Symposium Title: Executive Correlates Of Communication Skills in Youth with Three Neurodevelopmental Disorders: Implications for Identifying Diagnostically-Tailored Treatment Targets

Chair: Nancy Raitano Lee¹ & Gregory L. Wallace²

Discussant: Deborah Fidler³

Overview: Individuals with neurodevelopmental disorders often have impairments in language that impact academic success and independence. While many effective programs exist to improve oral and written language skills, achievement and independence in those with neurodevelopmental disorders continues to lag behind peers with typical development. Research on specific learning disorders suggests that gaining an understanding of the cognitive underpinnings of complex learning impairments (e.g., phonological processing skills in those with dyslexia) is important for intervention development and improving outcomes. Thus, research into the cognitive underpinnings of language impairments in those with neurodevelopmental disorders such as autism spectrum disorder (ASD) and chromosomal aneuploidies may help to identify new targets of intervention to improve outcomes for these groups. One such target is executive function, an umbrella term that describes higher-level cognitive skills such as working memory, inhibition, and cognitive flexibility. Research suggests that executive function skills are predictive of academic outcomes and independence in typical and atypical populations. However, their relation to language outcomes in youth with different neurodevelopmental disorders is poorly understood. Thus the current symposium will summarize research on executive function and its relation to different aspects of language in youth with ASD, Down syndrome, and Sex Chromosome Trisomy (47, XXY and 47, XXX). In addition, a model intervention program for targeting executive function difficulties in neurodevelopmental disorders will be presented and the implications for improving communication skills will be discussed.

Paper 1 of 4

Paper Title: Associations between Real-World Executive Functions And Both Structural and Pragmatic Language among Children and Adults with Autism Spectrum Disorder

Authors: Gregory L. Wallace³, Jason Crutcher⁴, Anna C. Armour⁵, Alex Martin⁴, Lauren Kenworthy⁵

Introduction: Executive functioning (EF) is an umbrella term applied to a critically important array of cognitive skills that are developmentally dynamic; such as flexibility in cognition and behavior, keeping information in mind in the service of a goal, and being able to inhibit a prepotent response. Classically, studies of EF in autism spectrum disorder (ASD) reveal prominent difficulties in behavioral and cognitive flexibility (Hill, 2004). Nevertheless, findings are mixed using laboratory and performance-based measures of EF, while ecologically valid approaches to EF assessment consistently reveal deficits among children and adults with ASD (Kenworthy et al., 2008; Wallace et al., 2016). Although pragmatic language difficulties are to some extent pathognomonic with ASD, links between these language skills and EF in ASD have not been thoroughly examined across development. The aim of the current study is to investigate associations between real-world EF profiles and both structural and pragmatic language in children and adults with ASD.

Methods: Children (n=129; Mean age=10+/2; Mean IQ=103+/18) and adults (n=30; Mean age=28+/12; Mean IQ=112+/17) with ASD without intellectual disability (diagnosed using DSM-5 criteria, the Autism Diagnostic Interview, and the Autism Diagnostic Observation Schedule) participated in the study and each had measures of real-world EF and structural and pragmatic language skills. For children, EF and (both structural and pragmatic) language were assessed based on parent report utilizing the

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Behavior Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Steven, & Kenworthy, 2000) and the Children’s Communication Checklist (CCC-2; Bishop, 2003), respectively. For adults, self-ratings from the BRIEF-Adult (BRIEF-A; Roth, Isquith, & Gioia, 2005) and the Communication Checklist-Self-Report (CC-SR; Bishop, Whitehouse, & Sharp, 2009) were utilized. Stepwise multiple linear regression analyses were completed to examine relationships between EF and language functioning. Step 1 included age, sex, and full-scale IQ as nuisance variables, while step 2 included the peak subtests from each index (Behavioral Regulation vs. Metacognition) of the developmentally appropriate version of the BRIEF in order to avoid issues of multicollinearity and multiple comparisons.

