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Explaining Brain-Behavior Relations: Inhibitory Control as an Intermediate Phenotype Between the N2 ERP and the Externalizing Spectrum in Childhood

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Abstract

Identifying neural and cognitive mechanisms in externalizing problems in childhood is important for earlier and more targeted intervention. Meta-analytic findings have shown that smaller N2 event-related potential (ERP) amplitudes, thought to reflect inhibitory control, are associated with externalizing problems in children. However, it is unclear *how* (i.e., through which cognitive processes) N2 amplitudes relate to externalizing problems. We examined whether inhibitory control may be a cognitive process that links N2 amplitudes and externalizing problems in early childhood. Children ($N = 147$, 74 girls) were assessed at four time points, spanning 3–7 years of age. Children's externalizing behavior was assessed via questionnaires completed by mothers, fathers, and teachers/secondary caregivers. Children's inhibitory control was assessed using eleven performance-based tasks and two questionnaires. Developmental scaling linked differing measures of inhibitory control and externalizing behavior across ages onto the same scale. Children's N2 amplitudes were extracted from electroencephalography data collected during a go/no-go task. Smaller N2 amplitudes were associated with externalizing problems and poorer inhibitory control. A concurrent analysis of indirect effects revealed that poorer inhibitory control partially explained the association between smaller N2 amplitudes and externalizing problems, even when controlling for the child's age, sex, and socioeconomic status. This is among the first studies to link N2 amplitudes, inhibitory control, and externalizing problems during early childhood. Findings suggest that smaller N2 amplitudes may be an early neural indicator of inhibitory control deficits and externalizing psychopathology. Moreover, inhibitory control may be an important target for early intervention in the development of externalizing psychopathology.

Keywords N2 ERP · Externalizing problems · Inhibitory control · Children · EEG · RDoC

Externalizing behavior problems consist of children's outward behaviors and reactions to external cues from the environment, such as aggression, inattention, hyperactivity, and conduct problems (Liu, 2004). The worldwide prevalence of externalizing disorders is ~ 5.7%, or 113 million children (Polanczyk et al., 2015). Moreover, individual differences in externalizing behaviors tend to be relatively stable throughout the life span and are associated with severe outcomes, including academic underachievement (Hinshaw, 1992), substance use (Petersen et al., 2015), and criminality (White et al., 1990). Therefore, it is crucial to identify mechanisms in the development of externalizing behaviors before these behaviors develop into severe problems later in life. It may be especially important to identify biological and cognitive mechanisms underlying externalizing behavior, because a given behavior (e.g., deficient self-regulation) can reflect different underlying substrates and can appear across several disorders. That is, the same behavior can occur for different reasons. Thus, behavior ratings are not sufficient to make conclusions about mechanisms in the development of psychopathology (Insel, 2014).

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Accordingly, the Research Domain Criteria (RDoC) initiative from the National Institute of Mental Health seeks to advance understanding of neural substrates of psychopathology (Insel et al., 2010). The RDoC initiative was developed to address shortcomings of traditional categorical conceptualizations of psychopathology that are based on a set of symptoms. Instead of using diagnostic categories, the RDoC framework uses dimensional conceptualizations of psychopathology, in which typical and atypical behavioral development are examined across the lifespan. The RDoC framework provides an organizational structure (i.e., matrix) for researchers to characterize the nature of psychopathology across units of analysis. The matrix specifies six major domains (e.g., Cognitive Systems) consisting of constructs (e.g., cognitive control), subconstructs (e.g., inhibitory control), and units of analysis (e.g., physiological, self-report, and behavioral data). Within the RDoC framework, it is important to identify neurobiological (and other) processes underlying the development of psychopathology. Notably, one initial criticism of the RDoC framework was that it largely excluded developmental data in its formulation (Conradt et al., 2021; Durbin et al., 2022). However, recent studies have sought to integrate developmental perspectives into the RDoC framework. For example, Vogel et al. (2021) used an RDoC approach to examine how trajectories of emotion dysregulation in positive (i.e., excitability) and negative (i.e., irritability) affect in childhood predicted emotion dysregulation in adolescence. Similarly, Damme et al. (2022) used the RDoC framework to examine associations between patterns of irritability in early childhood (i.e., preschool age and early school age) and later psychopathology (internalizing and externalizing symptoms) and neural outcomes in preadolescence. Thus, the RDoC framework provides a structure for researchers to examine trajectories of constructs across units of analysis, allowing researchers to examine the development of typical and atypical behavior (e.g., psychopathology) over time.

One possible biological process in the development of externalizing behavior is neural activity in the prefrontal cortex or anterior cingulate cortex, as indexed by the N2 event-related potential (ERP). The N2 ERP is commonly examined using tasks designed to assess inhibitory control. Inhibitory control is the ability to inhibit responses to irrelevant stimuli in pursuit of a cognitively represented goal (Simpson & Carroll, 2019). In the RDoC framework, inhibitory control is a subconstruct of the cognitive systems domain and cognitive control construct. A widely used paradigm to assess inhibitory control is the go/no-go task. During go/no-go tasks, children are presented with two stimuli: a go stimulus, which is paired with response activation (e.g., a button press), and a no-go stimulus, which is paired with response inhibition. Go stimuli are often presented more frequently than no-go stimuli to elicit a prepotent response and make inhibition more difficult. The N2 ERP, extracted using electroencephalography (EEG), is the second negative deflection in the waveform that occurs approximately 300–500 ms post stimulus in children to both go and no-go stimuli (Hoyniak, 2017). Importantly, the inhibitory (no-go/stop) N2 component has been widely associated with externalizing behavior in children. Meta-analytic work has shown that smaller (i.e., less negative) no-go N2 amplitudes are associated with more externalizing behavior in children (Hoyniak & Petersen, 2019). However, the mechanism underlying the association between no-go N2 amplitudes and externalizing problems is unclear.

Given the costs and practical challenges of using neural substrates in intervention and prevention efforts, it is important to identify cognitive intermediate phenotypes in the association between biological processes and externalizing behavior. Cognitive intermediate phenotypes between inhibitory N2 amplitudes and externalizing problems may capture early neural risk processes, while providing practical targets for intervention. Furthermore, identifying links between the brain and behavior is aligned with the RDoC framework, which encourages researchers to build a bridge that spans the same construct across multiple units of analysis. A cognitive process that may be a potential intermediate phenotype between no-go N2 amplitudes and externalizing problems is inhibitory control.

Although the functional interpretation of the N2 component is not yet established, research supports the interpretation of the N2 as an index of inhibitory control in inhibitory tasks (Jing et al., 2021; Jodo & Kayama, 1992), such as go/no-go tasks (Hoyniak, 2017; Hoyniak & Petersen, 2019). The N2 is larger to inhibition (i.e., no-go) stimuli than to activation (i.e., go) stimuli. Moreover, when experimentally manipulating effort by setting limits on adults' reaction time, Jodo and Kayama (1992) found that no-go N2 amplitudes were larger when greater effort was required to withhold the prepotent response. Research has localized the no-go N2 component to areas thought to support inhibitory control (Steele et al., 2013), including the anterior cingulate cortex, orbitofrontal cortex, ventral prefrontal cortex, and dorsolateral prefrontal cortex (Bokura et al., 2001; Lavric et al., 2004). Taken together, these findings provide evidence for the interpretation of the no-go N2 as an index of inhibitory control. However, other functional interpretations of the N2 have been proposed, including that the inhibitory (i.e., no-go and stop) N2 reflects conflict monitoring or attention to mismatched stimuli (Enriquez-Geppert et al., 2010; Folstein & Van Petten, 2008; Smith et al., 2010). Given the association between no-go N2 amplitudes and externalizing problems, it is important to clarify the functional interpretation of the N2 component.

