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Top-down auditory attention modulates neural responses more strongly in neurotypical than ADHD young adults

Jasmine A. Kwasa^{a,b,*}, Abigail L. Noyce^a, Laura M. Torres^b, Benjamin N. Richardson^a, Barbara G. Shinn-Cunningham^a

^a Neuroscience Institute, Carnegie Mellon University, 5000 Forbes Ave., Pittsburgh, PA, 15213, United States

^b Department of Biomedical Engineering, Boston University, 1 Silber Way, Boston, MA, 02215, United States

Abstract

Human cognitive abilities naturally vary along a spectrum, even among those we call “neurotypical”. Individuals differ in their ability to selectively attend to goal-relevant auditory stimuli. We sought to characterize this variability in a cohort of people with diverse attentional functioning. We recruited both neurotypical (N = 20) and ADHD (N = 25) young adults, all with normal hearing. Participants listened to one of three concurrent, spatially separated speech streams and reported the order of the syllables in that stream while we recorded electroencephalography (EEG). We tested both the ability to sustain attentional focus on a single “Target” stream and the ability to monitor the Target but flexibly either ignore or switch attention to an unpredictable “Interrupter” stream from another direction that sometimes appeared. Although differences in both stimulus structure and task demands affected behavioral performance, ADHD status did not. In both groups, the Interrupter evoked larger neural responses when it was to be attended compared to when it was irrelevant, including for the P3a “reorienting” response previously described as involuntary. This attentional modulation was weaker in ADHD listeners, even though their behavioral performance was the same. Across the entire cohort, individual performance correlated with the degree of top-down modulation of neural responses. These results demonstrate that listeners differ in their ability to modulate neural representations of sound based on task goals, while suggesting that adults with ADHD may have weaker volitional control of attentional processes than their neurotypical counterparts.

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* Corresponding author at: 4825 Frew St, A52A Baker Hall, Pittsburgh, PA 15213, United States. jkwsa@andrew.cmu.edu (J.A. Kwasa).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

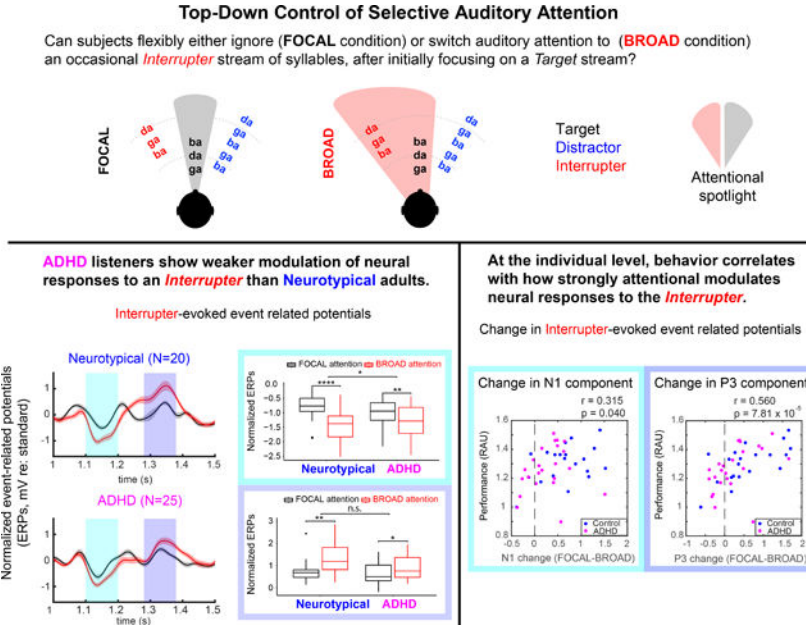
CRedit authorship contribution statement

Jasmine A.C. Kwasa: Conceptualization, Methodology, Software, Investigation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing, Project administration. **Abigail L. Noyce:** Writing – review & editing, Supervision. **Laura M. Torres:** Investigation. **Benjamin Richardson:** Formal analysis. **Barbara G. Shinn-Cunningham:** Methodology, Resources, Writing – review & editing, Funding acquisition, Supervision.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.brainres.2022.148144>.

Graphical Abstract



Keywords

Auditory Attention; Adult ADHD; EEG; N1; P3a

1. Introduction

Competing sounds, like a teacher's voice against the sudden trill of a cell phone, pose a challenge to attentional control. Listening in such environments depends upon a push-and-pull between goal-directed attention, allocated to a source (the teacher's voice), and automatic, involuntary shifts of attention to other salient, unexpected sounds (the ringing phone). The outcome of this attentional contest depends on the strength of an individual's "top-down" control of attention relative to their susceptibility to "bottom-up" attentional capture (Lavie, 2010; Pinto et al., 2013; Prior et al., 1985). In order to better understand cognitive control during auditory selective attention, we measured electrophysiological correlates of this push-and-pull dynamic in a neurodiverse population comprising neurotypical and Attention Deficit Hyperactivity Disorder (ADHD) subjects.

Top-down attention enhances neural responses to attended stimuli and suppresses those to ignored stimuli (Hillyard et al., 1973; Woldorff et al., 1993). Specifically, the magnitude of stimulus-elicited event-related potentials (ERPs) in electroencephalography (EEG) depends on attentional focus. The N1 response, a negative-going ERP component occurring approximately 100 ms after stimulus onset, is larger when listeners focus top-down attention on the evoking source and smaller when they focus attention elsewhere (Chait et al., 2010; Choi et al., 2013; Desimone & Duncan, 1995; Elhilali et al., 2009; Hillyard et al., 1998). The difference between the N1 magnitude in these two conditions, a metric of attentional modulation, yields a measure of top-down attentional control. Conversely,

bottom-up attentional orienting to new events depends largely on their salience, rather than a listener's goals. Salient events reliably elicit a family of positive ERP responses approximately 300 ms after stimulus onset called the *P3* or P300. This positive-going component response reflects attentional capture (Polich, 2007). The interplay between top-down focus and bottom-up salience ultimately determines what a listener truly "hears." Individual differences in cognitive functioning affect the ability to focus on goal-relevant stimuli and orient appropriately to new stimuli (Anderson et al., 2013; Choi et al., 2014). These differences are reflected in large individual differences in the magnitudes of N1 and P3 responses to the same stimuli, even among neurotypical, normal-hearing adults.

To ensure our study included a neurodiverse "attention population," we recruited people on the ADHD spectrum, a group that purportedly have a "natural lesion" of attentional functions (Bush, 2010). People with ADHD struggle with tasks requiring top-down control, including selective attention (Booth et al., 2005; Mihali et al., 2017; Willcutt et al., 2005). In controlled laboratory environments, these individuals may perform just like age-matched controls on cognitive tasks; however, they often engage different, compensatory executive processes, accompanied by reduced neural activity in the regions recruited by neurotypical brains (Hasler et al., 2016; Salmi et al., 2018). Recent neuroimaging results demonstrate an association of ADHD with hypoactivation in a distributed set of regions and attentional networks, especially the cingulo-frontal-parietal (CFP) cognitive-attention network as well as parts of parietal cortex (Alexander & Farrelly, 2018; Bush, 2011; Dickstein et al., 2006) and the temporal lobe (Rubia et al., 2007). These regions and networks span a wide variety of functional processes falling under the "executive function" umbrella. Specifically, functional deficits have been identified via fMRI in cognitive flexibility tasks (Smith et al., 2006), interference suppression tasks (Vaidya et al., 2005), and most relevant for our study, in top-down attentional control tasks (Heinrichs-Graham et al., 2014; Salmi et al., 2018; Silberstein et al., 2016). These deficits are largely recovered by typically prescribed stimulant therapies like methylphenidate (Kowalczyk et al., 2019) and by attentional training games using neurofeedback (Butnik, 2005; Moradi et al., 2022; Moreno-García et al., 2022).

