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Amygdala and hippocampal volumes in Turner syndrome: a high-resolution MRI study of X-monosomy

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Abstract

Turner syndrome (TS) results from partial or complete X-monosomy and is characterized by deficits in visuospatial functioning as well as social cognition and memory. Neuroimaging studies have demonstrated volumetric differences in the parietal region of females with TS compared to controls. The present study examined amygdala and hippocampus morphology in an attempt to further understand the neural correlates of psychosocial and memory functioning in TS. Thirty females with TS age 7.6–33.3 years (mean = 14.7 ± 6.4) and 29 age-matched controls (mean age = 14.8 ± 5.9; range = 6.4–32.7) were scanned using high resolution MRI. Volumetric analyses of the MRI scans included whole brain segmentation and manual delineation of the amygdala and hippocampus. Compared to controls, participants with TS demonstrated significantly larger left amygdala gray matter volumes, irrespective of total cerebral tissue and age. Participants with TS also showed disproportionately reduced right hippocampal volumes, involving both gray and white matter. Amygdala and hippocampal volumes appear to be impacted by X-monosomy. Aberrant morphology in these regions may be related to the social cognition and memory deficits often experienced by individuals with TS. Further investigations of changes in medial temporal morphology associated with TS are warranted.

Keywords

Turner syndrome; Amygdala; Hippocampus; X-monosomy; MRI

1. Introduction

Turner syndrome (TS) results from complete or partial X-monosomy in a phenotypic female (45, X) and is one of the most common sex chromosome abnormalities (Jacobs, 1992; Jones, 1997). TS is typically characterized by an uneven cognitive profile with strengths in verbal skills and deficits in visuospatial abilities (Ross et al., 2002; Zinn et al., 1998). Research has

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only recently begun to investigate the neural correlates of the TS cognitive profile. Neuroimaging studies indicate parietal lobe abnormalities as the most consistent finding in participants with TS. Decreased volume in this area is often related to visuospatial deficits (Murphy et al., 1993; Reiss et al., 1993; Reiss, Mazzocco, Greenlaw, Freund, & Ross, 1995).

However, abnormalities associated with TS also have been reported in other brain regions. Previous studies by our laboratory have shown functional activation deficits in the prefrontal cortex and caudate (Haberecht et al., 2001; Tamm, Menon, & Reiss, 2003). Volumetric studies of TS by our laboratory also have revealed aberrant morphology in the cerebellum, pons and medulla (Brown et al., 2002; Reiss et al., 1995). Murphy et al. (1993) indicated decreased caudate, thalamus and lenticular volumes in TS participants compared to controls.

In addition to the brain abnormalities described above, there appears to be converging evidence of temporal lobe differences in participants with TS. In a previous study of 30 females with TS and 30 age-matched controls, we demonstrated disproportionately increased right superior temporal gyrus (STG) volumes, involving both gray and white matter. Additionally, left STG white matter was increased in the TS group. Increased STG volume was associated with decreased cognitive function (Kesler et al., 2003). Medial temporal lobe alterations have been evidenced as reduced hippocampal volumes in females with TS. Furthermore, these participants scored significantly lower than controls on tests of memory functioning that are often associated with the hippocampus and other medial temporal areas (Murphy et al., 1993).

Other investigators have demonstrated memory deficits in TS that may be related to hippocampal dysfunction. A study of 10 participants with TS reported significant long-term memory impairment (Pennington et al., 1985) and another identified short-term memory deficits in a sample of 13 children with TS (Williams, Richman, & Yarbrough, 1991). In a large group of adults with TS ($N = 71$), Ross et al. (2002) also found impaired visual memory. The authors indicate that, while some memory dysfunctions in TS may improve with age, likely due to estrogen replacement, visual memory deficits tend to persist. A study conducted by Bishop et al. (2000) showed that individuals with TS actually performed better than controls on measures of immediate story recall. However, the TS group demonstrated deficits in both verbal and visual delayed recall and also showed more rapid forgetting of visual and verbal information. Given the involvement of the hippocampus in memory functioning (Squire & Zola, 1996), it seems likely that X-monosomy negatively impacts hippocampal development.