Several studies have examined the association between N2 amplitudes and inhibitory control in children (Brydges

et al., 2014; Espinet et al., 2012; Jing et al., 2021; Kaiser et al., 2006). A larger difference between go and no-go N2 amplitudes is thought to reflect more advanced inhibitory capacities (Jodo & Kayama, 1992). Thus, it might be expected that larger no-go N2 amplitudes would be associated with better inhibitory control, because smaller N2 no-go amplitudes may reflect insufficient recruitment of neural resources necessary for inhibition. However, mixed findings in children have emerged. Several studies have shown that larger no-go N2 amplitudes are associated with better inhibitory control in children (Grabell et al., 2017; Hoyniak, 2017; Ruberry et al., 2017). By contrast, meta-analytic work has found that *smaller* no-go N2 amplitudes are associated with better inhibitory control (Buss et al., 2011; Espinet et al., 2012; Hoyniak & Petersen, 2019). Given these inconsistent findings in children, it is important to consider developmental changes in N2 amplitudes and self-regulatory processes. On average, no-go N2 amplitudes decrease and self-regulation abilities increase with age during childhood (Berger, 2011; Hoyniak, 2017). Thus, if inhibition is successful, smaller no-go N2 amplitudes may reflect more efficient and mature neural processing. Further, it is possible that children who remain less efficient in the neural processes required for inhibition have larger no-go N2 amplitudes than typically developing children. That is, older children with poorer inhibitory control skills via less efficient neural processing may have larger no-go N2 amplitudes. This may explain why some studies have found that smaller no-go N2 amplitudes (more efficient processing) are associated with better inhibitory control, whereas others have found that larger no-go N2 amplitudes (more advanced inhibitory capacity) are associated with better inhibitory control. More research is needed to clarify the nature of the association between no-go N2 amplitudes and inhibitory control in children.

Nevertheless, inhibitory control deficits are robustly associated with externalizing problems (Schoemaker et al., 2013). Inhibitory control deficits predict later externalizing problems in children (Kahle et al., 2018) and growth in externalizing behaviors across development (Perry et al., 2018).

Given that (a) the no-go N2 may reflect inhibitory control processes, (b) inhibitory control deficits are associated with externalizing behavior, and (c) no-go N2 amplitudes are associated with externalizing behavior, inhibitory control may be an intermediate cognitive phenotype that explains the relation between the N2 component and externalizing behavior. To date, no studies have examined whether inhibitory control processes may be a mechanism that accounts for the association between no-go N2 amplitudes and externalizing behavior problems in children. Identifying the cognitive processes underlying the association between no-go N2 amplitudes and externalizing behavior could help identify intervention targets that are more clinically practical for intervention than neural processes.

The Present Study

The aim of the present study is to identify neural and cognitive processes underlying externalizing problems in childhood, and to determine whether inhibitory control is a cognitive intermediate phenotype between the no-go N2 ERP and externalizing problems in childhood. In the RDoC framework, it is important to identify intermediate phenotypes that explain how neural processes relate to behavior. Consistent with this framework, we aimed to examine the same construct (i.e., cognitive control or disinhibition) across multiple units of analysis, including physiology, paradigms, and behavior. To do so, we examined whether inhibitory control concurrently mediated the association between N2 amplitudes on inhibition (i.e., no-go) trials and externalizing problems in 3–7-year-old children. We hypothesized that no-go N2 amplitudes would be positively associated with externalizing behavior, such that smaller, less negative no-go N2 amplitudes would be associated with greater externalizing problems, consistent with prior studies (Hoyniak & Petersen, 2019). Second, we hypothesized that no-go N2 amplitudes would be associated with inhibitory control, but we had no a priori hypothesis about the sign of the association given mixed findings. Third, we hypothesized that inhibitory control would be negatively associated with externalizing behavior, such that better inhibitory control would be associated with fewer externalizing problems, consistent with prior research (e.g., Buss et al., 2014; Kahle et al., 2018; Perry et al., 2018). Finally, we hypothesized that inhibitory control would partially mediate the association between no-go N2 amplitudes and externalizing behavior. Specifically, we hypothesized that smaller, less negative no-go N2 amplitudes would be associated with inhibitory control, whose deficits in turn would be associated with externalizing problems.

The N2 may also be related to broader executive function-related processes, of which inhibitory control is a component (Espinet et al., 2012). However, the present study focuses on brain activity in response to a particular trial condition (no-go trials) of a specific inhibitory control paradigm (i.e., go/no-go). ERPs assess neural processes at a particular timing and are thought to index particular cognitive processes. Thus, we sought to identify the cognitive process related to the no-go N2 component with as much precision as possible. Because prior research suggests that no-go N2 amplitudes may reflect inhibitory control processes, we focus on inhibitory control in this study. This approach aligns closely with the dimensional approach of the RDoC framework, in which researchers

are encouraged to relate biological processes to simpler, lower-order, narrower subdimensions of psychological constructs (Macedo et al., 2021), including the subconstruct of inhibitory control.

Method

Participants

A community sample of children ($N = 147$, $M_{age} = 4.81$ years, SD = 1.18 years, 74 girls), and their caregivers participated in an ongoing accelerated longitudinal study. Participants were recruited at four ages: 36 ($n = 40$), 45 ($n = 38$), 54 ($n = 32$), or 63 ($n = 37$) months. The full sample of children spanned 3 to 7.5 years of age. The inclusion criterion to be recruited for the study was that the child was one of the target ages (described above). Exclusion criteria were: the child's primary caregiver did not speak English, or the child did not have a permanent guardian, did not have normal or corrected-to-normal vision and hearing, or was not capable of communicating or following basic instructions in English. Participants were recruited in 2018–2023 from the greater Iowa City community via university listservs, databases acquired from the University of Iowa Hospital and Clinics, local daycares and preschools, community flyers, social media, snowball sampling, and by word of mouth. Reasons for participant ineligibility and a flowchart of the final sample are in Supplementary Fig. S1. Reasons for missingness and tests of systematic missingness are in Supplementary Appendix S1. The sample consisted of children, their primary caregiver, the primary caregiver's parenting partner (as applicable), and a teacher/secondary caregiver (e.g., nanny, babysitter, or someone else who knew the child well).

