MIND, BRAIN, AND EDUCATION

Developmental Dyslexia and the Stress of Reading: A Social Stress Study of Neuroendocrine Response in Children

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ABSTRACT— Dyslexia is a neurodevelopmental disorder characterized by persistently slow and effortful reading. It is associated with core cognitive deficits in decoding words, but it also presents significant challenges associated with, for example, anxiety and stress related to academic performance. We asked, thus, whether, reading out loud would be associated with elevated stress for readers with dyslexia, relative to good readers, and we investigated stress-related hormone response in these two groups. We carried out an acute psychosocial stress test (Trier Social Stress Test-Children adapted for children, TSST-C), which included a reading out loud task. We carried out a quasi-experimental study with an experimental group of participants with Developmental Dyslexia ($n = 17$), and a control group, with good readers ($n = 18$). During the stress test, we collected six saliva samples for evaluation of two stress-related hormones, cortisol, and adrenocorticotropic hormone (ACTH) levels. We found a main effect for group for ACTH and for cortisol levels. We also found significantly higher levels of ACTH in the dyslexic group at the end of the task, and during the post-task recovery period. Results are discussed in the light of the less-understood emotional impact of dyslexia, and of a recently proposed role for stress as a trigger for increased risk of development of dyslexia. Lastly, we underscore the contribution for the evidence of the emotional impact of learning disorders, especially, as is the case, from a population generally underrepresented in cognitive neuroscience research (i.e., Latin-American children).

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INTRODUCTION

Developmental dyslexia (DD) affects nearly one in 10 adults and school-aged children (American Academy of Pediatrics, 2009; Singleton, 1999). It has pervasive impacts in educational attainment and in adult life, including income levels (McLaughlin et al., 2014; Undheim, 2009). The characteristic manifestation of DD is a core deficit in learning to map print to its speech counterparts, and in persistently slow and effortful reading, which are not the result of intellectual impairment or lack of adequate schooling (American Psychiatric Association, 2013; Bishop & Snowling, 2004; Shaywitz et al., 2002). The core deficit of DD and the associated alterations in brain morphology and function have been replicated across multiple languages (Buchweitz, Costa, et al., 2019; Cao et al., 2017; Cattinelli et al., 2013; Feng et al., 2020; Galaburda et al., 2006; Kronbichler et al., 2006; Martin et al., 2015; Paulesu et al., 2001, 2014; Ramus et al., 2018; Richlan et al., 2011; Seki et al., 2001; Tanaka et al., 2011). The familial risk for DD has also been well-established (Hulme et al., 2015; Lohvansuu et al., 2021; Shaywitz et al., 1990). However, there is increasing evidence for an interplay between emotional and mental health aspects in developmental risk for DD.

Learning disorders, such as DD, are associated with elevated stress and mood disorders. Struggling readers are more depressed, more anxious, and they report more somatic complaints than typical readers, even after adjusting for demographic variables and diagnosis of other disorders, like Attention-Deficit/Hyperactivity Disorder (ADHD) (Arnold et al., 2005). A large-scale study has shown an association between literacy difficulties, generalized anxiety disorder, and separation anxiety (i.e., "school phobia") (Carroll et al., 2005). Yet, the emotional impact of DD and its relationship to, for example, elevated stress, is far less understood. We asked, thus, whether reading would be associated with elevated stress for readers with dyslexia, relative to good readers. We investigated stress-related hormone responses in children with DD relative to good readers while they were asked to read out loud in front of adults, following the adaptation of a well-known social stress test paradigm. We used saliva samples to assess the levels of two stress-related hormones, cortisol, and adrenocorticotropic hormone (ACTH), during the social stress test paradigm.

Multifactorial Origins for DD and the Less-Understood Interaction with Stress

The etiology of DD is multifactorial. Reduced early brain plasticity and alterations in neuronal migration may underpin DD brain development differences (Galaburda, 2005; Galaburda et al., 2006; Kershner, 2019). Recently, it has been suggested that DD is associated with a dysregulation of excitation–inhibition processes in neuronal firing (Hancock et al., 2017), in other words, the timing of neural activity may be different. These alterations are due, in part, to familial risk factors, heritability, and the role they play in influencing changes in the path of brain development. Recent evidence-suggests, however, that stress may play a critical role in DD early on.

