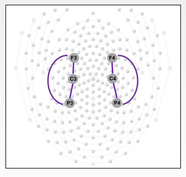
Stimuli and Procedure

- 100 word pairs: 50 related, 50 unrelated.
- 100 picture pairs: 50 related, 50 unrelated.
- Word/picture block order counterbalanced
- Participants were asked to judge whether the stimuli were related or unrelated.



EEG Data Acquisition and Preprocessing

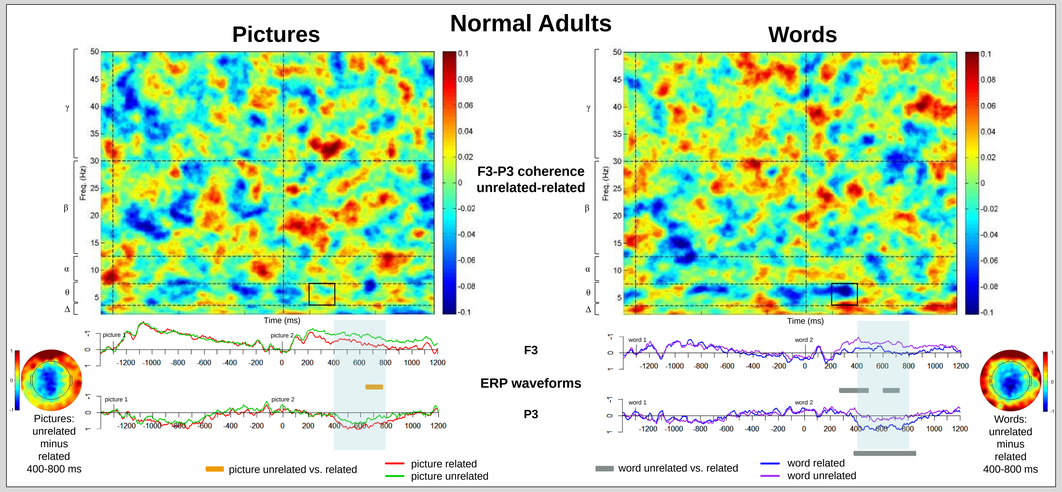
- EEG recorded at 250 Hz using an EGI GES 300 EEG System with 256-channel Hydrocel Geodesic Sensor Nets and NetStation 4.3
- Bandpass filtering 0.5-50 Hz.
- Motion and eye movement artifacts corrected using ICA