The sample of children was 66.7% Non-Hispanic White, 9.5% Hispanic or Latino, 6.8% Black or African American, 4.8% Asian, 6.1% multiracial, and 6.1% other race. For the consented primary caregivers ($n = 148$), and parenting partners ($n = 139$), 97% were biological parents, 1% were stepparents, 1% were adoptive parents, and less than 1% were grandparents or other caregivers. The level of educational attainment across primary caregivers and parenting partners was: 7.8% doctoral degree, 7.5% professional degree, 21.3% master's degree, 30.1% bachelor's degree, 11.3% associate degree, 14.4% some college, 5.6% high school graduate, 1.9% some high school (Grades 9–12, no degree). Additionally, among primary caregivers and parenting partners, 85.5% were married, 8.3% were single/never married, 3.4% were divorced, 1.5% were re-married, and 1.2% were separated.

Procedures

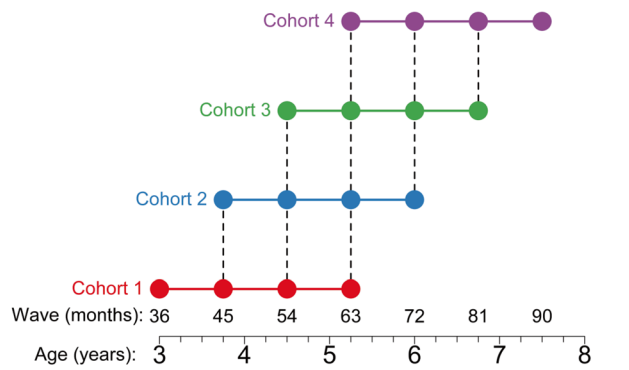
Children and their primary caregiver completed two lab visits, one week apart, every 9 months for four time points (see Fig. 1). During the first lab visit ($M_{minutes} = 152.51$, $SD = 20.80$ min), children completed behavioral tasks, including inhibitory control tasks, while the primary caregiver completed questionnaires, including ratings of their child's inhibitory control and externalizing problems. Parenting partners and secondary caregivers rated the child's externalizing problems via online questionnaires. During the second lab visit ($M_{minutes} = 89.75$, $SD = 18.83$ min), children completed several tasks, including a computerized go/no-go task while electroencephalography (EEG) was recorded. Video examples of procedures are available on Databrary (https://nyu.databrary.org/volume/1559).

Measures

The present study is part of a larger study, the School Readiness Study. Measures and hypotheses for the School Readiness Study were preregistered: https://osf.io/jzxb8. Data files, a data dictionary, analysis scripts, and a computational notebook for the present study are published online: https://osf.io/e2nkr. Descriptive statistics and bivariate correlations for all study variables are in Table 1. Estimates of reliability (inter-rater, internal consistency, cross-time stability) for study measures are in Supplementary Table S3.

Inhibitory Control

Thirteen measures, including questionnaires and laboratory tasks, were used to assess inhibitory control. Laboratory



Note. Accelerated longitudinal research design with four cohorts. The longitudinal design follows any given child for 2¼ years, with testing every nine months; the whole data set spans the ages of 3–7½ years. Circles reflect measurement points (four waves) for each cohort. Dashed lines indicate common measurement points across cohorts.

Fig. 1 Accelerated Longitudinal Research Design

Table 1 Correlations among Predictors, Outcomes, and Covariates

Variable	Age	Sex	SES	N2	IC	EXT
Age	—					
Sex	0.07	—				
SES	0.15**	-0.03	—			
N2	-0.16*	-0.11	0.03	—		
IC	0.60****	0.23****	0.25****	-0.23****	—	
EXT	-0.45****	-0.11**	-0.16****	0.17****	-0.38****	—
Obs	336	590	586	158	307	647
M	4.81	0.50	-0.10	-3.16	0.81	0.46
SD	1.18	0.50	0.80	6.10	0.67	15.70
Min	2.92	0.00	-3.38	-24.26	-0.65	-61.05
Max	7.80	1.00	3.47	15.24	2.63	43.77

Age is in years. Sex is coded such that 1 = female and 0 = male. Given the strong, cross-time rank-order stability of SES ($r = 0.90$, $p < .001$), we interpolated missing SES values at a given time point by carrying a participant's last observation forward. Sex values at later time points were interpolated by carrying a participant's last observation forward. That is, values for sex and SES were included in the data even when the child had not yet come in for a visit, which explains the larger number of observations of sex and SES compared to age, N2 amplitudes, and inhibitory control in the data used for analysis. 69% of children had available N2 data at one or more timepoints. Much of the greater missingness in the N2 amplitudes relative to questionnaire ratings of inhibitory control was due to COVID (see Supplementary Appendix S1). Correlations and descriptive statistics are presented using the data structured in long form. Correlations and descriptive statistics for all variables, except for externalizing problems, have one observation per participant at a given time point in the study (up to four timepoints). Correlations and descriptive statistics of externalizing problems included observations from up to three raters (i.e., primary caregiver, parenting partner, and secondary caregiver) at a given time point for a given participant (up to four time points), which explains the larger number of observations than the other variables

SES socioeconomic status, *N2* N2 amplitudes for correct no-go trials, *IC* Inhibitory control, *EXT* Externalizing problems, *Obs* number of observations for a given variable, *Min* minimum observed value, *Max* maximum observed value

*$p < 0.10$; **$p < 0.05$; ***$p < 0.005$; ****$p \leq 0.001$, all ps are two-tailed

tasks included: Bear/Dragon, Day/Night, Grass/Snow, Hand Game, Knock/Tap, Less is More, Peg Tapping, Shape Stroop, and Simon Says. Computerized inhibitory control tasks included: Fish/Sharks and Stop-Signal. Additionally, caregivers reported on their child's inhibitory control using the Behavioral Rating of Executive Function (BRIEF) and Children's Behavior Questionnaire (CBQ). Detailed descriptions of each measure are in Supplementary Appendix S2.

For developmental scaling, scores of each measure of externalizing problems and inhibitory control were converted to proportion of maximum (POM) scores to have the same possible range (0–1), with higher scores reflecting greater externalizing problems and inhibitory control, respectively. Proportion scores are widely recommended by longitudinal researchers for studying growth with different measures (Little, 2013; Moeller, 2015). For measures that had a minimum and maximum possible score, the POM score reflected the proportion of the maximum possible score. For measures that did not have a minimum or maximum possible score (i.e., Stop-Signal task), the POM score reflected the proportion of the maximum *observed* score. POM scores were calculated as: $\frac{\text{score}-\text{minimum}}{\text{maximum}-\text{minimum}}$, where minimum and maximum were the minimum and maximum possible or observed score. Tasks (Stop-Signal Task) and questionnaires (BRIEF) were adapted to accommodate the developmental capacity of the child and the changing expression of inhibitory control with age.

Bear/Dragon Bear/Dragon (Kochanska et al., 1996) is a go/no-go task. The child was asked to follow instructions from a bear puppet, and to ignore instructions from a dragon puppet, and then rules were reversed. There were 12 trials. Each no-go trial was scored from 1 to 4 (1 = full commanded movement, 2 = partial movement, 3 = wrong movement, and 4 = no movement). Scoring was reversed for go trials, consistent with Carlson and Moses (2001). Consistent with Eisenberg et al. (2013), a composite of children's inhibition was computed by multiplying mean scores from six inhibition (no-go) and six activation (go) trials; children who activated a behavior on go trials and inhibited on no-go trials received the highest scores, whereas children who never activated (or always activated) a behavior received low scores.