A genome-wide association study found evidence of increased risk for psychiatric cross-disorder susceptibility in DD, in addition to the known associations with educational attainment and alterations in brain morphology (Gialluisi et al., 2020). Children with familiar risk of DD experience more family stresses than their control counterparts; and family stresses predict poorer attention and behavior outcomes (Dilnot et al., 2016). DD may be a precursor to internalizing problems, such as higher risk for depression and anxiety, and it is associated with significantly lower levels of self-esteem (Boyes et al., 2016; Livingston et al., 2018). Children and adolescents with DD show elevated anxiety and emotional distress in anticipation of, for example, situations that involve school performance (Frederickson & Furnham, 2001; Lackaye & Margalit, 2006). Early life stress has been shown to alter systemic stress response in the hypothalamic–pituitary–adrenal (HPA) axis. These alterations, in turn, can impact the course of brain development (Chahal et al., 2020; Fareri & Tottenham, 2016; Grassi-Oliveira et al., 2016; Hanson et al., 2015). It has been suggested that early life stress may increase the risk for triggering the brain development alterations associated with DD (Theodoridou et al., 2021). In other words, early life stress may increase the risk that familial risk for DD will influence significant alterations in brain development.

Stress-Related Hormones in Neurodevelopmental Disorders

Psychological stress, such as that which results from reading or in anticipation of school performance for children with DD, can induce the activation of the HPA axis. In a nutshell, the mechanism of response to stress involves the HPA axis receiving neuronal signals associated with stress. Once these signals arrive at the paraventricular nucleus of the hypothalamus, they trigger the release of the corticotropin-releasing factor to the external zone of the pituitary gland in the brain (Armario et al., 2012). The anterior pituitary then releases the adrenocorticotropic hormone (ACTH). Circulating levels of ACTH are detected by the adrenal cortex, and systemically stimulate the synthesis and secretion of glucocorticoids (e.g., cortisol). Thus, this mechanism of systemic response to stress involves the expression of ACTH and cortisol, which are the two hormones investigated in the present study.

The presence of elevated stress has been investigated by assessing the relative systemic levels of hormones; in other words, by comparing stress-related hormonal responses between more or less stressed participants. Systemic levels of cortisol can be measured in saliva and hair samples. Elevated stress has been associated with increased salivary (Grassi-Oliveira, Ashy, & Stein, 2008) and capillary levels of cortisol. These elevated levels of cortisol have been further linked to alterations in brain function and increased risk for internalizing and externalizing problems (Buchweitz, de Azeredo, et al., 2019; Grassi-Oliveira et al., 2012). The interaction between stress, brain development and function has been identified in a variety of neurodevelopmental conditions, including ADHD (Chang, Su, Mondelli, & Pariante, 2021), autism spectrum disorder (Bozkurt, Şimşek, & Şahin, 2021), central coordination disorder, and fragile X syndrome (Hardiman & Bratt, 2016). Few studies, however, have investigated if stressful situations, such as cognitive challenges presented by academic performance, could result in hypo- or hyper-activation of the HPA axis in neurodevelopmental disorders. Anesiadou et al. (2021) compared salivary cortisol levels of children with ADHD, autism spectrum disorder, or specific-learning disorder, to those of typically developing counterparts. They found evidence of a distinct HPA axis response in children with neurodevelopmental conditions by analyzing cortisol levels pre- and post-

cognitive challenges. In the present study, we investigated if children with DD would present elevated stress (as construed by altered HPA axis response) in the face of a stressful situation of reading out loud. We assessed stress-related hormone response (i.e., ACTH and cortisol) in the saliva samples of readers with DD relative to good readers. To our knowledge, this is the first study to investigate social stress inoculation for DD and the neuroendocrine response to stress related to reading.

METHODS

Participants

We conducted a quasi-experimental, between-group comparison study with two groups: Developmental Dyslexia and Good Readers. The Developmental Dyslexia (DD) group included 17 participants (DD; 6 female); the Good Reader group included 18 age-matched controls, with no reading impairments (10 female). Participants were invited following their evaluation in a pro-bono Reading Clinic, which provided evaluation for children struggling to read, including diagnosis of DD. We did not invite participants who were undergoing psychotherapeutic treatment or using medication for depression, ADHD, or anxiety disorder, as per the medical history obtained in the Reading Clinic evaluation, or during an interview with parents or guardians prior to the study. We matched participants for age and screened for anxiety, using the State–Trait Anxiety Inventory (STAI) (Spielberger et al., 1983) and the Beck Anxiety Inventory (BAI) (Beck & Steer, 1993). We also screened for depression using the Children's Depression Inventory (CDI) (Kovacs, 1992). All tests have a published, validated adaptation to Brazilian Portuguese (Biaggio & Natalício, 1979; Cunha, 2001; Gorenstein et al., 1999; Gouveia et al., 1995).

