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Are attention and cognitive control altered by fMRI scanner environment? Evidence from Go/No-go tasks in ADHD

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Abstract

It is widely assumed that cognitive processes studied in fMRI are equivalent to cognitive processes engaged in the same experimental paradigms in typical behavioral lab settings. Yet very few studies examined this common assumption, and the results have been equivocal. In the current study we directly tested the effects of fMRI environment on sustained attention and response inhibition, using a Go/No-go task, among participants with (n=42) and without (n=21) attention deficit/hyperactivity disorder (ADHD). Participants with ADHD are characterized by deficits in these cognitive functions and may be particularly susceptible to environmental effects on attention. We found a substantial slowing of reaction time in the scanner for all participants, and a trend for enhanced sustained attention, particularly in ADHD participants with poor performance. We also report limited stability of individual differences in scores obtained in the lab and in the scanner. These findings call for cautious interpretation of neuroimaging task-related results, especially those obtained in clinical populations.

Keywords

ADHD, fMRI, sustained attention, response inhibition, reaction times

Introduction

Studying brain-behavior relations is of the ultimate goals of functional magnetic resonance imaging (fMRI) research. A common practice in cognitive neuroscience is to select a well-studied task designed to tap a certain cognitive construct, and present it to participants inside the MRI scanner, in order to study the neural underpinnings of that construct. However, fMRI studies rarely address the issue of how the setting of an MRI scanner may influence cognitive functioning, and how these changes in cognition and behavior might obscure the search for neural correlates.

Various factors might cause changes in one's behavior during an MRI scan. These include the loud noise, the supine position, the use of a response device other than a standard keyboard, and the magnetic field itself. Importantly, lying in an MRI scanner often entails discomfort or even stress, especially for participants who experience this setting for the first time. It has been shown that MRI scanning increases endocrinological stress responses (Eatough, Shirtcliff, Hanson, & Pollak, 2009; Peters, Cleare, Papadopoulos, & Fu, 2011; Tessner, Walker, Hochman, & Hamann, 2006) as well as subjective reports of anxiety (Muehlhan, Lueken, Wittchen, & Kirschbaum, 2011). Such changes in the mental state of participants can influence cognitive processes and performance by elevating arousal, increasing cognitive control, or altering attention (Eysenck, Derakshan, Santos, & Calvo, 2007).

Previous research on this topic, directly comparing performance during fMRI with performance in standard lab settings, has been scarce; and the reported results are mixed. Some studies reported prolonged reaction times in the scanner (Assecondi et al., 2010; Koch et al., 2003; van Maanen, Forstmann, Keuken, Wagenmakers, & Heathcote, 2016), but the opposite has also been found (Koten, Langner, Wood, & Willmes, 2013). It has been shown that scanner noise per se, when isolated from other scanner effects, is not driving differences in reaction times (Hommel, Fischer, Colzato, van den Wildenberg, & Cellini, 2012; Jacob et al., 2015) but may be effecting attentional demand (Tomasi, Caparelli, Chang, & Ernst, 2005) and cognitive control (Hommel et al., 2012). However, others found no effects on cognitive control during fMRI (Koch et al., 2003). Furthermore, some previous interpretations attributed behavioral differences in the scanner to reduced attentional allocation (a “divided-attention-like” situation (Gutchess & Park, 2006; van Maanen et al., 2016), while other argue for increased arousal leading to improved attention (Koten et al., 2013).

Importantly, all these studies have been conducted with neurotypical adult samples. Yet participants from clinical populations could be disproportionately affected by the scanner environment, especially by the aversive noise, attentional demand, and stress. In the current study we focus on participants with attention-deficit/hyperactivity disorder (ADHD), who might be specifically prone to behavioral changes during scanning, due to deficiencies in attention and in cognitive control (e.g. Barkley, 1997; Durston, de Zeeuw, & Staal, 2009; Hervey, Epstein, & Curry, 2004; Tsal, Shalev, & Mevorach, 2005; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005), and elevated levels of anxiety (Kessler et al., 2006; Schatz & Rostain, 2006). The ADHD fMRI literature is growing rapidly yet the underlying pathophysiology is incompletely understood (Cortese et al., 2012; Samea et al., 2019). Inspection of task-fMRI studies of ADHD show that they often fail to replicate well-known behavioral findings in data collected with fMRI, i.e. performance of ADHD participants in many fMRI studies seems to be intact and comparable to that of a neurotypical control group, even in paradigms where deficient performance of participants with ADHD is well documented in previous studies in standard lab settings (e.g. Congdon et al., 2014; Orinstein & Stevens, 2014; van Belle et al., 2015). This discrepancy in behavioral results, which might be partially rooted in the aforementioned effects of the scanner environment, complicates the interpretation of any imaging findings in these studies.

We examine the behavioral performance of adults with ADHD in a Go/No-go task during fMRI scanning, in comparison with performance of the same participants in a standard lab setting, and in comparison with the performance of neurotypical control participants (using the same lab and scanner conditions). We compared behavioral data from a couple of imaging studies of sustained attention and response inhibition (Kolodny, Mevorach, & Shalev, 2017; Kolodny et al., 2020) with unpublished behavioral data that were collected in a standard lab setting. We report substantial slowing in reaction times during fMRI

among all participants, and a trend for improved sustained attention performance among ADHD participants.

Methods

Participants

The study included 42 adult participants with ADHD (19 males, age range 19-39, mean=27.3 years) and 21 control participants (6 males, age range 19-37, mean=27.2). All were right-handed with normal or corrected to normal vision. The study conformed to the Declaration of Helsinki and was approved by the ethics committees of Sheeba medical center and Tel-Aviv University. All participants provided written informed consent. Each participant completed a behavioral session in the lab followed by an fMRI session, in different days. The Imaging data has been previously reported (Kolodny et al., 2017, 2020).

Participants with ADHD were recruited through advertisement within university and college campuses. All had a previous diagnosis of ADHD by a qualified clinician, and their current and childhood diagnosis was verified in a clinical interview conducted by a psychiatrist from our research team (author ST), conforming to DSM-5 criteria for ADHD. Participants were excluded if they had neurological or psychiatric disorders other than ADHD, including major depression, anxiety, OCD, or psychosis. Participants were not using any psychotropic medications other than psychostimulants customary to treat ADHD. Participants receiving psychostimulants had at least 24-hours washout period before each testing session (i.e. both before the lab session and before the scanner session). Control participants had no prior history of neurological or psychiatric conditions, no learning disabilities, and no indication of attention difficulties, as assessed by the Adult ADHD Self-Report Scale (ASRS)(Kessler et al., 2005; Zohar & Konfortes, 2010).