Day/Night In Day/Night (Gerstadt et al., 1994), the child was instructed to say "day" when they saw the card with the black moon and say "night" when they saw the card with the yellow sun. Sixteen test trials were scored incorrect (0), initially incorrect, but changed to correct (1), or correct (2). Scores were averaged across trials (0–2).

Fish/Sharks Fish/Sharks (Wiebe et al., 2012) is a go/no-go task and was administered on a computer using E-Prime software (version 2.0.10.356; Schneider et al., 2012). The child was shown cartoon images of fish (go stimuli) and sharks (no-go stimuli) on a touch screen and was instructed to touch the fish and not to touch the sharks. A composite of children's inhibition was computed by multiplying the proportion of correct inhibition (no-go) trials (20 trials) by the proportion of correct activation (go) trials (60 trials), consistent with Eisenberg et al. (2013).

Grass/Snow In Grass/Snow (Carlson & Moses, 2001), the child was instructed to touch a white square when they heard the word "grass" and a green square when they heard the word "snow." Twelve test trials were scored either correct (1) or incorrect (0), consistent with Carlson and Moses (2001). Final scores were averaged across trials (0–1).

Hand Game In Hand Game (Luria et al., 1964), the child was instructed to point a finger when the experimenter made a fist, and to make a fist when the experimenter pointed a finger. Fifteen test trials were scored incorrect (0), initially incorrect, but changed to correct (1), or correct (2), consistent with Kochanska et al.'s (1997) scoring of other inhibitory tasks. Scores were averaged across all trials (0–2).

Knock/Tap In Knock/Tap (Klenberg et al., 2001), the child was instructed to knock on the table when the experimenter tapped, and to tap the table whenever the experimenter knocked. In the second part of the task, the instructions changed. The child was instructed to make a side fist when the experimenter knocked, to knock when the experimenter made a side fist, and to do nothing when the experimenter tapped the table. Fifteen test trials were scored incorrect (0), initially incorrect, but changed to correct (1), or correct (2), consistent with Kochanska et al.'s (1997) scoring of other inhibitory tasks. Scores were averaged across trials (0–2).

Less is More Less is More is a motivationally salient symbolic representation task that assesses affective ("hot") inhibitory control (Carlson et al., 2005). The child chose a preferred treat from two options, white marshmallows and uniformly colored jellybeans. In front of the child were two bowls, one of which had a "naughty monkey" puppet, and the other bowl was the child's bowl. The child was told that "the monkey wants all the treats for himself." On each trial, two bags were presented to the child: one bag with five treats and one bag with two treats. The child was instructed to point to a bag among the two bag options presented and that the bag they point to goes to the monkey's bowl, and that the child receives the other bag (i.e., the bag they did not point to). Responses were scored as: 0 = child points to large treats bag; 1 = child initially points to the large treats bag, then changes to the small treats bag; 2 = child points to the small treats bag, consistent with Kochanska et al.'s (1997) scoring of other inhibitory tasks. Scores were averaged across 16 test trials (0–2).

Peg Tapping In Peg Tapping (Luria et al., 1964), the child observed sequences of a specific number of pencil taps on a table (either one or two) and was instructed to tap a pencil the opposite number of times of what they observed. For example, if the experimenter taps the pencil once, the child is to tap the pencil twice and vice versa. Sixteen trials were scored correct (1) or incorrect (0). Scores were averaged across trials (0–1).

Shape Stroop Shape Stroop (Kochanska et al., 2000) assesses children's perceptual inhibitory control. The task assessed the child's ability to identify a picture of a small fruit embedded within a picture of a different, larger fruit. Six test trials were scored from 0 to 2 (0 = incorrect, 1 = initially incorrect, but changed response to correct, 2 = correct). Scores were averaged across the three small fruit trials (0–2).

Simon Says In Simon Says (Strommen, 1973), the child was instructed to perform simple motor actions (e.g., clap your hands, stomp your feet) and was told to perform the action only if the instructions are preceded by the phrase "Simon Says." Each no-go trial was scored from 1 to 4 (1 = full commanded movement, 2 = partial movement, 3 = wrong movement, and 4 = no movement), consistent with Carlson and Moses (2001) scoring of a simplified version of Simon Says (Bear/Dragon); scoring was reversed for go trials. A composite score was computed by multiplying mean scores from 10 go trials and 10 no-go trials (20 trials total), consistent with Eisenberg et al. (2013).

Stop-signal Task In a stop-signal task adapted from Berger et al. (2013), the child was told to give purple food to the purple pig and green food to the green goat by touching the animal on the screen. The child was then shown a cartoon wizard and told that the wizard will try to trick them and turn the food into a car. The child was instructed not to feed cars to animals and not to touch the screen when they saw a car. Blocks two and three had the same structure, with different animals. The latency of stop signal after go stimulus onset (i.e., stop-signal delay [SSD]) was manipulated based on the child's performance to obtain as close to a 50% error

rate as possible on stop trials, which helped normalize task difficulty across ages. Stimuli were presented via E-Prime software (Schneider et al., 2012). Response inhibition was operationalized as the stop-signal reaction time (SSRT). The SSRT was calculated as the median reaction time on correct go trials minus the mean SSD from Blocks 2 and 3. Block 1 was not included in the calculation to allow the algorithm time to converge upon a 50% error rate on stop trials. Cases were excluded if the SSRT was negative (i.e., the median go reaction time was faster than the mean SSD). Scores were reverse scored so that higher scores reflected greater inhibitory control.

Behavior Rating Inventory of Executive Function (BRIEF) The BRIEF assesses children's executive functioning within the context of their everyday environment. Two versions were used based on the child's age. Parents completed the BRIEF–Preschool Version (BRIEF–P; Gioia et al., 1996) if the child was 3–5 years old or the BRIEF–2 (Gioia et al., 2015) if the child was 6–7 years old. Scores on the Inhibitory Control subscale were used for both versions of the questionnaire. Twenty-four items were rated on a 3-point scale (1 = never, 2 = sometimes, 3 = often) in terms of how often, in the last six months, the child's behavior had been a problem. To account for missing responses in the sum score, scores were averaged across items and then multiplied by the number of items. Scores were reverse scored so that higher scores reflected greater inhibitory control. Mothers' and fathers' ratings on the Inhibitory Control Composite were correlated ($r[152] = 0.38$, $p < 0.001$).

Children's Behavior Questionnaire (CBQ) The CBQ assesses children's temperament (i.e., reactivity and regulation). Parents completed the CBQ (Putnam & Rothbart, 2006). Secondary caregivers completed the CBQ–Teacher Short Form (CBQ–TSF, Teglasi et al., 2015). Scores from the Inhibitory Control scale (CBQ: 47 items; CBQ–TSF: 26 items) were used. Items were rated on a 7-point Likert scale (1 = extremely untrue, 7 = extremely true). Scores were averaged across items. Mothers' ratings on the Inhibitory Control scale were associated with ratings by fathers ($r[164] = 0.46$, $p < 0.001$) and secondary caregivers ($r[165] = 0.31$, $p < 0.001$). Fathers' ratings were associated with ratings by secondary caregivers ($r[112] = 0.35$, $p < 0.001$).

