Original Research Article

2nd to 4th Digit Ratio (2D:4D) – Is It a Marker for Dyslexia ?

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ABSTRACT

Background: Specific learning disorder in general called as dyslexia is a neuro developmental disorder, which occurs more commonly in males (Male:Female ratio is 4:1), there are evidence to suggest role of prenatal gonadal hormone exposure in neurodevelopment. However, studies on association between 2nd to 4th digit ratio and dyslexia are mixed. Objective: To compare the 2nd and 4th digit ratio (2D:4D) of both hands between children with dyslexia and children without dyslexia.
Methodology: A case control study, recruited 30 children with dyslexia and 30 age and education matched normal controls, after getting informed consent from their parents. Collected socio demographic details, applied CARS, Schonell's reading and spelling test, followed by detailed evaluation by psychiatrist and clinical psychologist, including psychological testing to confirm the diagnosis of dyslexia. The digit length of index and ring finger on both hands of all children were measured using Vernier Calliper by direct method.
Results: In both the hands 2D:4D ratio was more in children with dyslexia than normal children, but the difference was not significant (p – 0.146). Analysis of only male samples showed digit ratio is higher in dyslexic children than normal children; which were significant (p – 0.03).
Conclusion: Our study does not support an association between digit ratios and dyslexia; however, trend towards higher ratio in dyslexia especially in male children are interesting and needs further exploration. Need more studies in this area to form a definite conclusion.

Keywords: Dyslexia, Specific learning disorder, Digit ratio, 2D:4D, Biomarker.

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INTRODUCTION

Dyslexia is a neuro - developmental disorder, Prevalence of dyslexia ranges from 4 % to 17%. The prevalence is higher in males (Male: Female ratio is 4:1),[1]. This suggests there could be some factors that is different in either sex which plays a role in the development of this disorder. The neurobiology of dyslexia remains largely unknown but evidence suggests that neuronal migration and axon guidance pathways may be disrupted in dyslexia [2].

Normal brain is sexually dimorphic, due to the influence of gonadal hormones on neurodevelopment during antenatal period. Aberrations in neurodevelopment due to gonadal hormonal imbalance are one of the mechanisms for developing dyslexia. The relation between imbalance in gonadal hormones and dyslexia is very complex.

The absence of testosterone leads the central nervous system to develop passively, in a primarily female fashion, while the presence of testosterone induces the masculinization of the brain, indicating that the sexual dimorphism of the brain is mediated by the epigenetic action of gonadal steroids [3]. Geschwind and Galaburda suggested that testosterone inhibited the growth of certain areas of the left hemisphere and

facilitated the growth of the same areas in the right hemisphere. As a result, language skills would be negatively affected and hand preference would tend to shift toward the left. In extreme forms, this abnormal cortical development would render an individual incapable of handling effectively the linguistic tasks required for reading and writing [4]. Ramus, based on animal studies demonstrated that rodents with induced ectopias and microgyri exhibit learning deficits. Focal cortical abnormalities in specific areas of left perisylvian cortex are the primary cause of dyslexia. When foetal testosterone exposure is high, cortical disruption propagates to the thalamus, provoking additional sensory impairments as a consequence of the conjunction of high fetal testosterone exposure and ectopias or microgyri [5]. A study showed high prenatal testosterone may impair developing auditory perceptual processes and phonological processing in the left hemisphere. These impairments in phonology in turn can adversely affect development in reading [6].

But it's not possible to measure the prenatal gonadal hormone exposure directly. Hence, we need to evaluate it indirectly using an indicator which could predict gonadal hormones concentration in utero. The digit ratio is the ratio of the lengths of different digits, typically as measured from the basal / proximal crease of the finger to the tip of the finger. Androgen and Estrogen differentially regulate the network of genes that controls condrocyte proliferation, leading to differential growth of digits in males and females [7].

The ratio between the length of the 2nd and 4th digits is: (a) fixed in utero; (b) lower in men than in women; (c) negatively related to testosterone and sperm counts; and (d) positively related to estrogen concentrations [8]. 2D:4D ratio may be used as an indicator and predictive factor in a variety of disorders associated with a disturbed testosterone/estrogen hormone balance like Gender identity disorder, Autism, Dyslexia, Migraine, Stammering, Immune dysfunction, Infertility [8].