Tasks and procedure

Participants performed a Go/No-go task and were instructed to respond quickly when a Go stimulus – a red square – was presented in the center of the screen, and to withhold response to all other stimuli (Fig. 1). Two variants of this task were administered in each session, in a counter-balanced order across subjects: one with a high occurrence of Go trials and low occurrence of No-go trials (prevalent-Go condition), and the other with the opposite occurrence rate (rare-Go condition). The task administered in the lab was identical to a previously reported task (Visual Conjunctive Continuous Performance Task – CCPT-V; Shalev et al., 2011), with the addition of a prevalent-Go condition (identical in all parameters other than the percentage of Go trials; see Segal, Mashal, & Shalev, 2015). Each variant of the Go/No-go task included 320 trials and lasted 12 min, preceded by 15 practice trials. Stimuli were presented for 100 ms, interspersed with 1000, 1500, 2000, or 2500 ms intervals. The ratio of Go and No-go stimuli was 30%/70% in rare-Go condition and 70%-30% in the prevalent-Go condition. Behavioral responses were collected using

the space bar of a standard PC keyboard. The task administered in the MRI scanner (Kolodny et al., 2017) followed closely the apparatus of the behavioral task, with adjustments for fMRI scanning. Each variant of the Go/No-go task included 328 trials, presented in 2 blocks of 8 minutes each, separated by a short break. Stimuli were presented for 100 ms, interspersed with a random interval ranging from 1.8 s to 12 s, with a mean of 2.75 s. The ratio of Go and No-go stimuli was 25%/75% in rare-Go condition and 75%-25% in the prevalent-Go condition. Behavioral responses were recorded by button presses on an MR-compatible response box. The lab session always preceded the fMRI session. Tasks were performed in the lab session as part of a larger battery of tests, while the fMRI sessions typically took place on a separate day when no other testing took place.

Data analysis

Data were analyzed using Matlab and SPSS. Commission and omission error rates were calculated for each condition in each session. RT analyses were performed on correct Go trials only, after discarding extremely short responses (<150 ms) and responses where RT was above 4 standard deviations from a participants' mean in the respective condition and session (this procedure resulted in 0 to 4 discarded trials per participant and condition). We obtained ex-Gaussian parameters (μ, σ and τ) (Heathcote, Popiel, & Mewhort, 1991) for each subject by fitting the ex-Gaussian distribution to the RT data with maximum likelihood estimation, using the Simplex routine (Nelder & Mead, 1965) implemented in Matlab (https://github.com/bramzandbelt/exgauss). In order to inspect the fits and assure their quality, we simulated 10,000 data points from each set of ex-Gaussian parameters obtained, and generated a quantile-quantile plot visualizing the empirical against the simulated data (e.g. Shahar, Teodorescu, Usher, Pereg, & Meiran, 2014). A good fit was demonstrated (Section 1 and Figure S1 in the *Supplementary Materials*).

Four participants from the ADHD group were excluded from further analysis due to a high rate of omission errors (>10%) in the prevalent-Go condition in the fMRI session. Omission errors in the prevalent-Go condition are expected to be negligible (as opposed to omissions in the rare-Go, where such errors may reflect lapses of attention) and thus are suspected to result from fatigue or disengagement from the task. This resulted in a final sample size of 38 participants in the ADHD group.

A three-way repeated-measures analysis of variance (ANOVA) was performed separately for each measure: omissions, commissions, traditional RT measures (mean and SD), and ex-Gaussian parameters (μ, σ and τ) as a dependent variable. Environment (lab or fMRI) and condition (rare-Go or prevalent-Go) were within-subjects factors and group (ADHD or control) was a between-subjects factor. Significant effects are summarized in the main text, and full ANOVA tables are provided in Section 4 of the *Supplementary Materials*.

In order to check for the consistency of individual differences across the testing environments, we examined the agreement between the main measures of sustained attention and response inhibition – SD of RT and commission rate – as assessed in the lab and scanner sessions. We used Pearson coefficients to assess linear correlation, and complemented this approach with "limits of agreement" plots (Bland & Altman, 1986) to visualize the extent to which two methods agree on individual subjects' ratings.

Results

Participants performed a Go/No-go task in a standard lab environment and during an fMRI scan, on two separate days. Two variants of the task were administered in each session (Fig. 1): one with a high occurrence of Go trials and low occurrence of No-go trials (prevalent-Go condition), and the other with the opposite occurrence rate (rare-Go condition). The rate of commission errors (false alarms) in the prevalent-Go condition serves as the main measure of response inhibition, whereas sustained attention functioning is assessed by the standard deviation of reaction times in both task variants. However, for completeness and in order to get a fine-grained characterization of behavioral performance, we fully report all accuracy and reaction time measures from both task variants in both environments (lab and scanner), including ex-Gaussian parameters fitted to describe the RT distributions.

Error rates

Omission rates (Fig. 2A) were overall low, though higher in the scanner than in the lab (1.6% and 0.5%, respectively; $F(1,57)=23.3$, $p<.001$, $\eta_p^2=.29$), and higher in ADHD participants than in controls (1.6% and 0.5%, respectively; $F(1,57)=9.1$, $p<.005$, $\eta_p^2=.14$). No other effects were significant. Commission errors (Fig. 2B) were significantly more frequent in the prevalent-Go condition than in the rare-Go condition (4.7% and 0.7%, respectively; $F(1,57)=105.8$, $p<.001$, $\eta_p^2=.65$), as expected from the frequency manipulation. That is – prevalent Go trials created a tendency to respond, thus challenging response inhibition, which resulted in higher rate of commission errors. ADHD participants made more commission errors than controls (3.5% and 1.9%, respectively; $F(1,57)=10.5$, $p<.005$, $\eta_p^2=.16$), again as expected (Epstein, Conners, Sitarenios, & Erhardt, 1998). There was a significant interaction between group and condition ($F(1,57)=7.6$, $p<.01$, $\eta_p^2=.12$), with the group difference being larger in the prevalent-Go condition. No other effects were significant. Importantly, environment had no effect on commission errors ($F(1,57)=1.6$, *n.s.*), nor did it interact with any of the factors, indicating that response inhibition performance was not influenced by the fMRI setting.