There were no significant differences in age, anxiety, or depression scores. The socioeconomic questionnaire scores for the Good Readers were, on average, lower than those of the DD group. However, both average scores translate to socioeconomic substrata within the B strata for Brazil (A = Upper Stratum; B = Middle; C = Lower Middle; D = Upper Lower; E = Lower). DD were, on average, in B1 stratum and Good Readers, B2, which are both within the Middle-Class range; neither stratum are below the poverty line (World Bank, 2022). The descriptive statistics for the two groups are presented in Table 1. Reading fluency was evaluated using a standardized test for Brazilian Portuguese. The Good Readers showed adequate reading speed for their age, and the DD showed reading performance well below the expected levels for their age (Saraiva et al., 2006). A more detailed description of the DD evaluations can be found elsewhere (Bassôa et al., 2021; Buchweitz, Costa, et al., 2019; Toazza et al., 2017). The scores for reading fluency were significantly different between the groups, as expected (Table 1).

The present study relied on volunteer participation of DD children diagnosed by our pro-bono reading clinic (Costa et al., 2016; Toazza et al., 2017); our initial goal was to obtain two groups of 40 participants, a convenience sample size determined by the extent of fundings received for investigating neuroendocrine response. The continuation of the study and its sample size were significantly affected by the COVID19 pandemic, since the social stress test requires meeting and interacting in person with participants. As the pandemic subsided, funds, some team members, and the Reading Clinic were no longer in place.

Procedures

The evaluation of reading skills and the diagnosis of DD were carried out as part of two larger studies. DD participants were evaluated at our Reading Clinic, Good Readers were participants from a larger school cohort. These participants were invited to participate in the present study. The Reading Clinic was a pro-bono service for children aged 8–11 years who present persistent reading difficulties (Buchweitz, Costa, et al., 2019; Costa et al.,

Table 1
Descriptive Statistics for the Developmental Dyslexia (DD) and Good Reader groups (Average [*SD*])

	DD (n = 17; 6 female)	*Good readers (n = 18; 10 female)*	*p*
Age (years)	10.93 (1.23)	10.78 (0.87)	.664
SES	24.26 (4.84)	20.05 (4.50)	.015*
STAI state	44.62 (8.92)	43.61 (12.68)	.792
STAI trait	50.93 (8.81)	48.16 (14.45)	.511
BAI	13.37 (8.74)	9.98 (7.66)	.225
CDI	5.38 (2.59)	7.38 (5.33)	.222
Fluency (wpm)	52.3 (25.5)	114.5 (18.6)	<.001*

Note: BAI = Beck Anxiety Inventory (total score); CDI = Child Depression Inventory (total scores); Fluency = words per minute (SD) (Saraiva et al., 2006); SES = Socioeconomic Status based on Brazilian criteria (ABEP, 2016); STAI = State–Trait Anxiety Inventory (STAI): trait and state total scores.
*p value for Student's t-test for independent samples ($p < .05$).

2016; Toazza et al., 2017). The Clinic was part of a larger behavioral, neuropsychological and brain imaging study of dyslexia (Bassôa et al., 2021; Buchweitz, Costa, et al., 2019; Costa et al., 2016; Toazza et al., 2017). The Clinic provided free services for diagnosis of DD for 9 years, during which time hundreds of children and families sought the multidisciplinary evaluation of reading for struggling readers, a service that is generally scarce and inaccessible outside private services, in Brazil.

No financial compensation was provided to the participants. Families were provided with payments for transportation and meals. The present study was approved by the pertinent Research Ethics Committee (registration number CAAE 85239418.9.0000.5336), which is in accordance with the Declaration of Helsinki. All participants gave their informed consent and signed an Informed Consent Form as approved by the Research Ethics Committee.

Trier Social Stress Test

The Trier Social Stress Test (TSST) has been widely used as a tool in the investigation of neuroendocrine patterns associated with exposure to psychological stress (Dickerson & Kemeny, 2004; Ellenbogen, Hodgins, Walker, Couture, & Adam, 2006; Ellenbogen, Schwartzman, Stewart, & Walker, 2006; Wiemers, Sauvage, Schoofs, Hamacher-Dang, & Wolf, 2013). The TSST for adults consists of an anticipation period and a test period in which participants give a free speech, and then perform mental arithmetic, both in front of an audience. TSST may induce behavioral and physiological responses, such as those associated with social and stressful situations. It thus allows for the investigation of physiological responses in basic and clinical research (Dickerson & Kemeny, 2004).