The amygdala, located adjacent to the hippocampus in the medial temporal lobe, enhances memory for stimuli that are emotionally meaningful (McGaugh, 2002; Poldrack & Packard, 2003). Additionally, the amygdala has a role in recognition of facial emotion and in social judgment (Adolphs, 2003; Adolphs, Baron-Cohen, & Tranel, 2002; Grady & Keightley, 2002). Impairments in social functioning are common among individuals with TS (Ross et al., 2002; Skuse et al., 1997). Adolescent girls with TS are at greater risk for having problems related to lower social activity, poor social coping skills and increased immaturity, hyperactivity and impulsivity compared to their peers (McCauley, Feuillan, Kushner, & Ross, 2001). Girls with TS tend to have more difficulties maintaining relationships, relating to others, have fewer friends and tend to be more socially isolated than controls (Siegel, Clopper, & Stabler, 1998). Results from several investigations indicate significant impairments in face and emotion processing as well as interpreting gaze in individuals with TS (Lawrence et al., 2003a; Lawrence, Kuntsi, Coleman, Campbell, & Skuse, 2003b; Reiss et al., 1993; Ross, Feuillan, Kushner, Roeltgen, & Cutler, 1997; Ross, Stefanatos, Roeltgen, Kushner, & Cutler, 1995).

A recent neuroimaging study (Good et al., 2003) showed that females with Turner's syndrome have significantly enlarged amygdalae and orbital frontal cortex volumes compared to female and male control participants, and suggested that increases may be related to impaired social cognition. The Good et al. (2002) study used a voxel-based method as opposed to a manual, region of interest (ROI) measurement. Recent studies comparing VBM analysis and manual ROI delineation of amygdala and hippocampus volumes (Good et al., 2002; Testa et al., 2004) indicate that each of these methods has differential sensitivities to volume changes in these regions. Therefore, both neuroimaging techniques are important for investigating amygdalar and hippocampal morphology.

The study by Murphy et al. (1993) utilized ROI analyses and reported reduced hippocampal volumes in TS, but did not find any amygdala differences. However, half of their participants had a mosaic karyotype, which may have obscured group differences (Jones, 1997; Zinn et al., 1998). More importantly, the Murphy et al. study used a relatively large slice thickness (5 mm) to acquire images, which tends to decrease image resolution, particularly with respect to small structures such as the amygdala. The present study utilized high resolution MRI to conduct ROI analysis and further delineate hippocampal morphology in TS by including tissue specific (i.e. white and gray matter) measurements. Amygdalar volumes were delineated, also using ROI analysis, with the expectation that these would be aberrant in the TS group compared to controls.

The present study also includes an investigation of X-linked imprinting effects on amygdala and hippocampus in TS. Imprinting is a mechanism associated with differential gene expression based on parental origin (Constancia, Pickard, Kelsey, & Reik, 1998; Nicholls, 2000). Imprinted genes can have specific effects on brain development, particularly in terms of regional tissue growth and pruning (Keverne, 1997, 2001; Keverne, Fundele, Narasimha, Barton, & Surani, 1996). Some studies of TS suggest a possible association of imprinting with certain cognitive–behavioral deficits, particularly memory and social cognition. Individuals with Turner syndrome having a maternally derived X chromosome (45 X^m) showed greater deficits in these areas of function (Bishop et al., 2000; Donnelly et al., 2000; Skuse et al., 1997). Additionally, we previously demonstrated possible imprinting effects on STG volumes (Kesler et al., 2003) as well as on occipital white matter and cerebellar gray matter in participants with TS (Brown et al., 2002). Consistent with the cognitive–behavioral study of imprinting in Turner participants, these imaging studies suggested that females with the 45 X^m genotype showed the greatest brain abnormalities. The study conducted by Good et al. (2003) did not demonstrate any differences in amygdalar or orbitofrontal morphology based on parental origin. However, their sample of individuals with TS was much smaller than ours. Therefore, we hypothesized that individuals with TS who have a maternally derived X chromosome would demonstrate greater abnormalities in amygdalar and hippocampal volumes compared to those with a paternally derived X chromosome (45X^p) and to controls.

2. Methods

2.1. Participants

Participants included 30 individuals with Turner syndrome (mean age = 14.7 ± 6.4; range = 7.6–33.3) and 29 age-matched typically developing females (mean age = 14.8 ± 5.9; range = 6.4–32.7). Among the females with TS, 20 had a maternally derived X chromosome (mean age = 15.3 ± 6.9; range = 7.6–33.3) and 10 had a paternally derived X chromosome (mean age = 13.6 ± 5.5; range = 7.6–24.4). This 2:1 ratio of participants with 45 X^m to 45X^p was expected (Jacobs et al., 1990, 1997). Age was not significantly different between the parental origin groups ($P = 0.49$). Only participants with a non-mosaic karyotype were included in this study. Individuals with TS were recruited through the National Turner

Syndrome Foundation, the Denver Sex Chromosome Aneuploidy Study, the Human Growth Foundation, local physicians and the Stanford Psychiatry Neuroimaging Laboratory website.

