2D:4D finger ratio and language development

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2D:4D FINGER RATIO AND LANGUAGE DEVELOPMENT

Summary. Introduction. *A possible hormonal influence in language development has been suggested in the recent years. The 2D:4D finger ratio is an indirect measure for prenatal androgen exposure. It is negatively related to prenatal testosterone and positively related to prenatal estrogen, resulting in a lower ratio for men and a larger ratio for women. It can be explored in children as young as 2 years old.* Aim. *To study if an association exists between the 2D:4D finger ratio and language development (vocabulary) and/or language problems.* Subjects and methods. *The lengths of the second digit (index finger) (2D) and the fourth digit (ring finger) (4D) were measured in 97 preschoolers and the Language Development Survey was administered to the parents.* Results. *A weak negative correlation between language development (vocabulary) and right 2D:4D ratio was found in both sexes for children aged 4 or less years, significant only in boys. A strong negative correlation between language articulation problems and right 2D:4D ratio in both sexes for children aged 3 or less years, and a lower negative correlation between articulation problems and right 2D:4D ratio were found for boys aged 4 or less years.* Conclusion. *Findings suggest an important role for testosterone in language development (vocabulary) and a possible influence on articulation problems, probably through higher testosterone levels. [REV NEUROL 2009; 48: 577-81]*

Key words. *2D:4D ratio. Expressive language disorder. Language articulation problems. Language development. Sex differences.*

INTRODUCTION

Normal language development consists of a passive initial phase that includes listening and gradual understanding of others' speech between 4 to 6 months old, commonly known as receptive language. A subsequent active phase with word production and vocabulary expansion begins at about 12 months of age, with increasingly more complex functions appearing in the second year of life when simple grammar rules and word combinations appear. Practice and exposure to higher number of words, and complex language constructions help children build their verbal skills. However, several studies show that other environmental factors, such as family socioeconomic status (SES) [1-4] and maternal education and age at first birth also have important influences on vocabulary development [5-9]. Additionally, the possible hormonal influence in language development has been a source of speculation. Clinical and epidemiologic evidence demonstrates sex differences in language development. Several authors have shown that girls develop expressive language earlier than boys [10,11] particularly in vocabulary and verbal fluency measures [12,13]. However, other authors have established that this advantage is transient and smaller in older ages [14-18]. Some of the sex differences in language development associated with changes in brain morphology have been studied through diverse imaging techniques and postmortem studies, see Cosgrove et al [19] for an excellent review. Hormone release during the puberty period is responsible of the reorganizational effects in the brain, which are probably secondary to neurogenesis, changes in receptor expression, and neurite overgrowth [20]. During this period, several studies have shown that gray matter volume decreases while white matter volume increases in both sexes [21-27] but not consistently for boys [28]. Morphology changes are possible throughout life as revealed by several hormone therapy studies in men and woman with estrogen and testosterone [29-32]. Clinical studies show that prenatal hormones play an important role in brain organization and language performance. Disorders with low prenatal androgen levels, such as Congenital idiopathic hypogonadotropic hypogonadism (IHH) or Klinefelter have a detrimental effect on verbal fluency measures [33-35] which increase with testosterone supplementation treatment in Klinefelter [34]. Along the same lines, females with a more masculine appearance have an associated pattern of proficiency at verbal tasks [36]. In contrast, lower levels of circulating estrogen in Turner Syndrome are associated with less than average verbal fluency [37]. The effects of estrogen on language abilities have been investigated by Dorn et al [38], who studied a group of children with precocious puberty (PA) (8 girls, 1 boy) and compared their cognitive profile, with those 'typically developing' children. The PA group had higher estrogen levels and had significantly lower summary WISC III verbal scale scores, while no differences were noted on verbal fluency compared to the 'typically developing' group.

