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A volumetric study of parietal lobe subregions in Turner syndrome

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Abstract

Turner syndrome, a genetic disorder that results from the complete or partial absence of an X chromosome in females, has been associated with specific impairment in visuospatial cognition. Previous studies have demonstrated a relationship between parietal lobe abnormalities and visuospatial deficits in Turner syndrome. We used high-resolution magnetic resonance imaging to measure parietal lobe subdivisions in 14 participants with Turner syndrome (mean age 13 years 5 months, SD 5 years) and 14 age-matched controls (mean age 13 years 5 months, SD 4 years 7 months) to localize neuroanatomical variations more closely. Scans were acquired and analyzed for 14 females with Turner syndrome. Analyses of variance were used to investigate differences in regional parietal lobes. Females with Turner syndrome showed a bilateral parietal lobe reduction, specifically in the superior parietal and postcentral gyri. Full-scale IQ scores were significantly positively correlated with postcentral tissue volume in the Turner syndrome group. Structural differences in the parietal lobe are localized specifically to the anterior and superior parietal lobe and might be related to the visuospatial and visuomotor deficits associated with Turner syndrome.

Turner syndrome is a genetic disorder that arises from the complete or partial absence of an X chromosome in females. This genetic condition has often been associated with specific cognitive deficits in visuospatial skills (McCauley et al. 1987, Murphy et al. 1994). Neuroimaging studies in females with Turner syndrome have consistently pointed to structural and functional abnormalities of the parietal region of the brain. For example, functional imaging studies with positron emission tomography imaging have found abnormal patterns of metabolism in the parietal and occipital regions in participants with Turner syndrome compared with controls (Murphy et al. 1997, Clark et al. 2002). Recent functional magnetic resonance imaging studies have also pointed to activation deficits of the parietal cortex (Haberecht et al. 2001, Kesler et al. 2004). Similarly, structural imaging studies with magnetic resonance imaging have established the presence of decreased tissue volumes in parietal and occipital brain regions (Reiss et al. 1993, 1995; Brown et al. 2002). Thus neuroanatomical variations in the parietal region of the brain in females with Turner syndrome might contribute to their specific deficits in visuospatial processing. The purpose of this study was to investigate further morphological variations in individuals with Turner syndrome by measuring neuroanatomical subdivisions of the parietal lobe, including the postcentral, superior parietal, supramarginal, and angular gyri. On the basis of the cognitive profile of females with Turner syndrome, we expected to find neuroanatomical differences specifically in the superior parietal lobe, a region that has been strongly associated with visuospatial cognition (Harris et al. 2000, Ng et al. 2000).

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Methods

PARTICIPANTS

The study group consisted of 14 females with Turner syndrome (mean age 13 years 5 months, SD 5 years) and 14 agematched typically developing control females (mean age 13 years 5 months, SD 4 years 7 months). Participants with Turner syndrome were recruited through the National Turner Syndrome Foundation, local physicians, and the Stanford University website. Because the presence of a second 46,XX cell line might lessen the effects of the monosomic state of the X chromosome, only participants with monosomic 45,X karyotypes (non-mosaic) were included in this study. Control participants were recruited through newspaper advertisements and parental networks. All control participants were in good health and without evidence of neurological or psychiatric disorder, as determined from standardized screening procedures in our laboratory.

All participants were assessed using the Wechsler Intelligence Scale for Children – Revised (age less than 17 years; Wechsler 1991) or the Wechsler Adult Intelligence Scale Revised (age 17 years or more; Wechsler 1997). Mean Fullscale IQ and Verbal IQ scores for the groups were comparable (Table I). However, as expected, Performance IQ was significantly different between groups (F=17.8, df=1,23, p=0.0003). IQ scores were not available for one participant with Turner syndrome. In addition, two control participants did not have Performance IQ or Verbal IQ scores. After providing a complete description of the study to all participants and their caretakers, written informed consent was obtained under protocols approved by the Institutional Review Board at Stanford University.