Control participants were recruited through local newspapers and parent group newsletters. Controls were excluded for having any history of neurological, psychiatric or substance use disorders and also for current illicit substance and/or psychotropic medication use. This study was approved by the Institutional Review Board of Stanford University. The two groups were matched for handedness (Chi squared $P = 0.67$) which was determined using the Edinburgh Handedness Inventory (Oldfield, 1970). The TS group had 28 right handed and two left handed participants while the control group had 26 right handed and three left handed participants.

2.2. Genetic analysis

To determine parental origin of the X-monosomic, participants with TS, their parents and, when available, their siblings had testing of the androgen receptor (Xq11.2–Xq12), HPRT (Xq26.1–Xq26.1), DXS6809 (pter–Xqter) and DXS9895 (X chromosome). In cases where both parents were available, the parental origin of the patient's X was shown by clear differences in alleles. When only one parent was available, parental origin was determined by presence of an allele in the subject that was not present in the parent at one or more loci. When only one parent was available and parental origin was not clear, the following additional markers were used to determine parental origin: DXS6799 (Xpter–Xqter), DXS8378 (Xpter–Xqter), DXS9898 (X chromosome), DXS101 (Xq22–Xq22), DXS733 (Xq24–Xq26), DXS1120 (Xq22.2–Xq22.3), DXS731 (Xq27–Xq28), DXS1125 (Xq11.2–Xq13), DXS1190 (Xpter–Xqter) and DXS1123 (Xq27–Xq27/Xq28–Xq28).

2.3. Image acquisition

Given the increased incidence of anxiety and hyperactivity among individuals with TS, most participants were prepared for the scanning session using a mock scanner behavioral training program that desensitized scanner related fears and shaped compliant behavior. Magnetic resonance brain images were then obtained with whole body GE Signa Horizon scanners (GE medical systems, Milwaukee) at Stanford University School of Medicine (16 TS, 15 controls), Johns Hopkins University School of Medicine (11 TS, 11 controls), and the National Jewish Medical and Research Center in Denver (three TS, three controls). A coronal 3D volumetric spoiled gradient echo (SPGR) pulse sequence was acquired using the following parameters: TR = 35 or 45, TE = 6, flip angle = 45, number of excitations = 1, field of view = 20 or 24 cm and matrix size = 256 × 256 for 124 contiguous slices of 1.5 mm width. A study conducted by our laboratory confirmed the compatibility of MRI data collected from multiple sites using this protocol and included data from the sites used in the present study (Patwardhan et al., 2001).

2.4. Image analysis

All image processing was completed at Stanford University. Scans from other sites were delivered digitally via secure FTP transfer. MRI scans were imported into *BrainImage* (Stanford University, Stanford, CA) for semi-automated whole brain segmentation and quantification in the coronal plane using previously described and validated methods (Kates et al., 1999; Reiss et al., 1998). Interrater reliability obtained by interclass correlation exceeded 0.90.

The amygdala and hippocampus were manually delineated for each participant in the coronal plane according to previously described methods (Kates, Abrams, Kaufmann, Breiter, & Reiss, 1997), using gray-scale volume stacks derived from the whole brain analysis. These datasets were standardized in their orientation parallel to the axial plane

passed through the anterior and posterior commissures. The resolution of the standardized coronal datasets was then increased from 256 × 256 to 512 × 512 using a bicubic interpolation algorithm to increase visualization accuracy. The resultant amygdala and hippocampus ROIs were then measured on the participant's segmented gray and white matter fraction stacks.

The anterior border of the amygdala was defined as the coronal plane where the anterior commissure first crosses the midline of the brain and the amygdala is clearly present. The entorhinal sulcus and a white matter tract comprised the superior and inferior borders, respectively. Medial and lateral borders were defined by CSF in the medial margin of the temporal lobe and a white matter tract laterally. The posterior border of the amygdala was defined by the appearance of the hippocampus.

The anterior border of the hippocampus was defined by the alveus or the hippocampal sulcus. The alveus marked the superior border and white matter defined the inferior border. The temporal horn demarcated the lateral border and the ambient cistern the medial border. Measurement of the hippocampus proceeded posteriorly until the corpus collosum first fused with the fornix.

