

Neural correlates of schema encoding and the role of behavioral flexibility in children with autism spectrum disorder

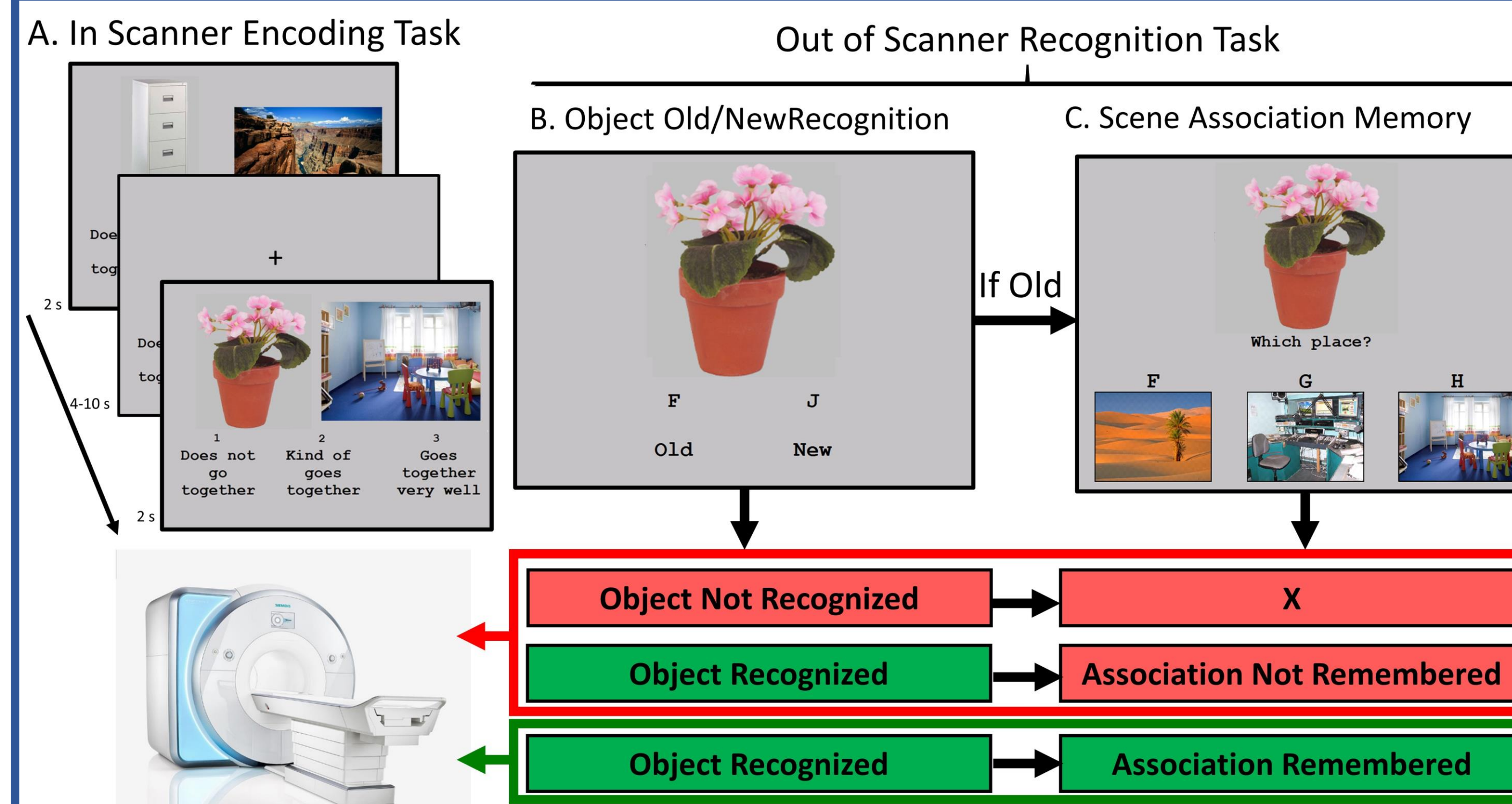
Cook KM¹, Cherry CBJ¹, You X^{1,3}, Merchant JM³, Skapek M², Powers M², Pugliese C², Kenworthy L², Vaidya CJ¹

