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Exploring the influence of the DRD2 gene on mathematical ability: perspectives of gene association and gene-environment interaction

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Abstract

Mathematical ability is influenced by genes and environment. This study focused on the effect of DRD2, a candidate gene for working memory, on mathematical ability. The results in child participants revealed associations between the DRD2 gene and mathematical ability. It was found that individual's mathematical ability was influenced by Single Nucleotide Polymorphisms (SNPs) in DRD2, both in the form of haplotypes and in the way of interaction with parental education. These findings suggest that dopaminergic genes are linked to mathematical ability. This study provides evidence for the genetic basis of mathematical ability and offers guidance for personalized intervention in mathematical education.

Keywords DRD2 gene, Haplotype, Mathematical ability, Gene-environment interaction

Introduction

Mathematical ability is heritable. Individuals vary more and more in their math performance as they get older, even if they are in similar levels of environment. Previous studies have conducted genome-wide association studies for math-related abilities and found that mathematical ability appears to be influenced by multiple genes [1, 2]. However, only candidate genes related to reading abilities have been investigated for their influence on mathematical ability [3]. Meanwhile, the impact of gene-environment interaction (G×E) on the development of mathematical ability cannot be ignored. Creating the most suitable environment for the development of children with different genotypes based on the results of gene-environment interaction can lead to targeted educational interventions, personalized learning plans, and early identification of children who might benefit from specific teaching strategies, as well as address learning disparities.

According to "Generalist Gene" hypothesis: genes that affect any aspect of a learning disability or learning ability can also affect other aspects of the disability; genes that affect one learning disability or learning ability may also affect other learning disabilities or learning abilities. Based on co-morbidities, we found that mathematical ability was mainly related to literacy, reading ability and educational achievement. Furthermore, working memory (WM), a pivotal component of the learning process, which allows for the control, maintenance, and manipulation of stored information is also important in completing mathematical tasks [4]. In mathematical problems (e.g., arithmetic, algebra, and geometry), solving them involves retaining partial information and processing new information to obtain a relevant solution, which often requires the utilization of WM resources [5]. A

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series of projects have supported the influence of WM on mathematical abilities, including training [6], intervention [7], and association studies [8].

DRD2 gene encodes the subtype of Dopamine (DA) receptor known as DRD2 receptor, which affects the transmission of DA by inhibiting the activity of adenylyl cyclase and the production of cAMP [9]. Within the cortex, DRD2 receptors are specifically found in the temporal, parietal, frontal, occipital, and anterior cingulate cortices [10]. It has been demonstrated that the DRD2 gene can influence cognitive processes [11] and WM [12, 13]. DRD2 gene has been associated with variations in DRD2 receptor density, thereby influencing WM performance in mice [14, 15]. The splicing variations of DRD2 receptors, driven by specific genetic variations (SNPs: rs1076560 and rs2283265), significantly impact the neural network involved in executive function, particularly when these receptors are expressed in different neurons receiving dopamine innervation [15]. These variations can consequently affect WM activities. There were also studies showing the impact of DRD2 on language-related abilities. Beaver et al. (2010) documented an association between DRD2 and language skills in adolescence and early adulthood, and the A1 allele of TaqI was associated with lower vocabulary skills [16]. Eicher et al. (2013) found that a SNP of DRD2-rs6278 was associated with non-word repetition and language comprehension deficits [17]. In addition, a recent study showed that an increase in the number of risk alleles for DRD2-rs6277 was associated with better performance in vocabulary and language fluency in patients at risk for psychosis [18]. These studies suggest that the DRD2 gene plays a significant role in learning-related abilities, including WM and language skills. From the "Generalist Gene" perspective, a hypothesis was derived (H1): Candidate gene of DRD2 associated with WM and language could also affect mathematical ability.

