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RESEARCH ARTICLE

To snack or not to snack: Using fNIRS to link inhibitory control to functional connectivity in the toddler brain

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Abstract

Inhibitory control (IC) emerges in infancy, continues to develop throughout childhood and is linked to later life outcomes such as school achievement, prosocial behavior, and psychopathology. Little, however, is known about the neural processes underpinning IC, especially in 2-year-olds. In this study, we examine functional connectivity (FC) in 2.5-year-olds while recording hemodynamic responses via functional infrared spectroscopy (fNIRS) during a traditional snack delay task. We found that *functional connectivity strength* between left frontal and parietal cortex and bilateral parietal cortex were positively associated with performance on this task. The current findings present the first neural data for toddlers during this IC task. Further, these data are the first to link this self-regulatory process to differences in brain development within this population. Implications for future directions and work with clinical populations are discussed.

KEYWORDS
fNIRS, inhibitory control, toddlers

1 | INTRODUCTION

Inhibitory control (IC) is the ability to suppress behavioral responses towards a target stimulus to achieve biological, social, or reward-oriented goals (Spinrad et al., 2007). IC can be measured as early as 6-months of age and develops through adulthood (Holmboe et al., 2018; Kochanska et al., 1998; Malloy-Diniz et al., 2008). Behavioral IC is predictive of self-control (e.g., inhibiting undesirable social behaviors; Duckworth et al., 2013), attentional regulation, and academic achievement (Jaekel et al., 2015). In 2- to 4-year-olds, IC is related to impulse control and suppression of prepotent responses in early childhood as well as later outcomes such as school success in middle childhood (Diamond, 2013; Gagne & Saudino, 2010; Jacobson et al., 2017; Quiñones-Camacho et al., 2019). Additionally, several prosocial behaviors in children are supported by the ability to exert IC: sharing behavior (Paulus et al., 2015), cooperative behavior (Ciairano et al., 2007), donating behavior (Hoa, 2017), distributive behavior (Reis & Sampaio, 2019), and reasoning ability (Lui et al., 2015). Thus, IC is an important construct for both analyzing cognitive control in lab-based settings and interpreting real-world behaviors.

IC laboratory tasks are calibrated to the specific developmental stage of the child (Petersen et al., 2016). A classic measure of early IC in 2 and 3 year-olds is the Snack Delay task (Diamond, 2013; Friedman & Miyake, 2004; Mischel, 1974). Individual differences in Snack Delay task performance are predictive of familial attentional vulnerabilities, and have been demonstrated to mediate the detrimental effects of crying, feeding, and sleeping issues on attention regulation throughout development (Baumann et al., 2019; Pauli-Pott et al., 2014). Generally, the literature documents the relationship between early IC behaviors and their neural correlates within adolescent and adult populations, specifically linking it to externalized behavioral issues and clinical outcomes such as anxiety in adulthood (Baumann et al., 2019; Filippi et al., 2021; Friedman et al., 2011; Lamm et al., 2014; Neppl et al., 2020). Despite it's predictive relationship with important outcomes, the literature on toddlers has not yet examined the neural underpinnings of IC (Paulus et al., 2015).

1.1 | Neural development associated with IC

Changes in IC during childhood and adolescence are dependent upon the development of frontal cortex (Durston et al., 2006; Lui et al., 2015; Ordaz et al., 2013). However, neural mechanisms related to IC in early development are not well understood or easily identifiable (Ciairano et al., 2007; Hoa, 2017; Lui et al., 2015; Reis & Sampaio, 2019). Although frontal cortex has been implicated as central to early regulation of IC, research with 2 and 3 year-olds shows that IC is mediated by increased activation in both prefrontal cortex and parietal cortex (Fiske & Holmboe, 2019; Fiske et al., 2021; Knight et al., 1999). Prefrontal cortex activation increases over time from childhood to adulthood during IC tasks (Fishburn, Hlutkowsky, et al., 2019), while functional connectivity (FC) within parietal cortex become more efficient (i.e., reduced widespread connectivity in favor of more specific connections) as well as less overall activation in specific regions of parietal cortex relative to increases in IC performance (Hwang et al., 2010). Using functional near-infrared spectroscopy (fNIRS) in children ages of 4–6 and adults, Mehnert et al. (2013) observed increased activation in bilateral frontal and parietal cortices during both response and inhibition trials. In contrast, adult counterparts displayed activation only in right frontal and parietal cortex and only during the response inhibition trials. These data suggest that children have not yet fully developed neural networks that are selectively engaged in response to inhibitory demands at 4–6 years. Thus, weaker connections between these regions in children prior to the age of four may be one potential neural mechanism driving the developmental of IC.