¹Georgetown University, ²Children's National Health System (CNHS), ³University of Maryland at College Park

Introduction

- Children with autism spectrum disorder (ASD) have **trouble generalizing** knowledge (Woods et al 2006)
- Generalization difficulties may result from impaired **schema use**. **Schemas** are broad knowledge representations that are believed to be necessary for flexible behavior (Ghosh & Gilboa, 2014)
- Schema relies on connections between the medial temporal lobe (MTL) to encode schema-incongruent and the medial prefrontal cortex (mPFC) congruent information, (Van Kesteren et al., 2013)
- In ASD, the mPFC is weakly connected to the default mode network (Washington et al., 2014) and the MTL is enlarged (Groen et al., 2010) suggesting that neural correlates of schema may be atypical in ASD
- We examined neural correlates of schema in children with ASD and whether they differ relative to typically developing (TD) children and assessed differences in relation to behavioral inflexibility**

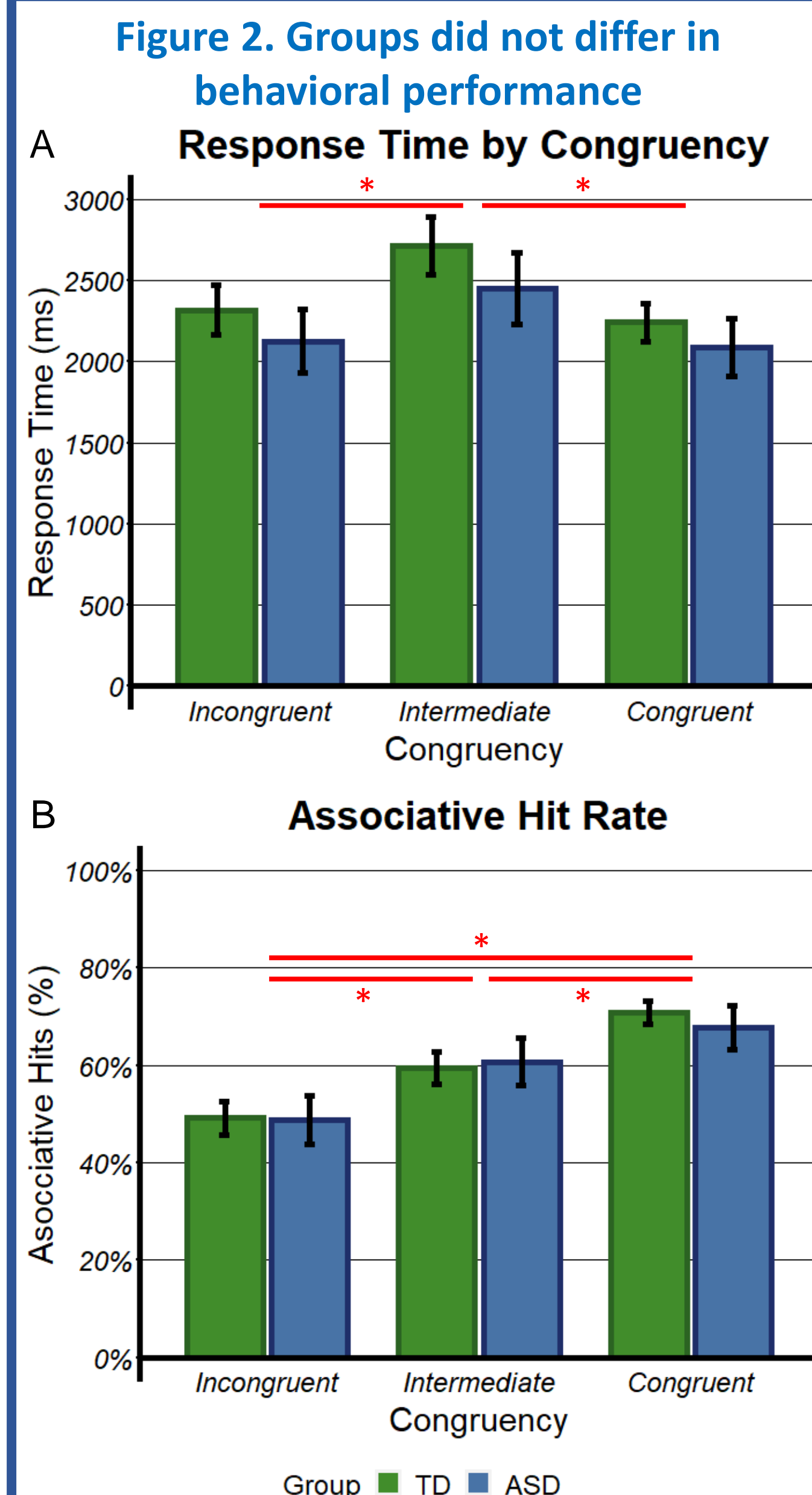
Methods



	Typical Developing	Autism Spectrum Disorders
N	19	12
Age	11.77 (2.51)	13.18 (1.73)
Gender (%M)	73.7%	75.0%
IQ Estimate	122.85 (12.86)	114.17 (13.19)
Maternal Ed	18.21 (3.29)	16.50 (3.45)