In addition, mathematical abilities appear to be influenced by parental genetics and the environment provided by parents [19, 20]. There is no doubt that gene-environment interactions play a role in shaping children's mathematical performance. The dopaminergic system, an important neurotransmitter system, is closely linked to the environment. Dopaminergic system is susceptible to environmental influences, whether it is exposed to chronic or acute stress, which can alter the concentration of dopamine release and thereby have adverse effects on cognitive and neurological disorders [21]. Similarly, under environmental enrichment, the number of dopamine neurons in the midbrain increases and modifies the brain's plasticity projected by Dopaminergic system [22]. These individual differences in neural system, resulting from genetic factors, are also confirmed in gene-environment interactions. In a study about dopaminergic polygenic composite by parental behavior interactions, dopaminergic genes associated with increased reward sensitivity showed an association with poorer executive function in children when negative parental behavior was present [23, 24]. We thus assume that DRD2 gene might be susceptible to external environmental stimuli, thereby potentially affecting an individual's mathematical ability.

Studies have found that parental education level (PE) is related to their children's academic performance [25], intelligence and language ability [26]. Therefore, parental education level represents higher environmental quality and serves as a proxy measure of home literacy/numeracy environment and family socioeconomic status. PE as a variable on the parental end of the spectrum, also influences both parental behavior and child behavior [27]. Higher-educated parents tend to provide richer environments or stimuli that can influence the neural development and functional connectivity of children's brains [28]. Children with low PE have limited access to resources and environments compared to children with high PE, resulting in poorer cognitive and academic performance. Previous studies have revealed interplay between genetics and PE [29, 30]. In one of our studies investigating the effects of gene-environment interactions on reading ability, the cumulative score of the KIAA0319 gene showed a significant effect on the interaction effect with PE [31]. Another study from our team which examined the interaction of individual SNP related to dyslexia with PE showed similar results [32]. However, the specific effects of gene-PE interactions on mathematical ability have not been fully elucidated. Therefore, we proposed a second hypothesis (H2): DRD2 gene and PE interactively influence children's mathematical ability, when PE is considered as an external environmental factor.

Although molecular genetics provides strong support for the"Generalist Gene" hypothesis between mathmatical ability and reading and more general cognitive ability [33], molecular genetic evidence for the G×E interaction effect on mathematical ability remained limited. Our last aim was to test the interaction models of DRD2 and PE on mathmatical ability. Two main models have been proposed for G×E interaction effect in learning ability: diathesis-stress model and differential-susceptibility model [34–38]. Diathesis-stress model proposes that individuals with a certain disease risk or vulnerability genotype have higher sensitivity to negative environment than normal individuals [34]. The diathesis-stress model only focuses on the G×E interaction effect in poor environments. In contrast, the differential-susceptibility model indicats that specific genetic traits predispose individuals to be more affected by both the negative impacts of harsh environments and the positive influences of enriching ones. Differential-susceptibility model leads to disordinal form in gene-environment interaction, indicating

that persons carrying risk allele may be more malleable [39]. Therefore, by clarifying the pattern of gene-environment (DRD2 by PE) interactions on mathematical ability, hypothesis 3 (H3) was proposed: A simple slope analysis of the correlation was employed in the current study to see which of the two models that the interaction was more likely to fit into. To sum, the current study aimed to investigate: (1) the effects of the DRD2 gene on mathematical abilities, including both individual SNPs and haplotypes; (2) whether haplotypes, as an aggregate of genetic variations, exert a greater genetic influence on mathematical ability as a complex phenotype; and (3) whether there is interaction between the DRD2 gene and parental education (PE) on mathematical abilities, and if yes, which the interaction pattern fit into diathesis-stress model or differential-susceptibility model.

Materials and methods

Participants

A cohort of primary school students from two provinces in the northwestern part of China, including Shaanxi province and Gansu province, aged from 7 to 13 (Mean age 9.59 years old) was recruited as participants for this study. We used convenience sampling, specifically we contacted and selected five primary schools that were willing to participate and able to provide support. To ensure a nationally representative sample, we selected schools in both urban and rural areas, as well as schools at different economic levels. Among them, the proportion of girls is 48.4%. We first excluded individuals with severe mental disorders and excluded individuals below three standard deviations based on their performance on the mathematics test (n=97). Nonverbal intelligence of these children was assessed using Raven's Standard Progressive Matrices and all children had normal IQ levels. Finally, a total of 1097 participants were eligible for subsequent genotyping and association analysis. This study received approval from the ethics committee of Shaanxi Normal University, and written informed consent was obtained from the parents of all participants.