The existing literature shows mixed results regarding the relation between digit ratio and dyslexia; there is also ongoing debate whether 2nd digit to 4th digit ratio is a reliable indicator of prenatal gonadal hormones exposure. Few researchers even question the proposed role of gonadal hormones in the development of dyslexia. This is an interesting area and has a wide scope for research. There are many studies on digit ratio in autism, but only very few studies in dyslexia. Hence this study is planned to examine the relationship between 2nd digit to 4th digit ratio and dyslexia. A reliable finding in this area of research would have a very significant clinical implication; this has prompted us to carry out this study.

The objective of the study was to compare the 2^{nd} to 4^{th} digit ratio (2D:4D) of both hands between children with dyslexia and children without dyslexia.

METHODOLOGY

Hypothesis

Children with specific learning disability (Dyslexia) will have smaller 2^{nd} digit to 4^{th} digit ratio compared to children without dyslexia.

Subjects and Procedure

We screened all children aged between 5 and 18 years old, who attended psychiatric outpatient department in PSG institute of medical sciences and research, between May 1st 2014 and July 31st 2014. PSG institute of medical sciences and research is a tertiary care general hospital. A final year MBBS student who got trained in applying Schonell reading test, Schonell spelling test and Childhood Autism Rating Scale administered these tests on all children. All children were evaluated in detail by a psychiatrist; the diagnosis of dyslexia and the type of dyslexia was confirmed only after further psychological testing by the child psychologist. We consecutively recruited 30 children with dyslexia who fulfilled the inclusion and exclusion criteria.

Control group had 30 age and education matched children who visited hospital for non psychiatric problems or were recruited from the community. Control group didn't had any academic difficulties or psychiatric problem according to parents, Schonell reading test, Schonell spelling test and childhood autism rating scale was administered to all children in control group as well, child suspected to have dyslexia or autism were referred to psychiatry for further evaluation.

Children were included in the study after getting informed consent from their parents and only if the child was willing to participate in the study. Children with autism, Asperger's syndrome, mental retardation,

attention deficit hyperactivity disorder, schizophrenia, medical or surgical condition which would interfere with measurement of digit length e.g., contractures, trauma, amputation etc, were excluded from the study. Children who were recruited for the study, the length of their index finger and ring finger (from the basal crease to the tip of the finger) of both the hands is measured using Vernier Calliper by direct method, which is an accurate as well as easy method to measure the digit length [9].
The study was approved by Institutional human ethics committee, PSG institute of medical sciences and research.

Materials

1. **Semi structured proforma:** This Proforma is used to get basic details of the cases and controls. It includes the name, age, sex, education medium, syllabus, socio economic status, height, weight, IQ, co morbidity.
2. **Childhood Autism Rating Scale (CARS):** It is a tool for assessing autism. This is scored based on the interview with the primary care giver and observation of the child. The child is diagnosed as having autism if they score above 30 [10].
3. **Schonell reading test:** A reading test that determines the reading age, however it does not test reading comprehension. The reading age is calculated from the number of words read correctly and compared to the student's chronological age to see if the student is reading at the level for their age, or are reading either below or above level for their age [11].
4. **Schonell spelling test:** A spelling test that determines the spelling age. It comprises of 100 words, and the child is asked to write 30 words (applicable for their class).The spelling age is calculated from the number of words wrote correctly and compared to the student's chronological age to see if the student is writing at the level for their age, or are writing either below or above level for their age [12].

STATISTICAL ANALYSIS

Statistical analysis was done using the Statistical package for social sciences (SPSS) version-18. Continuous variables were assessed using the unpaired t-test and categorical variables were assessed using the chi-square test. P value of less than 0.05 is considered as statistically significant.

RESULTS

Table 1 – Socio-demographic variables

		CASE (N=30)	CONTROL (N=30)	p Value
Age (Mean, SD) in years		11.60 ± 3.328	13.40 ± 2.568	0.092
Education (Mean, SD) in years		6.90 ± 2.998	8.50 ± 2.610	0.470
Sex	**Female**	3	18	0.001
	Male	27	12	
Medium	**English**	28	27	0.640
	Tamil	2	3	
Syllabus	**CBSE**	1	29	0.313
	Samachir	0	30	
SES	**Lower middle**	0	6	0.010
	Upper middle	27	24	
	Upper	3	0	

The mean age of cases and controls were 11.6 years and 13.4 years respectively, the difference in age between the 2 groups was not statistically significant. There is no statistical difference between the 2 groups on other socio demographic profiles like education, medium, syllabus and socioeconomic status. Most of the children

on either group were from upper middle socioeconomic class, studied in English medium and their syllabus was samachir, which is the most popular syllabus in the state of Tamil Nadu, India.
The children with dyslexia were predominantly males (90% of the cases) were as in control group only 40 % were males; this was statistically significant (p = 0.001).

