Enlarged Temporal Lobes in Turner Syndrome: An X-chromosome Effect?

Gender differences in brain morphology have previously been reported in the temporal lobe and an ‘X-chromosome dosage effect’ has been described in Turner syndrome (45,X). To examine this further, we investigated temporal lobe morphology, metabolism and function in nine children with non-mosaic Turner syndrome using magnetic resonance imaging, 1H magnetic resonance spectroscopy and neuropsychological testing and compared outcomes with results from nine age-matched control girls (46,XX). Turner subjects were found to have significantly larger superior temporal lobes (P = 0.004) and middle temporal lobes (P = 0.047) than controls. The size of the temporal lobe was found to correlate negatively with temporal lobe choline-containing compounds suggesting that increased temporal lobe size is associated with larger cells and/or decreased dendrites. This suggests a developmental failure to prune neurons. The degree of enlargement correlates negatively with functional performance on temporal-lobe associated tasks, suggesting that the enlargement may be a compensatory mechanism, or possibly causative in the case of semantic fluency performance. These temporal lobe abnormalities are discussed with reference to genes which are absent in Turner syndrome subjects and 46,XX controls.

Keywords: magnetic resonance spectroscopy, non-lexical reading, temporal lobe, Turner syndrome, X-chromosome

Introduction

The X-chromosome comprises some 5% of the human genome. In female humans of standard karyotype (46,XX) one of the pair of X-chromosomes is inactivated to allow dosage compensation with males (46,XY), although this inactivation is not complete for all regions of the X-chromosome (Carrel et al., 1999) and is variable between females (Brown and Robinson, 2000). The most common of the X-anomalies, 45,X, by contrast, results in the development of a syndrome named for the clinician who first described it in 1938, Turner syndrome (Turner, 1938).

Turner syndrome is relatively common, with an incidence of 1 in 3000–5000 live female births (Hook and Warburton, 1983). Chromosomal aberrations associated with the phenotype include complete absence of the X-chromosome, isochromosomes, rings and deletions with mosaicism for a second X-chromosome in 28–67% of subjects (Held et al., 1992). These aberrations are associated with short stature, gonadal dysgenesis and infertility, with the variable expression of other physical signs including webbed neck, coarctation of the aorta, renal malformations, cubitus valgus, lymphoedema, high arched palate and shield chest.

The combination of absence, or partial absence, of one X-chromosome with the lack of oestrogen is associated with a neuropsychological and behavioural profile. The most prominent findings suggest a specific visuo-spatial deficit characterized by a lowering of performance IQ (Alexander et al., 1966; Rovet, 1990; Downey et al., 1991), impaired spatial processing (Silbert et al., 1977; Nielsen and Wohltet, 1990; Rovet, 1990; Money, 1993) and dyscalculia (Bender et al., 1993; Rovet et al., 1994). Although verbal intellectual abilities are usually unaffected, specific linguistic impairments in naming (Waber, 1979) and oral fluency (Temple et al., 1996; Romans et al., 1997; Temple, 2002) have been reported. Recently, it has been suggested that there may be an ‘X-chromosome dosage effect’ on the Turner syndrome cognitive profile (Murphy et al., 1997) which manifests by decreased verbal scores and decreased verbal-spatial test score asymmetry as mosaicism decreases. These authors have also found that visuospatial ability in Turner syndrome correlates significantly with the degree of mosaicism, as measured by the percentage of lymphocytes with the 45,X karyotype (Murphy et al., 1995).

The primarily spatial nature of the cognitive deficits has been assumed to reflect a right hemisphere deficiency and reported brain deficits in Turner syndrome to date have also mostly been focused in the parietal and parietal/occipital regions (Clark et al., 1990; Murphy et al., 1993; Reiss et al., 1995; Elliott et al., 1996; Haberecht et al., 2001). Reported volumetric and metabolic deficits in these areas have been associated with altered function (Haberecht et al., 2001).

Morphological differences between male and female brains are documented, particularly in the planum temporale.
(Geschwind and Galaburda, 1985; Giedd et al., 1996; Harasty et al., 1997) although the differences are mostly confined to shape rather than size (longer, thinner left planum temporale and shorter, thicker right planum temporale). Females have also been reported to have proportionally more grey matter than males (Gur et al., 1999). Turner syndrome subjects differ genetically from the 46,XX population in that Turner subjects are lacking transcription from the section of the second X-chromosome which is not normally inactivated (Carrel et al., 1999) and differ from the 46,XY population in lacking transcription from the genes on the Y chromosome. These include pseudo-autosomal genes which are shared with the X-chromosome and which are not subject to inactivation in 46,XX females. Turner syndrome subjects therefore have less genetic material than either 46,XX or 46,XY subjects. Given the documented gender differences in the size of the planum temporale, it is pertinent to consider the effect of the Turner syndrome deletion on temporal lobe volumes.