Children whose mothers had been exposed to hormones during pregnancy have earlier development of speech and fewer disorders [39]. McCardle and Wilson [40] compared children with congenital adrenal hyperplasia (characterized by high levels of intrauterine testosterone), with children who have been diagnosed with idiopathic precocious puberty (IPP) (characterized by high levels of estrogen or testosterone). Children in the latter group performed better in the semantic tasks, while children exposed to high testosterone levels did better in the time and the memory dependent tasks. One study has been done examining fetal testosterone (FT) in routine amniocentesis and

Accepted: 17.03.09.

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LAG was distinguished with the Scholarship 'Mujeres ICyTDF: Rosalind Franklin'. Dedicated to the memory of Dr. Marcelo Salles Manuel.

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vocabulary size. In this study, Lutchmaya et al [41] reported an inverse relationship between FT and vocabulary size.

A less invasive indirect measure for prenatal androgen exposure is the finger ratio length of the 2nd (index) finger and 4th (ring) finger 2D:4D. This is a measure from the bottom crease to the tip of the finger, considered a well known marker of hormonal influence in the 6th week of intrauterine life. It is negatively related to prenatal testosterone and positively related to prenatal estrogen. It determines a lower ratio of 2D:4D for men and higher ratio for women [42]. Fetal testosterone (FT) and Fetal Estradiol (FE) obtained through amniocentesis and measured by radioimmunoassays were confirmed to have a negative association between the right 2D:4D ratio and FT/FE ratio Lutchmaya et al, [43]. Longitudinal studies using x-rays to measure the 2D:4D ratio have shown that this ratio is established by age 2, although recent studies have reported that sex differences in the ratio are present in human fetuses from 9 to 40 weeks of gestation [44]. In children, a pattern of slow growth continues until the age of 9 years, when the 2D:4D measurement becomes stabilized; later in puberty it becomes permanent [42]. The ratio is independent from weight and height and has racial and genetic influences demonstrated by some investigators [45]. The finger ratio may be related to traits or behavioral measures which have prenatal hormonal influence. Some studies in female adults have found associations between reactive aggression, sensation seeking, dishinibition, psychoticism and verbal fluency with low 2D:4D ratio (male type) finger type, while high 2D:4D ratio (female-type) was related to neuroticism [46].

Manning et al [47] studied autistic children with and without language, finding a lower but non-significant mean 2D:4D ratio in the latter. Until now, this ratio has not been investigated to evaluate its association with language development or as a predictor of language problems and delays in non autistic children. One study of verbal fluency in adults showed a relationship to lower ratios (male type) in women [48]. To our knowledge there have been no Mexican studies examining this ratio. The aim of this study was to determine if an association between 2D:4D ratio and language development in Mexican children exists.

SUBJECTS AND METHODS

Participants from a similar socioeconomic background were recruited from three community nurseries in Mexico City. School principals and parents gave consent to perform the ratio measurement during school hours. Two trained nurses measured the children's fingers, and in the first 10 children (5 boys and 5 girls), a second measurement was done to investigate interrater agreement. The sample included 97 children, 55.6% were males with an age range of 1-4 years old. The mean age of the male participants (3.6 ± 0.71 years-old) was similar to the mean age of female participants (3.6 ± 0.58 years-old). There were no significant differences between sex and age. Parents of these children completed the Language survey and the associated factors risk questionnaire. Children with known hypoacusia, deafness, or with intellectual disability were excluded.

Digit length ratio measurement

Diverse techniques of measurement have been used to study the 2D:4D ratio: photocopy, x-ray, direct measurement over the skin and outline drawings have been successfully used [49]. A similar method of outline drawings was chosen because of ease of use, suitability and appropriateness for young children. Four points of the perimeter of the fingers were marked on a sheet of paper and were later measured with a ruler. For this measurement, the child was first asked to abduct the fingers and place the palm flat on a sheet of paper. Marks were placed on the paper at the locations of the web spaces between the second and third and between the third and the fourth fingers.

The child was then asked to adduct the fingers and marks were placed at the locations of the tips of the second and fourth fingers. Lines were drawn from the web space marks to the appropriate finger tip marks and the lengths of the lines were measured.

