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Stress Response Variability in Preschoolers with Developmental Language Disorder: Genetic and Environmental Interactions

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Abstract: Children with Developmental Language Disorder (DLD) show a high prevalence of psychological problems, yet understanding of individual variability in stress responses is limited. This study looked at how genetic and environmental factors affect stress responses in 200 preschool children (ages 3–6) from a PAUD in Bangkinang, Indonesia, including 100 with Developmental Language Disorder (DLD) and 100 without. Children with Developmental Language Disorder exhibited significantly greater cortisol reactivity (over 50% AUCi, $p < .001$), more pronounced decreases in heart rate variability ($p < .001$), and markedly higher anxiety spikes ($p < .001$) compared to control subjects. The multivariable regression analysis indicated a significant interaction between environmental and genetic variables ($p < .001$), collectively explaining 42% of the variation in cortisol reactivity. Cluster analysis revealed three distinct groups characterized by varying genetic and environmental risk factors: moderate responders (53%), severe stress (25%), and resilient individuals (22%). Our findings indicate that genetic and environmental factors interact in complex ways to alter the stress response of DLD, thereby supporting the development of intervention plans tailored to individual risk profiles.

Keywords: Cortisol, Genetic; Developmental language disorder; Environmental interactions; Stress Response.

Introduction

A neurodevelopmental condition known as Developmental Language Disorder (DLD) affects around 5–7% of school-age children and is marked by notable difficulties in learning and utilizing language (Norbury et al., 2016). Bishop et al. (2017) claim that the condition cannot be brought on by clear causes such as hearing loss, intellectual handicap, or other neurological diseases. Though DLD is among the most prevalent neurodevelopmental diseases, especially in relation to stress response and emotion control, there is little study on comorbidity and related risk factors (Clair et al., 2019; Conti-Ramsden et al., 2019). Children with DLD have an extremely high incidence of psychological issues, with estimates ranging from 40% to 70% having at least one comorbid mental condition (Clegg et al., 2005; Eadie et al., 2018; Yew & O'Kearney, 2013).

Children with certain language problems are 2–3 times more likely than usually developing counterparts to acquire internalizing illnesses like anxiety and sadness (Bornstein et al., 2013; Curtis et al., 2018; Maggio et al., 2014; Snowling et al., 2006). But among the DLD youngsters, individual susceptibility to psychological issues varies greatly. While some kids struggle greatly, others show amazing resilience (Lloyd-Esenkaya et al., 2020). The evolution of focused therapies depends on an understanding of the factors driving this diversity. Individual variations in physiological and psychological stress reactions in children with DLD is one area that has not been much researched. A complex response, stress involves the activation of the autonomic nervous system

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(ANS) and the hypothalamic-pituitary-adrenal (HPA) axis (Chrousos, 2009; Mueller et al., 2022).

Dysregulation of both these systems has been linked to higher risk of internalizing disorders in the general population (McEwen et al., 2015). Recent studies indicate that the link between DLD and emotional issues is mostly influenced by hereditary variables. Toseeb et al. (2022) conducted twin research that revealed a substantial genetic connection between DLD and emotional disorders in children, suggesting that the same genes might be implicated in both issues. Moreover, this research indicated that those with DLD had greater genetic impact on internalizing disorders, indicating that it might raise genetic susceptibility to stress. This result supports the diathesis-stress theoretical paradigm, which holds that environmental variables might amplify genetic effects on psychopathology (Manuck & McCaffery, 2014). Environmental variables have also been shown to significantly influence the developmental results of DLD youngsters.

The quality of the early communication environment including parental attentiveness and linguistic stimulation at home predicts not just language development but also psychosocial outcomes in children with DLD (Attig & Weinert, 2020; Gibson et al., 2021; Toseeb et al., 2020). Psychosocial risk variables such parental stress and parent-child relationship quality moderated the link between DLD and emotional problems, according to a longitudinal research (Clair et al., 2019). Most of the research, nevertheless, have looked just at genetic or environmental elements apart from one another, ignoring their possible interplay. Developmental psychopathology studies have drawn increasing interest in the idea of gene-environment interaction (GxE). Life stress experiences mitigate the link between 5-HTTLPR genotype and depression (Bleys et al., 2018; Caspi et al., 2003; Culverhouse et al., 2018). Many research since then have shown how environmental variables change genetic vulnerability to certain psychiatric diseases (Belsky & Pluess, 2009; Keller, 2018; Schmitt et al., 2014). Still, GxE studies on DLD are somewhat few.