2.5. Cognitive testing

The intellectual functioning of TS and normal control participants was assessed using the Wechsler adult intellectual scale, third edition (WAIS-III) for participants 17 years of age and older and the Wechsler intellectual scale for children, third edition (WISC-III) for participants under the age of 17 (Wechsler, 1991, 1997). IQ information was not available for 1 TS subject. Additionally, because some of the cognitive data were archival, only full scale IQ (FSIQ) scores were recorded for four participants with TS and six controls. The social problems and anxiety/depression subtests of the child behavior checklist (CBCL) (Achenbach & Edelbrock, 1981; Hudziak et al., 2003) were used to assess social–emotional functioning in participants age 18 and younger. Measures of social–emotional functioning were not available for older participants.

2.6. Statistical analyses

For all statistical tests, an alpha of 0.05 was chosen as the threshold for statistical significance. Univariate analysis of covariance (ANCOVA) was used to examine group differences in total cerebral tissue with age as a covariate. A multivariate analysis of covariance (MANCOVA) was used to determine group differences in amygdalar and hippocampal total tissue volumes. The four dependent variables in this model included right and left hippocampal tissue and right and left amygdalar tissue. Age and total cerebral tissue were included as covariates. Group differences in amygdalar and hippocampal volumes between 45 X^m and 45X^p and control groups also were examined using MANCOVA with Bonferroni post hoc analyses. Non-parametric statistics were utilized when results indicated non-normal distribution for particular variables or when variance was unequal between groups.

3. Results

3.1. Demographics

Descriptive statistics for age and IQ appear in Table 1. Visual inspection of the IQ data indicated that they were not normally distributed. Therefore, Mann–Whitney tests were used and indicated significantly lower full scale (FSIQ; $U = 177.5$, $P = 0.000$), verbal (VIQ; $U = 192.5$, $P = 0.033$) and performance (PIQ; $U = 70.5$, $P = 0.000$) IQ scores in the TS group. Compared to controls, the TS group demonstrated significantly increased social problems

[$F(1,31) = 12.3$, $P = 0.001$] and anxiety/depression [$F(1,31) = 6.8$, $P = 0.01$]. There were no significant differences in IQ or CBCL scores between TS participants with X^m or X^p.

3.2. Amygdala and hippocampus volumes in TS and controls

As shown in Table 2, there was no significant difference in total cerebral tissue volumes between the two groups. Because of unequal variance between the groups, a Mann–Whitney *U*-test was used for this analysis rather than an ANCOVA ($U = 347$, $P = 0.18$). The MANCOVA for right and left amygdalar and hippocampal tissue volumes indicated a significant profile of differences between the TS and control groups [Wilks lambda = 0.646; $F(4,52) = 7.13$; $P = 0.000$]. Neither age nor total cerebral tissue was a significant covariate. Follow-up ANCOVAs revealed significantly increased left amygdalar [$F(1,55) = 13.2$, $P = 0.001$] and decreased right hippocampal [$F(1,55) = 7.7$, $P = 0.008$] volumes in the TS group compared to controls.

Visual inspection of the amygdalar and hippocampal total tissue data revealed that the right amygdalar volumes were not normally distributed. However, re-calculating the MANCOVA without the right amygdala and using a Mann–Whitney non-parametric test to examine right amygdalar differences between groups produced the same results (data not shown).

Post hoc analysis to determine which tissue substrates were driving the observed between group differences in left amygdalar and right hippocampal volumes were conducted with ANCOVA as described above. These analyses indicated that left amygdalar gray was significantly increased [$F(1,55) = 13.7$, $P = 0.000$], while both right hippocampal gray [$F(1,55) = 6.5$, $P = 0.01$] and white [$F(1,55) = 5.5$, $P = 0.02$] were significantly decreased in the TS group.

3.3. Amygdala and hippocampus volumes in parental origin groups

Bonferonni post hoc pairwise comparisons indicated no significant differences between the $45X^p$ and $45\ X^m$ groups in amygdalar or hippocampal volumes.

3.4. Relationship between psychosocial function and morphology

Controlling for total cerebral tissue volume, exploratory analysis of the associations between CBCL social problems and anxiety/depression, left amygdalar and right hippocampal volumes was conducted using bivariate correlations. However, no significant correlations were noted.