Reaction times

Mean RTs (Fig. 2C) were slower in the rare-Go condition than in the prevalent-Go (502 ms and 450 ms, respectively; $F(1,57)=193.8$, $p<.001$, $\eta_p^2=.77$), and slower for ADHD

participants than for controls (494 ms and 457 ms, respectively; F(1,57)=7.4, p<.01, η_p^2=.12). Importantly, RTs were dramatically longer in the scanner than in the lab (537 ms and 414 ms, respectively; F(1,57)=382.7, p<.001, η_p^2=.87). SD of RT differed significantly only between groups (Fig 2D), with higher variability in ADHD (83 ms) than controls (60 ms; F(1,57)=21.7, p<.001, η_p^2=.28), as expected (Kofler et al., 2013; Segal et al., 2015; Tamm et al., 2012). All other effects were not significant. Importantly, SD of RT did not differ between the lab and the fMRI sessions (F(1,57)=0.9, *ns*), implying that sustained attention performance was not different between the environments.

To further investigate the effect of RT slowing in the scanner, we fitted the data with ex-Gaussian parameters (Figure 3a-b): μ and σ reflecting the mean and standard deviation of the normal component, and τ reflecting the exponential component, which could be thought of as the "heaviness" of the right tail of the distribution. The ex-Gaussian analysis corroborated the main findings of the classic RT analysis: the larger intra-subject variability in ADHD is apparent throughout the RT distributions (Figure 3c), which are wider than controls' (control: σ=36 ms, ADHD: σ=44 ms; F(1,57)=6.7, p<.05, η_p^2=.11) and particularly more skewed (control: τ=45 ms, ADHD: τ=69 ms; F(1,57)=20.3, p<.001, η_p^2=.26), in line with the literature (Gmehlin et al., 2014; Leth-Steensen, Elbaz, & Douglas, 2000). RT distributions obtained in the fMRI session were robustly shifted to the right (Figure 3d; lab: μ=359 ms; scanner: μ=479 ms; F(1,57)=349.7, p<.001, η_p^2=.86). Interestingly, the ex-Gaussian fitting revealed that the RT distributions in the fMRI were also slightly narrower than those obtained in the lab, as reflected in a significant but small effect in σ (lab: σ=42 ms; scanner: σ=38 ms; F(1,57)=6.6, p<.05, η_p^2=.10); but are similarly skewed as reflected in equivalent τ (see Section 2 in the *supplementary material* for report of condition effects). Notably, the group difference was not affected by the testing environment, as reflected in the lack of interaction effects.

To follow up on the finding of smaller σ in the scanner, we examined whether certain subgroups of participants are more affected by the fMRI environment than others. Specifically, we hypothesized that participants who demonstrate difficulty sustaining attention, as reflected in SD of RT in the rare-Go condition in the lab session, would demonstrate improved performance in the scanner. We therefore re-grouped participants according to z-scores of performance in the lab session (z-scores based on data of 450 independent control participants; unpublished data from LS's lab): a low-performance group, with participants scoring below z=-1 (n=15, all ADHD), an average-performance ADHD group (n=23), and the control group (n=21). A post-hoc analysis (Figure 4) yielded significant interaction of group with environment (F(2,56)=7.2, p<.005, η_p^2=.21) and a triple interaction of group, condition and environment (F(2,56)=5.7, p<.005, η_p^2=.17), resulting from significantly reduced SD of RT in the fMRI session for the low-performance group in the rare-Go condition (118 ms in the lab session vs. 90 ms in the scanner session; t(14)=3.4, p<.005; all other paired comparisons t's<2, *n.s.*). This result reveals

that participants with initial low sustained attention performance perform better in the scanner, maybe due to increased arousal or increased cognitive control.

Individual differences: correlational analysis

Stability of individual differences is of particular importance when the behavioral measures are assumed to estimate individuals' ability or severity of impairment. Mean RT and SD of RT correlated moderately between the lab and scanner sessions (from r=.37 to r=.74, all p's<.01; see Figure 5), indicating modest consistency. Commission errors in the prevalent-Go condition had a correlation of r=.33 (p<.05) among ADHD participants and r=.09 (n.s.) among the control group (other error rates were negligible so correlations were not computed). The modest consistency of individual differences between sessions is further illustrated using limits of agreement plots (Figure S2, (Bland & Altman, 1986)), which demonstrate that while the average difference is close to zero both for SD of RT and for commissions, the limits of agreement are far apart.

Possible confounds

The Go/No-go task version used in the scanner was slightly different than the version used in the lab, as is usually the case when adapting a cognitive task from the lab to the scanner: the inter-stimulus intervals (ISI) were longer in the scanner, the task was broken into two runs, and the lab version was always administered first (as a practice preceding the scan). To examine the effect of these differences, we conducted a second independent control experiment, where the 'lab version' and the 'scanner version' were both administered to participants in a standard lab setting, in a counter-balanced order (n=20; non-ADHD; 2 males; mean age = 25.7, SD = 6.6). Performance in the 'scanner version' was not different than performance in the 'lab version' in neither of the accuracy or RT measures (Figure 6). This result suggests that prolonged ISIs, the break between runs, or any order effects, do not underlie the slowdown of responses observed in the fMRI scan in our main experiment; and that the shift in RT distributions is driven by the fMRI environment. Note, though, that this sample was comprised of individuals with average attentional performance, and thus this control experiment cannot speak to the differences observed in SD of RT in the low-performance ADHD group: we cannot rule out the possibility that participants with attentional difficulties will be differentially affected by these parameters.

Discussion

We investigated the effects of fMRI scanner environment on cognitive processes by measuring behavioral performance in a Go/No-go task. The most prominent finding is a substantial slowdown in reaction times, where responses in the scanner were dramatically slower than in the lab. Notably, this effect is both large and consistent,

apparent in all but one participant in the sample (see individual data points in Figure 4a). An ex-Gaussian analysis demonstrated that the RT distributions are shifted, while their shape is largely maintained, indicating that responses prolongation occurs in all trials to a similar extent and is not a result of individual deviant trials skewing the distribution. There were no effects on accuracy, and participants with ADHD were affected to a similar extent as neurotypical control participants. Such a uniform shift in RT distributions is likely to stem from non-cognitive factors, and could be a result of a motor slowdown, or a result of hardware differences between the lab and the scanner setups, for example differences in the response device (keyboard vs. response box) and differences in the relay of signal from the device to the recording computer. However, the latter technical factors are unlikely to fully explain the magnitude of the effect seen in our data (~100 msec). Thus, we conclude the most likely explanation is a delay of motor response, possibly related to the supine position of participants in the scanner.