Several molecular pathways clarify the link between DLD and mental issues. Language problems could first cause social isolation and peer rejection, which would then heighten the likelihood of internalizing illnesses (Matthews et al., 2015; Redmond & Rice, 1998). Second, shortcomings in emotional control—often linked with language disorders—could increase people's sensitivity to stress (Altena et al., 2020; Wegmann et al., 2017). Third, the brain networks supporting both language processing and stress control might share malfunction (Conti-Ramsden et al., 2019). Research on neurobiology reveals that those with DLD often have variations in the brain areas responsible for emotions including the prefrontal cortex and amygdala. These regions also significantly influence stress management, suggesting maybe common neurological underpinnings for DLD and stress dysregulation (Abbott & Love, 2023; Boerma et al., 2023; Kershner, 2020).

Moreover, research using brain imaging have shown that persistent stress changes functional connectivity within the language network, therefore implying a bidirectional link between stress and language function (Berken et al., 2016). From a developmental standpoint, the preschool years are a vital time for language growth and emotional control. Children often advance quickly in their communication abilities at this time, which lets them more clearly express feelings and participate in more intricate social interactions (Shank et al., 2019). For kids with DLD, language development delays could interfere with these mechanisms and maybe cause secondary problems in social functioning and emotional control (Clair et al., 2019; Cole et al., 2010). Knowing personal variation in stress reactions in kids with DLD has significant therapeutic relevance. Identifying groupings of children depending on their stress response profiles could help to guide more focused treatments. For instance, although individuals with more adaptable stress responses would need a different strategy, children with high stress reactions could benefit from programs emphasizing stress management and emotional control (Compas et al., 2017). Moreover, knowing genetic and environmental risk and protective variables might help one forecast and avoid problems. Should specific environmental variables be shown to mediate or modify genetic effects on stress reactions, these might be targets for preventative treatments. Such a strategy fits the present trend toward individualized medicine, in which treatments are customized to unique risk profiles (Fröhlich et al., 2018; Hamburg & Collins, 2010). Studies on DLD in Indonesia are in their infancy. Data from epidemiology on the frequency of DLD in Indonesia remains somewhat scant.

Global projections, therefore, indicate that around 5–7% of children might be impacted, which would mean hundreds of thousands of children in Indonesia (Watkins, 2016). Research in this setting is very crucial given the dearth of knowledge and resources for early detection and intervention. This research will focus on preschool-aged children in Early Childhood Education (PAUD) in Bangkinang City, Riau. Several factors influenced the choice of this site: Several factors influenced the choice of this site: Bangkinang is a small-medium city in Indonesia, therefore its picture may be

more representative of the majority of the population than large cities; PAUD in this region lacks a systematic screening program for DLD, reflecting the reality in many other parts of Indonesia; The socio-economic and family background diversity in Bangkinang allows for exploration of diverse environmental factors; and Local government and local educational institutions support research in the field of child development.

Method

This study used a numbers-based technique and a case-control design to see how toddlers with Developmental Language Disorder (DLD) handle stress differently from preschoolers with normal language development. The research also looked at how genetics and the environment impact how people respond to stress. It happened from January to June 2024 in a number of Early Childhood Education Centers (PAUD) in Bangkinang City, Riau, Indonesia. We considered about how well the place reflected the population, the absence of systematic DLD screening programs, the range of socioeconomic backgrounds, and the support from the local government when we chose it (Shonkoff & Phillips, 2000). The target group was preschoolers aged 3 to 6 in Bangkinang City, and the accessible group was those who were already enrolled in local PAUD programs. The study employed purposive sampling and a matched-pair design (Shadish et al., 2002). We utilized the approach with α=0.05, β=0.2, p_1=0.60, and p_2=0.30 (Hosmer et al., 2013) to find the sample size, which turned out to be 84 youngsters in each group. Taking into consideration a 15% dropout rate, the final sample included 100 kids in each group, for a total of 200 youngsters. Here are the rules for who may and can't be in the study, as well as the research variables.

Table 1. Inclusion Criteria, Exclusion Criteria, and Research Variables

Inclusion Criteria	Exclusion Criteria	Independent Variables	Dependent Variables
Children aged 3-6 years	Hearing impairments	DLD status (DLD vs. non-DLD)	Physiological stress response:
Enrolled in Bangkinang City PAUD	Intellectual disability (IQ < 70)	Genetic factors:	Cortisol reactivity (AUCi)
Case group: diagnosed with DLD (CELF-P2 < -1.25 SD)	Other neurological conditions (epilepsy, ASD, CP)	Gene polymorphisms (SLC6A4, BDNF, FKBP5, COMT, CNTNAP2)	Heart rate variability (HRV)
Control group: typical language development	Long-term medications affecting stress response	Family history of language disorders	Alpha-amylase levels
Informed consent from parents/guardians	Parent/guardian refusal to participate	Environmental factors:	Psychological stress response:
		Communication environment quality	Anxiety levels
		Parental stress	Withdrawal behaviors
		Parent-child relationship quality	Emotion regulation
		Socioeconomic status	
		Trauma/stress event exposure	