We used the adaptation of the TSST for children (TSST-C) (Buske-Kirschbaum et al., 1997) in its Brazilian Portuguese version (Viola et al., 2014). The TSST-C consists of a baseline phase, the TSST protocol, and a rest/recovery phase. The baseline lasts 20 min. The TSST protocol, in turn, is divided into 5 min blocks: Explanation, Preparation (Anticipation), and tasks (Free Speech and Mental Arithmetic). After, there is a recovery period. The TSST-C has been translated, adapted and validated for Brazilian Portuguese by our collaborators (Viola et al., 2014). We further modified the TSST-C to better fit the goals of the study. Rather than read a story (Free Speech task), and orally report on its continuation, we asked participants to read out loud from an age-appropriate passage of a well-known book for youths (Rowling, 2000) (see Data S1). The passage was read out loud during what originally was designed as the Free Speech phase (Viola et al., 2014). Other researchers in Latin America have also applied modifications to the TSST to better accommodate the goals of the study and the study population (Johnson et al., 2017). Figure 1 presents an illustration of the TSST-C protocol implemented in the present study (see Data S1 for a description of the phases of the TSST-C in the present study).

Saliva

A total of six (6) saliva samples were collected. The timing for the six saliva sample collections were T1 at baseline; T2 at Explanation; T3 at Preparation/Anticipation; T4 at Reading Out Loud and Mental Arithmetic; and T5 and T6 during Recovery. Saliva samples were obtained using a Salivette sampling device (Sarstedt, Nümbrecht, Germany). The cotton sliver of the Salivette was taken out and put in the sublingual of the participants about 1–3 min, and then put back to the Salivette and stored at 4°C refrigerator for further laboratory analysis.

Anxiety Symptoms

We evaluated levels of anxiety during individual debriefing interviews with the participants, as described in a previous study (Krämer et al., 2012). Participants were asked to report their perceived anxiety using the Iconic Self-Assessment of Anxiety in Children (ISAAC) (Schneider, Wilhelm, and Martin, 2005). Participants were asked about their perceived anxiety during the baseline period, before and after the TSST-C, and during the recovery period.

Data Analyses

Hormonal Response

Saliva samples were collected at six different points in time using the Salivette sampling device (Sarstedt, Nümbrecht, Germany): Baseline (T1); Anticipation (T2); Preparation (T3); TSST Free Speech (Reading Out Loud) and Mental Arithmetic (T4); Recovery 1 (T5); and Recovery 2 (T6) (Figure 1). The samples were centrifuged at 3000 rpm for 5 min. At least 1.0 mL of saliva was collected following the centrifugal process. Subsequently, the centrifuged saliva was stored at −80°C refrigerator for further laboratory analysis. Salivary cortisol and ACTH concentrations were detected using a high-sensitivity salivary cortisol enzyme-linked immunosorbent assay (ELISA) for cortisol (Salimetrics LLC, State College, PA, USA) and ACTH (Wuhan Fine Biotech Co., Wuhan, China) according to the manufacturer's instructions. Aliquots of each six saliva samples were used for the assessment of cortisol and ACTH based on the instructions of the ELISA assays. All samples were run in duplicates by the same researcher. The intra- and inter-assay coefficients of variation for salivary cortisol and ACTH analysis were below 10%, according to the manufacturer's instructions. Salivary Cortisol data are expressed in nmol/L.