This finding and interpretation are compatible with those of Koch and colleagues (Koch et al., 2003), who reported overall delayed RTs in a task-switching paradigm in the scanner, while maintaining expected RT differences between task conditions. Importantly, as discussed by Koch et al., although motor slowdown is essentially a non-cognitive source of RT prolongation, it may influence the measurement of cognitive processes, which is often time sensitive. A motor delay might occur in critical time windows in the task, for instance allowing the participant more time to select their response, or change a prepotent or dominant response. This could change the essence of certain tasks, particularly those aimed at response selection mechanisms, for example tasks of response inhibition (e.g. Go/No-go, Stop-signal), stimulus-response mappings (e.g. Simon-like), or interference control (e.g. Stroop-like, flanker). Moreover, slowdown of RTs can distort RT-based measures and change their distributional properties, for example in the case of intra-individual coefficient of variation (ICV, computed as SD divided by the mean of RT; e.g. Dankner, Shalev, Carrasco, & Yuval-Greenberg, 2017; Saville et al., 2011; Wagenmakers & Brown, 2007).

Our second important finding was a reduction in the variability of RT in the scanner among a subset of participants with ADHD, specifically those with initially high variability in the lab session. Changes to variability of RT, which serves as an index of sustained attention, are an indication that attentional functioning is affected, and that the processes that are elicited during imaging might be fundamentally different than those that are assessed in a similar behavioral experiment. It is worth noting that the ADHD sample in the current study comprised mainly of students in higher education, i.e. high-functioning adults, with mild attention impairments and/or good compensation and coping strategies. The scanner effects on attentional performance could be even more pronounced in a more representative sample of ADHD. ‘Normalization’ of deficient attentional functioning under fMRI scanner conditions, directly due to the scanner environment or due to other factors (e.g. differences in task design when adapted to the scanner, differences in the

administration procedure and session length in lab vs. scanner, differential effects of practice and administration order in lower performing individuals, etc.), may play a role in explaining the vast number of fMRI studies in ADHD that fail to replicate well-documented behavioral differences between ADHD and controls (Congdon et al., 2014; Orinstein & Stevens, 2014; van Belle et al., 2015), and threatens the validity of such studies.

Furthermore, all the results summarized thus far rely on group-level analyses. As the field of neuroimaging shifts from uncovering common principles of brain function to investigating individual differences in brain function and behavior (Dubois & Adolphs, 2016; Gratton et al., 2020), it is crucial to assure that individual differences in behavior are stable across measurements, and specifically for task-fMRI that behavioral assessment during the scan is reliable and valid. The moderate correlations demonstrated in the current study between attention measures inside and outside the MRI scanner (Figure 4b) raise concerns about the comparability of these measurements and the extent to which measures in the scanner reflect stable individual traits. Together, our results call for careful assessment of scanner environment effects on behavior when interpreting neuroimaging results. This assessment ought to be specific to the experimental paradigm used and to the studied population, since different age ranges and various clinical groups might be effected differentially.

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Declarations

Funding

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Conflict of interest

All authors declare that they have no conflict of interest.

Ethics approval

All of the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, and the applicable revisions at the time of the investigation.

Consent to participate

Informed consent was obtained from all participants for being included in the study.

Consent for publication

Not applicable

Availability of data

Data will be made available by the corresponding author by request.

Code availability

Not applicable

Author contributions

Author contributions included conception and study design (TK, MA and LS), data collection or acquisition (TK, PS, MA, YD and ST), statistical analysis (TK), interpretation of results (TK, CM and LS), drafting the manuscript work or revising it critically for important intellectual content (TK, CM and LS) and approval of final version to be published and agreement to be accountable for the integrity and accuracy of all aspects of the work (All authors).

Figure 1. Experimental design. Illustration of the Go/No-go task, in which participants were shown a series of stimuli. Participants were instructed to respond quickly when a Go stimulus - a red square - was presented in the center of a screen, and to withhold response to all other stimuli. Trials occurred in a randomized order within two types of blocks: (a) Prevalent-Go, and (b) Rare-Go.

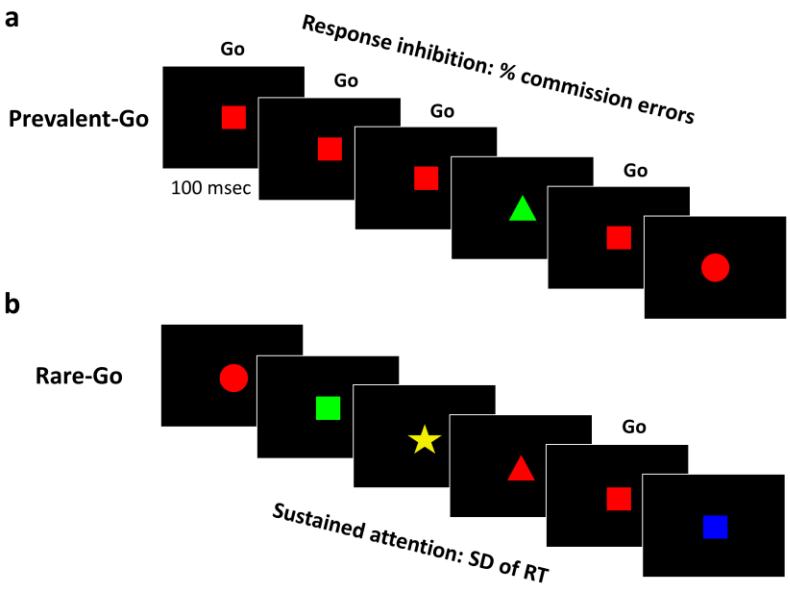


Figure 2. Behavioral measures in the lab and in the scanner. Means of (a) omission errors (%), (b) commission errors (%), (c) mean reaction time (RT; msec), (d) standard deviation of reaction time (SD of RT; msec); as a function of group (control or ADHD), condition (prevalent-Go or rare-Go) and environment (lab or scanner). Error bars represent standard errors of the mean.

