

# Developmental changes in hemodynamic cortical and thalamic activity associated with NREM slow waves: an EEG-fMRI study

Damiana Bergamo<sup>1</sup>, Giacomo Handjaras<sup>1</sup>, Flavia Petruso<sup>1,2</sup>, Francesca Talami<sup>3,4</sup>, Emiliano Ricciardi<sup>1</sup>, Francesca Benuzzi<sup>3</sup>, Anna Elisabetta Vaudano<sup>3,4</sup>, Stefano Meletti<sup>3,4</sup>, Giulio Bernardi<sup>1</sup>, Monica Betta<sup>1</sup>

1 MoMilab, IMT School for Advanced Studies Lucca, Lucca, Italy; 2 Sant'Anna School of Advanced Studies, Pisa, Italy; 3 Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; 4 Neurology Dept. Azienda Ospedaliera Universitaria di Modena, Italy

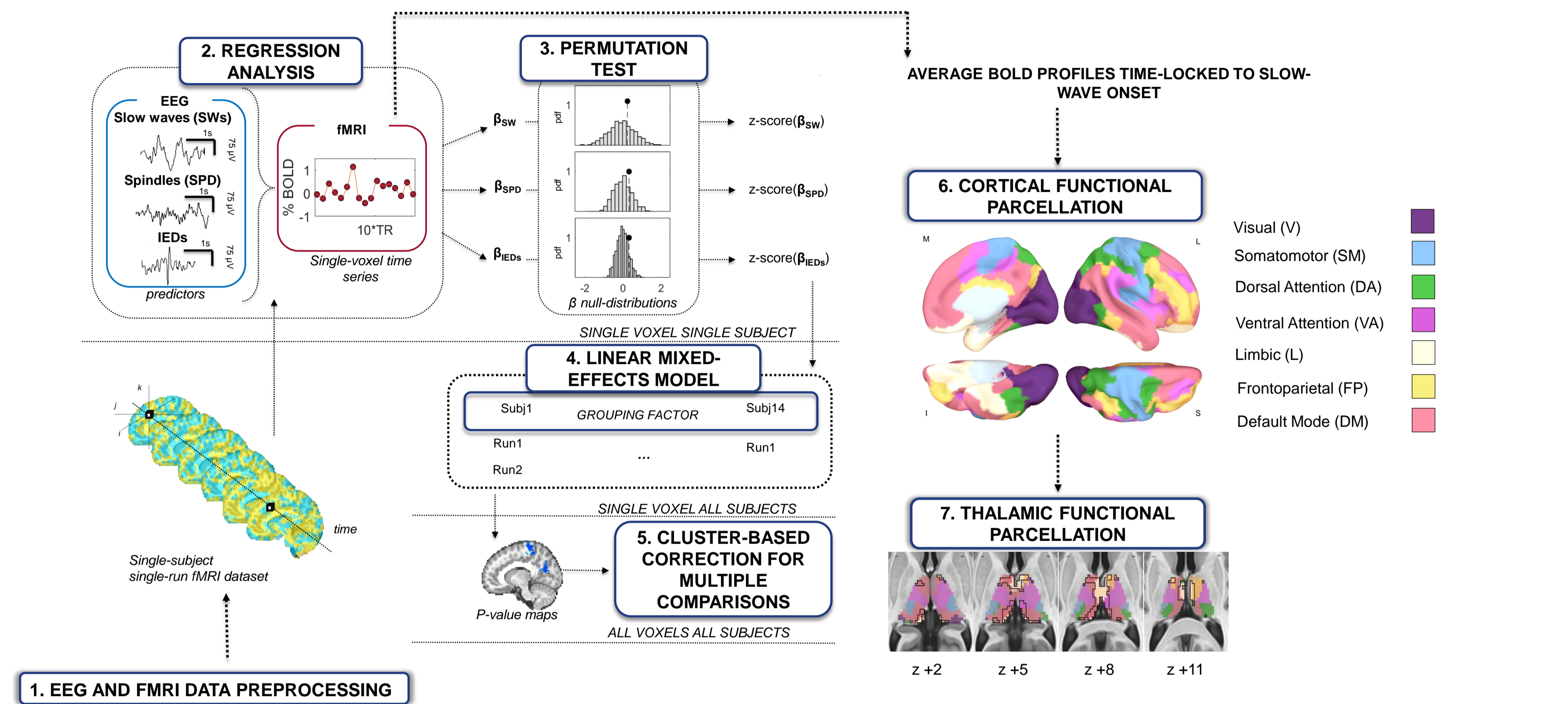
## INTRODUCTION AND METHODS

EEG slow waves (0.5-4 Hz) are a key feature of NREM sleep. While they are thought to represent primarily cortical events, the thalamus and brainstem influence their expression and coordination<sup>1,2</sup>. Slow waves are locally regulated as a function of experience