**Results:** Examination of the EF profile revealed uneven ratings (ps<.001), with peak difficulties in the domains of Shift and Working Memory among both children and adults with ASD. Among children with ASD, when submitted to stepwise linear regression analyses accounting for the influences of age, sex, and IQ, parent rated Shift scores from the BRIEF, in particular, were predictive (p<.01) of pragmatic language problems on the CCC-2. In contrast, the nuisance variable of IQ predicted structural language problems (p<.01), but EF difficulties did not in children with ASD. Among adults with ASD, self-rated Shift scores from the BRIEF-A again predicted pragmatic language problems on the CC-SR (p<.05). However, in contrast to findings among children, self-rated Working Memory scores from the BRIEF-A predicted structural language problems on the CC-SR among adults with ASD (p<.05). Finally, the nuisance variable of age was predictive of both self-reported pragmatic and structural language problems on the CC-SR (ps<.01).

**Discussion:** Children and adults with ASD demonstrate comparable real-world EF profiles wherein flexibility (BRIEF Shift scale) and working memory problems are most prominent. This suggests that (a) EF difficulties persist into adulthood in ASD and (b) a possible continuity in the EF profile across development (at the group level). Utilizing these peaks in the EF profile as predictors of language revealed specific linkages between shifting/flexibility difficulties and pragmatic language impairments, in particular, among both children and adults with ASD. Moreover, only among adults, working memory predicted structural language problems. This suggests that interventions targeting, for example inflexibility (e.g., *Unstuck and On Target*), might have positive downstream influences on pragmatic language functioning.

**References/Citations:**

**Paper Title:** Executive Correlates Of Structural and Pragmatic Language in Youth with DS: Evidence from Informant and Performance-Based Measures

**Authors:** Nancy Raitano Lee1, Mary Godfrey1, Taralee Hamner1, Megan Perez1, Alexandra Carolin1, Elizabeth Adeyemi4, Liv S. Clasen4, Jay N. Giedd4

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Introduction: Down syndrome (DS), the most common genetic cause of intellectual disability (ID), occurring in ~1/700 live births (Parker et al., 2010), is characterized by prominent impairments in language abilities (Abbeduto et al., 2007) that exceed global learning challenges. Understanding the cognitive underpinnings of the complex language learning difficulties in DS may help to identify new targets of treatment to improve language outcomes. Thus, the current research examines relations between executive function (EF), specifically measures of working memory (WM), inhibition (I), and cognitive flexibility (CF), and both structural and pragmatic language as measured by direct testing and parent report in two samples of youth with DS.

Methods: Sample 1 consisted of 22 youth with DS (10 females; Age: M=11 years; SD=4; IQ: M=52; SD=11) who were part of an ongoing study of reading and language at Drexel University. Sample 2 consisted of 32 individuals with DS (17 females; Age: M=13 years; SD=5; IQ: M=53; SD=14) who were a part of a larger study on brain and cognitive development completed at the NIH. A combination of direct testing and parent report of both language and executive function were used to evaluate study questions.

In sample 1, performance based measures of EF and language were used. They were as follows: the Test of Auditory Comprehension of Language - 4 (TACL-4) Vocabulary and Grammatical Morphemes subtests, the Missing Scan task (a measure of WM; [Roman et al., 2014]), the NIH Toolbox Flanker (a measure of I; [Zelazo et al., 2013]) and Dimensional Change Card Sort (a measure of CF; [Zelazo et al., 2013]) tasks. For this sample, the two TACL subtests were combined to make a structural language composite (STRUCT-TACL). The three EF measures were combined to make an EF composite (EF Test).

In sample 2, parent ratings on the Children’s Communication Checklist - II (CCC-2: Bishop, 2006) and the Behavior Rating Inventory of Executive Function (BRIEF; Gioia et al., 2000; Gioia et al., 2003) were used to evaluate everyday executive function and language skills, respectively. Analogous to the composites created for sample 1, in sample 2, the semantics and syntax measures from the CCC-2 were combined to create a structural language composite (STRUCT-CCC); parent report of WM, I, and CF from the BRIEF were used to create an EF composite (EF-BRIEF). Lastly, unlike Sample 1, sample 2 had data on pragmatic language from the CCC-2. Thus, the four pragmatic language scales of the CCC-2 were combined to create a pragmatic language composite for this sample (PRAG-CCC).

Results: To answer study questions, stepwise multiple linear regression was utilized to predict individual differences on the language composites with EF composites (measured concurrently) after accounting for the effects of age and sex.