Increases in the IC of proponent responding is one indicator of typical development. However, some children show delays in IC development or even detriments in their ability to employ IC during a snack delay task—such as those with ADHD (Einziger et al., 2018). The neural mechanisms driving this dysfunction in IC are still largely unclear as children undergo rapid approvements across executive functioning domains from toddlerhood to middle childhood; so much so that improvements in specific executive functions are interrelated. Currently, targeted interventions in children at risk for developing delays such as ADHD, are not possible due to the unclear nature of what is driving dysfunction once children are school age. IC more broadly includes emotional regulation and impulse control. Thus, understanding one facet of IC, and the neural mechanisms underlying snack delay performance in toddlers, might shed light on common mechanisms underlying the development of IC broadly in this group.

In summary, there is a gap in our understanding of when the neural mechanisms involved with individual variations in IC during early childhood begin to develop and when they become stable. Neuroimaging research has not been conducted during an IC task in the foundational toddler years, and research has not identified if other neural measures, such as FC measures, are associated with IC during early childhood. Understanding IC during this critical transitional age range will better inform early interventions targeting behavioral modification and emotional regulation during this time.

Research Highlights

- Increased functional connectivity between left frontal and parietal cortex is associated with improved inhibitory control performance in toddlers
- Increased functional connectivity between left and right parietal cortex is associated with improved inhibitory control performance in toddlers
- Differences in functional connectivity in frontal and parietal cortices may drive inhibitory control development
- fNIRS is a feasible method for collecting neural data during active laboratory tasks measuring executive functions in toddlers

1.2 | Current approach

In the current study we administered the Snack Delay task (Kochanska et al., 2000; Spinrad et al. 2007) to 26 2 year-olds while recording hemodynamic responses in bilateral prefrontal and parietal cortices using fNIRS. Correlated neural activity between brain regions, known as FC, is an important metric of communication between brain regions (e.g., Duan et al., 2012). We explore whether individual variability in IC is associated with FC between frontal and parietal cortex during toddlerhood. Patterns of FC during IC tasks in 2 and 3 year-olds as they relate to FC patterns has yet to explored. We hypothesized that children with greater IC in toddlerhood will also show stronger connections between frontal and parietal cortex as they perform the snack delay.

2 | METHODS

2.1 | Participants

Children in the current sample participated in a larger longitudinal attention battery. The snack delay task was administered at the end of the battery to ensure there was enough time between the child arriving and the end of the battery for a snack to be desirable. Meal, snack, and nap times were considered when scheduling children to avoid state-dependent factors further leading to self-selection in the current sample. In addition, children whom completed the snack delay task did not differ on trait-based temperament sub-scores or composite scores from the ECBQ. Thus, we are confident that, although self-selection might have occurred somewhat in the current sample, these data are representative of the general population (see Table S1).

For this battery, 37 2.5-year-old children were initially recruited ($M = 2.48$ years). Of this group, 26 children made it through to this final task. All 26 children who started the Snack Delay task finished it (Male: 11, Female: 15). All children included in the analysis had normal hearing and no known cognitive or neural developmental delays or abnormalities. Parental consent was obtained prior to the child participating in the study. Throughout the procedures, continuous verbal assent was maintained with all children. The study was approved by the Institutional Review Board for Research with Human Subjects at a major university in the Southeastern U.S.

2.2 | Procedure and stimuli

Questionnaires were completed by parents or legal guardians and were either administered with an Apple iPad Air 2 via quick response (QR) codes using Qualtrics© or by paper during each appointment. Data collection via the Apple iPad Air 2 and Qualtrics© was done via a secure network identity created for the laboratory.

Children were seated in a highchair. The circumference of the child's head was measured, and the vertex was measured (halfway between the pre-aural areas and halfway between the nasion and inion) and marked with hypoallergenic face paint. The appropriate fNIRS hat ranging from 52 to 54 cm was selected by adding 2 cm to head circumference for proper probe placement and fitting. fNIRS was collected at 25 Hz using a Techen CW7 system with wavelengths of 830 and 690 nm. Light was delivered via fiber optic cables that terminated in an array compiled of six sources and 12 detectors for a total of 16 channels. Sources and detectors were spaced 3 cm apart for each channels. Placement of the probe was aligned to the extended 10–10 system over left and right frontal cortex (AF3-4; F5-F6) and left and right parietal cortex (CP1-4; P1-4; PO3-4). Once the hat was placed, Polhemus Patriot digitization system was used to create a 3D digitization of the probe placement. This digitization was then checked for accuracy utilizing MatLab and AtlasViewer software (see Figure 1). Then, the amplification (gain) of the detectors was automatically adjusted by the system to maximize the signal-to-noise level for all measurement pairs. If needed, the head cap was adjusted to create better contacts between the NIRS sensors and the head by checking the existability of the systemic physiological noise (i.e., cardiac and respiration signals). The child was seated 63.5–65 cm from the display screen.

For the snack delay task, children first selected whether they preferred goldfish crackers or fruit gummy snacks. This was done to insure appropriate levels of motivation. Children were told they would get to eat some snacks during this game. The snack delay consisted of one practice trial to insure understanding and four test trials with varying delay durations (10, 15, 20, and 30 s; see standard task Spinrad et al., 2007). During all trials, a small clear cup was staged on the tray of the highchair (see Figure 2a). The following instructions were given during the practice trial: "I am going to place a gummy/goldfish snack under

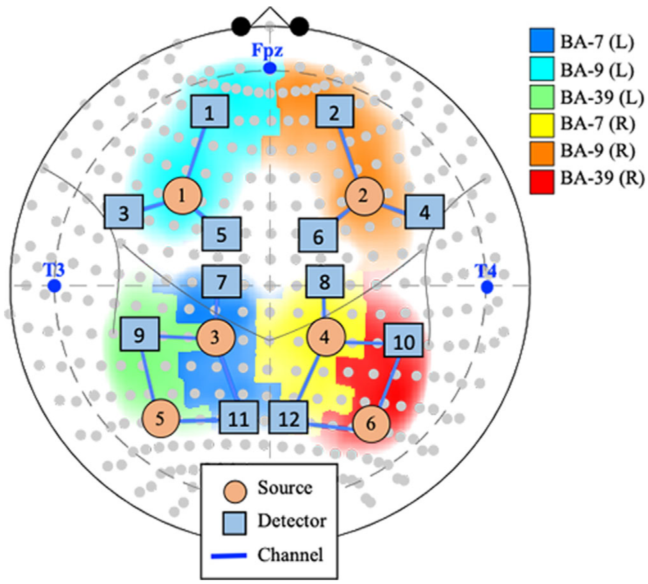

FIGURE 1 Configuration of current probe design. fNIRS probe placement in the International Extended 10-10 System, represented by gray dots in the current schematic. Blue text represents landmarks (i.e., nasion [Fpz], left preauricular [T3], ad right preauricular [T4]). Positioning of the 18 optodes, consisting of six sources (orange circle) and 12 detectors (blue squares) creating 16 channels. BA, Broadman area; L, left; R, right