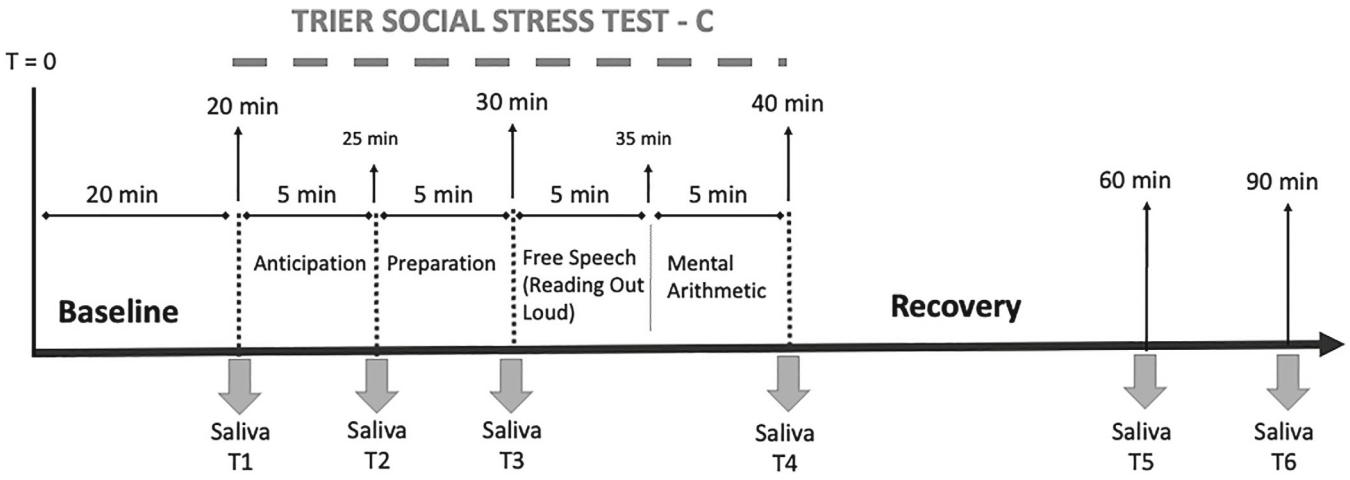

Fig. 1. Illustration of the adapted TSST-C version used in the experiment. Each salivary sample was collected at timepoints T1 to T6 (Note: distances between timepoints not to scale).

Statistical Analysis

We tested data for normal distribution and homogeneity of variance using Kolmogorov–Smirnov or Shapiro–Wilk tests, as well as for skewness, before statistical procedures were applied. These analyses revealed significant deviations in salivary cortisol and ACTH values. Therefore, the salivary cortisol and ACTH values were log-transformed to reduce the skewness and allowed for the use of parametric models in the analyses (see Table S1 for nonlog transformed data).

First, we compared ACTH and cortisol levels across groups using a one-tailed independent samples t-test. We also used a multivariate general linear model to investigate the main effect of group on ACTH and Cortisol levels. We modeled the dependent variable as each participant's time point (T1–T6) ACTH and cortisol log-transformed levels, the groups as the independent variable, and sex as a continuous covariate using 0 and 1. Indeed, stress studies have shown young men with higher stress-related cortisol responses than young women to real-life stress (e.g., academic exams) or inoculation of stress in experimental conditions (e.g., using the TSST) (Kirschbaum et al., 1995; Kudielka & Kirschbaum, 2005; Liu et al., 2017). Hence, we included sex as a covariate in the multivariate analysis.

We report the *p*-values and corrected model *p*-values, degrees of freedom and partial Eta for each comparison; we considered a *p*-value <.05 to be statistically significant for the analyses of hormonal response. For the *t*-tests across timepoints, we report *p* values and we used the Benjamini and Hochberg procedure to correct for multiple comparisons (Benjamini & Hochberg, 1995). All comparisons were performed using log-transformed hormone levels. All statistical analyses were performed using IBM SPSS Statistics (SPSS, Chicago, IL, USA).

RESULTS

Biological Stress Responses to the TSST-C: Significantly Different Mean ACTH and Cortisol for DD

The results show that DD participants' mean ACTH level ($M = 1.44$, $SD = 0.38$) was significantly higher than the Good Readers' mean ACTH level ($M = 0.95$, $SD = 0.37$): $t(18) = 2.879$ ($p = .005$); Cohen's d = 0.380 (Figure 2). The results also show DD participants mean cortisol level ($M = 0.74$, $SD = 0.29$) was significantly higher than the Good Readers' mean cortisol level ($M = 0.57$, $SD = 0.21$): $t(30) = 1.909$ ($p = .033$); Cohen's d = 0.255 (Figure 2).

The between-group comparisons for each timepoint showed ACTH levels were significantly higher for DD in timepoints T4, T5, and T6; the cortisol levels, in turn, were significantly higher for DD in timepoints T1, T2, and T3. We report the t-test results, and the corrections for multiple comparisons, in Table 2. Figure 3 shows a representation of the TSST-C trial and the average (nonlog transformed) salivary ACTH and cortisol for each group, at each time point (Figure 3).