Table I. Demographic characteristics, language scores and ratios (mean ± SD).

	Boys (*n* = 54)	Girls (*n* = 43)	*p*
Age	3.6 ± 0.71	3.6 ± 0.58	NS
Vocabulary (LDS)	152.4 ± 102.1	160.8 ± 111.2	NS
Socioeconomic status	7.1 ± 4.5	7.4 ± 4.3	NS
Right 2D:4D	0.88 ± 0.26	0.97 ± 0.14	< 0.04
Left 2D:4D	0.96 ± 0.02	0.97 ± 0.04	NS

NS: non significant; LDS: Language Development Survey.

Instruments

Language Development Survey (LDS) is a vocabulary checklist that can be used as a screening tool for the identification of language delay in 2-year-olds and as a measure of language development (vocabulary). The language survey questionnaire has good psychometric properties: reliability (0.97) and high test-retest reliability (0.97-0.99) [50-52]. Correlation of the LDS with other expressive language development measures range from 0.56 to 0.87 [12]. The LDS includes 310 words arranged into 14 semantic categories. Different studies have used a cut-off of fewer than 50 words to assess the prevalence of language delays at 24 months [51-53]. Parents were asked to complete the list of the words that their children use most commonly, a more demanding criterion than the original instruction which requires identifying the words spontaneously expressed by the children. This allows us to use the instrument in children older than 2 years of age. The survey also contains a questionnaire of risk factors for language delays, which examines the pregnancy and the birth, number of ear infections during the year, etc. Applicability among Latino populations has been tested by some studies [50,54]. An item which inquires about the presence of language articulation problem: (Does your child have pronunciation problems with words including the letters r, s, or others?) was added.

Statistical analysis

For group comparisons a Pearson's chi-square was used for categorical data, and *t*-tests for comparing continuous measures such as age, finger ratio and LDS scale scores. To test the finger ratio as predictor of language development we used multiple linear regression analysis.

RESULTS

The means and standard deviations for all the measures are shown in table I. Girls had better scores than boys in the LDS, but this difference was not significant. A cut off score of less than 50 words identified 14.4% of boys and 8.2% of girls with language delays.

Reliability

Intraclass correlation coefficients were performed to assess inter rater agreement showing an ICC 0.85 (95% CI = 0.58-0.98).

Finger-length ratios

Males had a smaller mean 2D:4D than females (0.88 ± 0.26 vs. 0.97 ± 0.14, $p < 0.04$ for right; 0.96 ± 0.02 vs. 0.97 ± 0.04, p = NS for left). Multiple regression analysis was done using the ratios as predictors of language development (vocabulary), language delay (cutoff less than 50 words), and language articulation problems informed by the parent (Table II). There was a weak negative association between the right 2D:4D ratio and language development and language articulation problems in boys aged ≤ 4 years, and a

TablE II. Multiple regression analysis of the relationships between 2D:4D ratios and LDS score, articulation problems and language delays.

Sex	Age	2D:4D ratios	Language	Partial regression coefficient *b*	*t*	*p*
Boys (*n* = 18)	≤ 3 years	Right	LDS score (vocab)	–0.05	–0.26	0.79
			Articulation	–0.50	–2	0.05
			Delay	0.25	0.58	0.60
		Left	LDS score (vocab)	–0.13	0.46	0.69
			Articulation	0.30	1.2	0.22
			Delay	–0.91	–2.1	0.12
Girls (*n* = 15)	≤ 3 years	Right	LDS score (vocab)	0.25	0.87	0.40
			Articulation	–0.73	–3.2	0.007
			Delay	–	–	–
		Left	LDS score (vocab)	–0.23	–0.8	0.43
			Articulation	0.06	0.27	0.78
			Delay	–	–	–
Boys (*n* = 54)	≤ 4 years	Right	LDS score (vocab)	–0.32	–2.5	0.01
			Articulation	–0.33	–2.5	0.01
			Delay	0.23	1	0.29
		Left	LDS score (vocab)	0.15	1.1	0.24
			Articulation	0.18	1.4	0.16
			Delay	–0.61	–2.8	0.06
Girls (*n* = 43)	≤ 4 years	Right	LDS score (vocab)	–0.18	–1.1	0.26
			Articulation	0.01	0.06	0.94
			Delay	0.66	2.3	0.06
		Left	LDS score (vocab)	0.03	0.24	0.81
			Articulation	–0.18	–1.1	0.26
			Delay	–0.63	–2.2	0.07