With regard to direct testing of semantic and syntactic skills (STRUCT-TACL) in Sample 1, EF-TEST accounted for unique variance in these abilities after the effects of age and sex were considered (R² change step 1: =.30; R² change step 2 =.20; F change Step 2 [1, 18]=7.4, p<.05 ). This relationship was not found when parent report of structural language and EF skills were examined using the CCC-2 and BRIEF, respectively in sample 2. In contrast, when parent report of pragmatic language was considered (PRAG-CCC) in sample 2, the EF-BRIEF predicted unique variance in everyday pragmatic language skills after the effects of age and sex were accounted for (R² change step 1: =.04; R² change step 2 =.40; F change Step 2 [1, 28]=20.2, p<.001).

Discussion: Thus, the current study suggests that the EF difficulties that characterize DS (Lanfranchi et al., 2010) may be closely related to the prominent language impairments associated with the syndrome. Support for this came from both direct tests of language and EF as well as parent report of both constructs. These results suggest that EF abilities may represent an important target of treatment for youth with DS that may have significant implications for language competencies. Given that EF and language were measured concurrently in this study, the direction of the relationship cannot be ascertained. Thus, longitudinal studies are needed to examine whether EF skills are predictive of language longitudinally. More importantly, research on EF interventions in DS and their effect on language abilities is needed.

References/Citations:
Introduction: Klinefelter (47, XXY) and Trisomy X (47, XXX) syndromes are sex chromosome aneuploidies that are characterized by the presence of a supernumerary X chromosome. While overall intellectual functioning is typically within the low average to average range (Leggett et al., 2010), youth with these sex chromosome trisomies have high rates of language learning impairments (Lee et al., 2012) and increased rates of attention-deficit/hyperactivity disorder (Tartaglia et al., 2012) and executive dysfunction (Lee et al., 2015). Moreover, males and females with 47, XXY and 47, XXX have been reported to have heightened social difficulties and impaired social cognition skills (van Rijn et al., 2015). Recent research suggests that executive dysfunction in these groups relates to their social cognitive impairments (van Rijn et al., 2015). Given close ties between social cognition and language, particularly, pragmatic abilities, it is likely that executive dysfunction contributes to language impairments as well. Thus, the current study examined concurrent relationships among parent report of executive function and both social (pragmatic) and non-social (structural) language skills in males and females with a supernumerary X chromosome.

Methods: The sample consisted of 24 youth, including 14 females with 47, XXX and 10 males with 47, XXY (Age: M=11 years; SD=4; IQ: M=52; SD=11), who were part of a larger study of brain and cognitive development completed at the NIH. Two parent-report measures, the Children’s Communication Checklist - II (CCC-2; Bishop, 2006) and the Behavior Rating Inventory of Executive Function (BRIEF; Gioia et al., 2000), were used to evaluate everyday executive function and language skills, respectively. Composite scores were made from these measures to reduce the number analyses. The four scales assessing structural (STRUCT) and four assessing pragmatic (PRAG) language were used to create CCC-2 composites. For the BRIEF, the Global Executive Composite (GEC) as well as the Behavioral Regulation Index (BRI) and Metacognition Index (MCI) were utilized. To answer study questions, stepwise multiple linear regression analyses were completed to predict individual differences on the CCC-2 STRUCT and PRAG composites (concurrently). Step 1 included age, sex, and nonverbal IQ. Step 2 included the BRIEF GEC. In order to examine the unique contributions of the BRI and MCI scales to structural and pragmatic language, another set of stepwise regressions were completed with step 1 the same as above and steps 2 and 3 including either the MCI or BRI scales.

Results: After accounting for the effects of age, sex, and nonverbal IQ in step 1, the BRIEF GEC contributed significant unique variance to performance on both the CCC-2 STRUCT and PRAG composites (STRUCT: $R^2$ change step 1: =.02; $R^2$ change step 2 =.33; F change step 2 [1, 17]=8.4, p<.05; PRAG: $R^2$ change step 1: =.1; $R^2$ change step 2 =.43; F change step 2 [1, 17]=15.9, p<.01). When examining the unique effects of MCI and BRI by alternating these indices in steps 2 and 3, we found the following. When predicting structural language, neither the MCI nor BRI predicted unique variance in Step 3 after accounting for the variance in the other index in Step 2. When predicting pragmatic language, only the BRI predicted significant unique variance in Step 3 ($R^2$ change step 2: =.28; $R^2$ change step 3 =.29; F change Step 2 [1, 16]=14.1, p<.01).