Parental education (PE) levels

A total of 798 participants in this study had information about their parents' educational levels, with 1 representing the lowest educational level and 8 representing the highest educational level: 1=primary school education, 2=junior high school education, 3=senior high school education, 4=junior college education, 5=undergraduate degree, 6=master's degree, 7=doctoral degree, and 8=post-docotoral experience. When both parents have access to information, the average score is given by their educational level, which represents the education level of the parents. We also define a 'single-family household' as a household in which only one parent lives with the child. If data are available for only one parent, we use the educational level of this parent as an indicator of PE [40, 41].

SNP selection and genotyping

First, 28 SNPs related to WM and language ability were selected (see Table S1). These SNPs were then included in the genotyping and imputation phases for the individuals under study. The parameters were minor allele frequency (MAF) over 1%. SNPs were eliminated if they showed a variant call rate<0.95, a missing genotype data (mind)<0.90, or a hardy-weinberg equilibrium (HWE)<10^{-5} with each dataset. We also impute DRD2 using the Genome Asia Pilot-GasP (GRCh37/hg19) reference panel on the Michigan Imputation Server (Minimac4). For quality control of all SNPs, please refer to the corresponding article [2].

Phenotypic measure

A Chinese version of Heidelberg mathematics test was used to assess the mathematical ability [42, 43]. The test includes 11 subtests associated with 11 categories of mathematical abilities, which are divided into three areas: arithmetic operations, mathematical reasoning and visuospatial skills. The arithmetic operations area assesses performance in six tasks, including addition, subtraction, multiplication, division, equation, and magnitude perception tasks. The mathematical reasoning evaluates that children complete the next three numbers of the sequence according to the potential rules. The visuospatial skills include visual size estimation, spatial conception, quantity counting, and visuomotor tasks. The reliability (Chronbach's alpha) of the total test was 0.88 and the validity of that was 0.91.

Data analysis

Linear regressions were performed to investigate the DRD2 genetic risk (28 SNPs) and phenotypes through PLINK. The interactions between PE and individual SNPs were analyzed using PLINK and the GLM model in R. Haplotypes were designated based on r^2 indicating linkage disequilibrium (LD) [44]. The main effects analyses of haplotype were performed using the PLINK haplotype linear association test. Haplotype by PE interaction analyses were also conducted using the GLM model in R (version 3.1.2). Rare haplotypes (frequency<0.02) were excluded from the linear association and interaction analysis (Table S1).

In all statistical assessments, Bonferonni's correction for multiple testing was applied to set appropriate significance thresholds. Adjusted p-value thresholds were set at $p \leq 0.0018$ (0.05/28) for single SNP analysis, and $p \leq 0.0018$ SNP×PE interaction analyses. Bonferonni-adjusted p-values for haplotypes and haplotype×PE interaction are $p \leq 0.0019$ (3 SNPs, 26 haplotypes), $p \leq 0.0020$

Table 1 Significant SNP x PE interaction analyses on phenotypes

SNP	A1	Phenotype	BETA	*P*
rs4648317×PE	A	Division	-0.9128	0.0016
rs4350392×PE	A	Division	-0.931	0.0012
		Equation	-0.7301	0.0020
rs4938019×PE	C	Division	-1.043	0.0003
		Equation	-0.8132	0.0005
rs10891556×PE	T	Division	-1.051	0.0003
		Equation	-0.7661	0.0010

(4 SNPs, 25 haplotypes) and $p \leq 0.0021$(5 SNPs, 24 haplotypes), respectively.

Results

Preliminary description

The skewness and kurtosis values of all phenotypes fall within the range of -2 to 2, suggesting that the data are close to a normal distribution for our analytical purposes. Most of the skewness and kurtosis values are between −2 and 2. These traits also showed moderate to high correlations (Table S1). To exclude the gene-environment correlations, the correlation analysis was conducted (Table S1). The relationship between SNPs and PE was not significant (r=−0.04-0.05, r_p = 0.15-0.91), thus PE can be used as an environmental variable in our study.