Main Effect of Group in ACTH, but no Effect in Cortisol

The multivariate analysis, in turn, suggested a main effect of group for higher salivary ACTH levels: $F(2, 13) = 3.072$, $p = .042$ (Pillai's Trace = 0.586; Partial Eta Squared = 0.586); but no main effect of group for salivary cortisol levels: $F(2, 24) = 1.082$, $p = .395$ (Pillai's Trace = 0.412; Partial Eta Squared = 0.206). No significant effect of the sex covariate was detected. The participants were matched for their anxiety scores prior to the study. The results showed no group differences in anxiety and depression screeners.

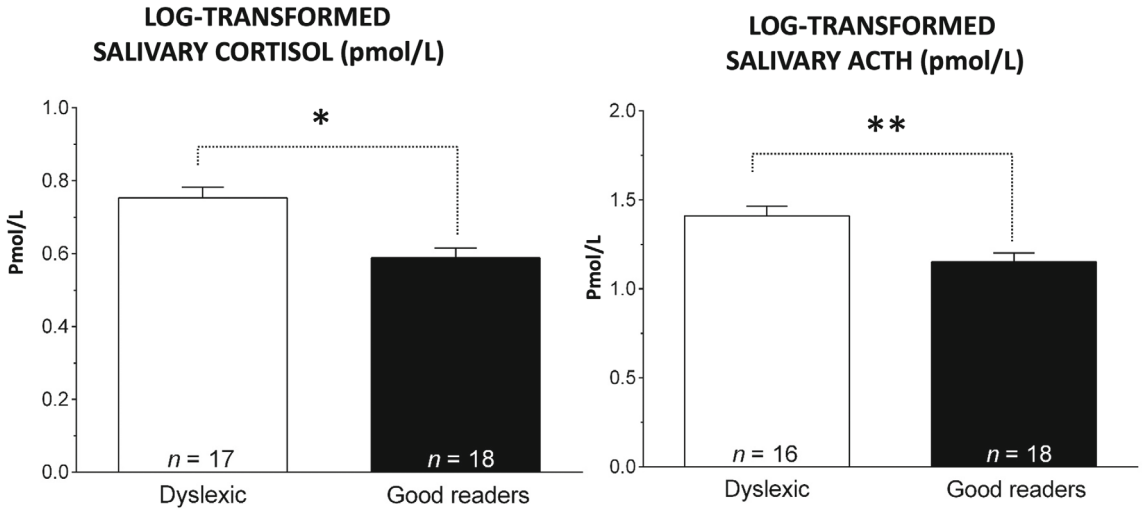

Fig. 2. Mean salivary cortisol and ACTH levels across groups. Means represent the log-transformed values; ** = $p < .01$; *$p < .05$.

Table 2
TSST salivary levels: ACTH and Cortisol

	ACTH			*Cortisol*		
	T (df)	*p*	*Cohen's d*	*T* (df)	*p*	*Cohen's d*
T1	1.547 (29)	.066	0.491	1.936 (33)	**.031***	0.240
T2	0.840 (29)	.204	0.302	1.779 (33)	**.042***	0.248
T3	1.361 (29)	.092	0.489	1.930 (33)	**.031***	0.305
T4	1.925 (29)	**.032***	0.695	1.001 (31)	.162	0.329
T5	2.476 (30)	**.010***	0.875	1.398 (32)	.086	0.480
T6	1.798 (25)	**.042***	0.693	0.591 (33)	.279	0.322

Note: t values and *df* (degrees of freedom); *p* values in bold <0.05.
**p* values do not remain significant after correction for multiple comparisons using Benjamini and Hochberg procedure for FDR = 0.05 (values remain significant for FDR = 0.1).

DISCUSSION

Our results suggest that DD participants had higher means of cortisol and ACTH, relative to good readers, in a modified version of a social stress test (Viola et al., 2014). Analyses of ACTH and cortisol at specific time points showed higher baseline DD cortisol at the start of the experiment and higher ACTH at later time points, after the task, and at the end of the experiment. The multivariate analyses showed a main effect of group only for ACTH, and not for cortisol. The participants were matched for anxiety and screened for depression. We found no group differences in the scores for anxiety and depression; although the literature shows that there are sex-related differences in hormonal responses to stress, we did not find a main effect of sex for ACTH or cortisol levels.

The elevated baseline cortisol levels found in DD could suggest a pattern of chronic hyperactivation of the HPA axis, or that prior to the TSST, children with DD were significantly more stressed than good readers due to anticipatory anxiety. The results suggest that the social stress test induced an elevated physiological stress response of ACTH in children with DD compared to the response of good readers. These findings suggest an altered HPA axis response associated with the anticipation and with the act of reading out loud and performing mental arithmetic tasks, with differences between ACTH and cortisol regarding the slope of the neuroendocrine effect observed in children with DD.