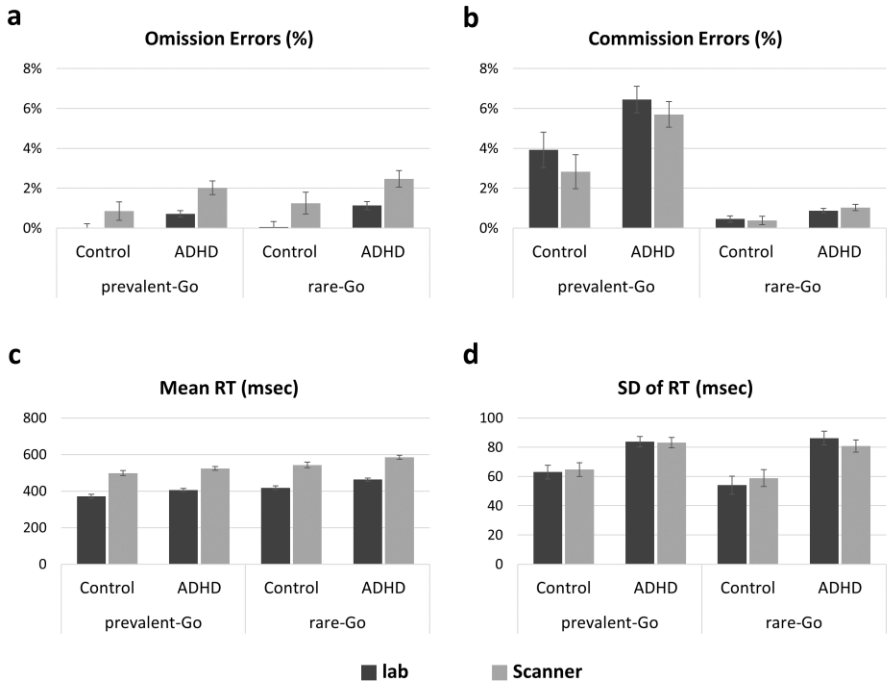
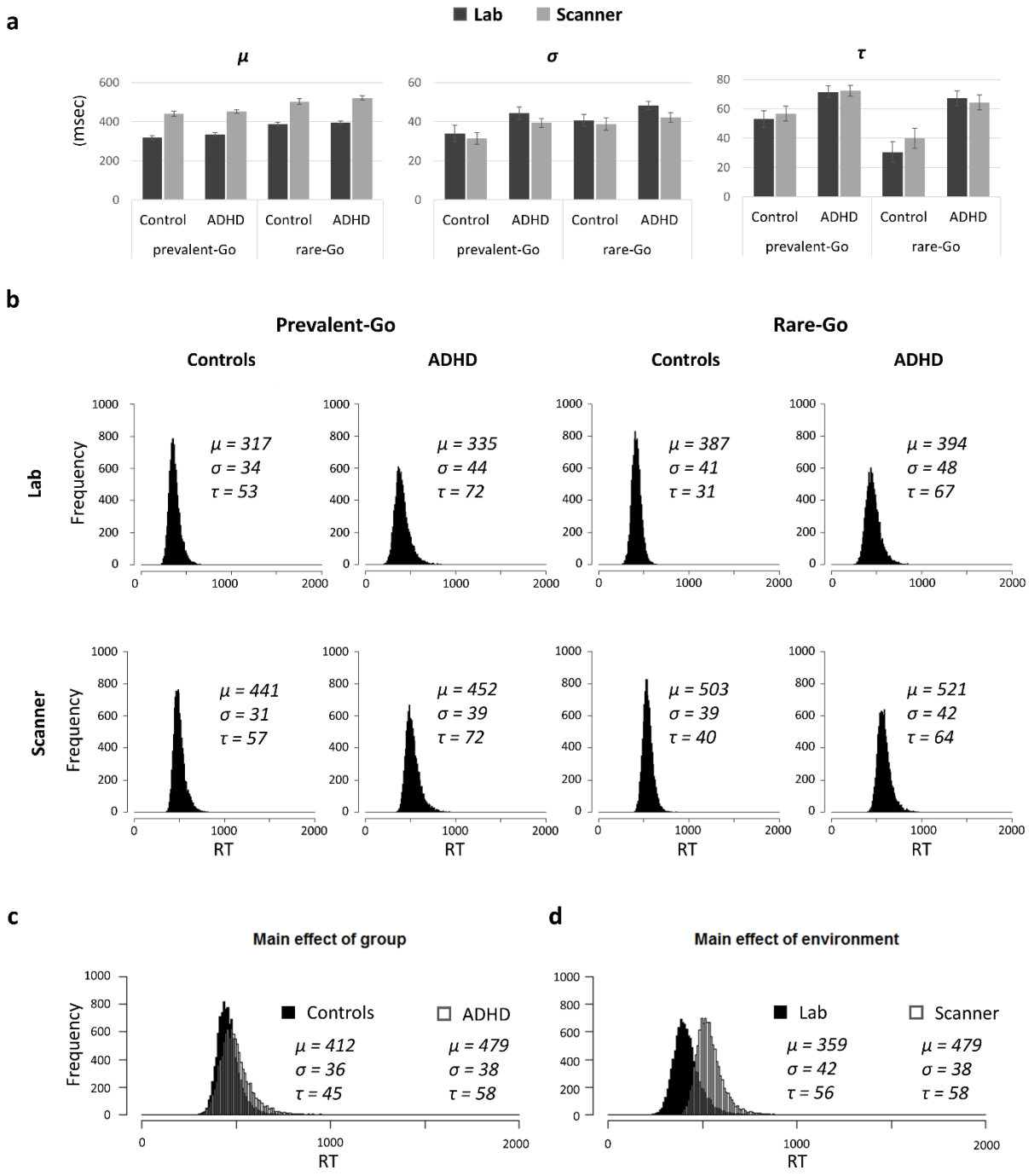


Figure 3. Ex-Gaussian analysis results. (a) Mean ex-Gaussian parameters μ, σ and τ, as a function of group (control or ADHD), condition (prevalent-Go or rare-Go) and environment (lab or scanner). Error bars represent standard errors of the mean; (b) Reaction time (RT) frequency distributions simulated from the mean ex-Gaussian parameters in (a); for different groups (control or ADHD), conditions (prevalent-Go or rare-Go) and environments (lab or scanner); (c) Reaction time distributions of ADHD participants are more skewed than RT distributions of control participants. Simulated distributions from ex-Gaussian parameters averaged across conditions and environments. (d) Reaction time distributions obtained in the fMRI scanner are shifted to the right compared to RT distributions obtained in the behavioral lab setting. Simulated distributions from ex-Gaussian parameters averaged across groups and conditions. μ, σ and τ are given in msec units.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ADHD
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Scanner
Frequency
RT
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τ = 53
μ = 335
σ = 44
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σ = 41
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τ = 67
μ = 441
σ = 31
τ = 57
μ = 452
σ = 39
τ = 72
μ = 503
σ = 39
τ = 40
μ = 521
σ = 42
τ = 64
c
Main effect of group
Controls
ADHD
μ = 412
σ = 36
τ = 45
μ = 479
σ = 38
τ = 58
d
Main effect of environment
Lab
Scanner
μ = 359
σ = 42
τ = 56
μ = 479
σ = 38
τ = 58

Figure 4. Standard deviation of reaction time (SD of RT; msec) compared among three groups, separating participants with ADHD into average-performance and low-performance groups according to scores in the lab session. The latter group demonstrates improved sustained attention performance in the scanner, as reflected in lower SD of RT in the rare-Go condition. Error bars represent standard errors of the mean.