Table 2. Research Instruments and Data Collection Procedures

Variable	Instrument	Reliability/Validity	Data Collection Procedure
DLD Screening	Clinical Evaluation of Language Fundamentals-Preschool 2 (CELF-P2)	α = 0.89-0.95 (Black et al., 2020)	Initial screening during recruitment phase
Genetic Factors	Genetic analysis (cheek swab)	Laboratory validation (Caspi et al., 2003)	DNA sample collection via cheek swab
	Family History Questionnaire	Content validity (Toseeb et al., 2022)	Parent interview
Environmental Factors	Home Communication Environment Scale (HCES)	α = 0.86 (Toseeb et al., 2020)	Parent-completed questionnaire
	Parenting Stress Index-Short Form (PSI-SF)	α = 0.91 (Johnson & R, 2015)	Parent-completed questionnaire
	Parent-Child Relationship Scale (PCRS)	α = 0.85 (Pianta et al., 1997)	Parent-completed questionnaire
	Socioeconomic Status Questionnaire	Content validity	Parent-completed questionnaire

Variable	Instrument	Reliability/Validity	Data Collection Procedure
	Life Events Checklist for DSM-5 (LEC-5)	α = 0.88 (Weathers et al., 2014)	Parent-completed questionnaire
Stress Induction	Trier Social Stress Test for Children (TSST-C)	Standardized protocol (Gunnar et al., 2021)	Public speaking and backward counting tasks
Physiological Stress Response	Salivary cortisol	CV < 10%	Saliva samples at 5 time points (pre-TSST, post-TSST, 15, 30, 45 minutes)
	Heart Rate Variability (HRV)	ICCs > 0.80	Portable heart rate detection device
	Alpha-amylase	CV < 8%	Saliva sample analysis
Psychological Stress Response	State-Trait Anxiety Inventory for Children (STAIC)	α = 0.87 (Spielberger et al., 2012)	Supplemented with visuals for preschoolers
	Child Behavior Checklist (CBCL)	α = 0.90 (Achenbach & Edelbrock, 1991)	Parent-completed
	Emotion Regulation Checklist (ERC)	α = 0.83 (Shields & Cicchetti, 1997)	Parent-completed

Data Analysis

Data analysis utilized SPSS version 26.0 and R Studio, encompassing: descriptive analysis for sample characteristics; independent t-tests or Mann-Whitney U tests to compare stress responses between groups; correlation analysis to assess relationships between variables; multivariable regression analysis to evaluate genetic and environmental factor contributions; gene-environment interaction analysis using regression models with interaction terms; cluster analysis to identify subgroups of children with DLD; and structural equation modelling to test causal models between DLD, genetic factors, environment, and stress responses (Conti-Ramsden et al., 2019; McEwen & Gianaros, 2010).

Result and Discussion

Participant Characteristics

A total of 200 preschool children participated in this study, comprising 100 children with Developmental Language Disorder (DLD) and 100 children with typical language development. Demographic and clinical characteristics of participants are presented in Table 3. Both groups showed similar distributions regarding age, gender, and socioeconomic background (all $p > .05$), demonstrating successful matching in the research design.

Table 3. Demographic and Clinical Characteristics of Participants

Characteristic	DLD Group (n = 100)	Control Group (n = 100)	p-value
Age (years)			
Mean ± SD	4.7 ± 0.9	4.6 ± 0.8	0.783
Range	3.1-6.0	3.2-5.9	
Gender, n (%)			
Male	62 (62.0)	61 (61.0)	0.887
Female	38 (38.0)	39 (39.0)	
Socioeconomic Status, n (%)			
Low	36 (36.0)	33 (33.0)	0.672
Middle	48 (48.0)	47 (47.0)	
High	16 (16.0)	20 (20.0)	
CELF-P2 Scores			
Mean ± SD	72.3 ± 8.5	106.8 ± 10.3	<0.001*
Family History of Language Disorders, n (%)	41 (41.0)	13 (13.0)	<0.001*

Note: $p < .05$ indicates statistically significant differences.

CELF-P2 scores were significantly lower in the DLD group (mean = 72.3, SD = 8.5) compared to the control group (mean = 106.8, SD = 10.3), $t(198) = 25.67$, $p < .001$. Additionally, the proportion of children with family histories of language disorders or neurodevelopmental conditions was significantly higher in the DLD group (41.0%) compared to the control group (13.0%), $\chi^2(1) = 19.82$, $p < .001$, indicating genetic factor contributions to DLD development.

Differences in Stress Response Between DLD and Control Groups

Physiological Stress Response

Analysis revealed significant differences in physiological stress responses between children with

DLD and those with typical language development, as shown in Table 4.