Externalizing Problems

Achenbach System of Empirically Based Assessment The Achenbach System of Empirically Based Assessment (ASEBA) assesses children's emotional and behavioral problems. Items were rated on a 3-point Likert scale according to how well the item described the child (0 = not true, 1 = somewhat or sometimes true, 2 = very true). Multiple versions were used based on the child's age and rater type. Parents completed the Child Behavior Checklist 1.5–5 (CBCL 1.5–5; Achenbach & Rescorla, 2000) if the child was 3–5 years old or the Child Behavior Checklist 6–18 (CBCL 6–18; Achenbach & Rescorla, 2001) if the child was 6–7 years old. Secondary caregivers completed the Caregiver–Teacher Report Form (C–TRF; Achenbach & Rescorla, 2001) if the child was 3–5 years old or the Teacher's Report Form (TRF; Achenbach & Rescorla, 2001) if the child was 6–7 years old. Scores on the Externalizing scale were used. Mothers' ratings on the Externalizing scale were associated with ratings by fathers ($r[178] = 0.56$, $p < 0.001$) and secondary caregivers ($r[174] = 0.46$, $p < 0.001$). Fathers' ratings were associated with ratings by secondary caregivers ($r[123] = 0.44$, $p < 0.001$). Age and sex norm-referenced T-scores had a mean of 46.35 ($SD = 9.73$). Using T-scores of 65 or greater as a clinical cutoff, ~ 2.4% of ratings in the study were in the at-risk or clinical range on the Externalizing scale; ~ 6.8% of children were in the at-risk or clinical range at one or more timepoints based on ratings from one or more raters.

Covariates

We examined models with and without covariates. Covariates included the child's age, sex, and family socioeconomic status (SES). Socioeconomic status was calculated as the average of three z-scored (relative to the sample) indices: income-to-needs ratio, parent educational attainment, and parent occupational prestige. Given the strong, cross-time rank-order stability of SES ($r = 0.90$, $p < 0.001$), we interpolated missing SES values at a given time point by carrying a participants last observation forward. A full description of covariates is in Supplementary Appendix S3.

Electrophysiological Recordings and Data Processing

Electrophysiological data were collected using an Electrical Geodesic, Inc (EGI) 128-electrode Hydrocel Geodesic Sensor Net with a Net Amps 400 series amplifier. Net Station Acquisition Software 5.4.2 (Electrical Geodesics Inc., 2018) was used to collect the continuous EEG data. EEG data were collected during a go/no-go task (i.e., Fish/Sharks), which was administered using E-Prime 2.0.10.356 (Schneider et al., 2012). A detailed description of the collection and pre-processing of the EEG data is in Supplementary Appendix S4.

Data were pre-processed in Net Station Tools 5.4.3 (Electrical Geodesics Inc., 2018). Continuous data were band-pass filtered from 0.1 to 30.0 Hz. Correct go and correct no-go trials were selected and segmented into 1200 ms epochs that began 200 ms prior to the presentation of each stimulus. Epochs were then automatically inspected for artifacts, which included identifying and removing "bad" channels. Epochs were marked bad if they contained more than

20 bad channels, an eye blink, or an eye movement. Channels were marked bad across all epochs if 20% or greater of the epochs were marked bad. Channels marked bad across all epochs were removed. Removed channels were interpolated based on the waveforms of surrounding electrodes. If a child did not have at least 10, artifact-free trials in each condition after automatic processing, epochs were manually examined for artifacts. After manually identifying and removing artifacts and bad channels, epochs were subjected to the same automatic inspection procedure described above. Epochs were then averaged within participants, and re-referenced to an average reference (i.e., the average of all scalp electrodes). Finally, epochs were baseline corrected by subtracting the average activity from each epoch's 200 ms baseline.

Data were excluded from analyses if the child did not have at least 8 correct, artifact-free trials in each condition after manual processing, consistent with prior studies with children (e.g., Hoyniak et al., 2018). Data were also excluded if the child refused to wear the EEG net, refused to complete the task (i.e., Fish/Sharks), or if there were technical errors during the EEG collection. A total of 102 children (69% of the full sample of children [$N = 147$]), had available EEG data. EEG data were more likely to be missing for children with poorer inhibitory control and for children from lower SES families. EEG data were not missing as a function of age, sex, ethnicity, or externalizing problems.

Following pre-processing, we conducted temporospatial principal component analysis (tsPCA) to decompose the EEG waveform. All PCA analyses were conducted using the ERP PCA Toolkit (version 2.98, Dien, 2010). We performed tsPCA separately for each condition (i.e., go versus no-go trials), consistent with prior research which found that a combined PCA (i.e., including both trial types in one PCA) misallocated substantial variance (Barry et al., 2018). For sensitivity analyses, we also performed tsPCA separately for two age groups across conditions, consistent with Scharf et al. (2022). PCAs were conducted for younger (36–54 months, $n = 81$ observations) and older children (63–90 months, $n = 77$ observations). However, the no-go N2 amplitudes from the age-combined versus age-separated PCA were strongly correlated ($r[472] = 0.64$, $p < 0.001$). Thus, we used the N2 amplitudes from the age-combined PCA to help ensure that we extracted the same ERP component across ages. A description of the tsPCA analyses and results is in Supplementary Appendix S5.

The grand averaged waveform is depicted in Supplementary Fig. S2. The temporospatial component, thought to correspond with the N2 component, was selected based on a priori hypotheses about the latency (typically 300–500 ms post stimulus onset), topography, and morphology of the component. The selected N2 component was characterized by a frontocentral negativity (see Supplementary Fig. S3) that peaked at 427 ms in the go condition, and 466 ms in the no-go condition. N2 amplitudes on inhibition (i.e., no-go) trials were extracted and used in analyses. Amplitudes were extracted from a cluster of electrodes whose loading on the N2 temporospatial component was 0.5 or greater (see Supplementary Fig. S3) at the peak latency (i.e., 466 ms; Scharf et al., 2022). The N2 tsPCA component waveform is depicted in Supplementary Fig. S4.

Statistical Analysis

Exploratory Factor Analysis

We first examined whether inhibitory control measures' scores were able to be modeled with item response modeling by examining their scores in exploratory factor analysis (EFA). Results of the EFA models supported item response modeling; see Supplementary Appendix S6.

Developmental Scaling Approach

We used developmental scaling to link scores from the different measures across ages onto the same scale (Hosch et al., 2022). In this way, we could estimate meaningful individual differences in inhibitory control and externalizing problems from age-differing measures across 3–7 years of age. To perform developmental scaling, we used a two-parameter Bayesian longitudinal item response model in a mixed modeling item response theory (IRT) framework. Details of the developmental scaling approach are in Supplementary Appendix S7.