A positron emission tomography study in Turner syndrome (Murphy et al., 1997) showed significant positive correlations between right–left cerebral metabolic asymmetries and performance–verbal asymmetries in Turner syndrome. X-chromosome dosage effects were reported between left mid-temporal florodeoxyglucose uptake and language ability. A study of men with non-mosaic Klinefelter syndrome (47,XXY; Patwardhan et al., 2000) reported decreased superior temporal gyrus grey matter on the left and right, although the difference was more marked on the left. There was also a trend for the decreased volume to be associated with reduced verbal fluency, measured using the controlled oral word association test. Taken together, these findings suggest a role for the X-chromosome in temporal lobe development and function.

In this study we investigated the effect of absence of the second X-chromosome and sex hormones on the morphology, function and metabolism of the temporal lobe, by the study of girls with non-mosaic Turner syndrome. These girls were compared with an age-matched group of control (46,XX) girls. All girls in the study were <12 years of age in order to minimize the possible effects of pubertal hormones. Cognitive test, magnetic resonance spectroscopy (MRS) and imaging (MRI) data were obtained on all subjects.

Materials and Methods

This work was conducted within the guidelines for human research as specified by the Australian National Health and Medical Research Council and approved by the appropriate human ethics committees. Informed consent was obtained from all participants and their parents or guardians.

Subjects

Nine non-mosaic subjects with Turner syndrome (45,X) were recruited through clinics. Subjects were aged between 7 and 12 years [mean age 119 (18), range 96–151 months]. None of the Turner syndrome subjects were oestrogen supplemented. Nine age-matched female controls [mean age 119 (15), range 95–141 months] were recruited through local schools.

Cognitive Testing

Tests were selected to measure a range of linguistic and visuospatial functions and to allow for possible dissociations in cognitive skills. Table 1 lists the tests used and abilities measured. Linguistic tasks included measures of naming, word knowledge, non-lexical and lexical reading, phonemic analysis, auditory and written rhyme judgements, category and letter fluency. Visuospatial tasks included measures of face processing, constructional, mental rotational ability and visual memory span.

Magnetic Resonance

All images and spectra were acquired with a Philips 1.5 T ACS-NT Gyroscan spectrometer and a quadrature head coil. Following acquisition of scout images, image planes were aligned perpendicular to the anterior-posterior commissure line and 3-D TR weighted (contrast prepared gradient echo) images were acquired in the coronal plane (TR = 4 ms, TE = 17 ms, flip angle = 20°, FOV = 250 × 166 mm (pixel size = 0.98 × 0.98 mm), matrix = 256 × 256, number of slices = 125, slice thickness = 1.5 mm, total acquisition time = 7 min). Images were reconstructed to 2 mm contiguous slices for volume analysis.

All 1H magnetic resonance spectra were acquired using the PRESS pulse sequence (τR = 2 s, TR = 136 ms), representing the sum of 64 transients from a 2 × 2 × 2 cm volume of interest. Full shim adjustments were carried out on each voxel placement. In addition, a single scan spectrum was acquired without water suppression for use as an internal standard. Spectra were acquired bilaterally from the superior temporal, and angular gyri (Fig. 1).

All images and spectra were stored by patient code and de-identified. They were all processed by an operator unaware of the patient’s karyotype.

Spectra were processed using jMRUI version 1.0 (Naressi et al., 2001). Quantification of the reconstructed signals was performed in the time-domain. AMARES (Vanhamme et al., 1997) was used to fit the resonances of NA (N-acetylaspargate, a marker of neuronal integrity), Cho (a composite peak arising from glycerophosphocholine, phosphocholine with a small contribution from free choline) and Cre (a composite peak arising from the N-methyl resonances of creatine and phosphocreatine) following removal of the residual water signal with HLSVD (Pijnappel et al., 1996; Harasty et al., 1999). A Lorentzian lineshape was fitted to the resonance arising from water in the spectrum acquired without water suppression. Results are expressed as peak ratios and also as concentrations relative to the water resonance (in arbitrary units, without correction for relaxation or number of scans).