Table 4. Comparison of Physiological Stress Responses Between DLD and Control Groups

Variable	DLD Group (n = 100) Mean ± SD	Control Group (n = 100) Mean ± SD	t	p-value	Cohen's d
Cortisol Reactivity (AUCi)	342.6 ± 98.4	227.5 ± 75.3	9.36	<0.001*	1.32
Heart Rate Variability (RMSSD)	21.4 ± 8.7	35.6 ± 11.2	-10.15	<0.001*	-1.43
Alpha-amylase (U/ml)	127.8 ± 42.5	86.3 ± 30.9	8.05	<0.001*	1.14

Note: AUCi = Area Under the Curve with respect to increase; RMSSD = Root Mean Square of Successive Differences; p < .05 indicates statistically significant differences.

Compared to controls, children with DLD demonstrated significantly higher cortisol reactivity (50.6% higher AUCi, $p < .001$), greater decreases in Heart Rate Variability indicating sympathetic nervous system dominance (39.9% lower RMSSD, $p < .001$), and elevated alpha-amylase levels (48.1% higher, $p < .001$). Cohen's d effect sizes for all comparisons showed large effects ($|d| > 1.0$), indicating substantial physiological stress response differences between groups.

Psychological Stress Response

Significant differences were also found in psychological stress responses between the two groups, as shown in Table 5.

Table 5. Comparison of Psychological Stress Responses Between DLD and Control Groups

Variable	DLD Group (n = 100) Mean ± SD	Control Group (n = 100) Mean ± SD	t	p-value	Cohen's d
Anxiety Level (STAIC)	42.7 ± 9.8	31.4 ± 7.5	9.27	<0.001*	1.31
Withdrawal Behavior (CBCL)	63.8 ± 12.3	52.1 ± 10.2	7.42	<0.001*	1.05
Emotion Regulation (ERC)	62.3 ± 10.5	78.6 ± 9.8	-11.36	<0.001*	-1.61

Note: STAIC = State-Trait Anxiety Inventory for Children; CBCL = Child Behavior Checklist; ERC = Emotion Regulation Checklist; p < .05 indicates statistically significant differences.

Psychologically, children with DLD showed significantly higher anxiety levels (35.9% higher STAIC scores, $p < .001$), more withdrawal behaviors (22.5% higher CBCL scores, $p < .001$), and poorer emotion regulation abilities (20.7% lower ERC scores, $p < .001$) compared to children with typical language development. Cohen's d effect sizes for all comparisons also demonstrated large effects ($|d| > 1.0$).

Genetic Factor Contributions to Stress Response

Analysis of specific gene polymorphisms revealed significant associations with stress response profiles in children with DLD, as shown in Table 6.

Table 6. Associations Between Gene Polymorphisms and Cortisol Reactivity in the DLD Group

Gene Polymorphism	Genotype	n (%)	Cortisol Reactivity (AUCi) Mean ± SD	F	p-value	η^2
SLC6A4 (5-HTTLPR)				14.27	<0.001*	0.227
	S/S	28 (28.0)	392.5 ± 105.7			
	S/L	47 (47.0)	341.8 ± 86.3			
	L/L	25 (25.0)	293.4 ± 77.2			
FKBP5 rs1360780				11.64	<0.001*	0.193
	T/T	12 (12.0)	403.2 ± 112.4			
	C/T	43 (43.0)	356.7 ± 91.8			
	C/C	45 (45.0)	309.5 ± 84.5			
BDNF Val66Met				9.85	<0.001*	0.169
	Met/Met	18 (18.0)	387.9 ± 107.3			
	Val/Met	49 (49.0)	348.2 ± 95.1			
	Val/Val	33 (33.0)	307.4 ± 83.6			
COMT Val158Met				8.31	<0.001*	0.147
	Met/Met	23 (23.0)	381.5 ± 103.2			

Gene Polymorphism	Genotype	n (%)	Cortisol Reactivity (AUCi) Mean ± SD	F	p-value	η^2
	Val/Met	50 (50.0)	339.4 ± 92.7			
	Val/Val	27 (27.0)	314.7 ± 89.5			
CNTNAP2 rs7794745				6.53	0.002*	0.119
	A/A	16 (16.0)	384.1 ± 108.9			
	A/T	46 (46.0)	343.5 ± 94.2			
	T/T	38 (38.0)	317.6 ± 88.1			

Note: AUCi = Area Under the Curve with respect to increase; η^2 = partial eta squared; $p < .05$ indicates statistically significant differences.

One-way ANOVA revealed that all investigated gene polymorphisms were significantly associated with cortisol reactivity in children with DLD (all $p < .05$). The largest effect size (η^2) was observed for the SLC6A4 (5-HTTLPR) polymorphism ($\eta^2 = 0.227$), with the S/S genotype showing the highest cortisol reactivity (mean = 392.5, SD = 105.7), followed by S/L (mean = 341.8, SD = 86.3), and L/L (mean = 293.4, SD = 77.2).

Environmental Factor Contributions to Stress Response

Environmental factors also contributed significantly to stress responses in children with DLD, as shown in the correlation analysis results in Table 7.