Flexibility Scale	17.74 (13.36)	61.67 (34.89)

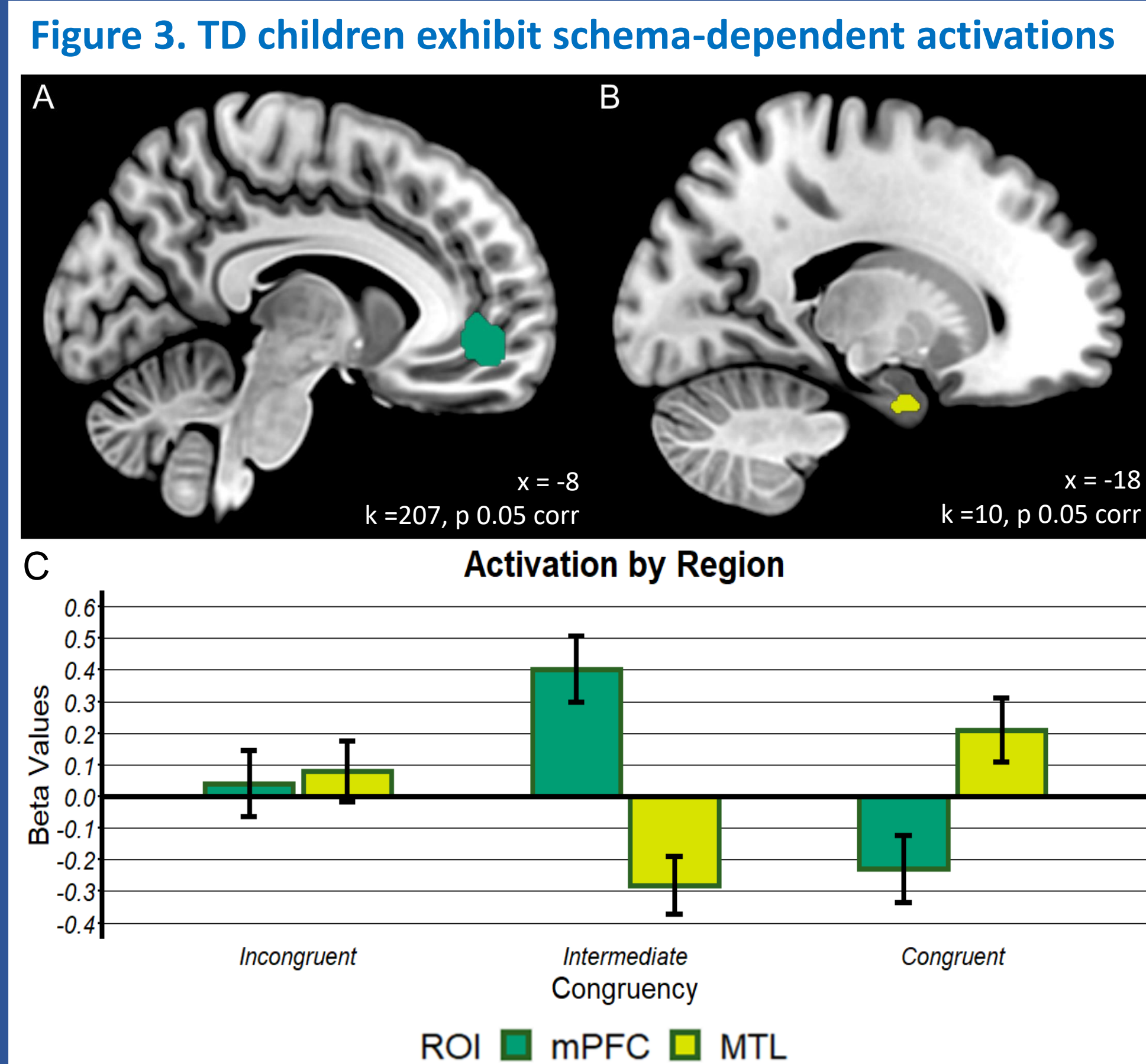
- TE/TR=30ms/2000ms, 3mm² voxels, 51 interleaved transverse ascending slices (width = 2.5mm, gap = 0.5mm, effective width = 3mm) on 3T Siemens
- Three 6:10 minute in-scanner encoding runs (1A) for 148 pairs
- Yes/no objection recognition and scene association (1B,C)
- Parents completed the Flexibility Scale (Strang et al., 2017)
- First Level Contrast: **Object-Scene Remembered vs Forgotten**
- Contrasts modeled with canonical HRF, temporal derivative, and dispersion
- Anatomically defined MTL and mPFC ROIs from AAL atlas