Children who are diagnosed with DD are usually well into second or even third grade when the clinical diagnosis is established (Gaab, 2019; Ozernov-Palchik & Gaab, 2016; Sanfilippo et al., 2020). Participants in our Reading Clinic had average age at diagnosis of 10.5 years. Thus, these children had attended at least 4 years of formal schooling (or 6 years including preschool) before they were properly

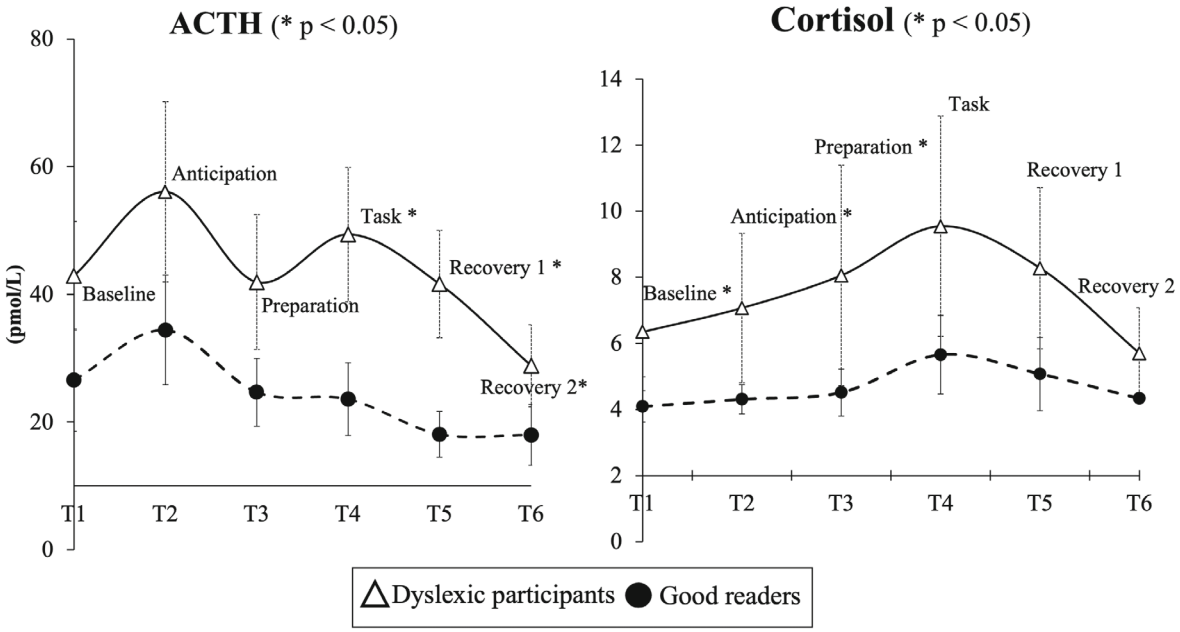

Fig. 3. Time course for means (± SEM) of physiological responses to the Trier Social Stress Test (TSST) in DD and good readers.

diagnosed (Costa et al., 2016; Toazza et al., 2017). More than two-thirds of DD children in the Clinic, over the years, had been held back 1 year or more in school, mostly due to lack of accommodation; the larger group of Clinic participants had an average age at diagnosis of 11 years (Costa et al., 2016; Toazza et al., 2017). School and institutional settings, and the anticipation of school performance may trigger anxiety and stress in any student. But children with dyslexia may find school performance to be significantly more stressful, especially if appropriate accommodations are not observed (Leitão et al., 2017; Shaywitz et al., 1990).

Neurodevelopmental disorders are associated with high rates of school absenteeism and dropout (American Academy of Pediatrics, 2009; American Psychiatric Association, 2013). They are also associated with increased risk for poorer quality of life and outcomes for youths and adults, especially if undiagnosed and untreated. These disorders show a high correlation with behavioral problems; moreover, there is a fivefold over-representation of ADHD among incarcerated youths (Young et al., 2015). For DD, in its turn, there is an over-representations at 50% or higher among offenders, which is between five and tenfold higher than the prevalence of 4%–10% among the general, nonincarcerated population (Baker & Ireland, 2007; Kirk & Reid, 2001; Samuelsson et al., 2000). Again, whether a result of DD or a coexisting behavioral or mental health comorbidity, cognitive and emotional aspects interact, and this interaction increases the risk of poorer outcomes for children with DD.