Table 7. Correlations Between Environmental Factors and Stress Responses in the DLD Group

Environmental Factor	Cortisol Reactivity (AUCi)	Anxiety Level (STAIC)	Emotion Regulation (ERC)
Communication Environment Quality (HCES)	-0.54**	-0.48**	0.59**
Parental Stress (PSI-SF)	0.47**	0.51**	-0.45**
Parent-Child Relationship Quality (PCRS)	-0.49**	-0.52**	0.56**
Socioeconomic Status	-0.35**	-0.31**	0.34**
Stress Event Exposure (LEC-5)	0.43**	0.49**	-0.41**

*Note: AUCi = Area Under the Curve with respect to increase; STAIC = State-Trait Anxiety Inventory for Children; ERC = Emotion Regulation Checklist; HCES = Home Communication Environment Scale; PSI-SF = Parenting Stress Index-Short Form; PCRS = Parent-Child Relationship Scale; LEC-5 = Life Events Checklist for DSM-5; *$p < .01$.

Pearson correlation analysis demonstrated that all environmental factors significantly correlated with both physiological and psychological stress responses in children with DLD (all $p < .01$). Strong negative correlations were found between home communication environment quality and cortisol reactivity ($r = -0.54$, $p < .01$) as well as anxiety levels ($r = -0.48$, $p < .01$), indicating that better communication environments are associated with lower stress responses. Conversely, strong positive correlations were found between parental stress and cortisol reactivity ($r = 0.47$, $p < .01$) as well as anxiety levels ($r = 0.51$, $p < .01$), suggesting that higher parental stress is associated with elevated stress responses in children.

Interactions Between Genetic and Environmental Factors

Multivariable regression analysis revealed significant interactions between genetic and environmental factors in influencing stress responses in children with DLD (Table 8).

Table 8. Multivariable Regression Analysis for Cortisol Reactivity in the DLD Group

Predictor	β	SE	t	p-value	95% CI
Block 1: Genetic Factors					
SLC6A4 (5-HTTLPR)	0.27	0.08	3.38	0.001*	[0.11, 0.43]
FKBP5 rs1360780	0.21	0.07	3.00	0.003*	[0.07, 0.35]
BDNF Val66Met	0.18	0.07	2.57	0.012*	[0.04, 0.32]
COMT Val158Met	0.14	0.07	2.00	0.048*	[0.01, 0.27]
CNTNAP2 rs7794745	0.13	0.07	1.86	0.066	[-0.01, 0.27]
$R^2 = 0.23$, $F(5, 94) = 5.62$, $p < .001$					
Block 2: Environmental Factors					
Communication Environment Quality (HCES)	-0.30	0.09	-3.33	0.001*	[-0.48, -0.12]
Parental Stress (PSI-SF)	0.23	0.09	2.56	0.012*	[0.05, 0.41]
Parent-Child Relationship Quality (PCRS)	-0.21	0.09	-2.33	0.022*	[-0.39, -0.03]
Socioeconomic Status	-0.10	0.07	-1.43	0.156	[-0.24, 0.04]
Stress Event Exposure (LEC-5)	0.17	0.08	2.13	0.036*	[0.01, 0.33]

Predictor	β	SE	t	p-value	95% CI
$\Delta R^2 = 0.14$, $\Delta F(5, 89) = 3.82$, $p = .003$					
Block 3: Interactions					
SLC6A4 × Communication Environment Quality	-0.21	0.08	-2.63	0.010*	[-0.37, -0.05]
SLC6A4 × Parental Stress	0.19	0.08	2.38	0.019*	[0.03, 0.35]
FKBP5 × Communication Environment Quality	-0.18	0.08	-2.25	0.027*	[-0.34, -0.02]
FKBP5 × Stress Event Exposure	0.17	0.07	2.43	0.017*	[0.03, 0.31]
BDNF × Parent-Child Relationship Quality	-0.16	0.08	-2.00	0.048*	[-0.32, -0.00]
$\Delta R^2 = 0.09$, $\Delta F(5, 84) = 2.61$, $p = .030$					
Overall Model					
$R^2 = 0.46$, Adjusted $R^2 = 0.42$, $F(15, 84) = 4.78$, $p < .001$					

Note: β = standardized beta coefficient; SE = standard error; CI = confidence interval; $p < .05$ indicates statistically significant relationships.

Hierarchical regression analysis showed that genetic factors (Block 1) explained 23% of variance in cortisol reactivity ($R^2 = 0.23$, $F(5, 94) = 5.62$, $p < .001$). Adding environmental factors (Block 2) significantly increased the explained variance by 14% ($\Delta R^2 = 0.14$, $\Delta F(5, 89) = 3.82$, $p = .003$). Importantly, adding interaction terms (Block 3) significantly increased the explained variance by an additional 9% ($\Delta R^2 = 0.09$, $\Delta F(5, 84) = 2.61$, $p = .030$). The overall model explained 42% of variance in cortisol reactivity in children with DLD (Adjusted $R^2 = 0.42$, $F(15, 84) = 4.78$, $p < .001$).