and learning<sup>3</sup> and are believed to have a direct role in regulating synaptic plasticity and metabolic waste removal<sup>4</sup>. During development, from childhood to adulthood, the peak of slow wave activity (SWA) shifts from posterior to frontal regions, mirroring the posterior-anterior gradient of cortical maturation and the acquisition of cognitive functions. Moreover, the propagation distance of slow waves increases due to the maturation of cortico-cortical connections<sup>6</sup>. Notably, the contribution of subcortical structures, particularly the thalamus, to these changes has not been yet investigated.

**AIM:** Here we used simultaneous EEG-fMRI to investigate developmental changes in the cortical and subcortical correlates of slow waves.

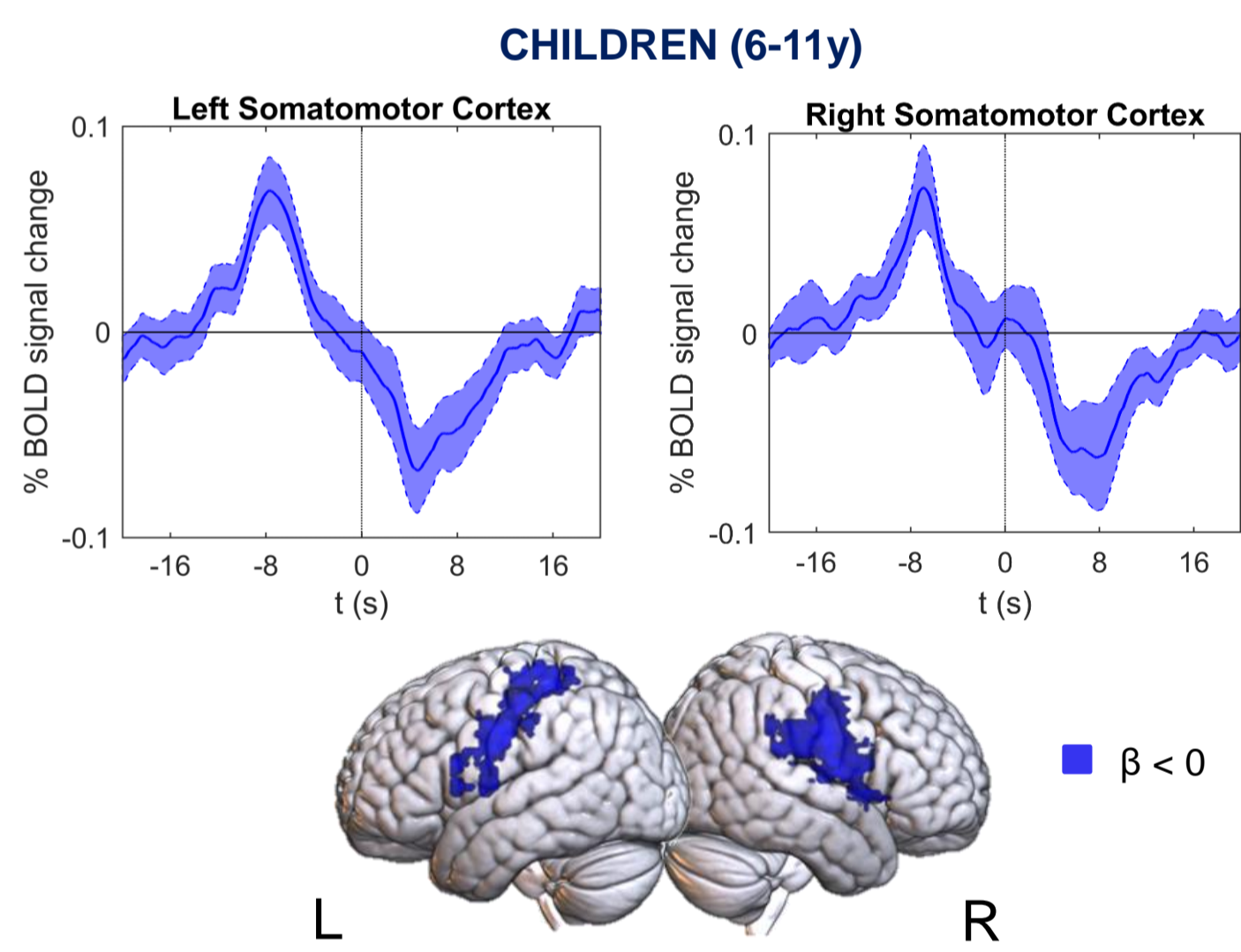
**SAMPLE:** 14 children (12M, 6-11y) and 2 adolescents (1M, 15-17y) with a diagnosis of idiopathic focal epilepsy who fell asleep during simultaneous EEG (32 electrodes) and fMRI (3T) recordings.