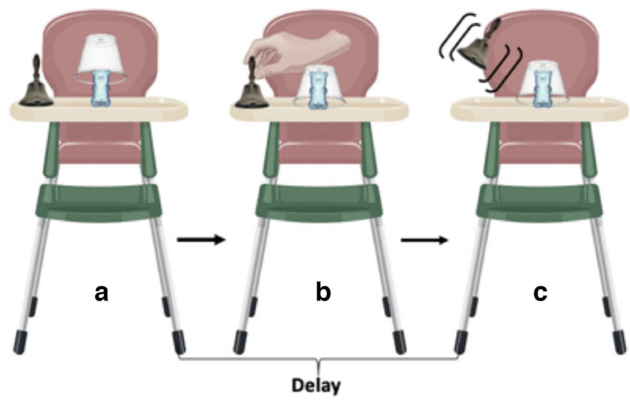

FIGURE 2 The snack delay task. This figure depicts the sequence of events in the Snack Delay where a) is the first half of the trial when the snack is placed, b) is when the bell is picked-up and not rung, and c) is when the bell is rung and the child can eat the snack. The delay between a and c consisted of either 10, 15, 20, or 30 s and were given in order is shortest to longest during the four testing trials

this cup here (*pointing to the clear cup*). When I ring the bell, you can eat the gummy/goldfish snack." The experimenter then rang the bell and let the child eat a snack to practice the procedure. During the test trials, these instructions were repeated only once during, at the beginning of the trail for the remaining four trials. Children received the delay durations in a fixed order from shortest to longest. Halfway through these durations (see Figure 2b), the experimenter reached for the bell and held it until the full duration had passed at which point, they rang the

TABLE 1 Scoring comparison for the snack delay task

Spinrad et al. (2007)		Current study	
Score (1–9)	*Behavior*	*Score (1–5)*	*Behavior*
1	Ate the snack right away	1	Ate the snack right away or touches bell, cup or snack immediately after the trial starts
2	Ate the snack after the experimenter lifted the bell	2	Ate the snack after experimenter lifted the bell
3	Touched (but did not eat the snack) in the first half of the trial	3	Touched the snack, cup, or bell in the first half of the trial
4	Touched the snack during the second half of the trial	4	Touched the snack, cup, or bell in the second half of the trial
5	Only touched the cup during the first half	5	Waited the entire time before eating the snack or touching anything on the tray
6	Touched the cup during the second half of the trial		
7	Waited the entire trial to eat the snack		
+ up to two additional points	Kept hands on mat in front of them		

bell indicating it was time to eat the snack (see Figure 2c). This procedure was followed even if the child ate the snack early.

2.3 | Survey and behavioral analyses

2.3.1 | Demographics

A demographics questionnaire was administered that was specifically designed to collect information concerning household income, parental education level, number of siblings and sibling order, eye-sight, race, sex, and childcare experience. Demographics were used for descriptive statistics and were not used in any of the other statistical analyses.

2.3.2 | Snack delay

Children's behaviors were coded from video recordings by two raters at three time points of interest for each trial: when the trial started (snack placed under the cup placed), when the researcher picked up the bell (half-way through the trial), and when the bell was rung (end of the trial). Children's snack delay performance was scored on a scale from 0 to 5 in a fashion similar to Spinrad et al. (2007) (see also Kochanska et al., 1996). Each delay duration received a score (see Table 1 for comparison scoring). Then, a total score was calculated by taking an average of all four scores. The scoring scale was adjusted due to variability in behaviors for the current sample to avoid artificial bimodal brain-behavior effects in the neural data due to behavioral coding.

2.4 | Neural data analyses

The NIRS Brain AnalyzIR Toolbox was used for all pre-processing and statistical analysis of fNIRS data (Santosa et al., 2018). Data were first converted to an optical density measure utilizing the Beer-Lambert Law (PPF = 0.6). To extract the individual FC measures, a robust correlation approach was taken by implementing iterative autoregressive least-square technique (for more details see Santosa et al., 2017). More concisely, the false discovery rate can be controlled by calculating the robust correlation coefficient of the temporally whitened signals. Santosa et al. (2017) demonstrated the robustness of this algorithm demonstrating that it yields more reliable estimates to serially correlated errors and statistical outliers due to motion artifacts (i.e., Temporal Derivative Distribution Repair; Fishburn, Ludlum, et al., 2019). Next, correlations were computed on the time series across channel pairs for each participant. Each trial was broken down into phases based on the trial structure. Specifically, the time period before the bell was rang, denoted first half of the trial, was analyzed separately from the second half of the trial due to the nature of the behavior you might see in these two phases (e.g., eating the snack after the bell is picked up or refraining). Correlations for each channel pair were calculated across participants to calculate both group and individual level FC scores (Wang et al., 2017). These scores were correlation coefficients in both these group and individual level channel-pair correlations. We focused our analyses on R-values generated from these FC analyses representative of the relationship between HbO_2 levels from each channel in relation to every other channel. Correlation coefficients on significant channel-pairs were used as a score for the strength of FC between those two cortical regions or channels (i.e., channel-pairs; Nguyen et al., 2018).