LDS score (vocab): Language Development Survey (vocabulary). Delay defined by less than 50 words on the LDS. The partial regression coefficient (*b*) is independent of age

strong negative correlation between language articulation problems and right 2D:4D ratio in both sexes aged ≤ 3 years. The low proportion of parents who reported risk factors made it impossible to perform a statistical analysis with these data.

DISCUSSION

In this study, girls had a higher non-significant mean total score in the LDS compared to boys. The prevalence rate for language delays was similar to other reports done with the same instrument [52]. We found sex differences in the 2D:4D ratio finger length significant only for the right hands, consistent with findings from other studies [55]. However the boys' right ratios in this study were lower than reported by Manning et al [47] for boys from the same age obtained by hand photocopies (0.88 ± 0.26 vs. 0.95 ± 0.036). This difference cannot be explained due to the different methods employed in the ratio measurement because Manning et al [56] showed in a study that differences in finger lengths from photocopies tended to be shorter or equal in length to direct measurements. A weak negative correlation between vocabulary and the 2D:4D right ratio was found in children from both sexes aged ≤ 4 years, but reached significance only in boys, suggesting that prenatal testosterone, manifested by a masculine type (low 2D:4D ratio), plays a role in normal language development (vocabulary) in children. A moderate to strong negative correlation was found between language articulation problems and a masculine type (right *lower* 2D:4D) ratio in children from both sexes aged ≤ 3 years. This effect was less prominent in boys aged ≤ 4 years. These results are contradictory because testosterone is implicated in normal language development as well as in language articulation problems. These conflicting results might be explained by a twofold testosterone role in neuronal function. Recent studies have shown that this hormone is essential for normal function of the central nervous system, particularly in neuronal development, differentiation, survival and neuroprotection. These responses are mediated through the intracellular androgen receptor [57-59]. However, higher levels of testosterone induce apoptosis in neuronal cells and have a detrimental effect on cognitive profiles and language.

A recent study explored high and low exposure to sex hormones and early language functions and their organization in the human brain. Friederici et al [61] used a phonological discrimination paradigm evaluated through event-related brain potentials (ERP). The low-T (testosterone) male group showed an automatic auditory discrimination with typical electrophysiological activation patterns (mismatch response, MMR) in the brain wave, in contrast to no activation response in the high-T males. No correlations with estradiol serum levels and brain potentials were found in any group. Results from a recent study [62] done with adults seem to support the idea that androgen exposure measured through finger ratio 2D:4D affects auditory processing functions by diminishing a grapheme to phoneme task. Unfortunately in this study no current or past language articulation problems were inquired so comparisons are difficult to establish. A developmental trend in 2D:4D right ratio and normal language vocabulary score for both sexes was noted. Girls aged ≤ 3 years showed a positive correlation (r = 0.25) and boys and almost neutral correlation (r = –0.05), both of which became negative; for boys (r = –0.32) and for girls (r = –0.18) aged ≤ 4 years. These results appear different from Lutchmaya et al [41] in which fetal testosterone was inversely predictive of vocabulary development. However, children's age in Lutchmaya et al study was 18 and 24 months for both sexes. According to our gradient hypothesis toward an association with testosterone, (higher to lower 2D:4D) children in that study would be at the beginning of the gradient and similar to the girls ≤ 3 years in our study. In our study, the low number of 24 month-old children does not allow us to detect associations.