Images were reconstructed with one degree of zero filling. Quantitative volumetric analysis was obtained on the left and right superior, middle and inferior temporal gyri and from Broca’s area using coronal slices. Superior temporal gyrus included the temporal pole, anterior superior temporal gyrus, planum temporale. Heschl’s gyrus and the
remaining posterior temporal gyrus. Broca’s area included all three Brodmann regions, area 44, 45 and 47 after Mohr’s definitive work in the area (Mohr, 1976). Middle and inferior temporal regions did not include any medial temporal gyri such as the parahippocampal gyrus. Regions were delineated by one operator using previously published highly reliable and consistent methodology based upon anatomical landmarks and previous cellular histological confirmation of the different regions (Harasty et al., 1996a,b). The proportional volume fraction of grey and white matter was analysed using Cavalieri’s method (Coggeshall, 1992). Grey and white matter were identified visually. To ensure reproducibility/reliability quantitative inter- and intra-subject ratings were determined as described previously (Rae et al., 2002a; Harasty et al., 2003). All ratings were conducted by persons blind to the subjects’ diagnosis and the study aims. Repeated measures showed high Pearson product-moment correlations of 0.98.

Non-parametric statistics were chosen due to the small sample size and as the data were not tested for normal distribution. Between-group comparisons were made using the Mann–Whitney U test and within-group comparisons using the Wilcoxon signed rank test. One-tailed tests were used for the analyses of cognitive findings where it was predicted that Turner syndrome subjects would perform below controls. Correlations were assessed using Spearman’s rank test. Statistical significance was assumed at $P < 0.05$.

**Results**

**Cognitive Assessment**

Cognitive test outcomes for Turner subjects and controls are presented in Table 2.

**Linguistic Abilities**

Significant group differences were found on PPVT ($z = -2.35$, $P = 0.009$), BNT ($z = -2.13$, $P = 0.015$), category fluency ($z = -1.86$, $P = 0.03$) and non-word reading ($z = -2.00$, $P = 0.03$). Turner syndrome subjects achieved lower scores than controls, indicative of poorer ability in word comprehension,
There were no significant group differences on irregular word reading, phoneme analysis, auditory or written rhyme judgements or letter fluency tests, with Turner syndrome subjects performing at comparable levels to controls (Table 2).

**Visual-spatial Abilities**

Significant group differences were found on the mental rotations ($z = -1.99$, $P = 0.03$), Object assembly ($z = -1.689$, $P = 0.05$) and face recognition ($z = -1.87$, $P = 0.03$) tests. In all cases Turner syndrome subjects performed significantly below controls. There was no difference between the groups on the visual sequential memory and block span tests.

**1H Magnetic Resonance Spectroscopy**

A significant increase ($P = 0.034$) was noted in left temporal lobe Cre/NA in Turner syndrome [0.73 (0.23)] compared to controls [0.55 (0.13)]. Reference to quantitative data for this region suggested that this was likely due to a decrease in NA [TS 7.62 (2.04), Ctl 9.65 (1.78), $P = 0.08$] rather than an increase in Cre [TS 5.37 (1.5), Ctl 5.2 (1.2), $P = 0.84$]. Significant asymmetries (left < right) were observed in the Cho resonance in Turner syndrome [left Cho 3.64 (0.80), right Cho 4.87 (0.9), $P = 0.0077$, Wilcoxon signed-rank] which did not exist in the control population [left Cho 4.35 (2.2), right Cho 4.33 (1.9)]. There were no such asymmetries in Cre or NA.

No differences in metabolite ratios or quantitative estimates of metabolites were seen in either the left or right angular gyrus.

**1H Magnetic Resonance Imaging**

Significant volume differences in the superior temporal gyrus were found between Turner syndrome girls and controls, with both left ($P = 0.0054$) and right ($P = 0.0031$) superior gyrus larger in Turner syndrome than control (Fig. 2). This was largely due to increased grey matter volume (left $P = 0.0051$, right $P = 0.0017$) than white matter (left $P = 0.12$, right $P = 0.06$).

Significant volume differences in the middle temporal gyrus were found between Turner syndrome girls and controls, with both left ($P = 0.031$) and right ($P = 0.047$) middle temporal grey
matter larger in Turner syndrome than controls. There was no difference in white matter ($P = 0.89$). In the inferior temporal gyrus, no significant volume increases were noted, although all mean volumes measured for Turner syndrome were larger than the corresponding mean of the volumes measured for controls. By contrast, no significant volume differences were found between Turner syndrome and control girls in Broca’s area ($P = 0.82$).

Correlations were found between temporal lobe MRS measures and volumes of the superior and middle temporal gyrus (Table 3). These correlations were mostly with levels of choline-containing compounds and were all negative. There were no such correlations in the control group.

Correlations were also found between measures largely associated with temporal lobe function (cognitive tests) and superior and middle temporal gyrus volumes (Table 3). These latter correlations all indicated that increased temporal grey matter size was associated with decreased cognitive performance. By contrast, correlations between cognitive task performance scores and volumetric measures in the control group were positive, indicating that a larger volume was associated with a better performance.