- The exclusion criteria were (I) any other epilepsy than childhood epilepsy with centro-temporal spikes or idiopathic childhood epilepsy of Gastaut, (II) pathological abnormality on conventional MRI, (III) other accompanying neurologic disorders, (IV) excessive head motion while scanning.
- Each subject underwent up to three 8-10-minute-long EEG-fMRI acquisition runs.

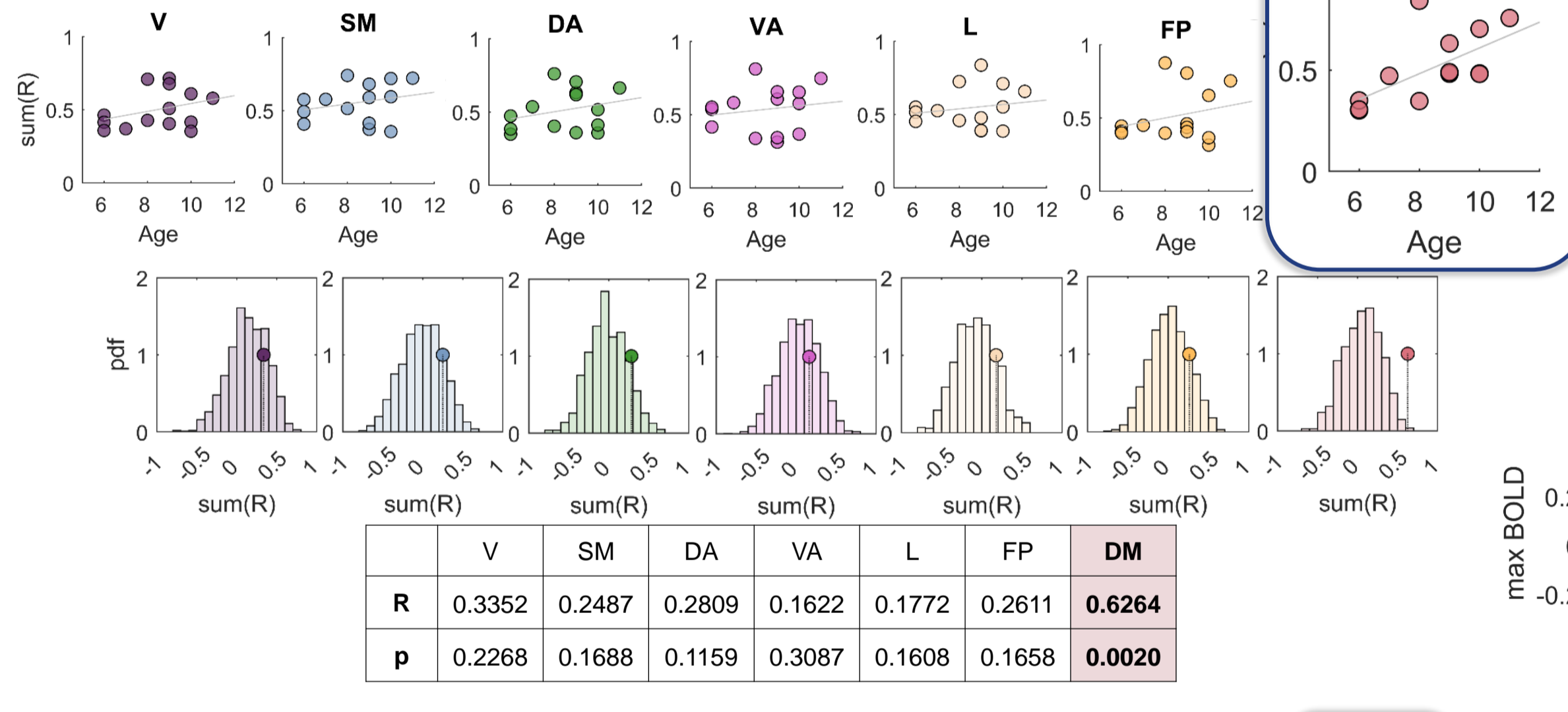


## RESULTS

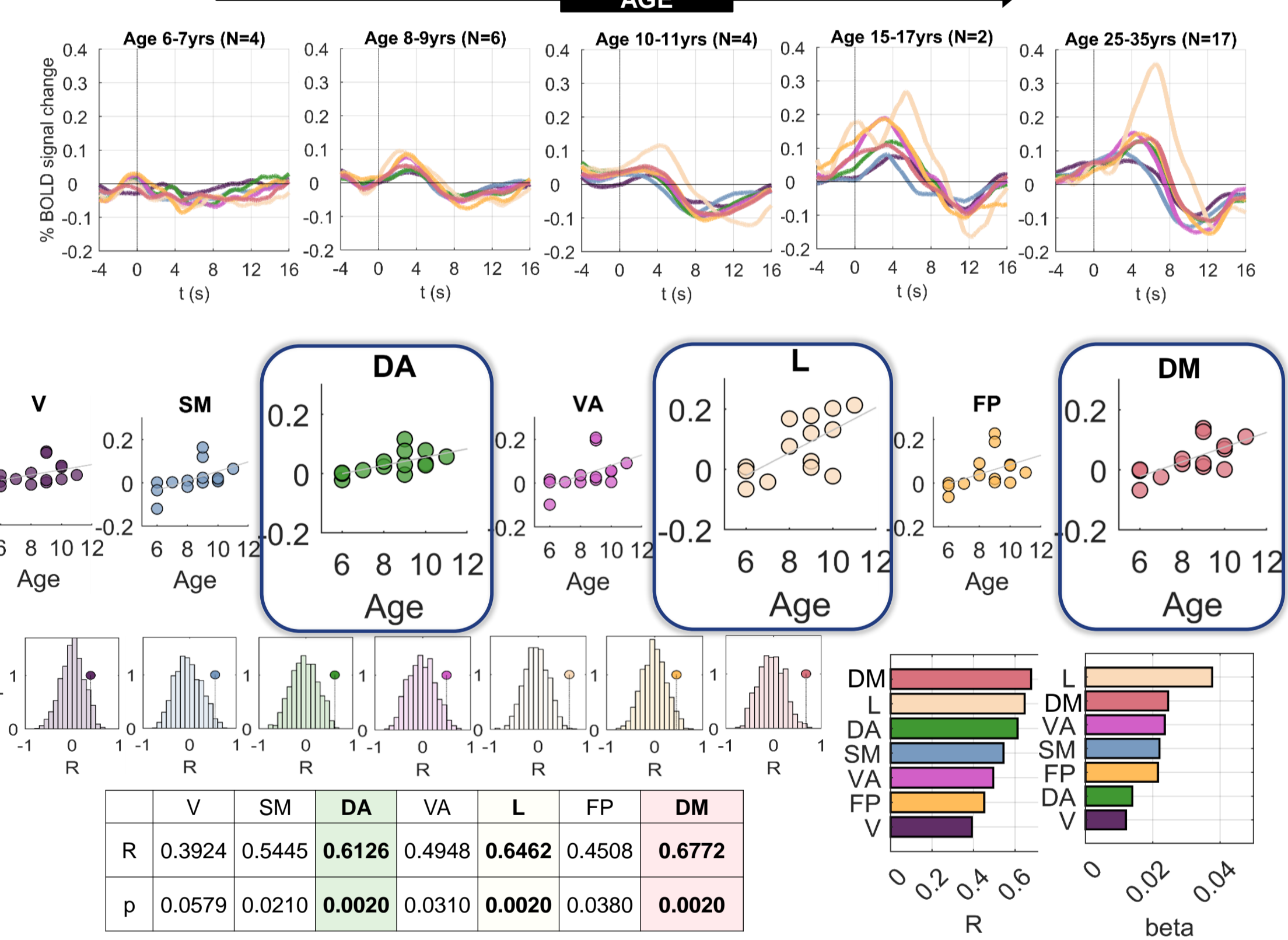
### BOLD SIGNAL CHANGES ASSOCIATED WITH SLOW WAVES IN CHILDREN vs ADULTS