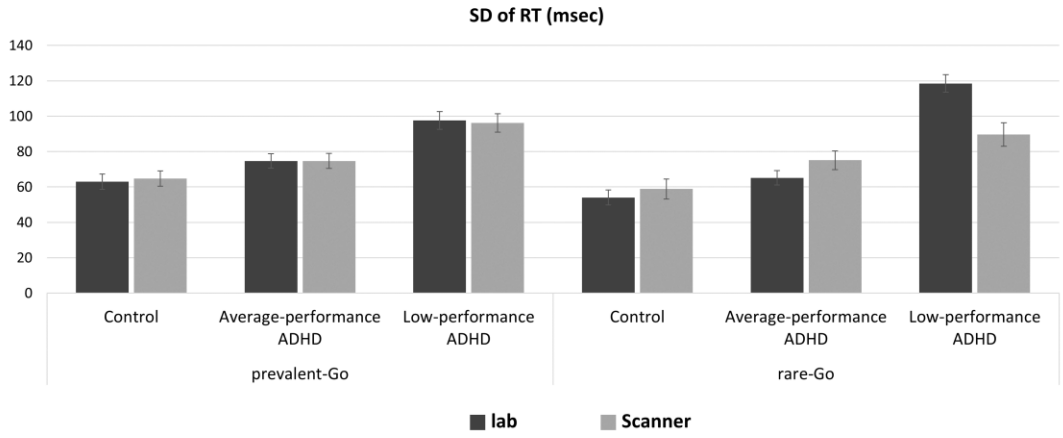


Figure 5. Correlations of mean reaction time (RT), standard deviation of reaction time (SD of RT) and commission errors, across environments. Measures from the scanner session are presented as a function of measures from the lab session. Data points close to the diagonal demonstrate equivalence between environments, data points far from the diagonal present poor compliance.

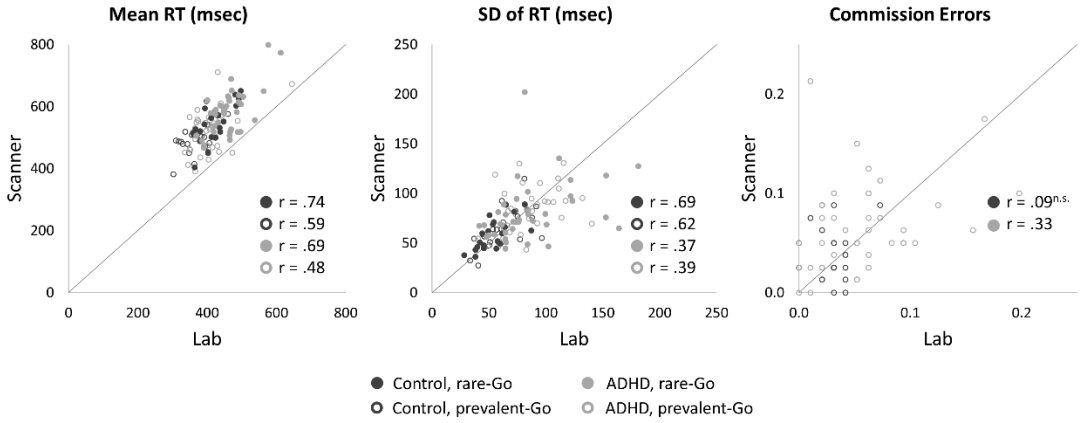
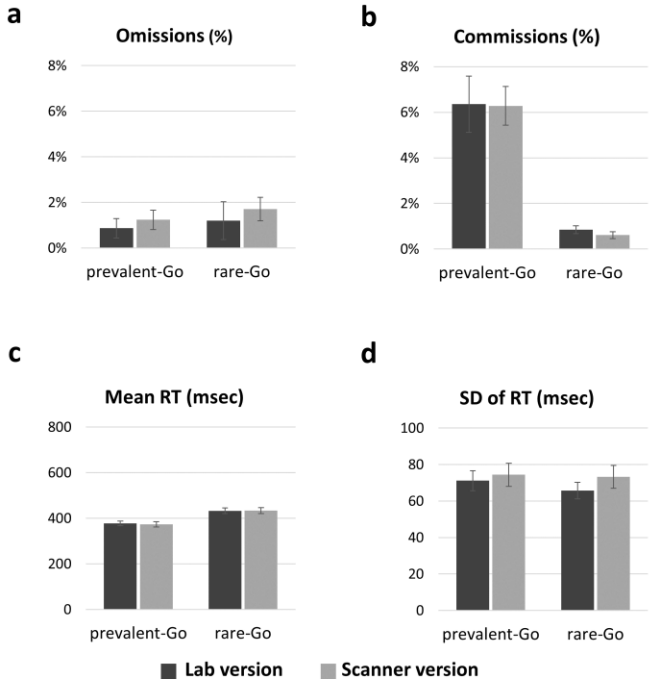


Figure 6. Results of the control experiment, comparing performance in the ‘lab version’ and ‘scanner version’ of the tasks when both were conducted in the lab environment. No differences in (a) omission errors (%), (b) commission errors (%), (c) mean reaction time (RT; msec), (d) standard deviation of reaction time (SD of RT; msec); as a function of task version. Error bars represent standard errors of the mean.



