**Keyword 2:** cerebrovascular disease
**Keyword 3:** dementia - Alzheimer's disease
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## Poster Session 07: Developmental | Pediatrics

1:45 - 3:00pm
Friday, 3rd February, 2023
Town & Country Foyer

### 1 Sluggish Cognitive Tempo in Children and Adolescents with Fetal Alcohol Spectrum Disorders: Associations with Executive Function and Subcortical Volumes

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**Objective:** Fetal alcohol spectrum disorder (FASD) is a common neurodevelopmental condition associated with deficits in cognitive functioning (executive functioning [EF], attention, working memory, etc.), behavioral impairments, and abnormalities in brain structure including cortical and subcortical volumes. Rates of comorbid attention-deficit/hyperactivity disorder (ADHD) are high in children with FASD and contribute to significant functional impairments. Sluggish cognitive tempo (SCT) includes a cluster of symptoms (e.g. underactive/slow-moving, confusion, fogginess, daydreaming) found to be related to but distinct from ADHD, and previous research suggests that it may be common in FASD. We explored SCT by examining the relationship between SCT and both brain volumes (corpus callosum, caudate, and hippocampus) and objective EF measures in children with FASD vs. typically developing controls.
**Participants and Methods:** This is a secondary analysis of a larger longitudinal CIFASD study that consisted of 35 children with prenatal alcohol exposure (PAE) and 30 controls between the ages of 9 to 18 at follow-up. Children completed a set of cognitive assessments (WISC-IV, DKEFS, & NIH Toolbox) and an MRI scan, while parents completed the Child Behavior Checklist (CBCL), which includes a SCT scale. We examined group differences between PAE and controls in relation to SCT symptoms, EF scores, and subcortical volumes. Then, we performed within- and between-group comparisons with and without controlling for total intracranial volume, age, attention problems, and ADHD problems between SCT and subcortical brain volumes. Finally, we performed correlations between SCT and EF measures for both groups.
**Results:** Compared to controls, participants with PAE showed significantly more SCT symptoms on the CBCL ($t$ [57] = 3.66, $p$ = 0.0006), more parent-rated attention problems and ADHD symptoms, lower scores across several EF measures (DKEFS Trail-Making and Verbal Fluency; WISC-IV Digit Span, Symbol Search, and Coding; effect sizes ranging from 0.44 to 1.16), and smaller regional volumes in the caudate, hippocampus, and posterior areas of the corpus callosum. In the PAE group, a smaller hippocampus was associated with more SCT symptoms (controlling for parent-rated attention problems and ADHD problems, age, and intracranial volume). However, in the control group, a larger mid posterior and posterior corpus callosum were significantly associated with more SCT symptoms (controlling for parent-rated attention problems, intracranial volume, and age; $r$ [24] = 0.499, $p$ = 0.009; $r$ [24] = 0.517, $p$ = 0.007). In terms of executive functioning, children in the PAE group with more SCT symptoms performed worse on letter sequencing of the Trail-Making subtest (controlling attention problems & ADHD symptoms). In comparison, those in the control group with more SCT symptoms performed better on letter sequencing and combined number letter sequencing of the Trail-Making subtest (controlling attention problems).
**Conclusions:** Findings suggest that children with FASD experience elevated SCT symptoms compared to typically developing controls, which may be associated with worse performance on EF tasks and smaller subcortical volumes (hippocampus) when taking attention difficulties and ADHD symptoms into account. Additional research into the underlying causes and correlates of SCT in FASD could result in

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improved tailoring of interventions for this population.

**Categories:** Prenatal/Perinatal Factors/Prematurity
**Keyword 1:** fetal alcohol syndrome
**Keyword 2:** cognitive functioning
**Keyword 3:** subcortical
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## 2 Choline as a neurodevelopmental intervention for children with fetal alcohol spectrum disorder: Long-term associations with white matter microstructure and executive function

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**Objective:** Fetal alcohol spectrum disorder (FASD) is a life-long condition, and few interventions have been developed to improve the neurodevelopmental course in this population. Early interventions targeting core neurocognitive deficits have the potential to confer long-term neurodevelopmental benefits. Time-targeted choline supplementation is one such intervention that has been shown to provide neurodevelopmental benefits that emerge with age during childhood. We present a long-term follow-up study evaluating the neurodevelopmental effects of early choline supplementation in children with FASD approximately 7 years on average after an initial efficacy trial. In this study, we examine treatment group differences in executive function (EF) outcomes and diffusion MRI of the corpus callosum using the Neurite Orientation Dispersion and Density Index (NODDI) biophysical model.
**Participants and Methods:** The initial study was a randomized, double-blind, placebo-controlled trial of choline vs. placebo in 2.5- to 5-year-olds with FASD. Participants in this long-term follow-up study included 18 children (9 placebo; 9 choline) seen 7 years on average following initial trial completion. The mean age at follow-up was 11 years old. Diagnoses were 28% fetal alcohol syndrome (FAS), 28% partial FAS, and 44% alcohol-related neurodevelopmental disorder. The follow-up evaluation included measures of executive functioning (WISC-V Picture Span and Digit Span; DKEFS subtests) and diffusion MRI (NODDI).
**Results:** Children who received choline early in development outperformed those in the placebo group across a majority of EF tasks at long-term follow-up (effect sizes ranged from -0.09 to 1.27). Children in the choline group demonstrated significantly better performance on several tasks of lower-order executive function skills (i.e., DKEFS Color Naming [Cohen's $d$ = 1.27], DKEFS Word Reading [Cohen's $d$ = 1.13]) and showed potentially better white matter microstructure organization (as indicated by lower orientation dispersion; Cohen's $d$ = -1.26) in the splenium of the corpus callosum compared to the placebo group. In addition, when collapsing across treatment groups, higher white matter microstructural organization was associated with better performance on several EF tasks (WISC-V Digit Span; DKEFS Number Sequencing and DKEFS Word Reading).
**Conclusions:** These findings highlight long-term benefits of choline as a neurodevelopmental intervention for FASD and suggest that changes in white matter organization may represent an important target of choline in this population. Unique to this study is the use of contemporary biophysical modeling of diffusion MRI data in youth with FASD. Findings suggest this neuroimaging approach may be particularly useful for identifying subtle white matter differences in FASD as well as neurobiological responses to early intervention associated with important cognitive functions.

**Categories:** Prenatal/Perinatal Factors/Prematurity
**Keyword 1:** fetal alcohol syndrome
**Keyword 2:** corpus callosum
**Keyword 3:** executive functions

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