Of the 26 children who completed this task, only 23 children were included in the final FC analyses. One child was dropped due to refusing to wear the fNIRS cap through the entire task, one child was dropped for excessive movement during the task (i.e., losing more than 20% of data due to motion), and one child was dropped for not meeting signal-to-noise ratio criteria for more than 80% of their channels. In the following analyses, we focused on measurements of HbO_2 during the first half of the trial, before the experimenter picked up the bell. Children that perform more poorly are likely eating the snack during the

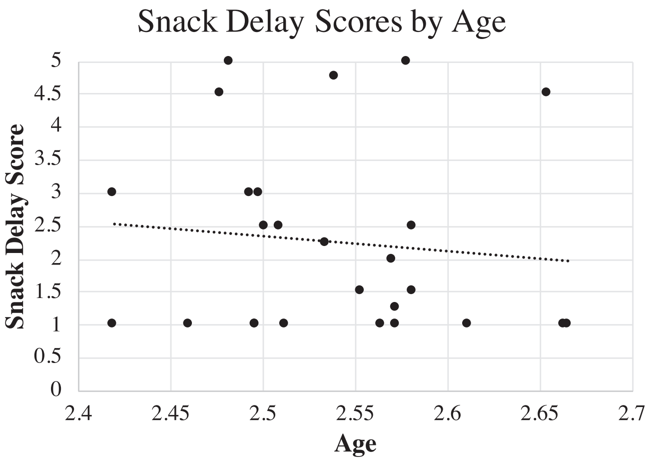

FIGURE 3 Performance on the snack delay task for toddlers by age. These data reflect the adjusted scoring used in the current study that reduces the binomial distribution of behavioral scores to retain the continuous metric of IC the task typically captures as we administered this to a much younger sample than typically seen in the literature

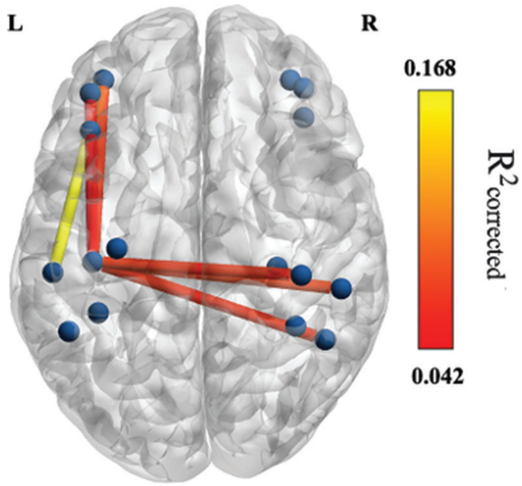

FIGURE 4 Significant effects of Snack Delay performance on FC. Location of the Nodes are illustrative only, and are based on approximate MNI coordinates for the current probe (i.e., channels 1–16, see Figure 1). That is, these locations are the approximated midpoint locations between each source and detector, calculated in AtlasViewerGUI within the Homer3 software package in Matlab. BrainNet Viewer was used to visualize significant FC predictive of IC (Xia et al., 2013)

second half of the trial compared to those who performed well and are still waiting for their snack, causing substantial movement-related, but not necessarily IC-related, group differences. Thus, only the first half of the trial is considered. Next, mixed-effects models optimized for connectivity analyses (see associated code in supplementals) were used to test our hypothesis that FC within and between frontal and parietal cortices would predict Snack Delay performance.