Mediation Models

Mediation models were fit in a structural equation modeling (SEM) framework. First, we fit separate models to estimate unadjusted associations (i.e., not controlling for covariates) of N2 amplitudes with inhibitory control and externalizing problems. Second, we estimated concurrent mediation models (i.e., analyses of indirect effects of concurrent associations) that included all three variables. We fit SEM models using the sem() function of the lavaan 0.6–16 package (Rosseel, 2012) in R 4.2.0 (Team, 2022). SEM models were fit with FIML estimation, which uses all available data and is the gold standard approach for handling missingness when data are missing at random or completely at random (Enders & Bandalos, 2001). Models were fit with a robust maximum likelihood estimator that provides robust standard errors to account for nonnormally distributed data. Following recommendations, the indirect effect was estimated with bias-corrected bootstrapped confidence intervals (Hayes, 2009; Shrout & Bolger, 2002). Confidence intervals were estimated from 10,000 bootstrap samples. Models were saturated—i.e., there were no degrees of freedom because only manifest

variables were included. Thus, fit indices indicated perfect model fit. Given the range of ages included in the study, we included the child's age as a covariate. To account for the nonindependence of data owing to multiple observations from the same participant, we also conducted a Bayesian multilevel mediation analysis with random intercepts for each child.

The effect size of the indirect effect was calculated with three estimates: (1) the standardized regression coefficient (beta, β) of the indirect effect, (2) the proportion of the effect that was mediated (P_M), which is the ratio of the indirect effect to the total effect (Wen & Fan, 2015), and (3) the proportion of variance in externalizing problems that was accounted for jointly by N2 amplitudes and inhibitory control (upsilon, υ; Lachowicz et al., 2018). Upsilon was estimated using the upsilon() function of the MBESS 4.9.2 package (Kelley, 2007) in R.

Data Structure

To leverage all time points of data for all participants for greater power, we stacked the data in long form for the structural equation models, so that each combination of participant, timepoint, and rater uniquely identified each row. Participants could have observations from up to three raters (i.e., primary caregiver, parenting partner, and/or secondary caregiver) and up to four time points (i.e., waves). Thus, each participant could have up to 12 rows of observations. When transforming the data from wide to long format, N2 and inhibitory control scores were unique for each combination of participant and timepoint and were thus applied to all rows of a given timepoint (i.e., wave) for that participant. Externalizing problem scores were unique for each combination of participant, timepoint, and rater. The structure of the data is depicted in Supplementary Table S6. Given modest cross-informant associations of externalizing problems, the long form data structure allowed us to make use of all raters' perspectives and all available information without losing information by averaging or aggregating across raters.

Sensitivity Analyses

We conducted several sensitivity analyses to (1) include cluster-robust standard errors, (2) account for additional covariates, (3) examine moderated mediation by sex, (4) examine models using latent variables of inhibitory control estimated by performance-based tasks and questionnaires separately, (5) examine the specificity of the N2 component, and (6) examine whether results changed when using N2 amplitudes extracted from different electrodes.

Results

N2 Amplitudes and Externalizing Problems

As expected, N2 amplitudes were positively associated with externalizing problems (β = 0.17, $p < 0.018$) in an unadjusted model, such that smaller (less negative) N2 amplitudes were associated with greater externalizing problems. This association was somewhat attenuated and only marginally significant after controlling for the child's age (β = 0.10, $p = 0.071$). Externalizing problems decreased with age (β = 0.042, $p < 0.001$).

N2 Amplitudes and Inhibitory Control

N2 amplitudes were negatively associated with inhibitory control in an unadjusted model (β = -0.25, $p < 0.001$), such that larger (more negative) N2 amplitudes were associated with better inhibitory control. This association held controlling for the child's age (β = -0.17, $p = 0.021$). Inhibitory control increased with age (β = 0.57, $p < 0.001$).

Inhibitory Control and Externalizing Problems

Consistent with hypotheses, inhibitory control was negatively associated with externalizing problems in an unadjusted model (β = -0.38, $p < 0.001$). That is, poorer inhibitory control was associated with greater externalizing problems. The association held controlling for the child's age (β = -0.17, $p = 0.006$).

Mediation Models

Without Covariates

First, we examined the indirect effect of N2 amplitudes on externalizing problems via inhibitory control without controlling for covariates. There was a significant total effect (β = 0.17, 95% CI [0.17, 0.66], $p = 0.001$). After accounting for inhibitory control, the direct effect of N2 amplitudes on externalizing problems was nonsignificant (β = 0.08, 95% CI [-0.05, 0.43], $p = 0.122$). Moreover, we observed an indirect effect of inhibitory control (β = 0.09, 95% Cl [0.14, 0.33], $p < 0.001$), which accounted for approximately 54% ($P_M = 0.536$) of the variance in the association between the N2 amplitudes and externalizing problems. The upsilon value estimate of the effect size of the indirect effect was $u_{adj} = 0.00752$.

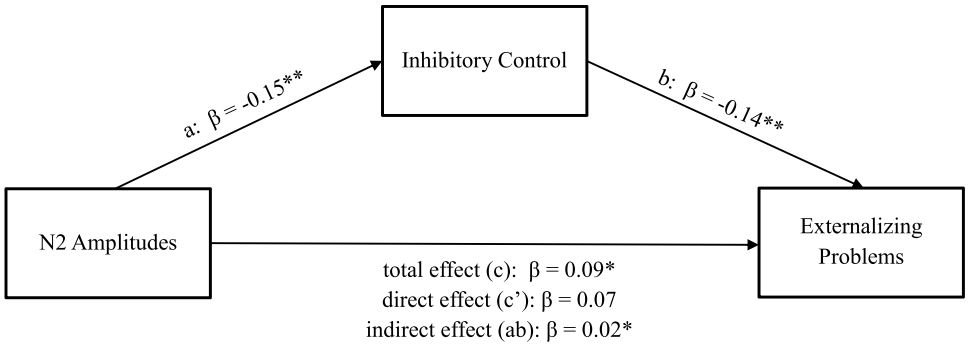


Fig. 2 Mediation Model with Covariates

Note. Mediation model controlling for child's age, sex, and family SES. * $p < .05$. ** $p < .01$.

With Covariates

After controlling for the child's age and sex, there remained a significant total effect (β = 0.09, 95% CI [0.002, 0.46], $p = 0.049$). The direct effect of N2 amplitudes on externalizing problems accounting for inhibitory control was not significant after controlling for covariates (β = 0.07, 95% CI [-0.06, 0.41], $p = 0.149$). There was a significant indirect effect of inhibitory control (β = 0.02, 95% Cl [0.02, 0.11], $p = 0.031$), which accounted for approximately 23% ($P_M = 0.229$) of the variance in the association between the N2 amplitudes and externalizing problems after controlling for covariates. The mediation model is depicted in Fig. 2. The regression coefficients for the mediation models (i.e., with and without covariates) are in Table 2.

Bayesian Multilevel Mediation Model

Without Covariates To account for the nonindependence of data owing to multiple observations from the same participant, we conducted an additional Bayesian multilevel mediation analysis with random intercepts for each child. Results were largely the same. N2 amplitudes remained associated with externalizing problems (i.e., total effect; $B = 0.48$, 95% ETI [0.20, 0.76]). After accounting for inhibitory control, the association between the N2 and externalizing problems was significant (i.e., direct effect; $B = 0.33$, 95% ETI [0.03, 0.64]). Additionally, there was a significant indirect effect of inhibitory control ($B = 0.14$, 95% ETI [0.01, 0.30]), which accounted for approximately 29% ($P_M = 0.288$) of the variance in the association between the N2 amplitudes and externalizing problems.

