

Early motor, cognitive, and neural predictors of schizophrenia spectrum disorders (SSDs)

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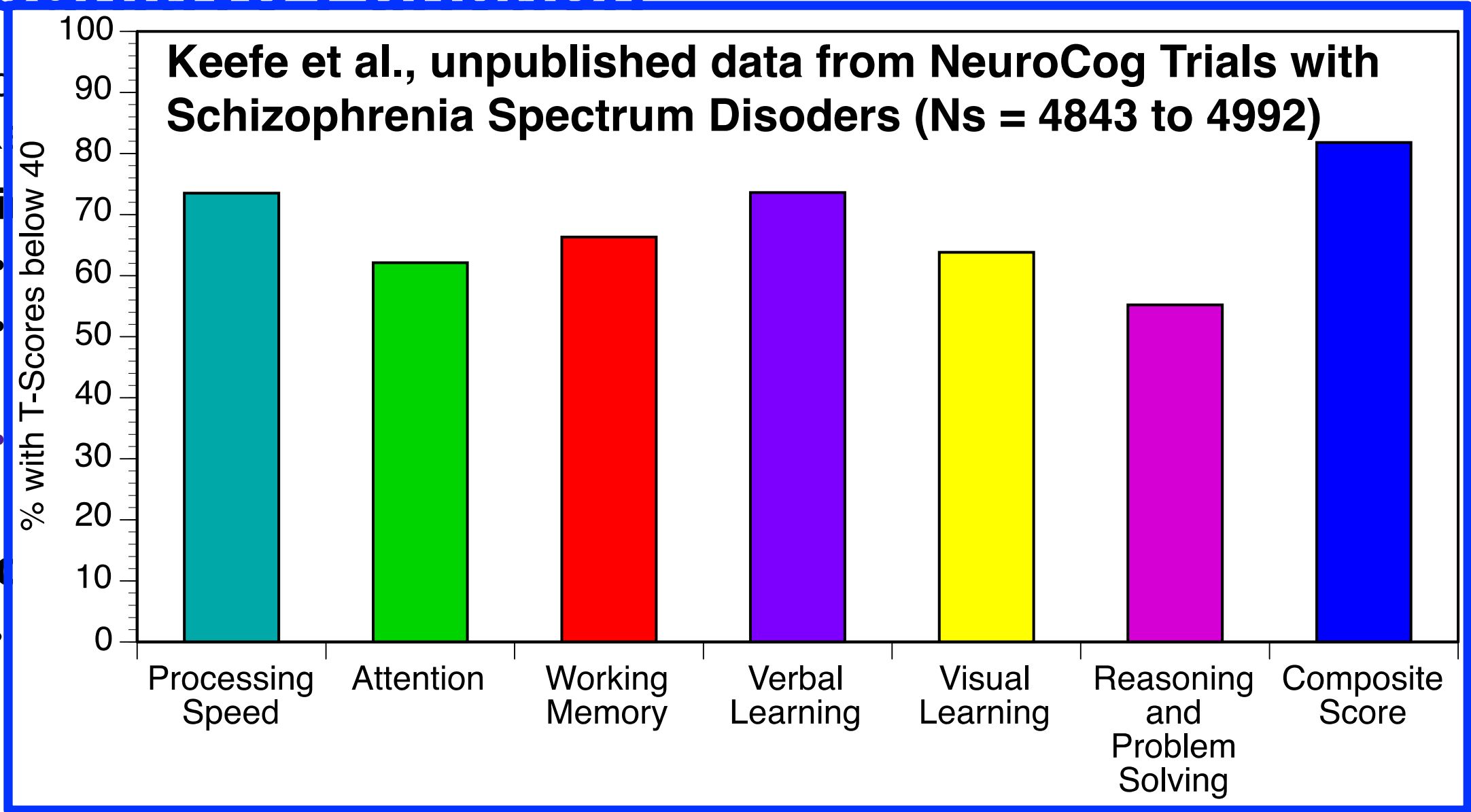
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Motor Abnormalities

- In SSD we see:
 - 50-65% with **neurological soft signs** (Heinrichs & Buchanan, 1988)
- **Predictors**
 - **Neurological soft signs** in infancy:
 - Odds ratio (OR) of 4.6; specific to SSDs (Cannon et al., 2002; Schiffman et al., 2009)
 - **Unusual movements/postural abnormalities** in infancy: ORs of 2-5 (Rosso et al., 2000)
 - **Neurological soft signs and motor coordination and** in middle childhood:
 - ORs up to 20 (Cannon et al., 2002);
 - Motor coordination specific to SSDs (Cannon et al., 2002; Leask et al., 2002)

Cognitive Function

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Intelligence (IQ)

- **61%** of individuals with SSD have “premorbid” **IQs** in the below average range (Keefe et al., unpublished)
- Low IQ in **middle childhood** strongly predicts the likelihood of developing schizophrenia in cohort-based and case-control studies
 - For each standard deviation *increase* in **IQ**, 42% *reduction* in lifetime odds of SSD (Koenen et al., 2009)
 - OR of 7.89 of having schizophrenia if **IQ** < 70
 - Prediction stronger if you also have genetic risk (Kendler et al., 2015)
 - But ... predicts reduced odds of many other disorders (Koenen et al., 2009; Osler et al., 2007; Sorenson et al., 2010)

Neural Impairments

- Individuals with SSDs show:
 - Meta-analyses show reduced volumes/thickness of **thalamus**, **hippocampus**, and **insula**, **anterior cingulate**, and **prefrontal cortex** (e.g., Haijma et al., 2013)
 - Meta-analyses show reduced **dorsolateral prefrontal cortex** activation in executive function and working memory tasks (Minzenberg et al., 2009)
 - Reduced **thalamic** to **prefrontal** and **cerebellar** connectivity, but increased **thalamic** to sensory motor areas (Review, Giraldo-Chica & Woodward, 2016)

Neural Impairments

- **Family High Risk Studies**

- Reduction in **inferior frontal gyrus** volume over time, 38% sensitivity, 96% specificity (Job et al., 2006)

- **Clinical high risk who developed SSDs:**

- Meta analysis → lower gray matter volume in **insula**, **anterior cingulate**, **prefrontal cortex** and **cerebellum** (Smieskova et al., 2010), with varying effect sizes across regions
 - But NAPLS did not see volume or thickness differences at baseline between converters and non-converters (Cannon et al., 2014)
- Greater **prefrontal** volume loss over time to conversion (Sun et al., 2009; Cannon et al., 2014)
- Reduced **thalamic** to **prefrontal** and **cerebellar** connectivity, but increased thalamic to sensory motor areas (Anticevic et al., 20016)

Next Steps

- Birth cohort and case-control studies that:
 - Assess range of cognitive domains, rather than only 1 or 2
 - Assess specificity to SSDs
 - Assess increased predictive utility when combined with other potential predictors
 - Assess neural predictors in children, ideally even in infants
 - **Adolescent Brain and Cognitive Development (ABCD)**
Study will provide very relevant data