EEG studies over the past decade have focused on biomarker identification and developing diagnosis classification methods for ADHD; however, such approaches show modest success, with about 60 % classification accuracy (Lenartowicz et al., 2018). Studies exploring effects of ADHD on EEG evoked responses corroborate the inhibition and attention-related deficits from the fMRI and behavioral literature. For example, children and adults with ADHD exhibit attenuated N1 responses and attenuation of a subset of *P3* responses related to decision-making (likely the P3b; see Barry et al., 2003 for a review). Additionally, in visual continuous performance tests as well as auditory oddball tasks, targets, task-relevant oddballs, and task-irrelevant oddballs all elicit weaker *P3* responses in ADHD subjects than in controls (Jonkman, 2005; Kaur et al., 2019); these results align with behavioral and ERP results showing a re-orienting deficit in ADHD when novel distractors are present (Gumenyuk et al., 2022). These EEG studies indicate that behavioral studies alone cannot identify important neural processing differences in ADHD, nor do they reveal whether selective attention deficits are due to poor top-down control of attention or to atypical bottom-up responses (Friedman-Hill et al., 2010). For these reasons, we included

young adults with ADHD to increase the heterogeneity of neural responses which can facilitate gaining insights into the mechanistic roots of the disorder.

We created a paradigm that stressed top-down cognitive control of attention. We assessed both the ability to focus on a single stream of sound and the ability to flexibly switch attention from a target stream to a new, interrupting sound. We included key conditions in which the stimuli were identical between trials, but the attentional focus differed, altering only the internal goal of the subjects. This allowed us to isolate and quantify effects of top-down attention on behavior. We used EEG to concurrently record neural responses and capture key ERP components whose strengths reflect top-down and bottom-up attention processes. We reasoned that even if behavioral metrics did not differentiate ADHD from neurotypical subjects, the neural signatures of attentional focus might.

We found that in the entire cohort, there was large variability in performance within groups, leading to no significant differences between groups. However, ADHD subjects exhibited weaker top-down attentional modulation of neural responses to interrupting sounds than did neurotypical listeners. We also observed that top-down attention modulates not only the N1, but a late, positive-going response akin to the P3a, previously described as driven exclusively by bottom-up mechanisms (Polich, 2012). At the individual subject level, attentional modulation of both the ERP N1 and these later positivities correlated with behavioral performance. Together, these results demonstrate that individuals differ in their ability to control top-down attention in the face of salient interruption's, and that this ability is weaker in ADHD than in neurotypical subjects.

2. Results

2.1. Paradigm

We recruited young adults (18–30 years old) with and without ADHD diagnoses to perform auditory selective attention tasks while we recorded concurrent EEG. On each trial, subjects began by focusing attention on a three-syllable “Target” stream of human speech, which was always diotic, with zero interaural time difference (ITD). The target consisted of the syllables /ba/, /da/, and /ga/, with the order randomly permuted from trial to trial (Fig. 1). Every trial also contained a five-syllable “Distractor” stream (each syllable chosen randomly, with replacement, from the same set of syllables), which started after the Target and was spatialized to the right (ITD $-700 \mu\text{s}$). Finally, two-thirds of trials contained a three-syllable “Interrupter” stream, which was a random permutation of /ba/, /da/, and /ga/, similar to the Target. The Interrupter was spatialized to the left (ITD $700 \mu\text{s}$) and either temporally overlapped with the Target (Early) or began after the Target syllables ended (Late).

On each trial, a visual cue instructed subjects to either ignore the Interrupter or to switch attention to it. On FOCAL trials, subjects were to maintain attention on the Target stream and, at the end of the trial, report the Target syllable order. On BROAD trials, subjects were to monitor the Target stream unless and until an Interrupter, coming from the left, occurred (Fig. 1B). If an Interrupter occurred (2/3 of trials), subjects were to switch attention away from the Target and instead report the Interrupter's syllables. On BROAD trials in

which no Interrupter appeared (1/3 of trials), subjects were to simply maintain focus and report the Target syllables. BROAD attention trials, therefore, were particularly challenging, as subjects had to monitor the Target stream but be prepared to switch attention to the Interrupter stream if and when it played.

Because No Interrupter, Early Interrupter, and Late Interrupter trials were randomly intermingled, subjects could not anticipate whether or when an Interrupter would appear on a given trial, forcing them to adopt flexible listening strategies. Syllable timings in all streams were staggered so that event-related potentials evoked by many of the syllable onsets could be temporally isolated, allowing us to analyze the modulatory effects of top-down attention on the neural representations of the corresponding syllables.

All behavioral analyses were performed on arcsine-transformed proportion-correct scores. All comparisons across condition and trial type are within-subject and all ADHD status comparisons are between-subject. See Materials and Methods for further details about the stimuli and analysis.

2.2. Stimulus features and attentional focus, but not ADHD status, affect task performance

The successful control of top-down attention allows subjects to identify and report the correct syllable order for the cued stream. Subjects in both cohorts reported the correct syllable order at rates far above chance (mean = 62.3%, std. dev. = 15.3%; Fig. 2).

Accuracy was significantly higher in FOCAL than BROAD attention ($F(1,41) = 85.40, p < .001$). There was also a main effect of Interrupter Type ($F(2,82) = 7.56, p < .001$), with lower accuracy on Late Interrupter trials than on either Early Interrupter ($t(85) = 3.10, p = .008$) or No Interrupter trials ($t(85) = 3.51, p = .002$). This is likely because the onsets of the Late Interrupter syllables aligned more closely in time with the onsets of syllables in the Distractor stream, resulting in greater perceptual interference (see Fig. S2 for visualization of the syllable overlaps). Consistent with past studies, there was no main effect of ADHD status on performance ($F(1,41) = 1.75, p = .193$), and no significant interaction of ADHD status with other factors, or any other significant interactions. To aid interpretation of this null result, we calculated a Bayes Factor (BF) to determine the degree to which the observed data supported the null rather than an alternative hypothesis. We found the BF to be 1.06, or “not worth more than a bare mention” (Kass and Raftery, 1995), under the hypothesis that neurotypical (NT) subjects perform better than ADHD. (In contrast, the BF was 398 under hypothesis that FOCAL performance was better than BROAD performance.). Thus, this analysis provided no evidence in support or against our a priori hypothesis that neurotypical individuals would show better behavioral performance than participants with ADHD.