4. Discussion

Consistent with our hypotheses, this study demonstrated aberrant amygdalar and hippocampal volumes in participants with TS compared to age-matched, healthy controls. The TS group demonstrated disproportionately enlarged left amygdalar volume, specifically involving gray matter. This group effect was irrespective of total cerebral tissue volume and age. Lesion, animal and human neuroimaging studies have consistently implicated the amygdala in a host of highly interrelated, socially relevant functions including processing emotional stimuli, interpreting eye gaze, recognizing facial expressions and making attributions about others, or “theory of mind” abilities (Adolphs, 2003; Emery, 2000; Zald, 2003). The amygdala lends affective significance to perceived stimuli, including facial and non-facial stimuli (Hariri, Tessitore, Mattay, Fera, & Weinberger, 2002; Yang et al., 2002), and may be especially sensitive to novelty (Schwartz et al., 2003) and fear (Morris, deBonis, & Dolan, 2002; Thomas et al., 2001). The amygdala also may function to warn of possible dangers. Bilateral amygdala lesions in monkeys result in a lack of fear responses to

previously feared stimuli (Amaral, 2002). Therefore, it has been suggested that social anxiety may arise from a hyperactive amygdala.

As indicated previously, individuals with TS tend to display deficits in a variety of amygdala regulated social abilities including emotion recognition and face processing, especially the perception of fearful facial expressions (Lawrence et al., 2003a; Lawrence et al., 2003b). Individuals with TS also are at risk for increased social anxiety compared to their typically developing peers (Lesniak-Karpiak, Mazzocco, & Ross, 2003). Participants with TS in the present study demonstrated significantly lower social functioning as well as increased emotional disturbance compared to controls. However, no relationship was found between amygdalar volume and social functioning. Additionally, no measure of social functioning was available for older participants.

Our finding of enlarged amygdalae in TS is consistent with results reported by another research group (Good et al., 2003), despite several methodological differences between their study and ours. For example, Good and colleagues used a fully automated whole brain analysis, each brain image was manipulated to fit a standard space, and amygdala volumes were computed based on an averaged template. On the other hand, our study assesses volumes drawn on each brain while in native space. Our method preserves individual anatomical boundaries and allows for the possibility of aberrant brain structure in this clinical population. Interrater reliability is critical to our method, and has been measured to be significantly reliable (intraclass correlation >0.90). Interestingly, our study included a younger sample (ages 7–33) than Good et al. (ages 15–44), suggesting that increased amygdala volumes in TS is not age dependent. Additionally, our findings of enlarged left amygdalar volumes in TS was irrespective of age.

The present study showed significantly reduced right hippocampal volumes in participants with TS, affecting both gray and white matter. The hippocampus is vitally important for consolidation of memory for specific events and facts as well as spatial information (Burgess, Maguire, & O'Keefe, 2002). Damage to the hippocampus can result in anterograde and/or retrograde amnesia (Squire & Zola, 1996). As indicated above, individuals with TS have impairments in visuospatial memory (Bishop et al., 2000; Ross et al., 2002). The study by Good and colleagues did not find volumetric differences in the hippocampus, but again, this may be due to their smaller sample size. Because this study was archival, no specific test of memory function was available to explore possible correlations with decreased hippocampal tissue. Further investigation of hippocampal morphology in TS using larger and, ideally, VIQ matched samples as well as visual and verbal memory assessment is necessary.

Individuals with TS show significantly low levels of estrogen compared to typically developing controls (Hojbjerg Gravholt, Svenstrup, Bennett, & Sandahl Christiansen, 1999). Sex steroid insufficiency may impact amygdalar development in individuals with TS. Estrogen has been shown to regulate several neuronal mechanisms including synaptogenesis, synaptic plasticity, neuronal density (Goldstein et al., 2001; Naftolin, Leranth, Horvath, & Garcia-Segura, 1996), long-term potentiation and excitatory postsynaptic potential amplitudes (Foy et al., 1999). The amygdala is replete with estrogen receptors (Cooke, Tabibnia, & Breedlove, 1999; Donahue et al., 2000; Goldstein et al., 2001).

Estrogen also has been shown to be vital for hippocampal development and growth (Gould, Woolley, Frankfurt, & McEwen, 1990; Gould, Woolley, & McEwen, 1991) as well as synaptic turnover (McEwen, 2002). Estrogen and growth hormone information was not available for all participants in the current study and therefore the possible effects of

hormone treatments on amydalar and hippocampal morphology could not be directly addressed in the current study. However, because estrogen treatment would likely affect only the older TS participants, an age effect would have been expected and none was found. Further investigation of the effects of age, estrogen replacement, amgydalar and hippocampal volume in TS is required.