Single SNP analysis

None of the investigated polymorphisms yielded statistically significant associations with any phenotypes in linear regressions using PLINK (Table S2). However, when SNP×PE interactions were investigated, the interactions reached statistical significance on division and equation solving (Table 1 and Table S3). Through simple slope analysis, we found that the homozygotes of the first allele (A1) of these 4 SNPs (rs4648317, rs4350392, rs4938019 and rs10891556) have a negative effect on the phenotype under the influence of environmental factors (PE) (Table S3)

The results of the slope analysis in GLM models using R verified the interaction between these 4 SNPs and PE on mathematical ability and further illustrated that the interaction patterns supported differential-susceptibility model (Figure S1 and S2). The resutls showed that in division (Figure S1) and equation (Figure S2) tasks, individuals with risk allele showed worse performance than other individuals, and better performance when PE is high.

Haplotype analysis

Haplotype analyses identified two haplotype blocks for polymorphisms reaching statistical significance (rs2734831-rs1125394-rs7103679 (TCC) and rs1125394-rs7103679-rs7125415 (CCC)) (Table 2 and Table S2). These two haplotype blocks affected mainly as 3 SNPs for magnitude perception and quantity counting. When we analysed 25 haplotypes consisting of four adjacent SNPs, rs2734836-rs2734831-rs1125394-rs7103679 (TTCC), rs2734831-rs1125394-rs7103679-rs7125415 (TCCC) and rs1125394-rs7103679-rs7125415-rs4648318 (CCCC) were found to be related to magnitude perception and quantity counting. Further analyses with haplotype combinations of 5 neighboring SNPs showed that 2 haplotype blocks were correlated with subtraction. Four SNPs (rs2734831, rs1125394, rs7103679 and rs7125415) were present in multiple haplotype blocks and had an effect on mathematical ability when combined.

Table 2 Haplotype association analyses and predicted betas for MA

SNPs	Haplotype	Phenotype	BETA	*p*
rs2734831-rs1125394-rs7103679	TCC	Magnitude perception	1.64	0.001
		Quantity counting	1.15	0.001
rs1125394-rs7103679-rs7125415	CCC	Magnitude perception	1.64	0.001
		Quantity counting	1.16	0.001
rs2734836-rs2734831-rs1125394-rs7103679	TTCC	Magnitude perception	1.744	0.0005
		Quantity counting	1.193	0.0008
rs2734831-rs1125394-rs7103679-rs7125415	TCCC	Magnitude perception	1.625	0.0011
		Quantity counting	1.117	0.0017
rs1125394-rs7103679-rs7125415-rs4648318	CCCC	Magnitude perception	1.698	0.0007
		Quantity counting	1.153	0.0013
rs1125394-rs7103679-rs7125415-rs4648318-rs12574471	CCCCT	Subtraction	1.68	0.0005
		Magnitude perception	1.807	0.0004
rs7103679-rs7125415-rs4648318-rs12574471-rs4274224	CCCTA	Subtraction	1.354	0.0012
rs2075654-rs2734836-rs2734831-rs1125394-rs7103679	TTTCC	Magnitude perception	1.744	0.0005
		Quantity counting	1.193	0.0008
rs2734836-rs2734831-rs1125394-rs7103679-rs7125415	TTCCC	Magnitude perception	1.734	0.0005
		Quantity counting	1.161	0.0012
rs2734831-rs1125394-rs7103679-rs7125415-rs4648318	TCCCC	Magnitude perception	1.657	0.0009

In Haplotype×PE interaction analyses (Table 3 and Table S4), we mainly performed interaction analyses between PE and haplotypes with 3 or 4 haplotype blocks. The results showed that the environment factor mostly moderated the effect of haplotypes on quantity counting, with four significant haplotypes. Rs1076560 can only influence mathematical reasoning as a risk SNP through haplotype×environment interaction (rs6275-rs1076560-rs2511521 (ACG and GAA), p=0.001). Rs4648318-rs12574471-rs4274224, rs12574471-rs4274224-rs4581480-rs7131056, and rs4350392-rs4938019-rs1799978-rs10891556 affected magnitude perception, subtraction, and spatial conception through haplotype × environment interactions, respectively.