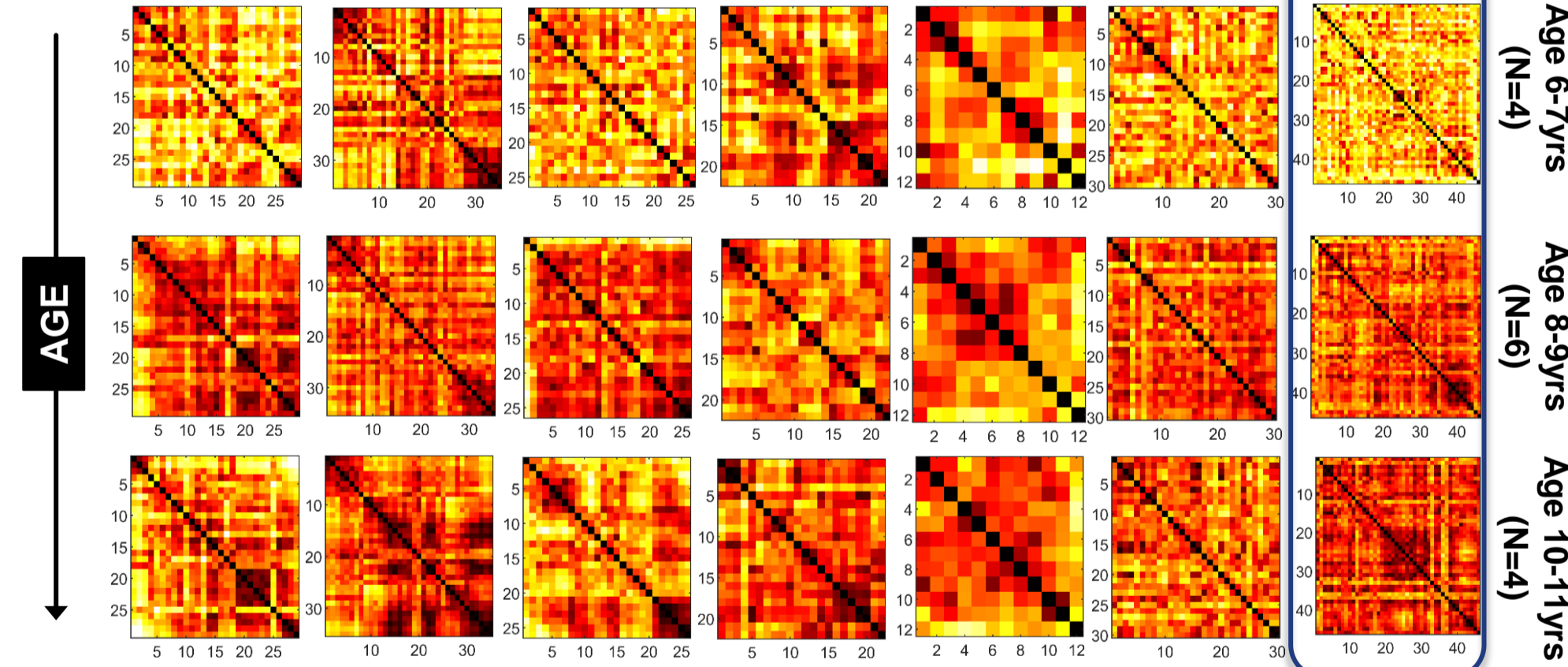
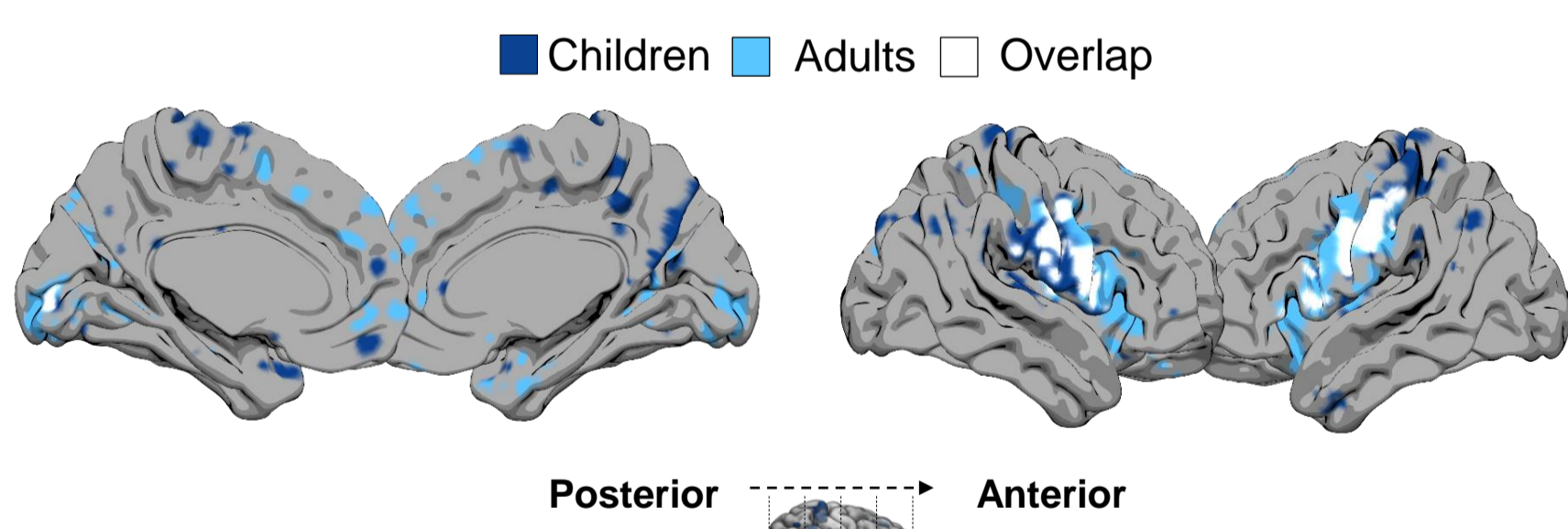
### RELATIONSHIP BETWEEN WITHIN-NETWORK REGIONAL CORRELATION AND AGE