Discussion: Consistent with reports that executive dysfunction contributes to social cognition impairments in youth with a supernumerary X chromosome, here we find that parent report of executive function as measured by the BRIEF predicts significant unique variance in both structural and pragmatic language abilities (after accounting for the effects of age, sex, and IQ). Moreover, it appears that behavioral regulation abilities, as measured by the BRI on the BRIEF, are a significant unique predictor of pragmatic language in particular, after accounting for metacognitive (MCI) abilities as well. These results highlight
the interconnectedness of language and executive function impairments in youth with SCAs and suggest that further research is warranted to examine this relationship over time.

References/Citations:

Paper 4 of 4

Paper Title: Cognitive-Behavioral Executive Function (EF) Intervention, Unstuck and On Target, Improves Social-Communication, as well as EF Abilities

Authors: Lauren Kenworthy, Alyssa Verbalis, Sydney Seese, Caroline Luong-Tran, Megan C. Wills, John Strang, Allison Ratto, Cara Pugliese, Kristina K. Hardy, Katerina Dudley, Anna C. Armour, Gregory L. Wallace, Laura G. Anthony

Introduction: Executive dysfunction is common in autism (ASD) and is linked to social-communication and emotional problems. We developed a school/home-based intervention targeting flexibility, goal-setting and planning called Unstuck and On Target (UOT; Cannon et al., 2011; Kenworthy et al., 2014) which remediates EF deficits through a cognitive/behavioral program that emphasizes self-regulatory scripts, guided/faded practice, and visual/verbal cueing in school/home.

Methods: Study 1: Included children: had IQ>70, met criteria for ASD, and were in 3rd-5th grade. Forty-seven (87%) male children received UOT, and 20 children (90% male) received a popular manualized social skills intervention (SS; Baker, 2003). The groups were well-matched for age, parent education, IQ, and percent minority. Thirty-one (28 males, 18 White) of the 47 children with ASD who received UOT were evaluated for follow-up 12-13 months after the completion of the intervention. Study 2: Included children had IQ>70 and were: from Title 1 (low income) schools in 3rd-5th grade, identified by school staff as being inflexible, and met diagnostic criteria for either ASD or ADHD. Of 145 participants (ASD n=48; ADHD n=97), only 29% were White, Non-Hispanic/Latino. Students received either UOT or contingency behavior management (CBM) interventions. ADHD and ASD participants in each intervention were equivalent regarding age, sex, and IQ and family income (t’s<1.54). Study 1 & 2: Schools were randomly assigned to intervention condition. Interventions were delivered in school by school staff in small groups;

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classroom teachers and parents were trained to reinforce lessons, with the same dose of intervention and training across intervention conditions.

Results: Study 1: There was significantly greater pre-post improvement in the UOT than the SS intervention on multiple measures of EF, but parent/teacher report and blinded social skills measures showed equivalent improvement following UOT and SS, (Estimated coefficient (SE) for treatment effect (UOT vs. SS) Challenge Task Social: 0.24(0.26); Social Responsiveness Scale (SRS) Parent Total t-score: -1.63(1.88); SRS Teacher Total t-score: -4.34(2.78). Benefit from UOT was maintained at follow-up when compared to pre-intervention performance on executive and a social lab task (CT Social: t =4.02, p<.001). Study 2: Observed behavior in the mainstream classroom improved for children with ASD following UOT (t=−2.6, p=.018) but not CBM (t=−0.99, p=.33), while children with ADHD improved with both interventions (UOT: t=−4.9, p<.001; PATSS: t=−3.9, p<.001). Parent reported BRIEF Emotional Control t-scores were significantly improved for both ASD and ADHD after UOT (p’s = .009 and .05 respectively), but not following CBM.

Discussion: In two studies, a cognitive behavioral intervention administered by school staff targeting flexibility, planning and organization, not only improved EF, but also lead to gains in social-emotional functioning per blinded observations and parent/teacher report. These data support previous findings showing that: intervention to improve EF enhances social reasoning (Fisher & Happé, 2005); and that EF is a precursor to, (Flynn, 2007), or is correlated with (Pellicano, 2007; Perner & Lang, 1999), theory of mind, and thus positively impacts broader social-communication.

References/Citations: