Aperiodic EEG and 7T MRSI evidence for maturation of E/I balance supporting the development of working memory through adolescence

Shane D. McKeon[1,2], Maria I. Perica[2,3], Ashley C. Parr[2,4], Finnegan J. Calabro[1,2,4], Will Foran[4], Hoby Hetherington[5,6], Chan-Hong Moon[7], Beatriz Luna[2,4]

1. Bioengineering, University of Pittsburgh, PA, USA. 2. The Center for the Neural Basis of Cognition, University of Pittsburgh, PA, USA. 3. Psychology, University of Pittsburgh, PA, USA. 4. Psychiatry, University of Pittsburgh, PA, USA.
5. Resonance Research Incorporated, Billerica, MA, USA. 6. Radiology, University of Missouri, Columbia, MO, USA . 7. Radiology, University of Pittsburgh, PA, USA

Introduction

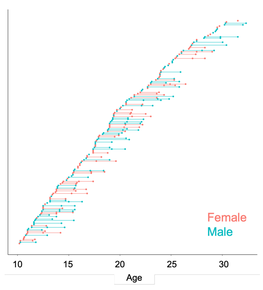
During adolescence, the prefrontal cortex (PFC) undergoes significant maturation, supporting improvements in cognitive control and executive functions[1].

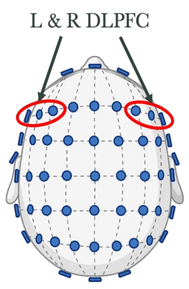
Using 7T MRSI we have found greater PFC glutamatergic excitatory over inhibitory GABAergic function disturbing excitatory/inhibitory (E/I) balance indicative of critical period plasticity. To further confirm this finding and understand neural function mechanisms underlying this process, we now extend these findings applying EEG measures of E/I balance in the same participants.

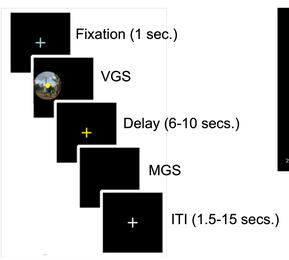
EEG broadband background aperiodic activity provides a unique measure of E/I balance using the Fitting Oscillations and 1/f (FOOOF) protocol, which derives the 1/f spectral slope (referred to as the aperiodic exponent) and an offset[3,4]. Thus, we aim to provide *in vivo* validation of the **underlying mechanisms of E/I balance in humans**, via EEG and MRSI derived measures, and their associations with working memory development, **supporting a period of PFC critical plasticity during adolescence.**

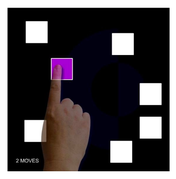
We hypothesized that MRSI measures of Glu/GABA balance would be associated with EEG aperiodic activity confirming recovery of E/I balance from adolescence to adulthood.

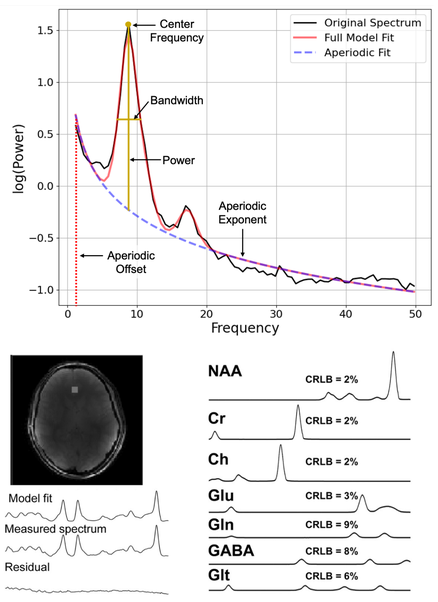
Methods











164 10-32yos completed an EEG and MRS study, up to 3 timepoints, for a total of 286 sessions.

Tasks included: Memory Guided Saccade (MGS), CANTAB Spatial Span, and resting state.

Electrodes corresponding to the left and right DLPFC (Right: F4, F6, F8; Left: F3, F5, F7) were used for analysis.

The Fitting Oscillations and One Over f (FOOOF) toolbox was used to assess the aperiodic component.