NEUROIMAGING

Magnetic resonance data were acquired on 1.5T GE Signa scanners at Stanford University School of Medicine, CA and Johns Hopkins University School of Medicine, MD, USA. Coronal three-dimensional volumetric spoiled gradient echo series were acquired with the following parameters: TR=35–45, TE=6, flip angle=45, number of excitations=1, FOV=20–24, slice thickness=1.5mm, matrix=256×192, for 124 contiguous slices.

IMAGING PROCESSING AND MEASUREMENT

Image data were imported into the BrainImage program (Stanford University) for semiautomated image quantification as previously described and validated (Subramaniam et al. 1997, Reiss et al. 1998). The processing of data included the removal of non-brain tissue, correction of image inhomogeneity, and segmentation into brain tissue and cerebrospinal fluid.

The parietal lobe was manually delineated by two raters in accordance with previously described methods (Duvernoy 1991, Kates et al. 1999). Interrater reliability for the parietal lobe and subdivisions exceeded 0.90 by intraclass correlations. The postcentral gyrus served as the anterior border of the parietal lobe and was demarcated axially by the central sulcus anteriorly by the postcentral sulcus posteriorly, and by the sylvian fissure inferiorly. The posterior border of the parietal lobe was delineated in the sagittal axis by drawing a plane through the parietal–occipital fissure. The cingulate gyrus served as the medial inferior border of the parietal lobe and was delineated separately by tracing the cingulate sulcus in the sagittal axis. The parietal lobe was drawn on coronal slices by using the contours of the postcentral gyrus, cingulate, and occipital lobe as boundaries.

After isolating the parietal lobe, the region was rotated into an axial orientation for subdivision into superior parietal, supramarginal, and angular gyri. The superior parietal gyrus included all brain matter superior to the intraparietal sulcus. The rest of the parietal

lobe was divided into the angular and supramarginal gyri by using iterative renderings of the cortical surface. The sulcus intermedius primus served as the dividing point between the supramarginal and angular gyri. The supramarginal gyrus was bordered by the postcentral sulcus anteriorly, the sulcus intermedius primus posteriorly, the intraparietal sulcus superiorly, and the sylvian fissure lateral-inferiorly. The angular gyrus was limited by the supramarginal gyrus anteriorly, the parietal–occipital sulcus posteriorly, the intraparietal sulcus superiorly, and the sylvian fissure inferiorly.

STATISTICAL ANALYSIS

Between-group differences in whole brain and parietal tissue volumes were examined by using a one-way analysis of variance (ANOVA). To determine whether a specific profile of tissue volume differences exist in the parietal lobes, a multiple MANOVA was used with the following eight dependent variables: right and left postcentral tissue, right and left superior parietal tissue, right and left supramarginal tissue, and right and left angular tissue. Follow-up ANOVAS were then used for subdivision comparisons to quantify group differences more precisely. Exploratory analyses of correlates of IQ with parietal volumes were also conducted. For all statistical tests, an alpha of 0.05 was chosen as the threshold for statistical significance.

Results

There was no statistical difference in whole-brain tissue volumes between participants with Turner syndrome and controls (Table II). We, therefore, did not adjust for whole-brain differences in subsequent analyses. Parietal volumes were decreased in females with Turner syndrome in comparison with controls in both the right (F=7.55, df=1,26, p=0.01) and left (F=5.08, df=1,26, p=0.03) hemispheres. A Wilks Lambda value of 0.01 (F=3.34, df=8,19) indicated the presence of significant group differences in the profile of parietal-lobe subregional volumes. Follow-up ANOVAs indicated that both right superior parietal tissue (F=4.61, df=1,26, p=0.04) and left superior parietal tissue (F=4.96, df=1,26, p=0.04) were reduced in participants with Turner syndrome. Similarly, right (F=13.55, df=1,26, p=0.001) and left (F=21.85, df=1,26, p<0.0001) postcentral tissue volumes were also decreased in participants with Turner syndrome. No statistical difference was found for the supramarginal or angular gyri.

Full-scale IQ was significantly correlated with total postcentral gyrus tissue volume in the Turner syndrome group (r=0.61, p=0.03) but not the control group (r=−0.26, p=0.41). The Fisher r to z transformation indicated that these correlations were significantly different (z=2.11, p=0.02). No other significant correlation between IQ scores and tissue volumes was found.