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Supplementary Materials

1. Ex-Gaussian fitting and quality assessment

Ex-Gaussian fitting of individuals' reaction time (RT) distributions was performed in order to get a more fine-grained characterization of RT in the task and to distinguish between various possible sources for slow mean RT. It is well known that RTs in most tasks violate the assumptions of normal distribution, and have a positive skew (Luce, 1986). It can be well modeled by an ex-Gaussian distribution, which is the convolution of a normal distribution with an exponential distribution (Heathcote, Popiel, & Mewhort, 1991). The ex-Gaussian distribution is described by 3 parameters: μ and σ reflecting the mean and standard deviation of the normal component, and τ reflecting the exponential component. The total mean RT of the distribution is given by the sum of μ and τ, and the variance of the overall distribution is given by the summed squares of σ and τ. When fitting ex-Gaussian parameters to an empirical RT distribution, τ reflects the 'heaviness' of the right tail of the distribution, consisted of infrequent but extremely slow responses, suggested to result from lapses of attention (Leth-Steensen, Elbaz, & Douglas, 2000). The μ and σ represent the mean and standard deviation (SD) of the majority of responses, in the main and centered part of the distribution. We obtained ex-Gaussian parameters (μ, σ and τ) for each subject by fitting the ex-Gaussian distribution to the RT data with maximum likelihood estimation, using the Simplex routine (Nelder & Mead, 1965) implemented in Matlab (https://github.com/bramzandbelt/exgauss). In order to inspect the ex-Gaussian fitting and assure its quality, we simulated 10,000 data points from each set of ex-Gaussian parameters obtained (i.e., per each participant, condition and environment). We generated a quantile-quantile plot visualizing the empirical against the simulated data by binning each set of RTs (empirical and simulated, per each participant, condition and environment) into five bins, and plotting the average of each RT bin (e.g. (Shahar, Teodorescu, Usher, Pereg, & Meiran, 2014). A poor fit will be visible by data points far away from the diagonal. As can be seen in Figure S1, the plot demonstrated a very good fit.

2. Ex-Gaussian analysis results

For the sake of succinctness and clarity, only the most prominent effects of interest (environment and group) were reported in the main text. For completeness, we hereby include the full report of the analysis, which was a three-way repeated-measures analyses of variance (ANOVAs), including a within-subjects factor of condition (rare-Go and prevalent-Go). ANOVAs were performed separately for each of the ex-Gaussian parameters η, σ and τ. Main effects of condition were found for all parameters (Figure 3 in the main text): the rare-Go had larger μ than the prevalent-Go condition, reflecting slowing of the normal component of the RT distribution (452 ms and 386 ms, respectively; $F(1,57)=253.6$, $p<.001$, $\eta_p^2=.82$). Interestingly, rare-Go had higher σ estimates than the

prevalent-Go, indicating more variance in the normal component of the distribution, but lower *τ*, indicating less skew (*σ*: 43 ms and 37 ms, respectively; F(1,57)=6.5, p<.05, η_p^2=.10*; τ*: 51 ms and 63 ms, respectively; F(1,57)=14.3, p<.001, η_p^2=.20). Main effects of group were found for both *σ* (control: 36 ms, ADHD: 44 ms; F(1,57)=6.7, p<.05, η_p^2=.11) and *τ* (control: 45 ms, ADHD: 69 ms; F(1,57)=20.3, p<.001, η_p^2=.26), but not for *μ*, indicating larger intra-individual variability of RT for ADHD participants in both the Gaussian and the exponential components of the distribution, in line with previous findings. Importantly, a large main effect of environment was found in *μ* (lab: 359 ms; scanner: 479 ms; F(1,57)=349.7, p<.001, η_p^2=.86) and a small though significant environment effect was observed in *σ* (lab: 42 ms; scanner: 38 ms; F(1,57)=5.4, p<.05, η_p^2=.09), but not in *τ*. No interactions were revealed for any combination of factors in any of the parameters (see full reports in Tables S5-7 below).

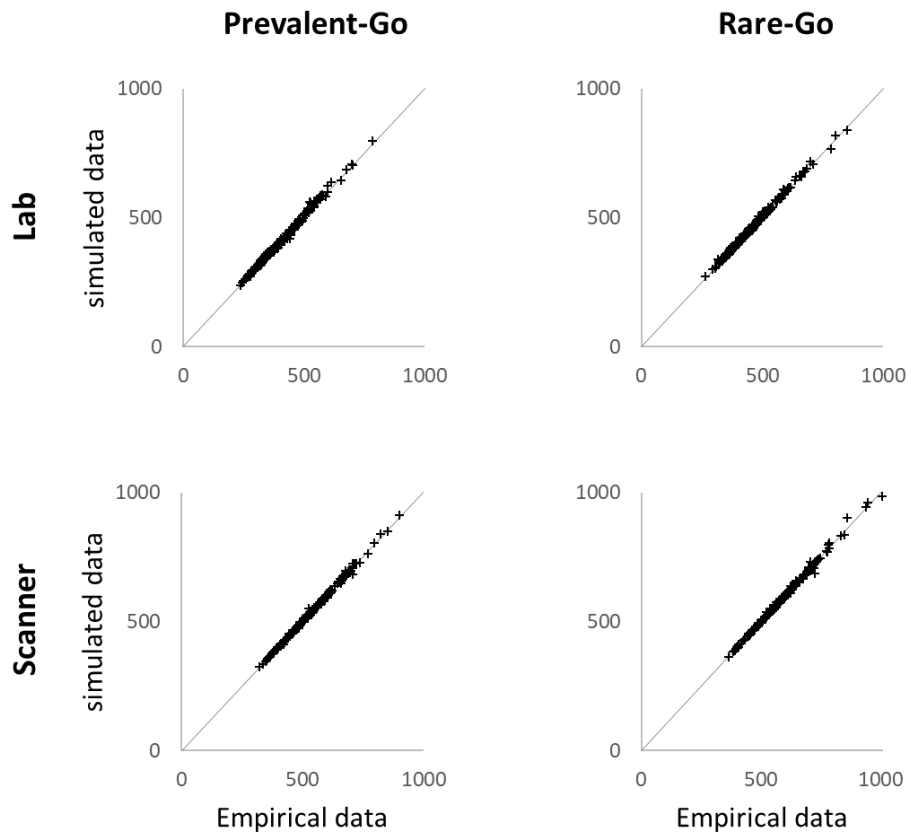

Figure S1. Quantile-quantile plot visualizing the empirical against the simulated data

3. Limits of agreement plots

To further illustrate the mediocre compliance of the measurements we present in Figure S2 “limits of agreement plots”, used to visualize and estimate the agreement between pairs of measurement tools (Bland & Altman, 1986). The difference between the scanner and the lab sessions is presented as a function of their mean, which is used as a best-available estimator of the true effect. The distance between the limits of agreement, which are lines denoting a 1.96 SD interval around the mean difference, is an estimate of the equivalence between measurements from the scanner and the lab sessions. As can be seen in the figure, the mean difference for mean RT is very large, reflecting RT being slower in the scanner than in the lab. Moreover, the limits of agreement are wide, reflecting the variability of individual data points. For SD of RT and commission errors, the mean difference is close to zero reflecting similar means in the lab and in the scanner. However, the limits of agreement are far apart, indicating low equivalence for individual data points. Overall, the Bland-Altman limits of agreement plots further assess the large effect of slow RT in the scanner, and the poor preservation of individual differences between environments.