Behavioral Performance



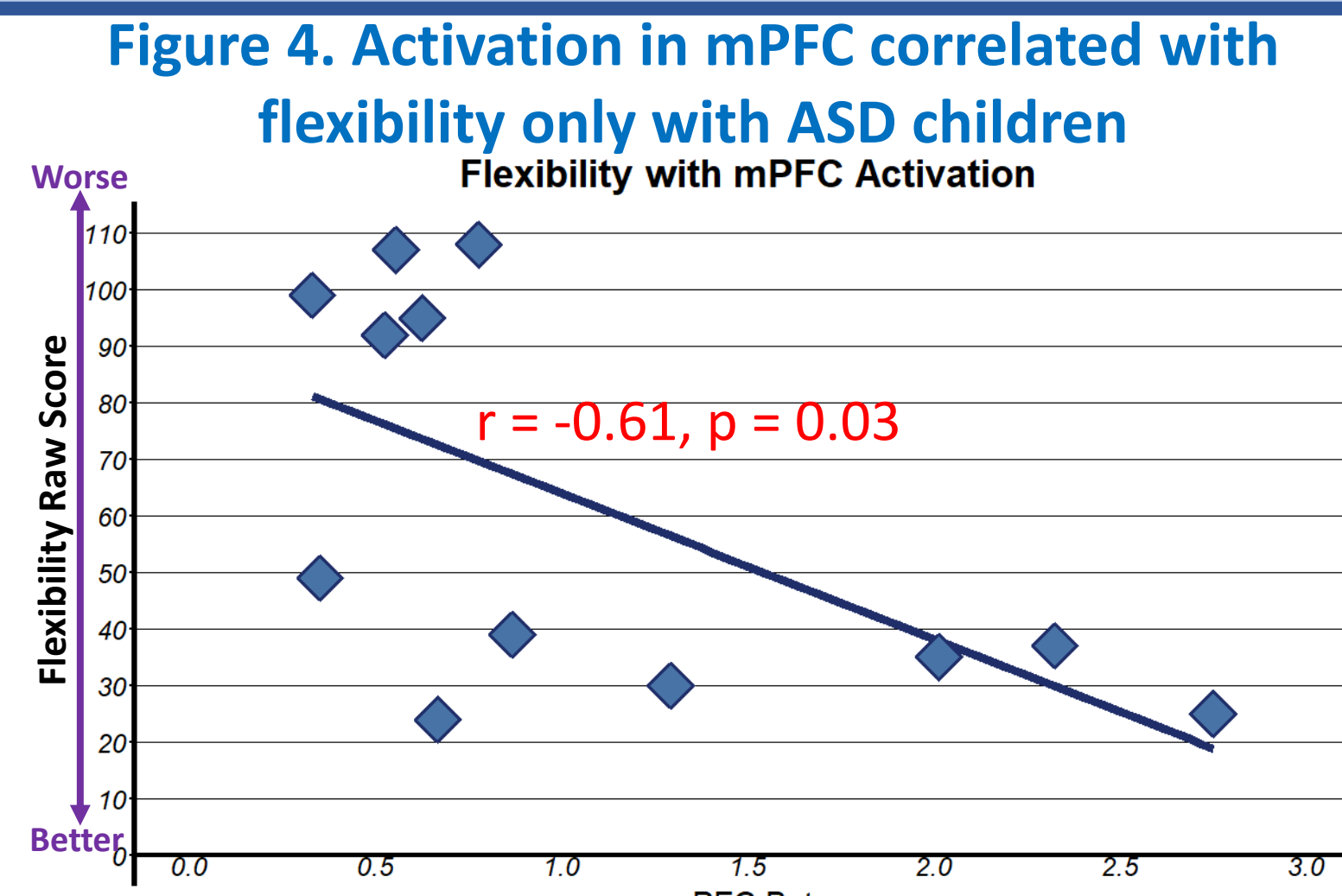
- Both groups were slower rating intermediate pairs (Fig 2A)
- Higher associative memory with increasing schema-congruency in both ASD and TD (Fig 2b)