The present study did not demonstrate X-linked imprinting effects on amygdalar or hippocampal morphology. The 45 X^m and $45X^p$ groups did not differ significantly from each other in terms of amygdalar and hippocampal volumes. They also were not significantly different in terms of cognitive–behavioral functioning. These findings may reflect low statistical power given the small number of participants with $45X^p$ and therefore further investigation with larger sample sizes is necessary.

The interpretation of disproportionately increased or decreased regional tissue volumes is difficult. It is unclear why amygdalar volumes of the TS group were enlarged while the hippocampus tended to be diminished. These findings may involve disruptions in synaptic/dendritic pruning, cell migration and/or neuroplasticity (Chechik, Meilijson, & Ruppin, 1999; Huttenlocher, 1984; Huttenlocher, & Dabholkar, 1997; Wolff, Laskawi, Spatz, & Missler, 1995). Disruption of these processes would likely lead to abnormal organization and distribution of tissue resulting in disproportionate increases and decreases of cell density in certain regions. Estrogen insufficiency also may play a role in abnormal synaptic organization (Olmos, Naftolin, Perez, Tranque, & Garcia-Segura, 1989).

Given the structural and functional connections between these two structures, it is possible that X-monosomy impacts directly upon only one, and the disproportionate volume in the other occurs on a secondary basis. From an anatomical perspective, direct projections travel from the primate amygdala to the ipsilateral hippocampus (Amaral, 1986). Therefore, we would predict that the left amygdala would influence the left hippocampus to a greater extent than the multisynaptic route to the contralateral hippocampus. In addition, the projections from the amygdala to the hippocampus are far more extensive than the reciprocal connections from the hippocampus back to the amygdala (Amaral, Price, Pitkanen, & Carmichael, 1992; Irwin et al., 2004), thus we would predict that the amygdala would have a greater influence on the hippocampus than the reverse. Based on this anatomy, we could interpret our findings as suggesting, for example, that an enlarged left amygdala is protective over decreases in left hippocampal volume. Whether X-monosomy affects the amygdala, the hippocampus or both, the precise mechanism is currently unknown and requires further investigation.

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Table 1

Age and IQ descriptive statistics

	TS	*N*	CON	*N*
Age	14.7 (6.4)	30	14.8 (5.9)	29
Age range	7.6–33.3	30	6.4–32.7	29
FSIQ*	97 (16)	29	113 (5.6)	29
VIQ**	103 (20)	26	114 (14.4)	23
PIQ*	89 (13)	26	111 (15.3)	23
Soc prob***	66 (15)	19	51 (1.9)	13
Anx/dep*	57 (8)	19	51 (1)	13

Table values refer to mean (standard deviation). TS: Turner syndrome; CON: control; FSIQ: full scale IQ score; VIQ: verbal IQ score; PIQ: performance IQ score; soc prob: social problems; anx/dep: anxiety/depression.

* Significant at $P \leq 0.01$ for TS <CON.

** Significant at $P < 0.05$ for TS <CON.

*** Significant at $P < 0.01$ for TS >CON.

Table 2

Amygdala and hippocampal volumes in participants with TS and controls

	TS	CON	Wilks' lambda	Omnibus *P*-value	ANOVA *P*-value
Total cerebral tissue	1036 (96)	1077 (83)			(U = 347) P = 0.18
Total amygdala & hippocampal tissue			0.65	0.000	
Amygdala & hippocampal tissue specific (gray/white)			0.74	0.003	
Left AMYG	2.4 (0.48)	2.1 (0.34)			0.001
Gray	2.2 (0.44)	1.9 (0.32)			0.000
White	0.23 (0.09)	0.20 (0.08)			0.24
Right AMYG	2.3 (0.70)	2.1 (0.51)			0.17
Gray	2.1 (0.63)	1.8 (0.47)			0.15
White	0.24 (0.14)	0.23 (0.09)			0.71
Left HIP	2.7 (0.52)	2.9 (0.56)			0.22
Gray	2.4 (0.46)	2.6 (0.47)			0.27
White	0.29 (0.13)	0.32 (0.11)			0.26
Right HIP	2.7 (0.50)	3.1 (0.54)			0.008
Gray	2.5 (0.46)	2.8 (0.45)			0.01
White	0.28 (0.11)	0.36 (0.13)			0.02

Table values refer to mean (standard deviation). TS: Turner syndrome; CON: controls; AMYG: amygdala; HIP: hippocampus.