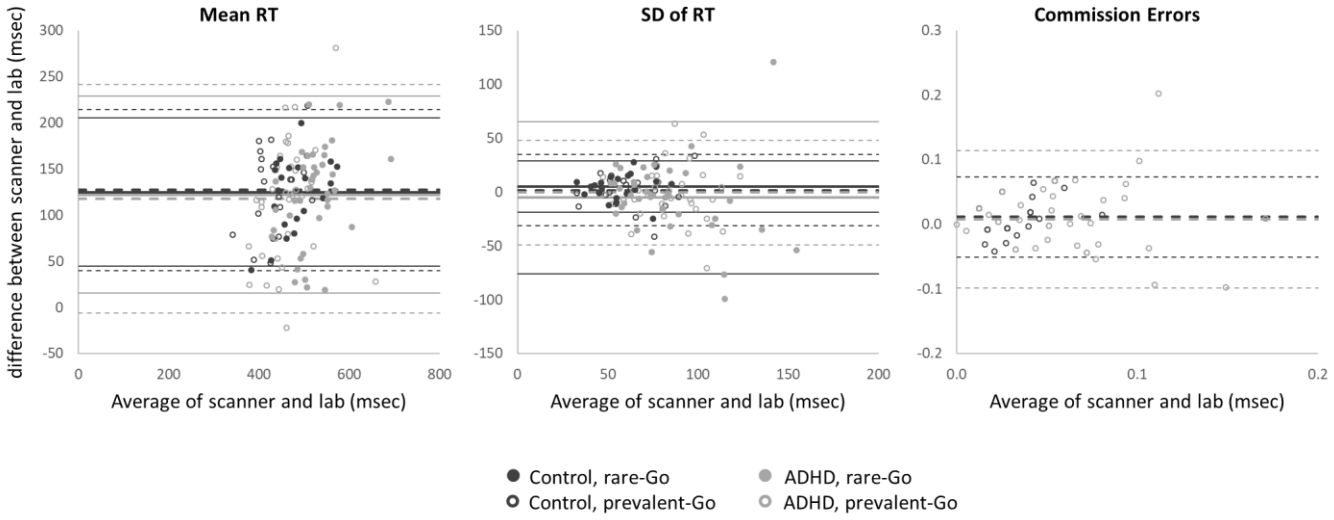

Figure S2. Limits of agreement plots. Thick horizontal lines correspond to filled circles data sets, thin horizontal lines corresponds to empty circles data sets. Continuous lines denote the mean difference, dotted lines indicate 1.96 standard deviations from the mean difference. The distance between the dotted lines of the same set within a plot captures the “limits of agreement” between the scanner and the lab measurements.

4. Full statistical reports

A three-way repeated-measures analysis of variance (ANOVA) was performed separately for each measure: omissions, commissions, traditional RT measures (mean and SD), and ex-Gaussian parameters (μ, σ and τ) as a dependent variable. Environment (lab or fMRI) and condition (rare-Go or prevalent-Go) were within-subjects factors and group (ADHD or control) was a between-subjects factor. Results are verbally summarized in the main text, presenting all significant effect. For completeness, we hereby provide the full ANOVA tables.

Table S1. *ANOVA summary table for omission errors.*

	df	*F*	*p*
Group	1,57	9.10	0.004
Environment	1,57	23.26	<.001
Condition	1,57	2.83	0.098
Group * environment	1,57	0.255	0.615
Group * condition	1,57	0.292	0.591
Environment * condition	1,57	0.340	0.562
Group * environment * condition	1,57	0.159	0.692

Table S2. *ANOVA summary table for commission errors.*

	df	*F*	*P*
Group	1,57	10.51	0.002
Environment	1,57	1.65	0.205
Condition	1,57	105.77	<0.001
Group * environment	1,57	0.18	0.671
Group * condition	1,57	7.57	0.008
Environment * condition	1,57	2.34	0.132
Group * environment * condition	1,57	0.10	0.922

Table S3. *ANOVA summary table for mean RT.*

	df	*F*	*P*
Group	1,57	7.44	0.008
Environment	1,57	382.68	<0.001
Condition	1,57	193.85	<0.001
Group * environment	1,57	0.24	0.624
Group * condition	1,57	2.80	0.100
Environment * condition	1,57	0.02	0.894
Group * environment * condition	1,57	0.22	0.640

Table S4. *ANOVA summary table for SD of RT.*

	df	*F*	*P*

Group	1,57	21.73	<0.001
Environment	1,57	0.00	0.950
Condition	1,57	1.96	0.167
Group * environment	1,57	1.51	0.225
Group * condition	1,57	2.00	0.163
Environment * condition	1,57	0.03	0.873
Group * environment * condition	1,57	0.62	0.433

Table S5. *ANOVA summary table for μ.*

	df	*F*	*P*
Group	1,57	1.16	0.286
Environment	1,57	253.57	<0.001
Condition	1,57	349.70	<0.001
Group * environment	1,57	0.01	0.918
Group * condition	1,57	0.02	0.895
Environment * condition	1,57	0.01	0.946
Group * environment * condition	1,57	1.12	0.294

Table S6. *ANOVA summary table for σ.*

	df	*F*	*P*
Group	1,57	6.69	0.012
Environment	1,57	6.55	0.013
Condition	1,57	5.44	0.023
Group * environment	1,57	0.87	0.354
Group * condition	1,57	0.97	0.329
Environment * condition	1,57	0.00	0.953
Group * environment * condition	1,57	0.08	0.778

Table S7. *ANOVA summary table for τ.*

	df	*F*	*P*
Group	1,57	20.32	<0.001
Environment	1,57	14.29	<0.001
Condition	1,57	0.74	0.395
Group * environment	1,57	3.92	0.053
Group * condition	1,57	1.43	0.238
Environment * condition	1,57	0.04	0.844
Group * environment * condition	1,57	0.58	0.450

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