Table 2: 2D:4D ratio between male and female children

Male Vs Female (n-39) (n-21)		t	df	Sig. (2-tailed)	Mean Difference	95% CI of Difference	
						Lower	Upper
Rt hand 2D:4D	Equal variances assumed	-0.761	58	0.450	-0.01239	-0.04498	0.02020
	Equal variances not assumed	-0.674	29.596	0.506	-0.01239	-0.04994	0.02517
Lt hand 2D:4D	Equal variances assumed	-0.761	58	0.450	-0.01239	-0.04498	0.02020
	Equal variances not assumed	-0.674	29.596	0.506	-0.01239	-0.04994	0.02517

Taken all 60 children together and divided them into 2 groups based on sex, male children had lower 2nd to 4th digit ratio on either hand when compared to controls, shown in (table 2), but the difference is not significant (p = 0.506).

Table 3: 2D:4D ratio between SLD and control groups

SLD Vs Control (n-30) (n-30)		t	Df	Sig. (2-tailed)	Mean Difference	95% CI of Difference	
						Lower	Upper
Rt hand 2D:4D	Equal variances assumed	1.490	58	0.142	0.02283	-0.00784	0.05349
	Equal variances not assumed	1.490	33.222	0.146	0.02283	-0.00833	0.05398
Lt hand 2D:4D	Equal variances assumed	1.490	58	0.142	0.02283	-0.00784	0.05349
	Equal variances not assumed	1.490	33.222	0.146	0.02283	-0.00833	0.05398

The comparison of 2nd to 4th digit ratio using independent t test between children with dyslexia and normal children showed that the mean digit ratio on both hands is more in children with dyslexia than normal children, which is in contrary to our hypothesis, however this was not statistically significant (p = 0.146). Our sample predominantly contained children with writing disorder (23/30 children). So, we decided to compare the 2D: 4D ratios between children with writing disorder only and controls.
As shown above in (table 4) the 2nd digit to 4th digit ratio in both right and left hand was higher in children with writing disorder than control group, but this again was not significant (p = 0.134). The sub-analysis comparing children with writing disorder and controls yielded a result similar to dyslexia group in general. Since the number of children with reading and mathematics disorder were very few, it was not possible to do a separate analysis on them. As dyslexia is more common in males and testosterone is expected to play a major role, a separate analysis was done comparing the digit ratio between male children with and without dyslexia.
The 2nd to 4th digit ratio on either hand was higher in male children with dyslexia compared to male children without dyslexia; the difference was statistically significant with a p value of 0.03. This is shown in (table 5).

Table 4: 2D:4D Ratio between dysgraphia children and controls

Dysgraphia Vs Control (n-23) (n-30)		T	Df	Sig. (2-tailed)	Mean Difference	95% CI of Difference	
						Lower	Upper
Rt hand 2D:4D	Equal variances assumed	1.372	51	0.176	0.02404	-0.01115	0.05923
	Equal variances not assumed	1.533	35.936	0.134	0.02404	-0.00776	0.05585
Lt hand 2D:4D	Equal variances assumed	1.372	51	0.176	0.02404	-0.01115	0.05923
	Equal variances not assumed	1.533	35.936	0.134	0.02404	-0.00776	0.05585

Table 5: 2D:4D Ratio in male children

Male children Case Vs Control (n-27) (n-12)		T	Df	Sig. (2-tailed)	Mean Difference	95% CI of Difference	
						Lower	Upper
Rt hand 2D:4D	Equal variances assumed	3.442	37	0.001	0.05263	0.02165	0.08361
	Equal variances not assumed	2.456	12.001	0.030	0.05263	0.00594	0.09932
Lt hand 2D:4D	Equal variances assumed	3.442	37	0.001	0.05263	0.02165	0.08361
	Equal variances not assumed	2.456	12.001	0.030	0.05263	0.00594	0.09932

DISCUSSION

There are very few studies in this area, to best of our knowledge this is the first study in India looking into the relation between 2nd digit to 4th digit ratio and dyslexia. We have taken 30 children with dyslexia (cases) and 30 normal age and education matched controls. There was a significant difference between the two groups with respect to gender distribution, predominance of male children in dyslexia group could be explained by the general prevalence of dyslexia, which is more common in males (Male: Female ratio is 4:1) and ours being a consecutive sampling.