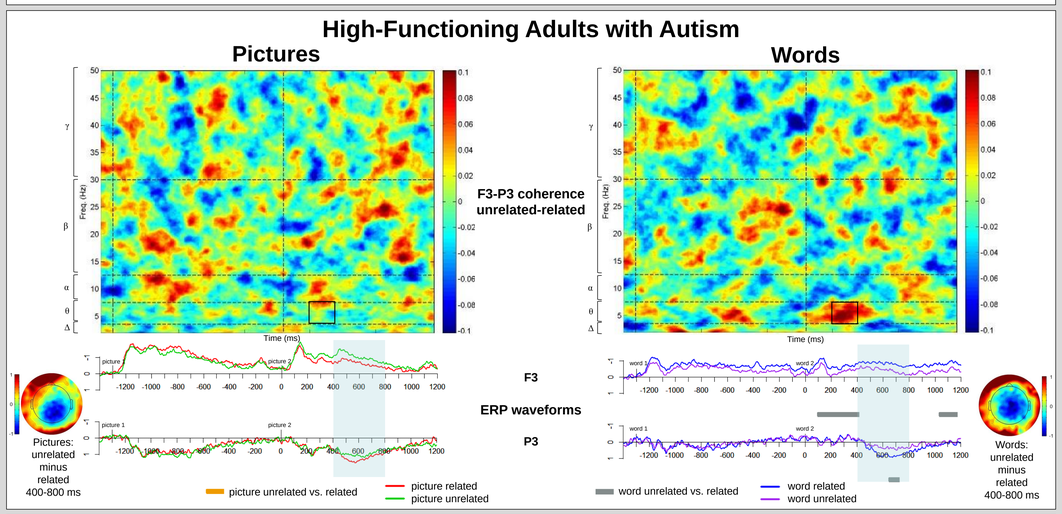


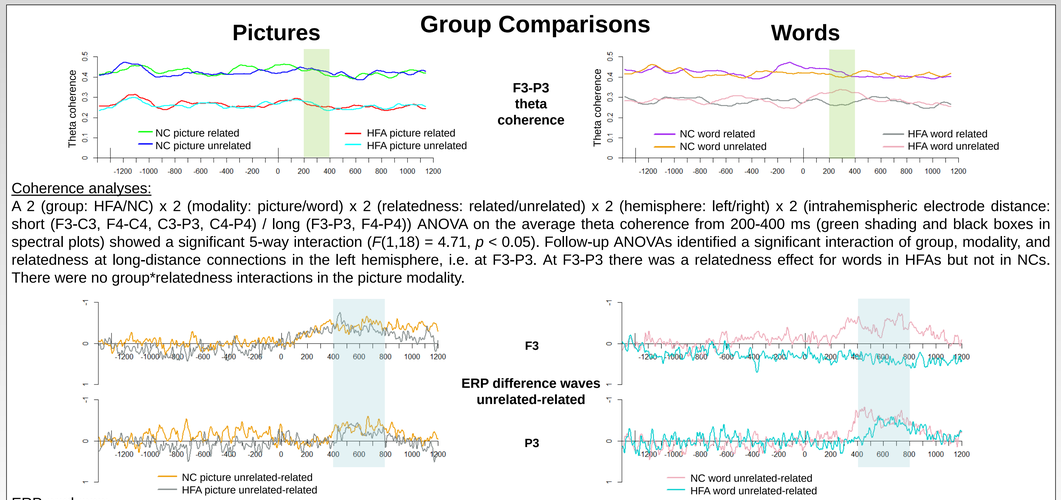
Time-frequency analysis

- Surface Laplacian estimate to account for voltage conduction effects; spectral decomposition using a Morlet wavelet of 2 cycles with expanding factor of 0.5 and Hanning taper
- Frequencies 2-50 Hz (delta: 2-3.5 Hz; theta: 3-7.5 Hz; alpha: 7.5-12.5 Hz; beta: 12.5-30 Hz; gamma: 30-50 Hz)
- 6 intrahemispheric connections between left and right frontal, central, and parietal sites

Results







Coherence analyses:

A 2 (group: HFA/NC) x 2 (modality: picture/word) x 2 (relatedness: related/unrelated) x 2 (hemisphere: left/right) x 2 (intrahemispheric electrode distance: short (F3-C3, F4-C4, C3-P3, C4-P4) / long (F3-P3, F4-P4)) ANOVA on the average theta coherence from 200-400 ms (green shading and black boxes in spectral plots) showed a significant 5-way interaction ($F(1,18) = 4.71$, $p < 0.05$). Follow-up ANOVAs identified a significant interaction of group, modality, and relatedness at long-distance connections in the left hemisphere, i.e. at F3-P3. At F3-P3 there was a relatedness effect for words in HFAs but not in NCs. There were no group*relatedness interactions in the picture modality.

ERP analyses:

A 2 (group: HFA/NC) x 2 (modality: picture/word) x 2 (relatedness: related/unrelated) x 2 (hemisphere: left/right) x 3 (site: frontal/central/parietal) ANOVA on the average ERP amplitude from 400-800 ms (blue shading) showed an interaction of group, modality, relatedness, and hemisphere ($F(1,18) = 6.61$, $p < 0.05$). Follow-up ANOVAs identified an interaction of group, modality, and relatedness in the left hemisphere (collapsed over sites) but not the right. In the left hemisphere there was a significant relatedness effect for words in NCs but not in HFAs. There were no group*relatedness interactions in the picture modality.

Discussion

Theta coherence effects (200-400 ms):

There were no significant group differences in relatedness effects in theta coherence for the picture modality, as predicted. In the word conditions, HFAs showed a statistically significant increase in theta coherence from F3-P3 for unrelated compared to related word pairs from 200-400 ms, whereas NCs showed no significant relatedness effects.

It is somewhat surprising HFAs did not show a relatedness effect in the picture modality and that NCs did not show a relatedness effect in either modality. One possibility is that these tasks were too easy for these participants, such that we are observing floor effects.

ERP effects (400-800 ms):

In the picture modality, there were no significant differences between groups in the magnitude of the N400 effect, as predicted. In the word modality, NCs showed a statistically significantly larger N400 effect than HFAs from 400-800 ms over the left hemisphere. The difference waves indicated a delayed N400 effect in HFAs compared to NCs at P3, which may suggest a reduced automaticity of semantic processing for words in HFAs.