The most significant interaction was observed between SLC6A4 (5-HTTLPR) and communication environment quality (β = -0.21, p = .010), indicating that the influence of risk genotype (S/S) on cortisol reactivity was reduced by high-quality communication environments. Similarly, a significant interaction was found between FKBP5 rs1360780 and stress event exposure (β = 0.17, p = .017), suggesting that the influence of risk genotype (T/T) on cortisol reactivity was amplified by higher stress event exposure.

Subgroup Identification Based on Stress Response Profiles

K-means cluster analysis identified three distinct subgroups among children with DLD based on their stress response profiles (Table 9).

Table 9. Subgroup Characteristics Based on Cluster Analysis in the DLD Group

Variable	Cluster 1: Moderate Responders (n = 53, 53.0%)	Cluster 2: High Stress (n = 25, 25.0%)	Cluster 3: Resilient (n = 22, 22.0%)	F	p-value	η^2
Cortisol Reactivity (AUCi)	338.4 ± 62.1	451.2 ± 84.3	217.5 ± 53.6	78.54	<0.001*	0.618
Heart Rate Variability (RMSSD)	22.1 ± 5.3	13.6 ± 4.1	30.8 ± 7.4	56.93	<0.001*	0.541
Alpha-amylase (U/ml)	124.5 ± 28.6	167.8 ± 39.7	84.1 ± 21.3	52.18	<0.001*	0.519
Anxiety Level (STAIC)	41.3 ± 6.8	52.7 ± 8.4	33.5 ± 5.2	54.39	<0.001*	0.531
Withdrawal Behavior (CBCL)	63.1 ± 9.2	76.4 ± 10.5	51.7 ± 7.8	44.79	<0.001*	0.481
Emotion Regulation (ERC)	63.8 ± 7.6	51.2 ± 8.3	73.1 ± 8.1	52.31	<0.001*	0.520
Genetic Risk Factors	2.6 ± 1.1	3.7 ± 0.9	1.5 ± 0.8	35.90	<0.001*	0.427
Environmental Risk Factors	2.8 ± 1.2	3.9 ± 0.8	1.6 ± 1.0	32.65	<0.001*	0.403

Note: AUCi = Area Under the Curve with respect to increase; RMSSD = Root Mean Square of Successive Differences; STAIC = State-Trait Anxiety Inventory for Children; CBCL = Child Behavior Checklist; ERC = Emotion Regulation Checklist; η^2 = partial eta squared; $p < .05$ indicates statistically significant differences.

Cluster analysis identified three distinct subgroups: Cluster 1 (Moderate Responders, 53.0%) showed moderate levels of physiological and psychological stress responses; Cluster 2 (High Stress, 25.0%) demonstrated very high physiological stress responses (extremely high cortisol reactivity, very low HRV) and significant psychological problems (high anxiety and withdrawal behaviours, poor emotion regulation); and Cluster 3 (Resilient, 22.0%) showed relatively low physiological stress responses and better psychological functioning despite having DLD.

One-way ANOVA confirmed that the three clusters significantly differed across all measured variables (all p < .001). Clusters also differed in the number of genetic and environmental risk factors, with Cluster 2 (High Stress) showing the highest number of genetic ($F(2, 97) = 35.90$, $p < .001$, $\eta^2 = 0.427$) and environmental ($F(2, 97) = 32.65$, $p < .001$, $\eta^2 = 0.403$) risk factors.

Discussion

This study aimed to characterize stress response variability in preschool children with Developmental Language Disorder (DLD) and explore the contributions and interactions of genetic and environmental factors on these stress responses. Our findings show that children with DLD have noticeable differences in how their

bodies and minds react to stress compared to children with typical language development, and we also found specific genetic and environmental factors that affect these stress responses in children with DLD.

Differences in Stress Response Between Children with DLD and Typical Language Development

Our results show that children with DLD have stronger physical stress reactions, indicated by higher cortisol levels, bigger drops in heart rate variability (HRV), and more alpha-amylase in their bodies. These findings align with previous studies showing that children with neurodevelopmental disorders often display dysregulated physiological stress systems (McEwen et al., 2015). The increased cortisol reactivity in children with DLD indicates that their HPA axis is working too hard, which is connected to a higher chance of developing mental health issues.

Our research also revealed that children with DLD show higher anxiety levels, increased withdrawal behaviors, and poorer emotion regulation abilities compared to their typically developing peers. These findings match earlier studies (Clegg et al., 2005; Eadie et al., 2018), which showed that children with specific language impairments are 2-3 times more likely to have emotional issues. Several mechanisms may explain the relationship between DLD and emotional difficulties. First, communication challenges can lead to frustration, anxiety, and social withdrawal in children with DLD (Matthews et al., 2015; Mulvey et al., 2017). Second, deficits in language skills may disrupt emotion regulation developmental processes, as language plays a crucial role in developing self-regulation strategies and emotional processing (Fujiki et al., 2002; Wegmann et al., 2017). Third, as mentioned by Clair et al. (2019); Conti-Ramsden et al. (2019); Côte-Sainte-Catherine (2015), the brain networks that help with language and managing emotions might not work properly in people with DLD.