The current study did not show any difference in the 2nd to 4th digit ratio between children with dyslexia and normal children, neither the right hand comparison nor the left hand comparison between groups showed significant difference, which is in contrast to the observation made by Manning et al 2002 who reported 2nd digit to 4th digit ratio is low in dyslexia compared to Non dyslexic individuals. But our finding is in concurrence with the findings of two other studies, which also reported no association between 2D:4D ratio and dyslexia. A study done in Netherland on children with dyslexia with a phonological deficit showed no evidence for an association between reading disabilities and the 2nd digit to 4th digit ratio, also showed no support for the assumed relation between the 2nd digit to 4th digit ratio and prenatal testosterone[10]. Another study showed digit ratios were sexually dimorphic 'male lower than female' pattern, no difference in digit ratio between dyslexic and normal reading children. Digit ratios were not related to any sensory measure.[11]

The present study showed that 2nd to 4th digit was lower in children without dyslexia than in children with dyslexia, which is contrary to our own hypothesis that 2nd to 4th digit ratio will be low in dyslexic children compared to normal children, and contradicts those studies which shows an association between digit ratio and dyslexia. This finding is difficult to explain by any existing literature on dyslexia and digit ratio. However similar finding was reported in a study on 2nd to 4th digit ratio among 107 individual across all departments and all academic grades, who completed an Internet-based questionnaire on autism or dyslexia in self and family members, the study showed an association between autism and lower 2nd digit to 4th digit ratio, whereas interestingly dyslexia was associated with a higher 2nd to 4th digit ratio in that study [12].

Males had a lower digit ratio compared to females irrespective of being dyslexic or not, points in favour of the concept of sexual dimorphism in digit ratio as suggested by a study [13], however could not agree fully because the difference was not significant.

Some of the theories put forward to explain dyslexia and digit ratio are testosterone theory in the context of cerebral lateralization with testosterone suppressing certain areas in left hemisphere, Extreme male brain theory which suggests excess masculinization of brain leading to dyslexia.

In this study there is no difference in the digit ratio between left hand and right hand nor there do any association of digit ratio in either of this hand and dyslexia. Comparison of only male samples between groups also revealed a higher ratio in children with dyslexia than normal children; this was significant ($p = 0.03$). These findings are in contrast to theories explaining dyslexia and digit ratio.

Our finding does not support an association between digit ratio and dyslexia; neither has it supported the cerebral lateralization theory or extreme male brain theory. The reasons could be digit ratio depends on the production of testosterone and sensitivity of digits to foetal testosterone, which can vary across different ethnic groups, this can explain why there is no difference in digit ratio between groups but this can't explain the reason for lower ratio in controls.

May be there is no real association between dyslexia and digit ratio as supported by studies, 2nd to 4th digit length may not be an indicator of prenatal gonadal hormone exposure 14 and most of the studies supporting the association has not directly compared dyslexia with normal children, it was either done on children with family history of dyslexia or comparing individuals in different academic fields [12]. So, findings in these studies could be influenced by some confounding factors.

Strength of the study

The sample in our study is homogenous and it's a direct comparison between children with dyslexia and without dyslexia. We recruited the children consecutively so any bias in sampling is avoided. Exclusion of comorbid condition like autism, Asperger's syndrome etc which could have confounded the findings if present, as studies also show an association between these disorders and digit ratio.15 All children in dyslexia group were evaluated in detail by a psychiatrist and clinical child psychologist. Using direct method to measure digit ratio by Vernier Calliper, which is an accurate as well as easy method to measure digit length.

Limitations of the study

The findings of this study should be interpreted with caution because of small sample size, possibility of type II error could not be ruled out. The investigator was not blind to the diagnosis, however any bias in measurement was unlikely as the results contradicts our own hypothesis. Measurement was done by a single investigator; having 2 or 3 persons to measure the digit could have added more reliability and validity to the findings. Controls were recruited based on the parents report on their children's academic performance, physical and mental status, not evaluated by psychiatrist or clinical psychologist, it's possible that children with subtle psychological disturbance are missed and mistakenly recruited as normal controls. Despite all these limitations, the finding of this study is unique and cannot be dismissed.

CONCLUSION

This study does not support the association of 2nd digit to 4th digit ratio and dyslexia; neither do the theories put forward to support such an association. However, this study has certain limitations, we need more studies in this area with a larger sample size to overcome above limitations and form a definite conclusion.

The finding children with dyslexia having a higher digit ratio than controls especially in male samples are interesting and needs further exploration.

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