Table 2 Regression Coefficients for the Mediation Models

Pathway	*B*	β	SE	*p*	95% CI
Model without Covariates					
N2 → IC	-0.02	-0.23	0.004	< 0.001	[-0.03, -0.02]
IC → EXT	-9.22	-0.38	1.33	< 0.001	[-11.85, -6.62]
N2 → EXT (direct effect)	0.19	0.08	0.12	0.122	[-0.05, 0.43]
N2 → EXT (total effect)	0.41	0.17	0.13	0.001	[0.17, 0.66]
indirect effect	0.15	0.09	0.05	< 0.001	[0.14, 0.33]
Model with Covariates					
Age → N2	-0.73	-0.14	0.27	0.007	[-1.24, -0.19]
Age → IC	0.32	0.57	0.02	< 0.001	[0.29, 0.36]
Age → EXT	-4.53	-0.34	0.60	< 0.001	[-5.71, -3.34]
Sex → N2	-1.21	-0.10	0.55	0.029	[-2.32, -0.13]
Sex → IC	0.23	0.17	0.03	< 0.001	[0.16, 0.30]
Sex → EXT	-1.03	-0.03	1.16	0.376	[-3.26, 1.28]
N2 → IC	-0.02	-0.15	0.004	< 0.001	[-0.02, -0.01]
IC → EXT	-3.27	-0.14	1.15	0.005	[-5.57, -1.07]
N2 → EXT (direct effect)	0.17	0.07	0.12	0.149	[-0.06, 0.41]
N2 → EXT (total effect)	0.23	0.09	0.12	0.049	[0.002, 0.46]
indirect effect	0.05	0.02	0.02	0.031	[0.02, 0.11]

Age is in years. Sex is coded such that 1 = female and 0 = male. The models with and without covariates were fit separately

N2 N2 amplitudes for correct no-go trials, *IC* Inhibitory Control, *EXT* Externalizing problems, *CI* Confidence Interval

With Covariates After controlling for the child's age and sex, the total effect was no longer significant ($B = 0.24$, 95% ETI [-0.03, 0.52]). The direct effect of N2 amplitudes on externalizing problems accounting for inhibitory control remained significant after controlling for covariates ($B = 0.31$, 95% ETI [0.03, 0.59]). Additionally, the indirect effect was somewhat attenuated and was significant at a trend level after accounting for covariates ($B = -0.07$, 95% ETI [-0.16, 0.001]). Unexpectedly, inhibitory control scores were *positively* associated with externalizing problems in the mediation model (despite having a negative bivariate association: $r = -0.38$). It appears that the unexpected sign of the association between inhibitory control and externalizing problems was likely due to controlling for a variable (age) that was strongly associated with both (age and inhibitory control: $r = 0.60$; age and externalizing problems: $r = -0.45$). After removing age as a covariate, inhibitory control was negatively associated with externalizing problems, as expected. The indirect effect held ($B = 0.14$, 95% ETI [0.001, 0.289]), and it accounted for approximately 28% ($P_M = 0.284$) of the variance in the association between the N2 amplitudes and externalizing problems.

Sensitivity Analyses

We conducted several sensitivity analyses, as described in Supplementary Appendix S8. Notably, results did not substantially differ when controlling for additional covariates, examining questionnaire- and task-based measures of inhibitory control separately, or when extracting N2 amplitudes from Fz or the peak negative channel. Indirect effects were specific to the timing of the N2 but were not specific to the frontocentral region; similar effects were observed with a positive-going waveform that was likely a dipole of the N2 and was centrally distributed. The child's sex did not moderate the indirect effect.

Power Analysis

We conducted a post-hoc power analysis to estimate the statistical power of detecting an indirect effect given our sample size and observed effect sizes (see Supplementary Appendix S9). We had power of 0.83 to detect significance in the observed indirect effect.

Discussion

The current study integrated information across physiological (i.e., the N2 ERP) and cognitive (i.e., inhibitory control) units of analysis to inform our understanding of externalizing behavior problems in early childhood. Previous research has shown that smaller N2 amplitudes may be an early neural biomarker of externalizing behavior problems in children (Hoyniak & Petersen, 2019). However, is it unclear *how* N2 amplitudes relate to externalizing problems. Cognitive intermediate phenotypes in the association between neural substrates (e.g., the N2 component) and externalizing behavior may provide more practical targets for intervention than neural substrates. Furthermore, the RDoC framework encourages researchers to examine the same construct (i.e., common process) across multiple units of analysis. Consistent with this framework, a potential cognitive intermediate phenotype between N2 amplitudes and externalizing behavior is inhibitory control. Research supports the interpretation of the N2 component as an index of inhibitory control when examined using go/no-go tasks (Jodo & Kayama, 1992), particularly in children (Hoyniak, 2017; Hoyniak & Petersen, 2019). Moreover, deficits in inhibitory control have been widely associated with externalizing problems (Buss et al., 2014; Kahle et al., 2018; Perry et al., 2018). Thus, we investigated whether the RDoC subconstruct inhibitory control concurrently mediated the association between physiological processes (i.e., the N2 ERP) and disinhibited behavior (i.e., externalizing problems). That is, we aimed to examine the same construct—cognitive control or disinhibition—across several units of analysis, including physiology, behavior, and paradigms, consistent with the RDoC framework.

We examined these associations in a community sample of young children (ages 3–7). A community sample is relevant because externalizing problems are considered a dimensional spectrum (Markon et al., 2011). Examining basic processes that underlie dimensional differences in externalizing problems is consistent with aims of the RDoC framework, which uses dimensional conceptualizations of psychopathology and encourages researchers to examine typical and atypical behavioral development. It also aligns with other emerging nosologies, such as the Hierarchical Taxonomy of Psychopathology (HiTOP; Kotov et al., 2017).

As expected, we found a positive association between the N2 component and externalizing behavior. This finding replicates prior meta-analytic work, which has found that smaller, less negative N2 amplitudes are associated with more externalizing behavior problems in children (Hoyniak & Petersen, 2019). N2 amplitudes were negatively associated with inhibitory control, such that smaller N2 amplitudes were associated with poorer inhibitory control. We also observed negative associations between inhibitory control and externalizing behavior. This is consistent with prior literature, which has found that poorer inhibitory control skills predicted greater externalizing problems (Buss et al., 2014; Kahle et al., 2018; Olson et al., 2005; Perry et al., 2018). Moreover, we found an indirect effect of N2 amplitudes on externalizing problems via inhibitory control. That is,

inhibitory control—including questionnaire and task-based operationalizations—partially mediated the association between N2 amplitudes and externalizing problems. Moderation models demonstrated that the indirect effect did not differ for boys and girls, suggesting that the mediation process operated similarly for boys and girls. Interestingly, the indirect effect showed some specificity to the timing of the N2 but not specificity to the frontocentral region; similar effects were observed with a likely positive-going dipole of the N2 that was centrally distributed.