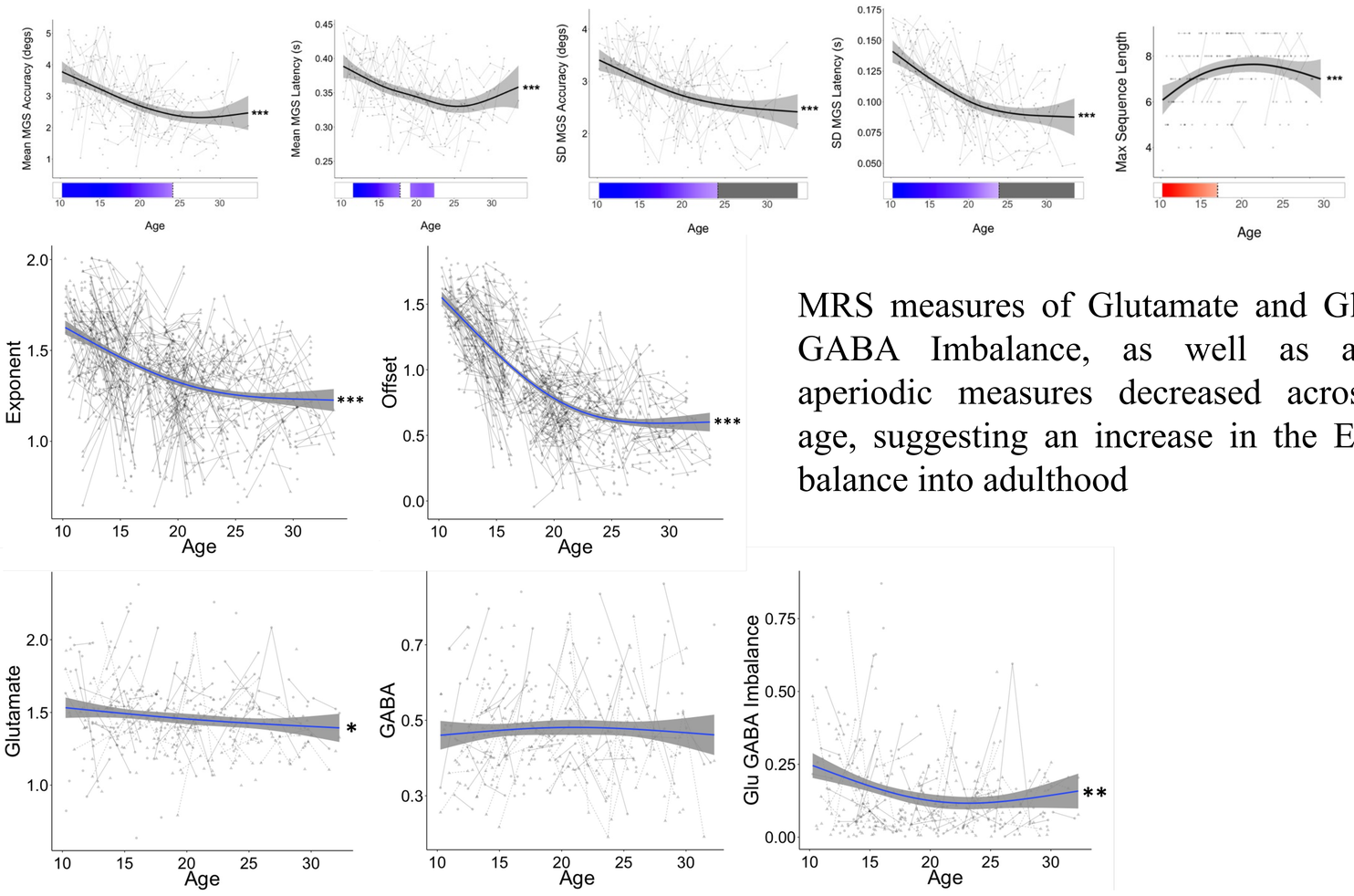
Oblique slice of 24x24 voxels (1.0x0.9x0.9mm) using a J-refocused MRSI sequence (TE/TR = 35/1500ms)

Neurotransmitters (NT) quantified using LCModel and reflect the NT relative to creatine (Cr, Glu/CR & GABA/Cr).

Glu/GABA balance was determined by taking the absolute value residual of the linear model of the association between Glu/Cr and GABA/Cr.