Genetic factors contribute to stress responses in children with DLD

Our research identified several gene polymorphisms significantly associated with stress responses in children with DLD. The SLC6A4 (5-HTTLPR) polymorphism was most strongly linked to how children with DLD react to stress, with the S (short) version of the gene connected to stronger stress responses. This finding supports earlier studies that showed the S allele of 5-HTTLPR is linked to stronger stress reactions and a greater risk of stress-related disorders. The S allele is linked to lower levels of serotonin transporter gene activity, which results in less serotonin outside of cells and may lead to stronger stress reactions.

The FKBP5 rs1360780 gene variation was strongly linked to how much cortisol children with DLD produced, with those having the T/T version showing the highest cortisol levels. FKBP5 makes a protein that helps control how sensitive our bodies are to stress hormones, and changes in this gene have been linked to different reactions to stress and a higher risk of mood disorders. Similar to our findings, Matsudaira et al. (2019) & Skolariki et al. (2023), found that individuals with the T/T genotype showed enhanced cortisol responses to acute psychosocial stress. This result suggests that FKBP5 gene variations may contribute to stress response variability in children with DLD.

The BDNF Val66Met variation was also strongly linked to cortisol responses in our group, with the Met/Met type showing the highest cortisol levels. BDNF plays a crucial role in neuroplasticity and serves as a key modulator of stress adaptation (McEwen & Gianaros, 2010). The Met variant is linked to lower levels of BDNF release when the brain is active, which might impact how stress is managed through areas of the brain like the limbic system and prefrontal cortex. Additionally, several studies have found that the BDNF Val66Met genetic variation interacts with stress exposure to help predict internalizing disorders in children.

Overall, our results support the view that stress responses in children with DLD are influenced by multiple genetic variants in genes involved in stress regulation and neuroplasticity. These findings are consistent with research by Toseeb et al. (2022), which indicated that the relationship between DLD and emotional problems is partially influenced by genetic factors. However, it's important to note that the influence of these genetic factors may be moderated by environmental factors, as demonstrated by our gene-environment interaction analyses.

The contributions of environmental factors to stress responses in children with DLD are outlined below

Our research identified several environmental factors significantly associated with stress responses in children with DLD. Home communication environment quality showed the strongest negative correlation with cortisol reactivity and anxiety levels, indicating the protective effect of high-quality communication environments. This finding aligns with research by Toseeb et al. (2020), which reported that rich preschool communication environments predicted better emotional outcomes in individuals with language disorders. Supportive communication environments can provide opportunities for children with DLD to develop emotion regulation strategies and express their needs, thereby reducing frustration and stress (Lloyd-Esenkaya et al., 2020).

Parental stress also significantly correlated with heightened stress responses in children with DLD. This is consistent with previous research showing that parental stress can negatively impact child development, including increased emotional and behavioral problems (Clair et al., 2019). Parental stress can affect children's stress responses through several mechanisms, including maladaptive modeling, inconsistent parenting practices, or exposure to family conflict (Nair et al., 2020). Children with DLD may be particularly vulnerable to the influence of parental stress due to their limitations in understanding and expressing emotions.

Parent-child relationship quality was also a significant predictor of stress response, with better relationships associated with lower cortisol reactivity and improved emotion regulation. This is consistent with research showing that secure attachment and warm parent-child relationships can serve as buffers against stress in developmentally vulnerable children (Clair et al., 2019; Conti-Ramsden et al., 2019; Côte-Sainte-Catherine, 2015). Positive parent-child relationships can facilitate the development of emotion regulation skills and provide a safe environment where children with DLD can experience and cope with stress (Clair et al., 2019; Cole et al., 2010).

Stress event exposure also significantly correlated with increased stress responses in children with DLD. This aligns with the diathesis-stress model, which suggests that individuals with underlying vulnerabilities (in this case, DLD) may be more susceptible to the negative effects of stressful life experiences (Manuck & McCaffery, 2014). Children with DLD may struggle to process and cope with stressful events due to language skill limitations, which can lead to excessive stress responses and emotion regulation problems (Bishop et al., 2017).

Overall, our findings emphasize the value of environmental factors in shaping stress responses in children with DLD. These environmental factors, particularly those related to family context and communication quality, can serve as either risk or protective factors, influencing how children with DLD respond to and adapt to stress. This information has important implications for intervention, as targeting these environmental factors may help reduce excessive stress responses and enhance resilience in children with DLD.