It is noteworthy that, although there were differences in the way SNPs were combined in individual haplotype analyses and in interaction analyses, rs7125415-rs4648318 not only had a separate genetic effect, but was also affected by modulation by PE level.

Discussion

This study reported that DRD2 gene demonstrated a significant effect on mathematical ability in a sample of Chinese children. The finding suggests that DRD2 can be considered as a generalist gene, as DRD2 as a candidate gene that can affect WM is also associated with mathematical ability. Particularly, when children engage in more complex mathematical tasks, the genetic effects of DRD2 become even more pronounced. The results support the "Generalist Gene" hypothesis, which states that there are common genes affecting most learning abilities.

First, our results provide evidence that DRD2 is a generalist gene by showing that DRD2 is not only associated with reading abilities and other cognitive abilities, but also influence mathematical ability. For the studies of complex diseases or quantitative traits, haplotype-based association analyses often provide more robust evidence when the single SNP exhibit low statistical power [45]. In the context of mathematical ability, a complex trait characterized by genetic variations arising from interactions between

Table 3 Haplotype×PE interaction analyses, *p*-values and betas. Bold *p* values passed Bonferroni correction

Phenotype	SNPs	Haplotype×PE	Beta	*p*
Magnitude perception	rs4648318-rs12574471-rs4274224	CTA×PE	1.54532	**0.0009**
	rs7103679-rs7125415-rs4648318	TCC×PE	1.83133	0.0023
	rs7103679-rs7125415-rs4648318-rs12574471	TCCT×PE	3.62023	0.0076
Subtraction	rs12574471-rs4274224-rs4581480-rs7131056	CGTC×PE	-5.561375	**0.0011**
	rs12574471-rs4274224-rs4581480	ATC×PE	3.110731	0.0093
Equation	rs4648318-rs12574471-rs4274224	CTA×PE	1.40115	0.0078
		CTG×PE	2.22024	0.0062
Division	rs4648317-rs4350392-rs4938019-rs1799978	GCTT×PE	1.31617	0.0076
Mathematical reasoning	rs6275-rs1076560-rs2511521	ACG×PE	-24.02675	**0.0010**
		GAA×PE	-23.9267	**0.0010**
	rs7103679-rs7125415-rs4648318	TCC×PE	-2.292862	0.0059
Quantity counting	rs7103679-rs7125415-rs4648318	TCC×PE	1.5394	**0.0006**
		TCT×PE	1.24921	**0.0005**
	rs2734849-rs1800497-rs10891549-rs6278	AGTC×PE	-0.84662	**0.0017**
	rs1800497-rs10891549-rs6278-rs6279	GTCG×PE	-0.85659	**0.0018**
	rs7125415-rs4648318-rs12574471	CTC×PE	1.31382	0.0083
	rs4648318-rs12574471-rs4274224	CTG×PE	-1.94551	0.0042
	rs7131056-rs4648317-rs4350392	GTC×PE	-0.65991	0.0098
	rs10891549-rs6278-rs6279	CGG×PE	-0.8382	0.0020
	rs1800497-rs10891549-rs6278	GTC×PE	-0.65991	0.0098
	rs2511521-rs2283265-rs12363125-rs2075654	GCCC×PE	-0.76791	0.0061
	rs12363125-rs2075654-rs2734836-rs2734831	CTTT×PE	0.76726	0.0056
	rs1125394-rs7103679-rs7125415-rs4648318	CTCT×PE	-1.55994	0.0084
	rs7103679-rs7125415-rs4648318-rs12574471	TCTC×PE	1.59475	0.0094
	rs4648318-rs12574471-rs4274224-rs4581480	CTGC×PE	-1.64561	0.0071
	rs12574471-rs4274224-rs4581480-rs7131056	TATC×PE	-2.34369	0.0095
Visual size estimation	rs4648318-rs12574471-rs4274224	CTA×PE	-2.72252	0.0038
Spatial conception	rs4350392-rs4938019-rs1799978-rs10891556	CTTG×PE	0.94203	**0.0017**
	rs4350392-rs4938019-rs1799978	CTT×PE	0.83099	0.0043
	rs4938019-rs1799978-rs10891556	TTG×PE	0.90643	0.0036
	rs2511521-rs2283265-rs12363125	GCC×PE	-0.76791	0.0061
	rs4648317-rs4350392-rs4938019-rs1799978	GCTT×PE	0.86894	0.0031