3 | RESULTS

3.1 | Behavioral results

Children were able to choose which snack they wanted from a choice of gummy snacks (N = 15) and goldfish (N = 11). Snack choice was not associated with significantly different behavioral outcomes, $t(24) = -0.097$, $p = 0.924$. Our examination of behavioral data indicates our sample consisted of both children who succeeded and struggled during the task ($M = 2.32$, SD = 1.50, see Figure 3) that is typical in the literature (e.g., Spinrad et al., 2007).

3.2 | FC results

In our analysis of FC and snack delay performance, significant associations (i.e., $p < 0.005$) between FC and snack delay performance was seen between left frontal and parietal cortex and between bilateral parietal cortex (see Table 2; Figure 4). There was no significant relationship between interregional channel-pairs and snack delay performance. All R2 values represent the strength of the correlation between HbO synchrony within channel-pair controlling for physiological artifacts. Santosa et al. (2018) has demonstrated that when randomly selecting two experimental time courses of fNIRS data from different subjects collected at different times, 70%–80% of the samples were falsely correlated at better than $p < 0.05$. This is an indication of a clear problem with uncontrolled Type-I Error in the standard analysis methods, which have previously been used for resting-state FC analysis in fNIRS studies. Our autoregressive algorithm used pre-whitening which removes autocorrelation data and whitens the frequency content of the signal. This important step will reduce false-discovery and greatly reduces the appearance of spurious global connectivity across the brain. We believe when the literature shows high correlation in their connectivity, those studies still include the systemic noise. However, in our method, Santosa et al. (2018) has shown the robustness technique to reduce those global systemic noises indicating proper control type-I error, which results in smaller R values. Thus, if the R is small but still very significant, it is still accurate.

4 | DISCUSSION

In the current study, we explored the relationship between behavioral IC and FC in toddlers using fNIRS. The main finding from this study was that toddlers showing increased IC (i.e., higher scores on the Snack Delay task) had *stronger connections* between left frontal and parietal cortices and parietal cortices. These findings supported our original hypothesis that connectivity *between* these regions is predictive of greater IC. However, our data did not support the hypothesis that stronger FC *within* frontal and parietal cortices would be associated with greater IC. These data provide one of the first windows into the neural substrates of IC in toddlerhood as it first emerges.

TABLE 2 Functional connectivity predicts snack delay performance

Statistical results	Channel-pair and region		$R^2_{corrected}$	p
Main effect of snack delay performance	1–8	Inferior lPFC←→ Superior lPC	0.062	<0.001
	1–13	Inferior lPFC←→Inferior lPC	0.168	<0.001
	2–8	lPFC←→Superior lPC	0.042	0.005
	8–11	Superior lPC ←→ Superior rPC	0.061	<0.001
	8–15	Superior lPC←→ Inferior rPC	0.067	<0.001
	8–16	Superior lPC←→ rPC	0.060	<0.001

Abbreviations: rPC, right parietal cortex; lPC, left parietal cortex; rPFC, right prefrontal cortex; lPFC, left prefrontal cortex.

In infancy and early childhood, IC is related to parietal cortex activation and over time is related to both PFC and parietal cortex as executive functions develop (see review, Fiske & Holmboe, 2019). As other cortical areas, such as PFC, involved in higher order cognitive processing (i.e., executive functioning) develop, IC performance improves in tandem to aid in goal directed behavior (e.g., Fiske et al., 2021; Knight et al., 1999; Hwang et al., 2010). Our findings provide evidence of frontal-parietal and bilater-parietal cortex FC being associated with improved performance on IC tasks as early as 2.5-years-old, suggesting that FC between these regions is important for the development of IC in very young children. Previous literature provides evidence for continued development of fronto-parietal networks in aid of IC at 4- and 5-years-old, while highlighting the instability of IC behaviors at age 2 (e.g., Fiske & Holmboe, 2019). Individual differences in IC in preschool predict long-term outcomes (Diamond, 2013; Gagne & Saudino, 2010; Jacobson et al., 2017; Jaekel et al., 2015; Quiñones-Camacho et al., 2019).