Along the same lines, adults' digital ratios investigated by Burton et al [48] showed negative correlations between digital right ratios and language fluency scores for both sexes; (–0.32) for men and (–0.24) for women. This result suggests that the gradient of association with testosterone is later fixed in adults, especially if they have higher verbal fluency. Another possible explanation for these results might come from the Geschwind and Galaburda [63] hypothesis, which proposes sex differences in cognitive abilities by relating them to lateralization of cerebral functions. They suggest that differences in maturation rates between the cerebral hemispheres are mediated by circulating testosterone levels (higher in males) which delay the development of certain cortical regions of the left hemisphere; the consequence is a greater development of the right hemisphere. Reduced language ability, with enhanced visuospatial skills is a profile found in males, and is the consequence of this asymmetry. These changes are not present in newborns; Lenneberg [64] and Zangwill [65] proposed a critical period of neurological development between 2 and 12 years of age, which is responsible for the observed differences in language development. It is more probable that this decisive time would be between 2 and 5 years old when language development is prominent. The shift from a positive to a negative correlation might reflect this critical period, which might be due to a small hormone effect between 3 and 4 years old that becomes fixed until adulthood. A recent magnetic resonance study supports the hypothesis that testosterone might be involved in changes of neuroanatomical dimensions by finding associations between hormone levels, 2D:4D ratio and corpus callosum size changes in young healthy women [66]. There was a low (non-significant) correlation between a positive (right higher 2D:4D) ratio feminine type and language delay problems in boys at 3 and 4 years old and in girls at 4 years old, the correlation was higher (0.66) but non-significant. The deleterious estrogen effect on language abilities has been reported by Dorn et al. [38] who studied a group of children with precocious puberty (PA) (8 girls, 1 boy) and compared their cognitive profiles with those of 'typically developing' children. The PA group had higher estrogen levels and significantly lower summary WISC III verbal scale scores, while no differences were noted in verbal fluency compared to the control group.

Results from this study show that testosterone indirectly measured through 2D:4D ratio is associated with early normal language development of Mexican children (significant only in boys aged ≤ 4 years). Larger effects were found for the role of testosterone and expressive language problems reported by parents in children from both sexes aged ≤ 3 years. No effects were found for the 2D:4D ratio and language delay (less than 50 words) in children from the community.

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ÍNDICE DIGITAL D2:D4 Y DESARROLLO DEL LENGUAJE

Resumen. Introducción. *En años recientes, se ha sugerido una posible influencia hormonal en el desarrollo del lenguaje. El índice digital D2:D4 es una medida indirecta de la exposición prenatal a andrógenos. Se relaciona negativamente con la testosterona prenatal y positivamente con el estrógeno prenatal, lo que determina un índice bajo en varones y alto en mujeres. Puede explorarse a partir de los dos años de vida.* Objetivo. *Estudiar si hay una asociación entre el índice digital D2:D4 y el desarrollo de lenguaje (vocabulario) y/o los problemas del lenguaje.* Sujetos y métodos. *Se midieron las longitudes del dedo índice (D2) y el dedo anular (D4) en 97 preescolares y sus padres contestaron el sondeo del desarrollo del lenguaje.* Resultados. *Se encontró una correlación débil negativa entre el desarrollo de lenguaje (vocabulario) y el índice digital derecho D2:D4 en niños de ambos sexos de 4 o menos años de edad, significativa sólo en los varones. Se halló una fuerte correlación negativa entre los problemas de articulación y el índice digital derecho D2:D4 para niños de ambos sexos de 3 o menos años, y una correlación negativa baja entre los problemas de articulación del lenguaje y el índice digital derecho D2:D4 para niños de 4 o menos años.* Conclusión. *Estos resultados sugieren que la testosterona influye en el desarrollo de lenguaje (vocabulario) y en los problemas de articulación, probablemente a través de dosis mayores. [REV NEUROL 2009; 48: 577-81]*

Palabras clave. *Desarrollo del lenguaje. Diferencias sexuales. Índice D2:D4. Problemas de comunicación. Problemas de lenguaje expresivo.*