multiple variants [1, 46]. Consistently, our present findings did not reveal significant effects at the level of individual SNPs. Instead, our findings highlighted the remarkable influence of haplotypes on mathematical ability. Notably, our study identified rs2734831-rs1125394-rs7103679 and rs1125394-rs7103679-rs7125415 as haplotype combinations demonstrating higher significance in the test of association analysis, even when involving three or more haplotypes in the DRD2. In haplotype analysis, we observed a moderation effect of haplotypes on basic mathematical abilities in children. According to these findings, we propose that DRD2 is related to mathematical ability. The association between variants and mathematical abilities might be due to the influence of DRD2 on mathematical abilities through WM. However, as we did not include analyses of WM in the current study, we cannot conclude whether the effect of the DRD2 gene on mathematical ability is dependent on WM, which suggest future research directions.

Second, the present study supports the hypothesis that the influence of dopamine system on mathematical ability is susceptible to modulation by the surrounding environment. Parental characteristics are important for the expression of genes in the dopamine system, especially for dopamine system related to cognitive abilities [47]. Our findings indicate that the genotypes of intron rs1076560 and rs2283265, when considered individually, did not exert a significant influence on mathematical ability. However, when moderated by parental education, both variants exhibited an impact on children's mathematical reasoning and mathematical spatial ability as haplotypes.

Specifically, the DRD2×PE interaction was mainly on children's more advanced mathematical abilities, such as division, equations, quantity counting, and mathematical reasoning. Through simple slope analysis, we found that the homozygotes of the first allele of these 4 SNPs (rs4648317, rs4350392, rs4938019 and rs10891556) have a negative effect on the phenotype under the influence of environmental factors (PE), i.e., at higher PE the phenotypes descend with the presence of homozygotes. The high PE makes subjects more vulnerable to these gene variants.

Third, we found the interaction to be consistent with the differential-susceptibility model through a simple slope analysis of the individual SNP and PE interactions. We find that the differential-susceptibility model provides a more relevant framework for demonstrating advanced mathematical ability. This model emphasizes the interaction between genetic and environmental factors that lead to variability in the performance of individuals facing complex mathematical tasks. In other words, individuals with risk allele, who were more affected by their parental education, showed worse mathematical performance than other individuals in poor environments, and better mathematical performance when the environment became positive. The interaction of haplotypes-PE on mathematical ability showed different effects, which may indicate a complex interaction between genetic and environmental factors in the development of mathematical ability. Given the current limited statistical methods, it is not possible to tell which model the interaction between haplotype and environment fits.

As a remote environment in the development of children, family socioeconomic status is usually measured by PE level and/or parental income. In a study on socioeconomic status (SES) and children's cognitive ability in Chinese families, it was noted that parental education level and income were two important indicators of family SES, and results show that PE rather than income is positively associated with their children's cognitive abilities [48]. Qi et al. (2022) also found that relative to family income and parental occupational levels, the key variable significantly linked with children's education as measured by their Chinese and math scores is parental educational level [49]. Compared to parents of low PE, parents of high PE tend to invest more material and interpersonal involvement in the development of children. Equally, in accordance with compensatory advantage mechanism [50], the adverse outcomes initially stemming from genetic influences can often be mitigated by parents of higher socioeconomic status (SES). Children from low-PE backgrounds, thus, face a double disadvantage: the genetic risks they carry are not compensated for within the home environment, exacerbating educational inequality. Our research indicates that students with certain genetic traits can benefit from a positive educational context. Although SES and parental education levels are immutable factors, the detrimental genetic effects can be offset by interventions that enhance school quality or alleviate poverty [51, 52]. Consequently, children from low-SES backgrounds can receive compensatory support through schools, thereby reducing their risk of developing mathematical disabilities.