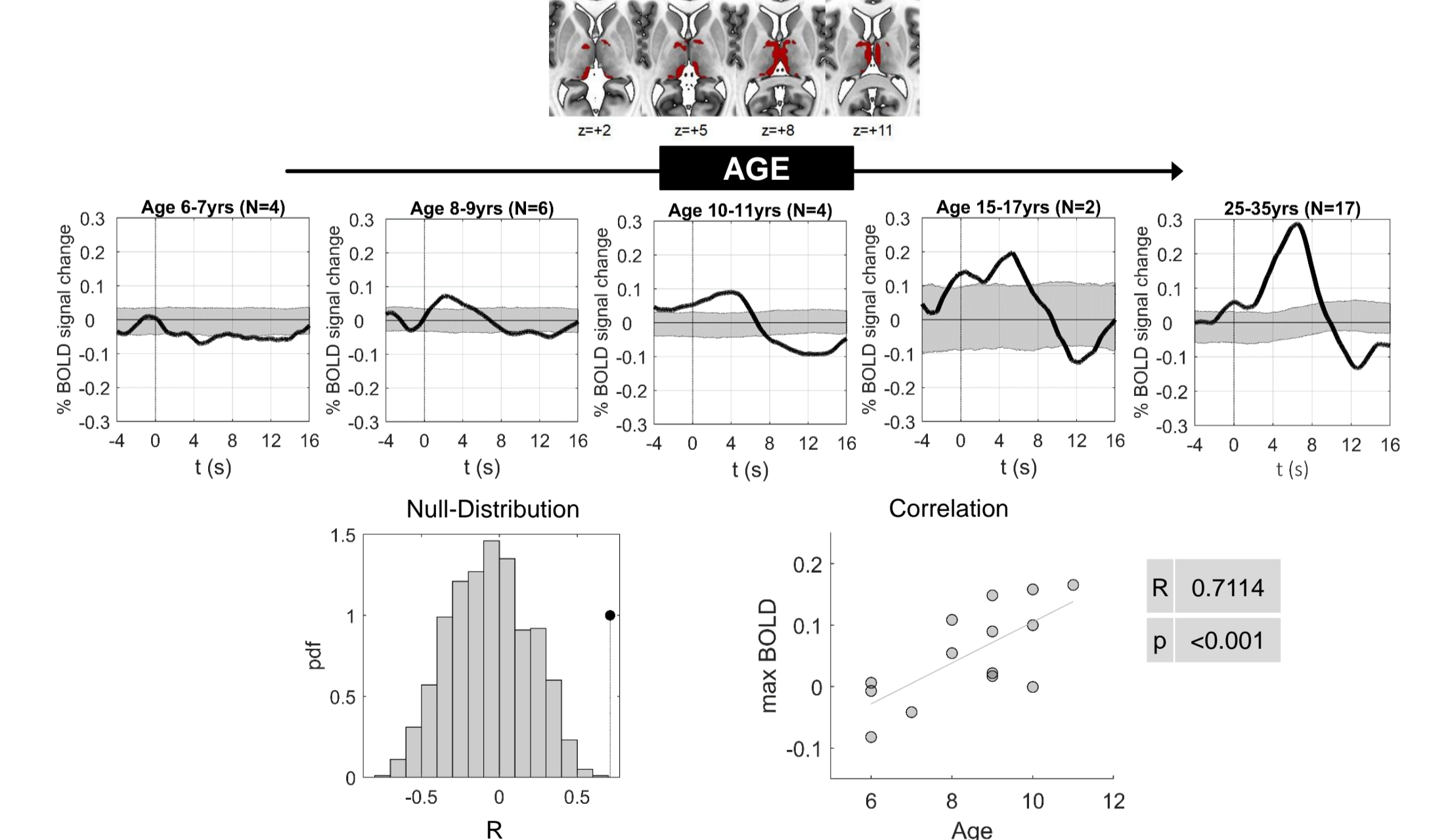
### CORRELATION BETWEEN THALAMIC HEMODYNAMIC CHANGES AND AGE



### CHILDREN (6-11y) vs ADULTS (25-35y)



### SIGNIFICANT SW-ASSOCIATED THALAMIC PORTION IN ADULTS



## CONCLUSIONS

- At the cortical level, our results are in line with previous research indicating that the distribution of SWA changes during development, shifting from posterior to anterior brain areas. However, we also showed that the somatomotor cortex could represent a key hub for the generation and expression of sleep slow waves in both children and adults, and thus, potentially, throughout the entire lifespan.
- The involvement of regions belonging to the DMN in sleep slow waves increases during development, likely mirroring the structural and functional maturation of this particular network. This result supports the potential value of slow waves as a marker of local and long-range brain connectivity changes.
- Thalamic involvement related to the occurrence of slow waves increases during development. Based on this finding, we hypothesize that maturation-dependent thalamic changes might have a relevant role in determining physiological changes in the regulation and expression of NREM slow waves from childhood to adulthood.

## REFERENCES

- Crunelli et al., *Nat Neurosci*, 13:9-17 (2010)
- Betta et al., *J. Neurosci*, 236:118117 (2021)
- Huber et al., *Nature*, 430: 78-81 (2004)
- Fultz et al., *Science*, 366: 628-631 (2019)
- Kurth et al., *J. Neurosci*, 30:13211-13219 (2010)
- Kurth et al., *SLEEP*, 40:zsx121 (2017)