Interactions Between Genetic and Environmental Factors

One of the most important findings from our research is the presence of significant interactions between genetic and environmental factors in influencing stress responses in children with DLD. This aligns with the idea of gene-environment interaction (GxE), which suggests that genetic factors affect traits differently depending on environmental conditions, and environmental factors can also influence how genes affect traits.

The most significant interaction we found was between the SLC6A4 (5-HTTLPR) polymorphism and communication environment quality, with high-quality communication environments mitigating the influence of the risk genotype (S/S) on cortisol reactivity. This finding is consistent with research (Belsky & Pluess, 2009), which showed that certain polymorphisms, including 5-HTTLPR, can increase individual sensitivity to environmental influences, both negative and positive. In this case, children with the S/S genotype may be more vulnerable to the negative effects of poor communication environments but also benefit more from supportive environments.

The interaction between FKBP5 rs1360780 and stress event exposure was also significant, indicating that the influence of the risk genotype (T/T) on cortisol reactivity was amplified by higher stress exposure. This is consistent with the diathesis-stress model, which suggests that stress can "unmask" underlying genetic vulnerabilities (Manuck & McCaffery, 2014). We also found that the quality of the parent-child relationship significantly interacted with BDNF Val66Met, meaning that good relationships can lessen the effects of risk genotypes.

Overall, our findings support the bioecological model of child development (Shonkoff & Phillips, 2000), which emphasizes the complex interaction between biology and environment in shaping developmental pathways. In the context of DLD, these gene-environment interactions can help explain why some children show remarkable resilience despite language challenges, while others develop significant stress and emotion regulation problems.

Subgroup Identification Based on Stress Response Profiles

Our cluster analysis identified three distinct subgroups among children with DLD based on their stress response profiles: Moderate Responders (53%), High Stress (25%), and Resilient (22%). This is consistent with previous research showing significant heterogeneity in the DLD population (Conti-Ramsden et al., 2019). The "High Stress" group showed extremely high physiological stress responses, significant emotion regulation problems, and the highest number of genetic and environmental risk factors. Children in this group may require more intensive interventions targeting stress management and emotion regulation, in addition to traditional language support. Such interventions might include adapted cognitive-behavioral therapy,

stress management strategies, and support for parents in managing their stress and creating more supportive environments (Compas et al., 2017).

The "Resilient" group (22%) showed relatively low physiological stress responses and better emotional functioning, despite language difficulties. Children in this group had the fewest genetic and environmental risk factors, which may contribute to their resilience. Examining the distinct traits of this group can yield significant understanding of protective factors that other children with DLD can potentially strengthen. This resilience may be related to parenting relationship quality, supportive communication environments, better emotion regulation skills, or a combination of these factors (Toseeb et al., 2020).

The "Moderate Responders" group (53%) was the largest and showed moderate levels of physiological and psychological stress responses. Children in this group may benefit from more tailored approaches that target their specific risks while strengthening existing protective factors. The identification of these subgroups supports the importance of personalized approaches for children with DLD, taking into account not only their language profiles but also their stress response patterns and risk and protective factors. This approach is consistent with current trends toward personalized medicine, where interventions are tailored to individual risk profiles (Hamburg & Collins, 2010).

Conclusion

This study explored stress response variability in preschool children with Developmental Language Disorder (DLD) and the interaction between genetic and environmental factors in influencing these stress responses. Our findings reveal that, compared to children with typical language development, children with DLD show higher cortisol reactivity, greater decreases in heart rate variability, and more psychological problems such as anxiety, withdrawal behaviors, and emotion regulation difficulties. Genetic factors, including polymorphisms in the SLC6A4 (5-HTTLPR), FKBP5, BDNF, COMT, and CNTNAP2 genes, were significantly associated with stress responses, with SLC6A4 (5-HTTLPR) showing the strongest association. Environmental factors, particularly home communication environment quality, parental stress, and parent-child relationship quality, also contributed significantly to stress response variability. Importantly, we found significant interactions between genetic and environmental factors, with supportive communication environments mitigating the influence of genetic risk and stress event exposure increasing genetic vulnerability. Cluster analysis identified three distinct subgroups in the DLD population: Moderate Responders (53%), High Stress (25%), and Resilient (22%), characterized by different stress response patterns and risk factors. These differences highlight heterogeneity in the DLD population and support personalized approaches to assessment and intervention. Overall, our findings support the bioecological model of child development, emphasizing the interaction between biology and environment in shaping developmental outcomes. Our findings have important implications for clinical practice, including the importance of comprehensive assessment, multimodal intervention approaches, parent involvement, early intervention for high-risk children, and personalized intervention strategies. Future studies should use long-term research methods, include more participants, explore a wider range of genetic factors, and conduct specific clinical trials to better understand how children with DLD respond to stress and to create effective intervention strategies. This research represents an important step toward better understanding the complex relationships between language, stress, and emotional development in children with DLD.

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Conflicts of Interest

The authors declare no conflict of interest.

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