Limitations

First, the cohort size utilized in this study can be considered exploratory and should be substantiated by larger studies and validated in independent replication cohorts. Second, although PE was considered as an environmental factor, it might also include genetic correlates, despite we found absence of a correlation between PE and DRD2. This study shows that children's mathematical ability can be influenced by their parents. Further analyses are needed to determine whether PE is an intergenerational or environmental influence in gene-environment interaction. Third, the DRD2 gene cannot fully account for all aspects of mathematical ability. Future studies should examine the development of mathematical skills influenced by the interaction of multiple genes. Fourth, since we used Gaussian distributions to fit the model results for haplotypes and environmental interactions during the calculations, there may be numerical instability in the matrix inversion or iterative algorithms, resulting false positives in some haplotype results.

Therefore, rigorous and robust models will need to be fitted for haplotypes and environmental interactions in the future. Finally, future studies should include analyses of WM and other possible neural mechanisms to determine their relationship with DRD2 gene expression and mathematical ability.

Conclusion

In this study, we explored the effects of the DRD2 gene and environmental interactions on children's mathematical ability. The DRD2 gene affects children's mathematical ability more as a form of haplotypes. Although gene-environment interactions demonstrate different patterns in basic mathematical calculations and more complex math abilities, the universal importance of positive PE in the development of children's mathematical skills is evident. Our findings also provide important implications for personalized interventions [53]. The discovery of generalist genes holds significant importance for the development of children's education. Identifying these genes not only aids in recognizing various cognitive and learning disabilities in children but also facilitates the development of targeted intervention strategies for these conditions. By accurately identifying the genotypes that affect children's learning performance, combined with consideration of environmental factors, we can implement more personalized intervention strategies. Balancing the needs of children with different genotypes, thereby maximizing their learning potential.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40359-024-01997-y.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

Author contributions

Jingjing Zhao conceived of the presented idea. Qing Yang and Ximiao Zhang performed data analysis. Chen Cheng and Liming Zhang collected the behavioral and genetic data. Qing Yang and Jingjing Zhao designed the study. Qing Yang, Ximiao Zhang, and Jingjing Zhao wrote the manuscript. All authors read and approved the final manuscript.

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Data availability

The raw data are not publicly available due to legal or ethical restrictions. Data were analyzed using R version 4.0.0 (R Core Team, 2020) and Plink 1.90. Codes used in this study are available from the authors upon request.

Declarations

Ethics approval and consent to participate

All experimental procedures have been authorized by the Shaanxi Normal University and written informed consent was obtained from all participants' parents. Shaanxi Normal University did not assign Ethic Approval Code for their Ethic Committee before 2020. Therefore, we provide the Ethic Committee Name: A study on the genetic mechanism of reading ability and mathematical ability in Chinese children and Approval Date: 27th November 2017.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Transparency and openness

The beta values of the SNPs in this paper can be found in previous studies (Zhang et al., 2023). The statistical methods and statistical data available from the corresponding author upon reasonable request. The raw data are not publicly available due to legal or ethical restrictions. Data were analyzed using R version 4.0.0 (R Core Team, 2020) and Plink 1.90.

Declaration of Helsinki

This study adheres to the Declaration of Helsinki and is conducted in strict accordance with ethical principles and the protection of research participants' rights and interests in the study of genetic data. We ensure their informed consent while safeguarding their personal privacy and data security. The collection, storage, analysis, and reporting of genetic data will be closely monitored and regulated to respect the privacy and personal information security of research participants. We remain committed to maintaining integrity and transparency, advancing the science of genetic data research, and safeguarding the interests and rights of our participants.

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