Schema-Dependent Activations



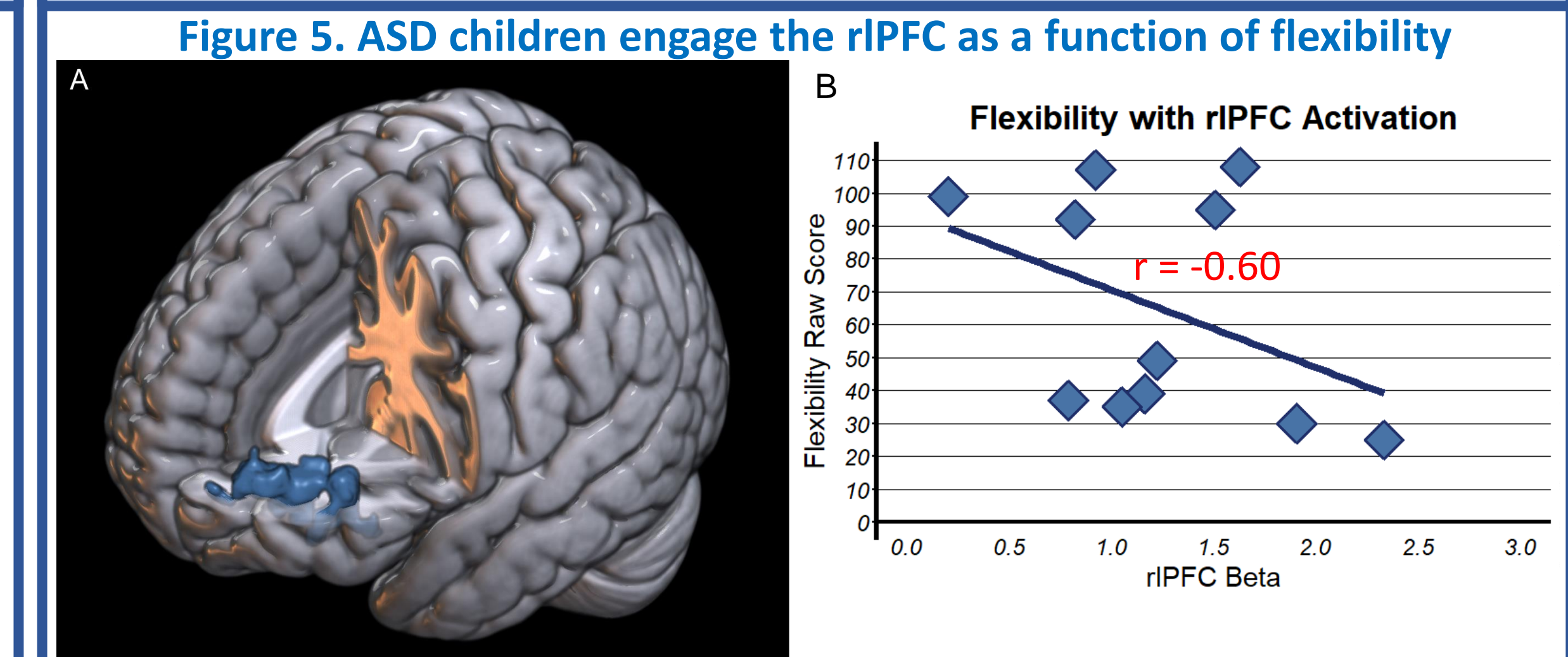
- One way ANOVAs for congruency were performed individually in each mask for each group separately
- TD showed two significant clusters (Fig 3A,B) while ASD children exhibited no clusters sensitive to schema.
- Extracted cluster betas were assessed offline in TD children with an ROI by Congruency 2x3 ANOVA
- TD children exhibited a significant interaction with more mPFC and less MTL activation at encoding for intermediate pairs, and the opposite pattern for congruent (Fig 3C)
- Results hold even after controlling for response time, number of associate hits, age, and when only male participants were included

mPFC Activation and Inflexibility



- Figure 3A,B clusters used as ROIs, betas were then extracted and correlated with flexibility individually for each congruency condition
- ASD children with better flexibility (lower scores) engaged mPFC more for intermediate pairs
- No significant MTL correlations with either group
- No significant correlation in TD children likely due to restricted range

Whole Brain Voxel-wise Correlation with Inflexibility



- Exploratory whole brain voxel-wise correlations were performed with Flexibility Raw Scores for both groups separately, within each of the three congruencies
- The TD group exhibited no correlations with flexibility within any level of congruency in the whole brain
- The ASD group exhibited a significant relationship for the intermediate pairs, such that those who were more flexible (lower score) recruited an additional left rIFPC region.

Conclusion

- TD children exhibit MTL and mPFC activations sensitive to schema in similar locations to adults (Van Kesteren et al, 2013) and young children (Brod & Shing 2019). Unlike previous studies, TD children engaged the MTL for congruent and the mPFC for intermediate pairs. There differences may be attributable to effortful encoding of ambiguous associations resulting from weakly established schema
- The absence of schema dependent activations in children with ASD suggests aberrant schema use in these children. The relationship between mPFC utilization and flexibility establishes a link between behavioral rigidity in these children and impairments in schema use
- Recruitment of the rIFPC has been associated with abstract and relational thinking (Dumontheil 2014), showing more flexible children with ASD are recruiting additional abstract reasoning regions alongside the mPFC for ambiguous associations; a relationship not seen in TD children
- This study is the first to characterize neural correlates of schema-dependent memory in typical development and in ASD and reveal association with behavioral flexibility**