Performance was significantly higher on FOCAL than on BROAD attention trials at each level of Trial Type and ADHD status (post-hoc $p < 0.001$, Bonferroni adjusted for 6 comparisons). This is particularly interesting for the No Interrupter trials, in which subjects heard statistically identical stimuli and never had to shift attention away from the Target; these trials differed only in whether subjects were focusing exclusively on the target (FOCAL) or preparing to switch attention to an Interrupter (BROAD). Thus, there is a

performance cost of broadening attention: subjects are more accurate in reporting the Target in FOCAL trials than in BROAD trials even when no Interrupter appears.

2.3. Before an interrupter occurs, neural responses are similar for broad and focal attention and don't differ across groups

We hypothesized that the amplitudes of neural responses might reflect the cost of broadening attention that we observed in accuracy. Specifically, we posited that Target-evoked N1 amplitudes might be smaller in BROAD trials compared to FOCAL because listeners who were anticipating a task-relevant Interrupter might be less focused on the Target. We analyzed neural responses to all Target syllables in No Interrupter and Late Interrupter trials (Fig. 3A). (Early Interrupter trials were excluded because the Interrupter began while the Target was still ongoing.) N1 responses evoked by the Target syllables were not affected by Condition ($F(1,41) = 0.26, p = .610$), ADHD status ($F(1,41) = 0.03, p = .867$), or their interaction ($F(1,41) = 0.155, p = .695$).

We also hypothesized that subjects with weaker top-down control of attention might be worse at filtering out responses to the always-ignored stream, the Distractor. We analyzed N1s evoked by all Distractors in the No Interrupter trials. Although ADHD subjects exhibited slightly larger Distractor N1s than Neurotypical subjects, this difference was not statistically significant ($F(1,41) = 1.98, p = .167$). In addition, neither Condition ($F(1,41) = 0.06, p = .817$) nor the interaction of ADHD Status and Condition ($F(1,41) = 1.218, p = .276$) significantly affected N1 amplitude. Individual differences in Target and Distractor N1 responses are shown in Fig. S3.

Post-hoc, we performed a non-parametric cluster-based test (Maris & Oostenveld, 2007) to find any other ERP components modulated by attention or ADHD status. We tested from 0 s, when the Target begins to play, to 1.5 s, before the Late Interrupter begins. We detected no time windows in which the FOCAL and BROAD attention conditions significantly differed in both the ADHD and Neurotypical groups (see traces in Fig. 3A).

2.4. ADHD subjects exhibit weak top-down modulation of neural responses to an interrupting event

We hypothesized that top-down attention would modulate N1s evoked by an Interrupter. We therefore analyzed the responses evoked by the first syllable in the Early Interrupter (Subsequent onsets of the Early Interrupter and all onsets of the Late Interrupter could not be isolated from other temporally adjacent events; see Materials and Methods). Overall, the first syllable of the Early Interrupter, which occurs before the final syllable of the Target stream, elicits larger N1s in BROAD than in FOCAL trials ($F(1,41) = 41.2, p < 0.001$; Fig. 3B). This demonstrates that volitional attention modulates this neural response, either by enhancing the Early Interrupter N1 during BROAD attention, suppressing it during FOCAL attention, or some combination of the two. Importantly, attention modulates this Early Interrupter N1 more weakly in ADHD subjects than Neurotypical subjects (Condition \times ADHD Status interaction $F(1,41) = 6.790, p = .013$), although there was no main effect of ADHD Status ($F(1,41) = 0.002, p = .968$). This result demonstrates that ADHD subjects exhibit weaker

top-down modulation of the neural responses evoked by the Interrupter in this complex listening environment.

2.5. Attentional focus modulates a late, orienting response

Prior work suggests that the P300 response elicited by unexpected stimuli, the P3a, is influenced only by stimulus features (Polich, 2012)—although at least one study shows that cognitive disorders affect the amplitude as well (Risling et al., 2013). We thus hypothesized that the orienting-like, bottom-up response of the late positivity would be stronger in ADHD subjects due to their high distractibility (Marzinzik et al., 2012) and did not expect attentional state to affect the magnitude of the response in either subject group. We found that the late positivity elicited by the first onset of the Early Interrupter was modulated by attention in both ADHD and Neurotypical subjects. Specifically, the Early Interrupter positivity was larger in the BROAD condition, when the Interrupter was behaviorally relevant, than in the FOCAL condition, where it was to be ignored ($F(1,42) = 19.80, p < .001$). There was no main effect of ADHD status ($F(1,42) = 2.52, p = .120$). While this top-down modulation of the positivity tended to be weaker in ADHD than Neurotypical subjects, similar to the N1 response modulations, the difference did not reach statistical significance (Condition \times ADHD Status interaction: $F(1,42) = 3.62, p = .064$; see Fig. 3C).

2.6. At the individual level, the degree to which neural responses change with task goals correlates with behavioral performance on the task

While we found significant group differences in the strength of top-down modulation of the N1 evoked by the first syllable of the Early Interrupter, there was significant individual variability of these responses within each group and significant overlap across groups in both behavioral and neural measures. We therefore tested whether there is a relationship between task performance and attentional modulation of the Early Interrupter N1 and the positivity at the individual subject level. For each subject, we calculated the degree of attentional modulation for the Interrupter N1 ($N1 = N1 \text{ peak in FOCAL} - N1 \text{ peak in BROAD}$) and positivity ($P3a = P3a \text{ peak in BROAD} - P3a \text{ peak in FOCAL}$), each defined so that large positive values indicate strong attentional modulation. Both $N1$ and $P3a$ significantly and positively correlate to accuracy on the Early Interrupter trials ($r(41) = .32, p = .040$ and $r(42) = .56, p < .001$, respectively; Fig. 4), demonstrating that individual differences in top-down control of attention relate directly to differences in performance. Fig. S4 shows this same data for subjects both on and off medication. When split by ADHD status, this correlation remained for the $P3a$ component and behavior, but did not persist for the $N1$ component, the weaker correlation. Specifically, the $N1$ s do not correlate for the ADHD group ($r(24) = .17, p = .430$) and marginally correlate for the Neurotypical group ($r(19) = .42, p = .063$). The $P3a$ modulations and behavior correlate significantly for both groups (ADHD: $r(24) = .48, p = .018$; NT: $r(19) = .65, p = .002$).

3. Discussion

3.1. Overview

We designed a demanding auditory experiment that exercised different attentional demands to explore how top-down attention control interacted with bottom-up attentional capture in a cohort of diverse cognitive abilities. Subjects displayed a range of abilities in flexible control of attention, which was reflected in how strongly attentional focus modulated neural responses. ADHD subjects exhibited weaker modulation, consistent with past work describing compromised preparatory-related neural responses in ADHD and reduced activation of networks involved in both bottom-up and top-down processing, even when there are no behavioral group differences (Friedman-Hill et al., 2010; Hasler et al., 2016; Salmi et al., 2018). Altogether our work highlights that although individual variability in behavior alone might not stratify neurotypical and disordered functioning, neural responses may be useful in identifying processing deficits.

3.2. Neural responses

3.2.1. Early Interrupter N1 responses are modulated by top-down attention—

The N1 response's peak magnitude is strongly modulated by top-down attention (Dai & Shinn-Cunningham, 2016; Hillyard et al., 1998; Kappenman & Luck, 2012; Laffere et al., 2020), and the degree of this modulation correlates with performance on selective attention tasks (Choi et al., 2014). We hypothesized that N1 modulation would be reduced in ADHD subjects, reflecting reduced efficacy of attentional control. We contrasted N1 responses elicited by FOCAL trials, where listeners always reported the Target stream, and BROAD trials, where they began listening to the Target but had to be prepared to switch attention to an Interrupter, if it occurred.

We did not observe any attentional modulation, in either subject group, of the neural responses elicited in the early portion of trials. This likely reflects the similarity of task demands in this period. In all conditions, listeners had to initially focus or re-orient on the Target and ignore the Distractor; only towards the end of a trial, if an Interrupter appeared, did they sometimes have to switch attention from the Target. This likely explains why Distractor- and Target-evoked ERPs early in the trial are similar for FOCAL and BROAD conditions.

In the latter portion of trials, we found strong attentional effects on the magnitude of N1 responses evoked by the salient and unpredictable Early Interrupter. The N1 was larger in BROAD trials, presumably because listeners needed to shift focus to the Interrupter, than in FOCAL trials, where the Interrupter was not task relevant. This difference was reduced in subjects with ADHD, suggesting that ADHD listeners are less able to use top-down attention to modulate responses to salient, interrupting events. This supports the account of ADHD as a deficit or alternative solution to executive functioning.

3.2.2. Early Interrupter Late ERP positivity responses are modulated by top-down attention—

We found that for both neurotypical and ADHD subjects, the late positivity evoked by the Early Interrupter was stronger in the BROAD than the FOCAL

2013; Jahshan et al., 2012; Light et al., 2007) and ADHD self-report scales (Marquardt et al., 2018), but to our knowledge, none show the top-down attentional modulation of this response (see also Marzinzik et al., 2012 for diminished novelty P3 modulation in ADHD). Additionally, the context of selective attention is important for our findings: foundational work showed no behavioral deficits in children with ADHD (Prior et al., 1985) during selective attention, similar to our results, but as paradigms and methods have advanced, both behavioral measures and EEG show clear deficits in both the early (N1) and later responses (P3) (Jonkman, 2005; Salomone et al., 2016). Our finding, specifically controlling for bottom-up contributions to selective attention, further supports the idea that ADHD manifests as a reduced ability to deploy top-down attentional control of sensory inputs at will. Future studies should directly address this ability in this population.

Finally, there were group differences in the extent that attention modulated neural responses, despite large individual subject differences. These individual differences are not random; instead, performance correlates with how strongly top-down attention modulates the N1 and late positivity evoked by interrupting events. Listeners who perform best are those who more strongly suppress neural responses to an event when it is task irrelevant compared to when it is task relevant. This correlation suggests that the differences in the strength of top-down attentional control relate directly to differences in behavioral ability and thus may provide a more nuanced measure of the ability to ignore salient distractions than does a categorical label.

At least two issues deserve additional investigation. First, we need to further explore the influence of top-down attention on the late positivity to confirm such effects, for instance, by isolating the response in different experimental paradigms, and to confirm the response's identity. Second, further research into the mechanisms that lead to individual differences in top-down control should be conducted. One avenue for future research is to explore whether there are signatures of ADHD in oscillatory brain activity. For instance, the ratio between theta waves (4–8 Hz) and beta waves (12–20 Hz) has shown promise as a neural marker of ADHD, but not one sensitive or selective enough to be clinically relevant (Arns et al., 2013; Deng et al., 2020; Loo et al., 2013; Putman et al., 2014; Saad et al., 2015). Similarly, lateralization of parietal alpha (8–14 Hz) oscillations are associated with spatially directed attention, with increases in alpha power in the hemisphere representing to-be-ignored visual or auditory events (Foxe & Snyder, 2011; Kelly et al., 2006; Payne & Sekuler, 2014; Zumer et al., 2014). Follow up studies exploring these oscillations and their relationships to successful attentional control may reveal more about the sources of variability in this skill (see Supplementary Fig. S6 for initial oscillatory analyses in the alpha band).

3.4. Clinical implications for ADHD

Our results support the idea that behavioral assessments are less sensitive than neural measures of ADHD (Marquand et al., 2016a, 2016b; Marzinzik et al., 2012). Still, as in many prior studies, our effect size is too small to be clinically useful for diagnosis or prognosis (Arns et al., 2013; Loo et al., 2013; Putman et al., 2014; Saad et al., 2015).

Increased distractibility in the ADHD population has been well-documented in both research and clinical settings (Marzinzik et al., 2012), as has disrupted preparatory processing

and performance monitoring in psychophysical tasks. The under-arousal theory of ADHD proposes that these issues are due to compromised attentional orienting in these individuals (Marquardt et al., 2018; Nesterovsky et al., 2015). This account is consistent with our finding that ADHD listeners are less able to modulate neural responses evoked by salient, task-irrelevant interrupters than are neurotypical subjects. We argue that, compared to controls, ADHD subjects are less effective at filtering out salient but irrelevant events; ADHD biases the attentional systems to focus on salient stimuli, regardless of their behavioral importance.

3.5. Caveats

It is worth noting that we did not separate our ADHD sample into the three subtypes of ADHD (inattentive, hyperactive/impulsive, and combined) identified in the DSM-5. Executive function deficits greatly vary within the ADHD population (Loo & Makeig, 2012; Thorell, 2007), and this could explain some of the inter-subject variability amongst ADHD subjects. Similarly, ADHD status in our sample was determined by self-report of previous diagnosis. The heterogeneity of the sample was exacerbated since subjects had been diagnosed by different physicians and psychologists at different developmental points, which in turn likely affected coping mechanisms and comorbidities. Finally, our sample was largely comprised of students from relatively high socioeconomic backgrounds and enrolled in a highly selective American university. Future work should consider these factors and attempt to understand their role in ADHD and attention.

3.6. Conclusions

During a demanding auditory task, neural responses evoked by an unpredictable interrupting sound are larger when that interrupter is behaviorally relevant than when it is to be ignored. This modulation affects not only the sensory N1 response, but also a late positivity, which strongly resembles a P3a-like automatic orienting response. Individual differences in how well listeners perform on this demanding auditory task correlate with how strongly they modulate neural representations based on task demands. Despite substantial overlap between neural signatures of attentional control in ADHD and neurotypical listeners, ADHD listeners demonstrate weaker top-down modulation of neural responses evoked by an unpredictable interrupting sound. Future work should be undertaken to confirm the effects of top-down attention on P3a responses, and to explore whether the group differences we see between ADHD and neurotypical listeners manifest similarly in attentionally demanding tasks in other sensory modalities.

4. Experimental procedure

The Boston University Internal Review Board (IRB) approved all study procedures. All participants gave written informed consent.

4.1. Participants

We recruited 95 volunteers with and without ADHD to complete an online intake survey (via Qualtrics, Provo, UT) reporting demographics, mental health and drug use history, and current mood and anxiety. We invited a balanced number of Neurotypical and ADHD

subjects who met our inclusion criteria (ages 18–30 years, normal or corrected vision, and normal hearing) to complete a lab visit. They gave written informed consent, completed a hearing screening, and performed an abbreviated practice test of the auditory experimental task.

To continue in the study, listeners had to have auditory detection threshold levels at or below 20 dB HL for pure tones between 250 and 8,000 Hz (in octaves) and performance at or above 66 % correct on the practice test. Fig. 5 shows the recruitment pipeline of both ADHD and neurotypical (NT) subjects retained or lost at each stage. Of the 45 subjects who continued to the main experiment and had useable data, 25 self-reported that they had been diagnosed with ADHD and who held current prescriptions of ADHD medications. We refer to these participants as ADHD subjects (19 female, 6 male; age 21.4 \pm 2.7) the remaining 20 we call Neurotypical subjects (14 female, 6 male; age 21.8 \pm 3.0). All subjects were compensated for their time and offered bonuses for good task performance.

ADHD subjects were initially tested once while either on or off their stimulant medications, assigned randomly. A subset of the ADHD subjects ($N = 14$) completed a second session of the same experiment on a subsequent day in the other medication state. Nine of these subjects performed on-medication first; five performed off-medication first. Post-hoc, we identified a strong practice effect: performance almost always increased on the second day, regardless of medication status. This effect was large enough to overwhelm any differences in performance due to medication status. Therefore, we include results in the main text from each subject's Day 1 data. The Supplemental Information includes results showing ADHD subject data from both days, including within-subject comparisons (on vs off medication) for the 14 participants who completed both experimental sessions.

4.2. Auditory experiment

4.2.1. Stimuli—Stimuli were streams of human speech comprising sequences of /ba/, /da/, and /ga/ syllables. Syllables were recorded by a male, native English speaker using an AudioTechnica AT4033 large diaphragm condenser microphone (Audio-Technica U.S. Inc., Stow, OH) in a sound-treated booth. These plosive syllables were selected because their abrupt onsets elicit strong ERPs. Individual syllables were recorded in isolation, cropped to be 437 ms long, and then concatenated with inter-stimulus intervals (ISIs) to form streams of randomly permuted syllables. Sound stimuli were presented via Etymotic ER-1 insert headphones (Etymotic, Elk Grove Village, IL). Syllables were spatialized to one of three stream locations using interaural time differences (ITDs) of 700 μ s (left of center), 0 μ s (center), or -700μ s (right of center). Stimulus creation and experimental control were via custom software created in MATLAB (The MathWorks Inc, Natick, MA) using the PsychToolbox (Brainard, 1997; Kleiner et al., 2007).

4.2.2. Experiment design and task—Every trial contained a three-syllable “Target” stream heard from the center and a five-syllable “Distractor” stream spatialized to the right. The Target always began playing first, followed 200 ms later by the Distractor (Fig. 1A).

The Target syllable onsets were always presented at 0, 0.5 s, and 1.25 s. The Distractor syllable onsets were presented with one of two “rhythms:” 0.2 s, 0.7 s, 1.45 s, 1.95 s,

and 2.7 s (rhythm 1) or 0.2 s, 0.95 s, 1.45 s, 2.2 s, and 2.7 s (rhythm 2). Two-thirds of trials contained a third “Interrupter” stream which was spatialized to the left and began either 1 s (Early Interrupter) or 1.5 s (Late Interrupter) after the Target. We balanced the design so there were equal numbers of No Interrupter, Early Interrupter, and Late Interrupter trials (Fig. 1B). Each Interrupter was created to have one of two syllable rhythms, with onset times of 0 s, 0.5 s, 1.25 s (rhythm 1) or 0 s, 0.75 s, 1.25 s (rhythm 2). These were then delayed overall by either 1 s, to create an Early Interrupter, or 1.5 s, to create a Late Interrupter, before being added to the Target and Distractor. In all trials with Interrupters, only Distractor rhythm 1 was used to reduce the amount of overlap between competing syllables. All syllable timings are depicted in Fig. S2.

Subjects were instructed to keep their eyes open and focused on a central fixation dot. Each trial began with a visual cue indicating the attentional state required. On FOCAL attention trials (diamond cue), subjects were to maintain attention on the Target and report the order of the /ba/, /da/, and /ga/ syllables presented in it. On BROAD attention trials (left-pointing arrow cue), subjects were to attend to the Target unless and until a (left-lateralized) Interrupter occurred. If an Interrupter began, subjects were to reorient attention to it and report its syllables, in order. The BROAD attention condition, therefore, was particularly challenging, as subjects had to both monitor the Target and be prepared to switch their attention to the Interrupter if it appeared (which could happen either Early or Late in the trial). Subjects were to always ignore the (right-lateralized) Distractor. Note that 1/3 of both FOCAL and BROAD attention trials were No Interrupter trials, letting us test the effect of attentional state in the absence of an attentional shift. Pilot versions of this task presented the target with either left or right distractors, paired with right or left interrupters. However, this required several hours of testing per subject to obtain a sufficient number of trials in each spatial configuration. Moreover, neither behavioral nor neural pilot results showed any left–right asymmetries, and no differences were found between the lateralization patterns. We therefore opted to test only a single spatial configuration (Distractor to the right and Interrupter to the left) to reduce the experiment duration to fit within a single session. After all stimuli ended (3.2 s after the Target onset), a circle appeared at the fixation point to cue subjects to respond. Listeners withheld responses until this signal to prevent motor planning and motor artifacts from distorting the sensory-evoked EEG responses. We did not analyze reaction times.

Subjects reported back the required sequence (either Target or Interrupter, depending on the trial) using the keys 1, 2, and 3 to indicate the order of /ba/, /da/, and /ga/ syllables, respectively. Each subject trained on this mapping before the experiment began. After entering their response and before the start of the next trial, subjects received feedback as to whether or not their response was correct. In addition to hourly pay, subjects were given a \$0.01 bonus for each correct response during the experiment (maximum bonus: \$4.80).

4.3. Behavioral performance analyses

We calculated the proportion of trials that were correctly reported. A trial was labeled correct if each of the three syllables in the proper stream (either the Target stream or

Interrupter stream, depending on the trial) was correctly identified, in order (Studebaker & a., 1985).

We used R version 4.0.2 (R Core Team, 2020) and the `rstatix`, `tidyverse`, and `ggpubr` packages to perform mixed within/between 3-way ANOVAs to assess the effects of ADHD status, attention condition (FOCAL vs BROAD), and Interrupter Type (Early, Late, or None) on behavioral performance on the task. There were no extreme outliers, the data were normally distributed (Shapiro-Wilk $p > 0.05$), and there was adequate homogeneity of variances (Levene $p > 0.05$). All behavioral analyses were performed on arcsine-transformed proportion-correct scores. We additionally calculated the Bayes Factor (BF), a more easily interpretable statistical test for null results, using the `BayesFactor` package in R (Morey et al., 2015).

4.4. EEG acquisition

Subjects performed the experiment in front of an LCD monitor in a sound-treated booth. A BioSemi ActiveTwo system and accompanying ActiveView acquisition software recorded EEG from 64 channels arranged in the standard international 10–20 setup. Data were sampled at 2048 Hz. Auditory stimuli were presented through Tucker-Davis Technologies System 3 (TDT, Alachua, FL) hardware, which also inserted time-locked event flags into the EEG recording. Three external electrodes collected EOG responses from eye movements: two beside the eyes and one below the left eye.

4.5. EEG processing

Continuous EEG data were referenced against the average of the mastoid channels, then downsampled to 256 Hz. Data were bandpass filtered between 1 and 20 Hz with a zero-phase Kaiser filter to remove slow drift below 1 Hz and high-frequency noise above 20 Hz, including line noise. Independent components analysis (EEGLAB, 57) allowed us to isolate eye blinks, saccades, and other artifacts; components corresponding to such artifacts were identified by inspection and projected out of the data. Altogether, the average number of ICA components rejected was 3.69 for NT subjects and 3.25 for ADHD subjects out of 67 total. A 2 sample t -test showed no significant difference between the two samples ($t(55) = -1.1703$, $p = 0.247$). Data from each trial were then epoched from one second before the visual cue onset to the end of the presentation period (4.5 s). Any processed epochs with amplitudes exceeding $\pm 100 \mu\text{V}$ were rejected from further processing. Datasets with 3 or fewer non-adjacent, erratic channels (determined by visual inspection of ICA topographies and raw signal traces) underwent interpolation (Delorme & Makeig, 2004). A final visual inspection removed any remaining contaminated trials.

4.5.1. Event related potential (ERP) calculations—The ERP components that we report are the peak magnitudes of the N1 and P3a responses. For each subject, trial type, and condition, we computed an average ERP across a broad cluster of 10 fronto-central channels, where auditory-evoked responses tend to be maximal (Fz, FC1, FCz, FC2, C1, Cz, C2, CP1, CPz, and CP2). Individuals' N1 peaks were calculated by averaging epochs of EEG from trials of the same type and condition, then employing a custom peak-finding algorithm to identify the peak negativity in a window from 75 to 150 ms after each

stimulus onset in all the streams. Individuals' ERP P3as were calculated similarly, but for a peak positivity in a window from 280 ms to 380 ms after stimulus onsets. Our time windows are derived from prior literature on N1 and P3 components (e.g., Luck, 2005) in conjunction with visual examination of the windows' fit to individual subjects ERP peaks. The full experiment comprised 240 trials, leaving each condition (2 options) and trial type combination (3 options) with a maximum of 40 trials for ERP calculation before artifact rejection. Overall, the average number of trials for all participants was 34.7 (ADHD = 34.9; NT = 34.5) after removing noise-contaminated trials and trials on which the listener made an incorrect response. Because the number of trials that remained after artifact rejection varied across subjects and conditions, we used a Monte Carlo down sampling procedure to obtain usable ERP component estimates. For each subject, we calculated that subject's minimum number of valid trials across all conditions (mean = 26.2, std dev = 5.50), then randomly selected this number of trials per condition for that subject. We repeated this procedure 100 times for each subject and then assigned the median N1 and P3a values calculated over all samples to that particular subject, condition, and trial type.

4.5.2. ERP statistical analyses—ERP peaks were used in four hypothesis-driven analyses. To test the effects of ADHD Status and Attention Condition on task-relevant Targets and task-irrelevant Distractors, we considered (1) all Target-elicited N1s in No Interrupter and Late Interrupter trials, and (2) all N1s elicited by Distractor onsets in No-Interrupter trials. To test the effects of ADHD Status and Attention Condition on the process of shifting attention to the Interrupter, we computed (3) N1 and P3a peaks elicited by the first Interrupter onsets in Early Interrupter trials. Other onsets were contaminated by temporally adjacent stimuli, preventing us from extracting ERP components of interest.

For each analysis, we computed each subject's mean peak amplitude in each condition, and again used mixed within/between ANOVA to statistically test for differences.

We followed up with a non-parametric permutation test to further identify significant differences between the two Attention Conditions in No Interrupter and Late Interrupter trials up until $t = 1.5$ (Maris & Oostenveld, 2007). For each subject, a paired sample t -value was calculated for each time point between the trial-length ERP for each Attention Condition. A null distribution for the t -test was derived from 1000 bootstrapped permutations of the data, in which time points were swapped between the Attention Conditions and within-subject. Time clusters over a certain pre-defined threshold were labeled significant.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

Data will be made available on request.

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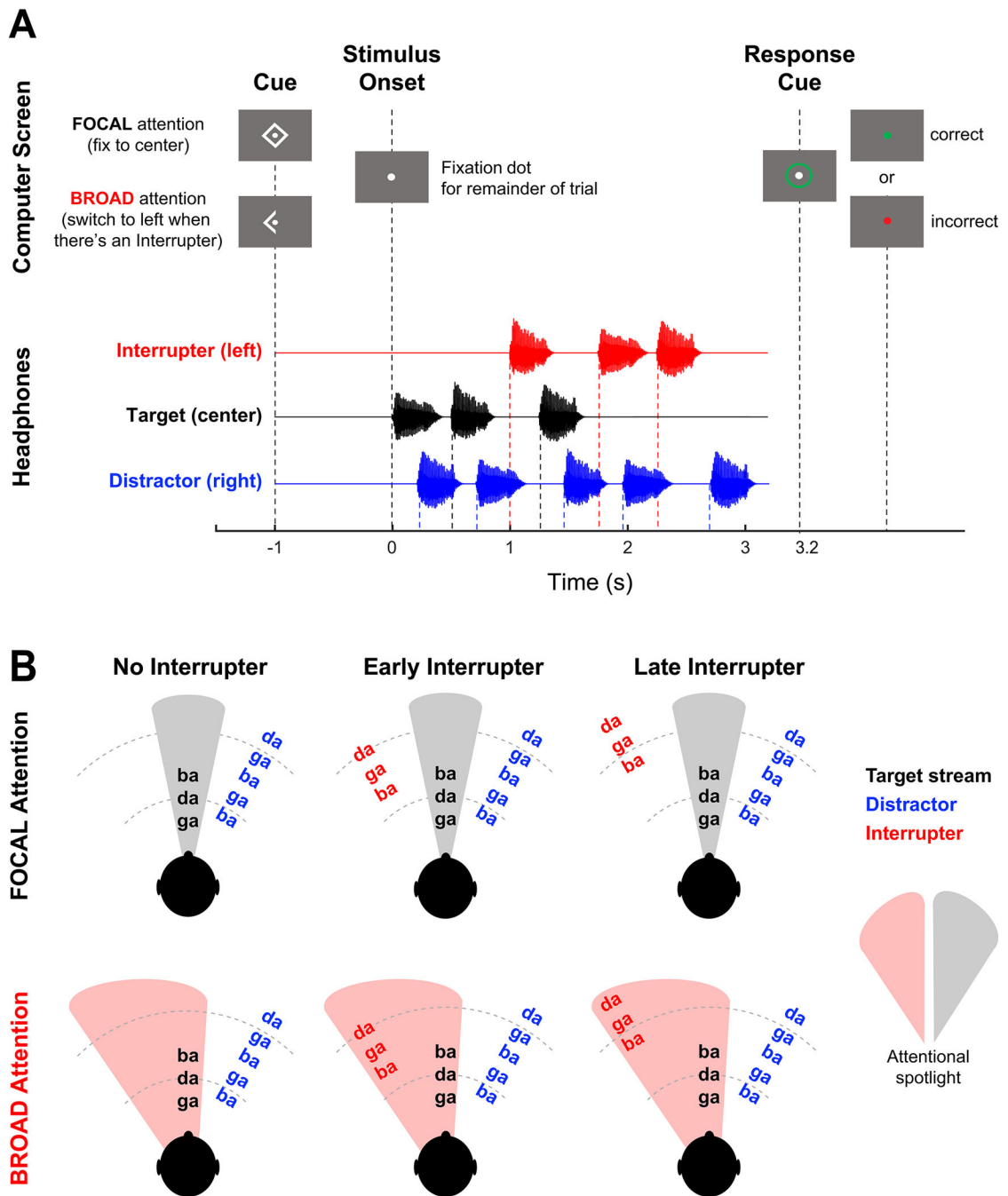


Fig. 1. Experimental Setup. (A) Order of events in an “Early Interrupter” trial. A visual cue instructed subjects to either engage in FOCAL attention, monitoring only the central Target stream, or in BROAD attention, in which they needed to monitor for the onset of a left-lateralized Interrupter stream and, if an Interrupter occurred, switch their attention to it. (B) Schematic of our factorial experiment design. Across the columns are the approximate relative timing of the three stimulus streams in No Interrupter, Early Interrupter, and

Late Interrupter conditions. In rows are the hypothesized attentional states required of the FOCAL and BROAD attention tasks.

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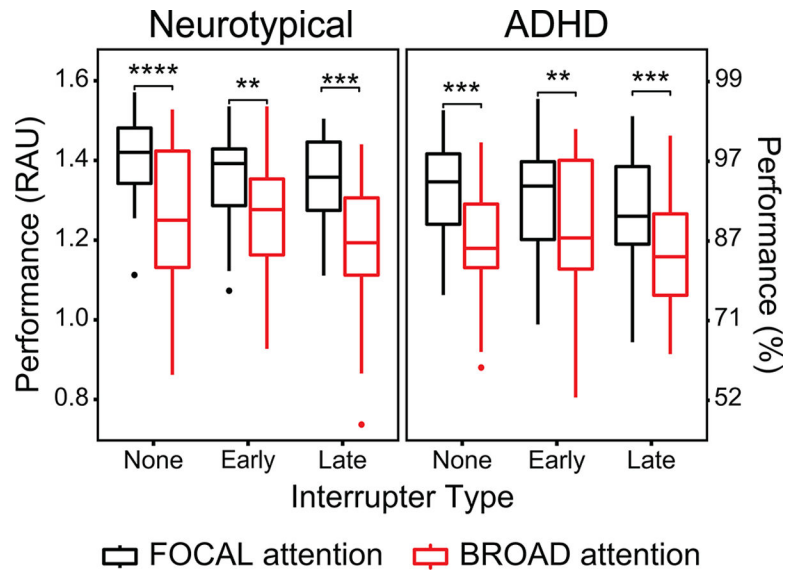


Fig. 2. Behavioral Performance. Performance for Neurotypical (left panel, N = 20) and ADHD (right panel, N = 25) groups in rational arcsine units for each Interrupter Type (None, Early, or Late), separately for FOCAL (black) and BROAD (red) attention conditions. Subjects performed worse in the BROAD condition compared to the FOCAL condition in all Interrupter Trial Types and for both ADHD and Neurotypical groups. In the No Interrupter trials, this worsening of performance without the presence of an interrupter represents a cost of broadening attention.

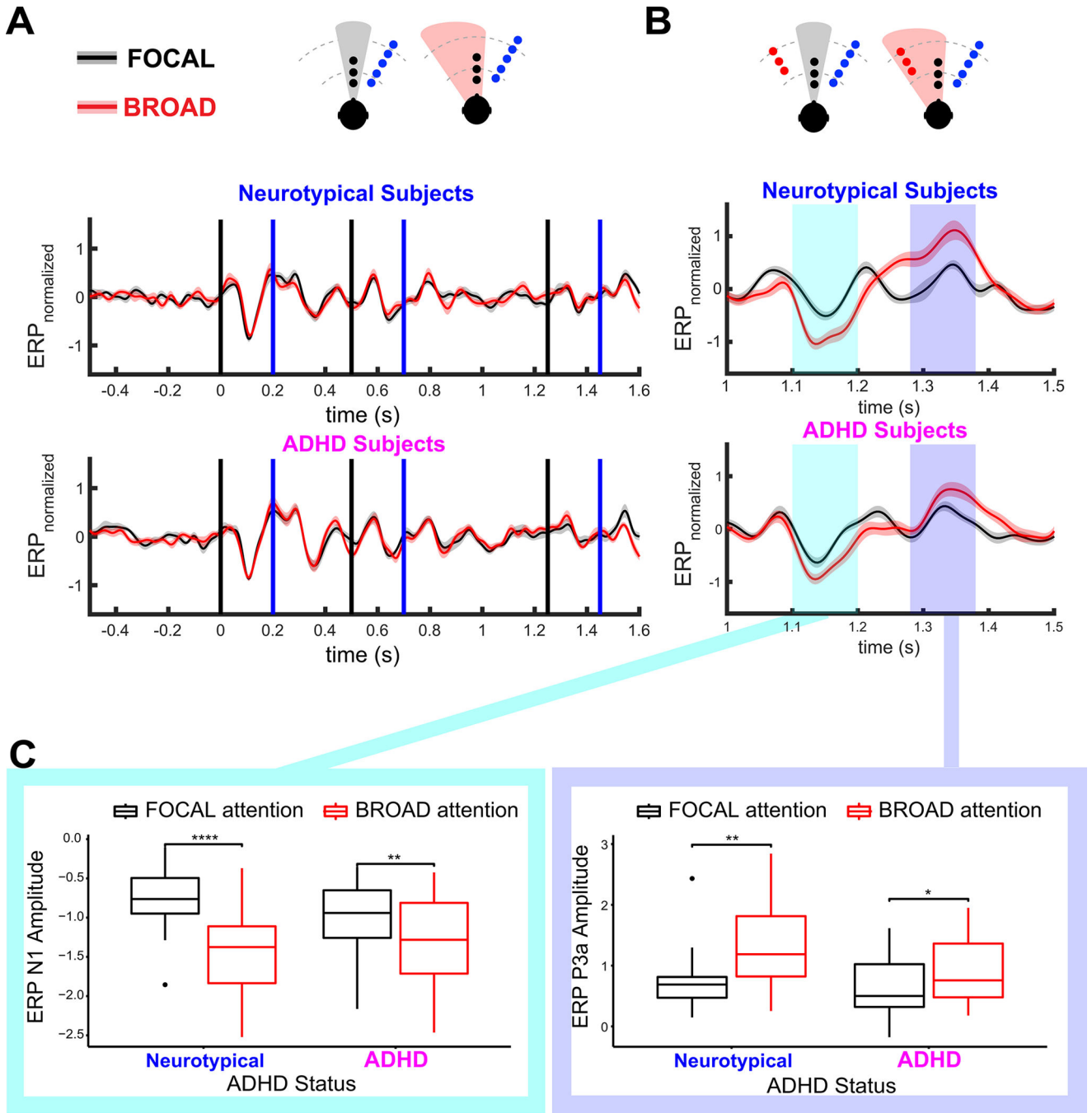


Fig. 3. ERP component neural responses. (A) Trial structures (top) and grand average ERP (bottom) for trials without an Interrupter in the first 1.5 s (i.e., No Interrupter and Late Interrupter trials). Event-related potentials are shown separated by ADHD status (top panel: Neurotypical, bottom panel: ADHD) and condition (FOCAL in black, BROAD in red, and error patches depict standard error). Vertical lines depict onset times for Target (black) and Distractor syllables (blue). (B) Trial structures (top) and grand average ERP (bottom) for the first Early Interrupter (t = 1.0 s). ERP peak amplitudes were calculated within the

highlighted regions (left: N1; right: P3a). These traces are also shown separated by ADHD status (top panel: Neurotypical, bottom panel: ADHD) and condition (FOCAL in black, BROAD in red). (C) Boxplots showing ERP N1 (left) and positivity (right) amplitudes, separated by ADHD status ($N = 25$) and Condition ($N = 20$).

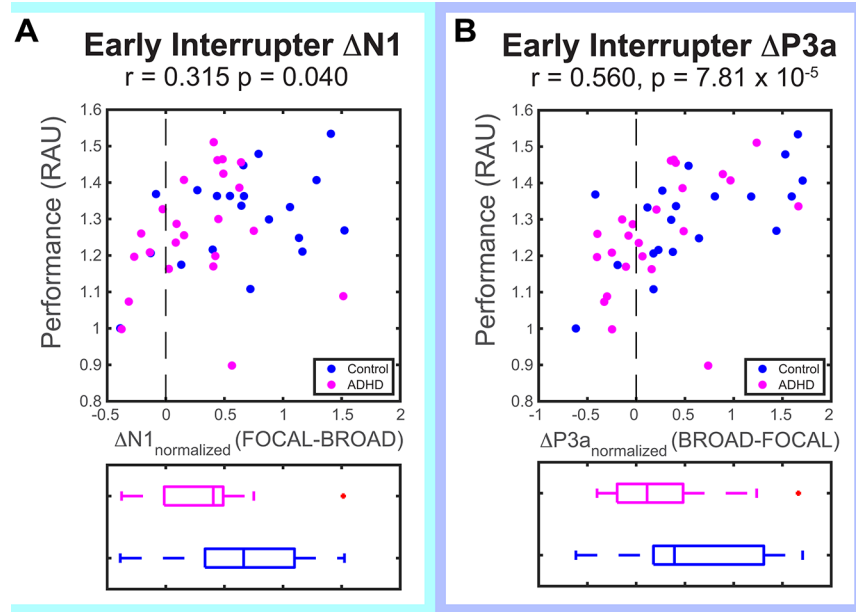


Fig. 4. Individual differences in neural responses. (A) Individual differences in total Early Interrupter trial performance plotted against individuals' N1s (FOCAL-BROAD) to the first Early Interrupter, depicting a significant correlation between the attention modulation and performance. The bottom panel shows the spread of individuals' N1 according to the population (ADHD in magenta and Neurotypical in blue). (B) Same data as (A) but for P3 (BROAD-FOCAL). The correlation between attention modulation and performance is strongly significant. ADHD status significantly affects N1 ($t(41) = 2.61$, $p = 0.0127$) and marginally affects P3 ($t(42) = 1.90$, $p = 0.0640$).

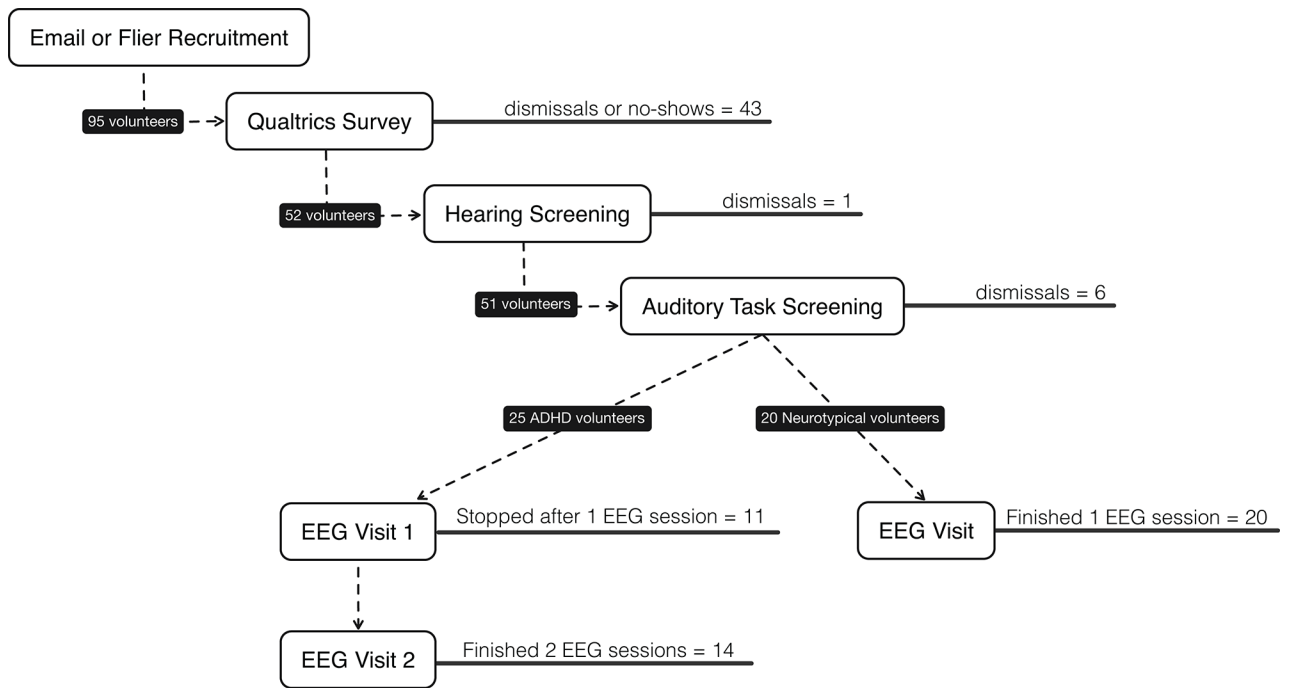


Fig. 5. Subject recruitment pipeline. Subject numbers for all phases of the study. In this paper, we present data from 45 subjects, 25 with ADHD and 20 without a prior diagnosis, who are labelled Neurotypical.