Implications

This is among the first studies to identify associations between N2 amplitudes, inhibitory control, and externalizing problems during early childhood. Findings provide additional evidence for N2 amplitudes as an early neural indicator of externalizing psychopathology, consistent with prior research (Hoyniak & Petersen, 2019). Notably, however, the magnitude of the association between N2 amplitudes and externalizing behavior (i.e., the total effect) was small ($\beta s = 0.09 - 0.17$). Thus, it may be important to consider additional neural risk processes for externalizing problems. For instance, work in adults has shown that the P3 ERP may better capture processes related to response inhibition when using a stop-signal paradigm (Wessel & Aron, 2015). There are likely other neural processes, e.g., the error-related negativity (ERN) ERP, that contribute to the development of externalizing problems (Lutz et al., 2021).

We also found that larger N2 amplitudes were associated with better inhibitory control. This is consistent with some previous research (Grabell et al., 2017; Ruberry et al., 2017), but inconsistent with other studies, including a prior meta-analysis (Hoyniak & Petersen, 2019). It is possible that age-related differences in the N2 could explain why larger N2 amplitudes are associated with better inhibitory control in some children but not others. However, there are inconsistencies between studies examining children of similar ages. Studies with similar age ranges (i.e., ages 3–5) have found that both larger (e.g., Grabell et al., 2017; Ruberry et al., 2017) and smaller (e.g., Buss et al., 2011; Espinet et al., 2012) N2 amplitudes are associated with better inhibitory control. Thus, there may be reasons other than age for the inconsistent findings. It is possible that the relation between N2 amplitudes and inhibitory control is non-linear, in which extreme variation in either direction (i.e., small or large N2 amplitudes) may confer risk for inhibitory control deficits. Speculatively, excessively small N2 amplitudes may reflect the insufficient recruitment of neural resources that are necessary for inhibition. By contrast, excessively large N2 amplitudes may reflect over-recruitment of neural resources, reflecting inefficient processing. Ultimately, more research is needed to clarify the nature of the association between N2 amplitudes and inhibitory control in children.

Results from the present study suggest that inhibitory control may be a cognitive intermediate phenotype between N2 amplitudes and externalizing problems. Inhibitory control deficits may capture early neural risk processes for externalizing psychopathology. Moreover, these findings suggest that inhibitory control may be a key target for early intervention in the development of externalizing problems. Thus, interventions targeting inhibitory control skills, or self-regulation, may be useful for the prevention of later externalizing problems. Studies suggest that curriculum-based interventions, such as Tools of the Mind or Red Light, Purple Light, may be effective and practical interventions to improve self-regulation in children (Diamond et al., 2019; McClelland et al., 2019; Pandey et al., 2018). Notably, inhibitory control accounted for approximately 23–28% of the variance in the association between N2 amplitudes and externalizing problems. Thus, it is important to consider additional cognitive processes through which neural processes such as the N2 ERP may lead to externalizing problems. Future research should examine additional cognitive processes, such as conflict monitoring or attention processes, that may also help explain the association between N2 amplitudes and externalizing psychopathology (Enriquez-Geppert et al., 2010; Folstein & Van Petten, 2008; Smith et al., 2010).

Strengths

The study had several strengths. First, the predictor (i.e., N2 amplitudes), mediator (i.e., inhibitory control), and outcome (i.e., externalizing problems) were assessed via distinct methods, which reduces the extent to which the indirect effect could be accounted for by method bias. Moreover, our assessment of inhibitory control included several measurement methods, including behavioral tasks and questionnaires to reduce the effects of common method variance. In addition, our latent variable of inhibitory control was estimated using several tasks beyond the task in which N2 amplitudes were extracted (i.e., Fish/Sharks), reducing potential measure-specific bias. Second, questionnaire data were collected from multiple informants, including mothers, fathers, and teachers or other caregivers to gain a more accurate estimate of children's real-world functioning and behavior across contexts. Third, we applied methods (i.e., developmental scaling) to maintain the developmental relevance of measures across a wide age range. We linked scores from age-differing measures onto the same scale, which allowed us to examine individual differences in inhibitory control and externalizing behavior across ages 3–7. Fourth, findings held across many sensitivity analyses, providing greater confidence in our inferences.

Finally, it is notable that we observed these associations in a community sample, in which externalizing behaviors were less prevalent compared to a clinical sample. It will be valuable for future work to replicate and extend these findings in clinical samples. We also make our data and analysis scripts freely available to promote dissemination.

Limitations

The study also had limitations. First, the study was correlational and examined concurrent associations. Thus, we cannot make causal inferences. Because of the ongoing nature of this study, we would currently be underpowered to examine lagged associations. Specifically, we were constrained by limited data available at time points three and four ($n = 51$), which would be needed for a fully longitudinal mediation model. Future research should examine the longitudinal relations between the N2 component, inhibitory control, and externalizing problems. Second, we had some missingness in ERP data, much of which was due to COVID. Nevertheless, the study had a larger sample of participants with ERP data ($n = 102$) than many studies of young children. Third, there were some differences in missingness as a function of demographic characteristics. N2 amplitudes were more likely to be missing for children with poorer inhibitory control and for children from lower SES families. Inhibitory control scores were more likely to be missing for children from lower SES families and for boys. Externalizing problems ratings were more likely to be missing for older children, for children from lower SES families, for boys, and for children of "other" race. Systematic missingness may limit the generalizability of our findings. However, effect sizes of systematic missingness were small, and findings did not substantially change after including the child's age, sex, and family SES as control variables in our models. Fourth, cross-informant associations of inhibitory control ($rs = 0.31 – 0.46$) and externalizing behavior ($rs = 0.44 – 0.56$) were modest. However, these associations are similar in magnitude to those observed in prior studies (Carneiro et al., 2021). Our modeling approaches estimated latent variables from the common variance of measures, which may miss context-specific behavior. Thus, it may be beneficial in future studies to examine these associations separately for parents and teachers.

Conclusion

Small N2 amplitudes are a commonly studied neural marker of externalizing behavior in children. However, the mechanisms that explain how the N2 is associated with externalizing problems are unclear. In the RDoC framework, it is important to identify intermediate phenotypes that explain how neural processes relate to behavior. Intermediate phenotypes (e.g., cognitive processes) may provide more practical targets for intervention. Thus, the current study examined whether inhibitory control mediated the association between N2 amplitudes and externalizing problems in young children. We found that smaller, less negative N2 amplitudes were related to externalizing problems, consistent with prior research (Hoyniak & Petersen, 2019). Smaller N2 amplitudes were also associated with poorer inhibitory control, which in turn was associated with externalizing behavior problems. That is, inhibitory control partially mediated the association between N2 amplitudes and externalizing problems. This study is the first to examine cognitive intermediate phenotypes of the association between neural processes and externalizing psychopathology in childhood. Findings suggest that inhibitory control deficits may be an early indicator of biological risk for externalizing psychopathology. Inhibitory control may be an important target for early intervention.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10802-023-01162-w.

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Data Availability The present study is part of a larger study, the School Readiness Study. Measures and hypotheses for the School Readiness Study were pre-registered: https://osf.io/jzxb8. Data files, a data dictionary, analysis scripts, and a computational notebook for the present study are published online: https://osf.io/e2nkr.

Compliance with Ethical Standards

Conflict of Interest We have no conflicts of interest to disclose.

Ethical Approval The present study was approved by the University of Iowa Institutional Review Board (Study #: 201708761).

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