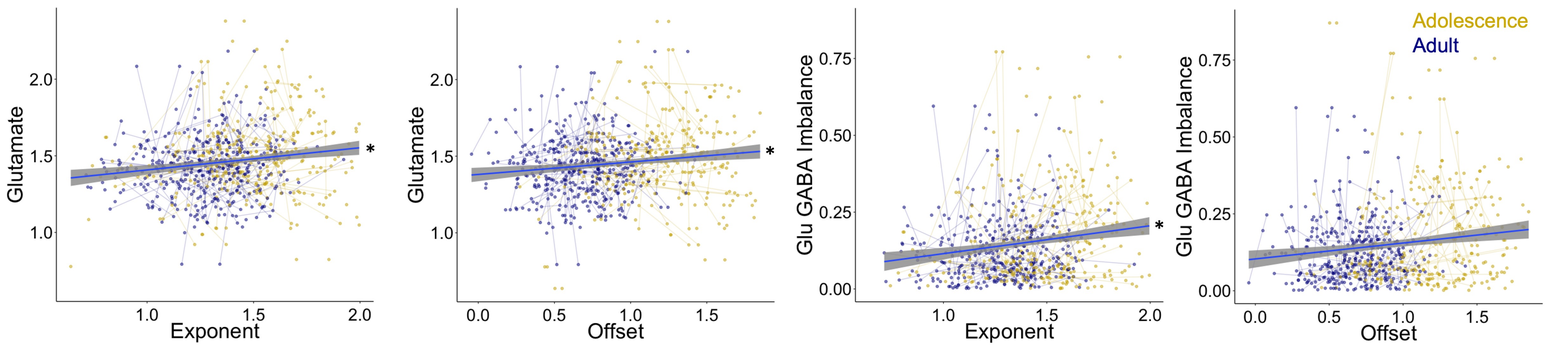
Results

As expected, MGS accuracy, latency, their variability, as well as spatial span performance improved with age

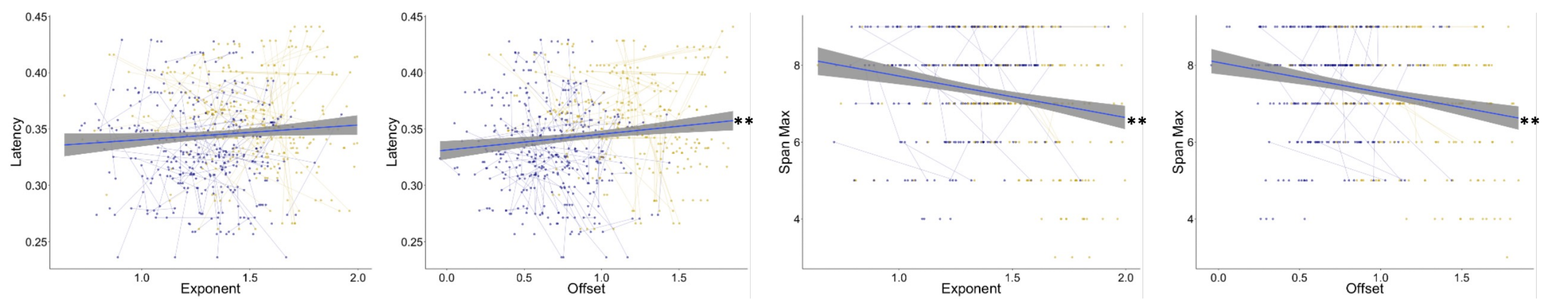


MRS measures of Glutamate and Glu GABA Imbalance, as well as all aperiodic measures decreased across age, suggesting an increase in the E/I balance into adulthood

Glutamate was associated with exponent and offset, while the Glu GABA Imbalance measure was only associated with exponent



Decreases in offset were associated with improved response latency, while increases in spatial span sequence length was associated with decreases in both exponent and offset



Discussion

Age related decreases in PFC EEG aperiodic offset is indicative of E/I balance maturation. Given past research, age decreases in aperiodic offset may underlie overall decreases in spike rate of cortical neurons, which also corresponds with the age-related decreases in glutamate.

The association between Glu/GABA balance and EEG aperiodic activity provides further support that PFC E/I balance is increasing into adulthood reflecting critical period plasticity. Importantly, the correspondence of EEG aperiodic offset and MRSI Glu/GABA balance supports that these methods are reliable characteristics of E/I balance.

Associations between exponent and WM latency (MGS) and capacity (Spatial Span), suggest that PFC E/I balance may optimize PFC processing supporting cognitive development

These findings provide novel *in vivo* evidence of plasticity in PFC from adolescence to adulthood underlying cognitive development supporting proposals that adult neurocognitive trajectories become established after adolescence. These results inform basic understanding of protracted specialization of higher order executive cortex that informs possible risks for the emergence of psychopathology but also opportunities to correct trajectories.

Contact Info
sdm63@pitt.edu
Personal Website

Acknowledgement

We thank Matthew Missar, Laurie Thompson, Alyssa Famalette, and Vivian Lallo for data collection. This work was supported by: UL1TR001857, MH067924, MH019986, the Staunton Farm Foundation, and support from the Department of Bioengineering, University of Pittsburgh.

References

1. Luna, B., et al. An Integrative Model of the Maturation of Cognitive Control. *Annu Rev Neurosci* (2015). 2. Caballero, A., et al. Developmental regulation of excitatory-inhibitory synaptic balance in the prefrontal cortex during adolescence. *Seminars in Cell & Developmental Biology* (2021). 3. Manning, J. R., et al. Broadband Shifts in Local Field Potential Power Spectra Are Correlated with Single-Neuron Spiking in Humans. *J. Neurosci.* (2009) 4. Donoghue, T. *et al.* Parameterizing neural power spectra into periodic and aperiodic components. *Nat Neurosci* (2020). 5. Larsen, B. & Luna, B. Adolescence as a neurobiological critical period for the development of higher-order cognition. *Neurosci Biobehav Rev* (2018).