IC to prepotent responding, such as refraining from eating a desirable snack, is extremely difficult for young children. Diamond (2013) reviews the interconnectedness of IC, such that IC is necessarily reliant on working memory (i.e., remembering the rules of the snack delay task). Further, working memory is reliant on IC and IC is necessary for other processes such as maintaining attentional selectivity in the face of conflict, competing information, or irrelevant distractors. In the current study, IC in toddlers is predicted by the strength of connectivity between frontal and parietal cortex. Frontal and parietal cortex have been a historical focus for fNIRS works assessing attentional control, working memory, and inhibitory responding in young children (e.g., Kerr-German & Buss, 2020; Moriguchi & Hiraki, 2013). Further, long-range connections between these cortical regions are associated with more adaptive executive functioning where both attention and inhibition, as well as working memory are required for successful performance (see also Buss & Kerr-German, 2019). Thus, global executive functioning ability (i.e., cognitive processes that overlap with IC in frontal and parietal cortex; Gagne & Saudino, 2016) could be contributing to the relationship between toddler's snack delay performance in the current study and FC. However, systematic probing of these questions is beyond the scope of the current study and should be considered in future work with toddlers.

It is possible that neural differences associated with IC performance at 2.5 years old might shed more light on what neural mechanisms drive typical and atypical trajectories and if delays that are present at 2-years-old persist into risk for poor outcomes later in development. Understanding the neural underpinnings of better performance on this classic IC task in typically developing children at an early age might allow us to better identify children at risk for behavioral dysfunction. For example, IC is important for early identification of externalizing behaviors such as Attention Deficit Hyperactivity Disorder (Eisenberg et al., 2001; Eisenberg & Spinrad, 2004; Gagne et al., 2011; Schachar et al., 1995). The pathophysiology of behavioral problems may improve the identification and treatment of those behavioral problems in young children (Saudino & Carter et al., 2008). To accomplish this, it is important to establish normative data for toddlers and young children across domains of potentially disrupted behavior (e.g., Cicchetti & Toth, 2009), including behavioral IC and the neural dynamics of IC, in order to better understand how these might unfold in children with atypical trajectories.

Importantly, this is the first application of functional neuroimaging analyses in toddlers during an IC task. These data support the feasibility of this methodological approach with children in the 2nd year of life. The current analyses are tolerant of motion allow more data to be extracted from less trials (e.g., Wang et al., 2017), making this approach optimal for toddlers. The application of fNIRS to study neural systems very young children should expand to domains of functioning beyond IC in order to better understand neural development during toddlerhood.

4.1 | Limitations

Although the current data shed light on the relationship between FC and one lab-based measure of IC, it is still unclear whether other measures of cognitive control play a role in the development of the brain networks involved in IC. The current study is limited due to small sample size. Sample size in this age range is a general challenge due to the high attrition rates in neurocognitive methods for toddlers. Additionally, this task was a part of a larger battery of tasks, thus it is possible children who made it to this part of the protocol were more advanced than their counterparts who fussed out. However, given the paucity of neuroimaging research in this age group, and the distribution of behavioral scores, these data remain representative of the age group and impactful.

5 | CONCLUSION

The relationship between IC and frontal-parietal and bilateral parietal cortices is apparent as early as 2.5-years-old. Specifically, greater FC between left frontal and parietal cortex, as well as between left and right parietal cortex, is associated with better IC during the snack delay task. These findings suggest demonstrate that the development of IC has measurable neural correlates indicative of established IC networks at 2.5-years-old. These data support the feasibility of using fNIRS to map brain development in very young children during active laboratory tasks. This work may further our ability to begin to detect atypical trajectories in IC at the neural level at a very young age.

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CONFLICT OF INTEREST

There are no declared financial conflicts of interest from any of the authors involved in this manuscript.

ETHICS STATEMENT

The research protocols used in this research were approved by the ethics committee of The University of Tennessee, Knoxville, United States.

DATA AVAILABILITY STATEMENT

Due to the sensitive nature of the questions asked in this study, survey respondents were assured raw data would remain confidential and would not be shared with identifying information. Deidentified neural and behavioral data will be shared upon request from Journal or for use in a metanalysis.

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SUPPORTING INFORMATION

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