Discussion

Results of this study support the hypothesis that abnormal parietal morphology in females with Turner syndrome is present bilaterally in the superior parietal gyrus. Functional imaging studies have consistently indicated the importance of the superior parietal lobe in cognitive rotation tasks, suggesting that this region is essential in visuospatial processing (Harris et al. 2000, Ng et al. 2000). Neuroanatomical alteration of the superior parietal gyrus might, therefore, contribute to the visuospatial deficits observed in individuals with Turner syndrome (McCauley et al. 1987, Murphy et al. 1994). Interestingly, we did not find any volume differences in the supramarginal or angular gyri in females with Turner syndrome, two regions that have both been implicated in language-related functions including semantic and syntactic processing (Jessen et al. 1999, Sakai et al. 2001). Relatively intact or preserved

inferior parietal anatomy would be consistent with findings of preserved verbal functioning in females with Turner syndrome (Romans et al. 1998).

The finding of decreased tissue volume in bilateral postcentral gyri was unexpected. To our knowledge, no study has reported abnormalities in somatosensory function in females with Turner syndrome. However, previous studies have suggested that the postcentral gyrus is involved in other capacities, in addition to somatosensory function, including visuomotor learning and spatial working memory (Inoue et al. 1997, Thomas et al. 1999, Frutiger et al. 2000). Furthermore, decreasing tissue volume was significantly correlated with lower IQ scores in the Turner syndrome group, suggesting that tissue loss in this area is associated with deficits in cognitive function. It is possible that brain regions, such as the postcentral gyrus, might serve different cognitive functions in females with Turner syndrome in comparison with typically developing individuals, analogous to the functional plasticity seen after injury to the central nervous system (Weiller and Rijntjes 1999, Chen et al. 2002). Thus atypical brain morphology associated with Turner syndrome might result in unexpected functional correlates. Further investigation is warranted to determine how a reduced volume of the postcentral gyrus might be associated with the neuropsychological profile of females with Turner syndrome.

In summary, this study provides evidence of selective volume differences in the parietal lobe subregions in individuals with Turner syndrome that might be associated with the visuospatial deficits reported in this syndrome. Future studies should investigate possible correlations between parietal subregion volume and cognitive function and examine the association of morphological alterations with brain activation through functional neuroimaging.

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Table I

Mean (SD) IQ scores for females with Turner syndrome and controls

Test	Turner Syndrome	Controls	F	df	df
FSIQ	103.8 (13.4)	111.4 (11.8)	2.45	1, 25	0.13
VIQ	112.7 (15.2)	118.4 (10.2)	1.20	1, 23	0.28
PIQ	92.8 (12.4)	112.4 (10.7)	17.8	1, 23	0.0003

FSIQ, Full-scale IQ; PIQ, Performance IQ; VIQ, Verbal IQ.

Table II

Mean (SD) tissue volumes (millilitres) for females with Turner syndrome and controls

Structure	45,X	Controls	F	p
Total cbrl tissue	749.4 (64.2)	761.4 (57.0)	0.50	0.482
Rt pl lobe	86.7 (12.7)	99.7 (12.5)	7.55	0.011
Rt pl lobe	88.2 (0.6)	98.9 (14.3)	5.08	0.033
Rt postcent gyrus	13.4 (2.0)	16.6 (2.5)	13.55	0.001
Lt postcent gyrus	13.5 (2.2)	17.4 (2.2)	21.85	<0.0001
Rt sup pl gyrus	31.4 (5.9)	36.0 (5.5)	4.61	0.041
Lt sup pl gyrus	31.8 (5.1)	36.2 (5.4)	4.96	0.035
Rt supra gyrus	23.4 (6.3)	26.5 (5.7)	1.79	0.192
Lt supra gyrus	26.0 (6.3)	27.0 (5.8)	0.17	0.684
Rt angular gyrus	18.4 (5.3)	20.6 (6.8)	0.93	0.345
Lt angular gyrus	16.8 (4.6)	18.3 (6.2	0.50	0.484

cbrl, cerebral; Rt, right; pl, parietal; Lt, left; postcent, postcentral; sup, superior; supra, supramarginal.