Some research suggests that individuals with autism perform similarly to NCs when prompted to attend to semantic relations between language stimuli (Koolen et al., 2014). As the semantic priming task promoted semantic processing (participants were asked to judge whether the stimuli were related), this could account for the fact that an N400 effect did occur in HFAs, albeit later than in NCs.

Overall interpretations:

Compared to NCs, HFAs showed a greater difference in early theta coherence between related and unrelated word pairs, but a delayed N400 effect for these stimuli. The coherence increase may reflect an overcompensation of functional connectivity to deal with difficulties in semantic integration, as reflected by the delayed N400.

HFAs also showed overall reduced theta coherence from F3-P3 compared to NCs, which supports previous findings of reduced functional connectivity in autism, particularly between left frontal and parietal regions (Just et al., 2004; Kana et al., 2006).

Conclusions

HFAs showed a delayed N400 effect and a greater difference in theta coherence for unrelated vs. related word stimuli compared to NCs, whereas no group differences occurred for picture stimuli. These findings suggest differences in functional connectivity during semantic processing of words, but not of pictures, in HFAs.

References

Brock, J., & Brown, C. (2002). The temporal binding deficit hypothesis of autism. *Development and Psychopathology*, *14*, 209–224.

Frith, U. (1989). *Autism: Explaining the enigma*. Oxford: Blackwell.

Just, M. A., Cherkassky, V. L., Keller, T. A., & Minshew, N. J. (2004). Cortical activation and synchronization during sentence comprehension in high-functioning autism: evidence of underconnectivity. *Brain*, *127*, 1811–21.

Kamio, Y., & Toichi, M. (2000). Dual access to semantics in autism: is pictorial access superior to verbal access? *Journal of Child Psychology and Psychiatry*, *41*, 859–867.

Kana, R. K., Keller, T. A., Cherkassky, V. L., Minshew, N. J., & Just, M. A. (2006). Sentence comprehension in autism: thinking in pictures with decreased functional connectivity. *Brain*, *129*, 2484–2493.

Koolen, S., Vissers, C.Th.W.M., Egger, J.I.M., & Verhoeven, L. (2014). Monitoring in language perception in high-functioning adults with autism spectrum disorder: Evidence from event-related potentials. *Clinical Neurophysiology, 125*(1), 108-123.

Kutas, M. & Federmeier, K.D. (2011). Thirty years and counting: Finding meaning in the N400 component of the event-related brain potential (ERP). *Annual Review of Psychology, 62*, 621-647.

Maguire, M.J. & Abel, A.D. (2013). What changes in neural oscillations can reveal about developmental cognitive neuroscience: Language development as a case in point. *Developmental Cognitive Neuroscience, 6*, 125–136.

McCleery, J. P., Ceponiene, R., Burner, K. M., Townsend, J., Kinnear, M., & Schreibman, L. (2010). Neural correlates of verbal and nonverbal semantic integration in children with autism spectrum disorders. *Journal of Child Psychology and Psychiatry*, *51*, 277–286.

Tager-Flusberg, H., Paul, R., & Lord, C. (2005). Language and communication in autism. In F. Volkmar, R. Paul, A. Klin, & D. Cohen (Eds.), *Handbook of Autism and Pervasive Developmental Disorders* (3rd Edition, pp. 335–364). New York: John Wiley & Sons.

Pijnacker, J., Geurts, B., van Lambalgen, M., Buitelaar, J., & Hagoort, P. (2010). Exceptions and anomalies: An ERP study on context sensitivity in autism. *Neuropsychologia, 48*, 2940-2951.

Sahyoun, C. P., Soulières, I., Belliveau, J. W., Mottron, L., & Mody, M. (2009). Cognitive differences in pictorial reasoning between high-functioning autism and Asperger's syndrome. *Journal of Autism and Developmental Disorders*, *39*, 1014–1023.

ACKNOWLEDGEMENTS

This work was supported by The Therapeutic Cognitive Neuroscience Fund and the Benjamin and Adith Miller Family Endowment on Aging, Alzheimer's, and Autism Research.

Presented at the 2015 Annual Meeting of the Cognitive Neuroscience Society, March 28-31, San Francisco, CA