The inclusion of students with DD has been increasingly leveraged by regulations, which ensure the equality of access for children, adolescents and college students (Kirkland, 2009; Leitão et al., 2017; Livingston et al., 2018; Pino & Mortari, 2014; Shaywitz, 1998). Special provisions for students with DD include more time for reading and taking tests, audio support (e.g., audiobooks) and technological assistance. In Latin America, these provisions are usually lagging for reasons that range from lack of infrastructure and training to political pushback from stakeholders in the education sector against diagnosis of neurodevelopmental disorders. It was only in 2021 that Brazilian federal regulations included Developmental Dyslexia and ADHD among developmental disorders that should be provided educational accommodations. Though the law has been signed, it still requires implementation policies for the public education system. We argue that our results help underscore the need for the implementation of clear policies for accommodation and evaluation of DD. Reading will always be more laborious for readers with DD, but there are ways to mitigate the effects of the disorder. We underscore the pressing need for early and proven assessment and interventions (Lonigan & Shanahan, 2002; Scarborough, 2001; Scarborough, 1998) coupled with policies that establish accommodations and professional development for stakeholders, especially infor the underserved populations of Latin American children (Fortes et al., 2016; Gaab, 2019; Silva et al., 2022).

Recent evidence suggests that DD and stress may be associated in more intricate ways than a commonsensical,

one-way, cause and effect relationship. This may come as no surprise to developmental psychology or cognitive neuroscience, but not necessarily so for stakeholders outside these fields. We underscore that it is the interplay between stress and neurodevelopmental disorders that should be further understood. Early exposure to elevated stress has sustained effects on brain development (Arnsten, 2015; Birn et al., 2017; Bremne & Vermetten, 2001; Chaby et al., 2020). Early stress is associated with risk for alterations in the brain's typical functional asymmetries between hemispheres found in DD (Berretz et al., 2020); it can lead to increased risk for DD as it affects maturational timing and neuroplasticity (Kershner, 2020, 2021; Theodoridou et al., 2021; Zakopoulou et al., 2019). A recent theory postulates alterations in neural excitability and neural "noise" (random variability in the firing of neural networks) as mechanisms that contribute to alterations in DD brain function (Hancock et al., 2017). The interaction between stress and neural development may increase the chances for changes in neural excitability and firing; roughly, in the ability that neurons have to communicate with one another. The role of stress in DD underscores the potential protective effects of early childhood healthcare and educational assistance.

In the present study, baseline cortisol levels suggest that children with DD show elevated levels of stress relative to their peers. We advocate that whether stress emerges because of anticipation of task performance, whether it is intrinsically more elevated in DD, or whether it is both, it plays a role in creating more obstacles for school-related behavior and performance. Of note, the DD participants were from a higher socioeconomic substratum than the good readers, which highlights the pervasive challenges of access to reliable multidisciplinary evaluation services in Brazil, and the pervasive consequences of DD. To our knowledge, there is no national evaluation of DD, or an evaluation with a representative sample that would allow for establishing an average age at DD diagnosis in Brazil. However, studies report diagnosing patients old as 12 years, and working with participants who were diagnosed only at an adult age (Basso et al., 2017; Germano et al., 2009; Lima et al., 2020; Navas et al., 2017).

The reading out loud task was carried out in a laboratorial, or clinical, setting. In this sense, we cannot generalize to the effects of reading out loud in a classroom setting, in the presence of peers; however, we postulate that reading out loud in the classroom setting may be more stressful for the DD reader than the laboratory setting. As reported in the Methods section, the population sample size was affected by the pandemic. To be sure, the present finding needs to be replicated by more studies of social stress test of DD and their peers. In particular, owing to the small sample size, our analyses of testing time and interaction effects may have been underpowered.

Ultimately, our data show children with DD have higher cortisol and ACTH levels in salivary samples, thus suggesting a pattern of chronic activation of the HPA axis. Altered HPA axis functioning may increase sensibility to the effects of psychosocial stressors and is associated with the emergence of a myriad of neuropsychiatric disorders (Cullen et al., 2022; Kudielka & Kirschbaum, 2005). Our findings underscore that children with DD present neuroendocrine alterations that might render them more vulnerable for comorbid psychopathology later in life.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. ACTH and Cortisol salivary concentration (nonlog transformed)

Data S1. Supplementary Methods

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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