**Discussion**

**Cognitive Testing**

The finding of widespread impairments across linguistic and visual spatial domains, in Turner syndrome subjects supports previous claims that the cognitive deficits reflect both left and right hemisphere pathology (Pennington et al., 1982). However, the impairments were not generalized and there was evidence of dissociations within linguistic and spatial domains consistent with multifocal rather than diffuse pathology.

Linguistically, Turner syndrome subjects exhibited impaired naming and vocabulary scores suggestive of underlying semantic difficulties. There was also evidence of impaired category fluency and non-word reading, indicating additional difficulties in word retrieval and non-lexical reading. Overall, these results are consistent with previous reports of naming and retrieval deficits (Waber, 1979) and reduced verbal fluency in Turner syndrome (Temple et al., 1996; Romans et al., 1997; Temple, 2002). However, the findings on the reading tests were unexpected. Although reading typically has been reported to be intact or advanced in Turner syndrome (Temple and Carney, 1996) previous work has not analysed specific components of the reading process. In this study Turner syndrome subjects showed deficits in non-word reading but intact regular word reading, indicating that these children have acquired to a normal degree the ability to read aloud via the lexical (‘dictionary lookup’) procedure while specifically failing to acquire to a normal degree the ability to read aloud via the non-lexical (letter-to-sound rule) procedure. Their intact performance on letter fluency indicating relatively preserved access to orthographic knowledge and on phonological processing (phoneme analysis and rhyme judgement) tasks suggested that their impaired non-lexical reading was attributable to specific deficits in knowledge and application of letter-to-sound rules. These results on naming, fluency and reading tasks implicate left temporal and parietal areas.

Widespread but specific and dissociable deficits were also present in spatial processing. Turner syndrome subjects performed significantly below controls on object assembly and mental rotation tasks consistent with previous reports of abnormalities in constructional (McGlone, 1985; Temple and Carney, 1995) and mental transformation skills (Money and Alexander, 1966; Rovet and Netley, 1982). Their reduced performance on face recognition tasks further suggested impairments in face processing. These cognitive deficits are typically associated with disruption of right posterior hemisphere circuitry involving ventral visual pathways. In contrast the lack of group differences on spatial working memory tasks (visual sequential memory and block span) suggests that dorso lateral prefrontal and inferior parietal areas are relatively preserved.

**Temporal Lobe Abnormalities in Turner Syndrome**

The finding of magnetic resonance spectroscopy differences in the temporal lobe in Turner syndrome is novel. This study included only Turner syndrome girls who displayed a ‘non-mosaic’ karyotype, and who may, given the reported X-chromosome dosage effect (Murphy et al., 1997), be more

| Table 3 |
| Correlations between superior temporal morphological measures and temporal lobe MRS measures or temporal lobe function (cognitive test) results |
| Karyotype | Volume | $\rho$ | $R_\xi$ |
| 45,X ($n = 8$) | Left ST grey | Left Cho/NA | 0.089 | -0.60 |
| | Left MT total | Left Cho/NA | 0.034 | -0.75 |
| | Left ST total | Left Cho/Cr | 0.059 | -0.67 |
| | Left MT grey | Left Cho | 0.073 | -0.63 |
| | Total MT grey | Left Cho | 0.031 | -0.77 |
| | Left MT total | Total MT | 0.013 | -0.88 |
| | Total MT | Total MT | 0.034 | -0.75 |
| | Right MT grey | Total MT | 0.038 | -0.073 |
| | Right ST grey | Right Cho | 0.034 | -0.75 |
| | Right MT total | Right NA | 0.08 | -0.62 |
| | Right ST grey | Right Cho/Cr | 0.047 | -0.70 |
| $n = 9$ | Right ST total | Semantic fluency | 0.035 | -0.72 |
| | Left ST grey | Left Cho | 0.07 | -0.6 |
| | Right ST total | Right Cho/Cr | 0.03 | -0.72 |
| | Right ST grey | Verbal fluency | 0.026 | -0.79 |
| | Right MT grey | Left ST grey | 0.026 | -0.78 |
| | Left ST grey | Auditory rhyme (%) | 0.011 | -0.86 |
| | Right ST grey | Right MT grey | 0.017 | -0.80 |
| | Left MT grey | Left ST total | 0.024 | -0.76 |
| | Left ST total | Right ST total | 0.013 | -0.84 |
| | Right ST total | Left ST total | 0.017 | -0.80 |
| | Left MT total | Left ST white | 0.043 | -0.71 |
| | ST total white | Written rhyme % | 0.022 | -0.79 |
| 46,XX ($n = 9$) | Left ST grey | Left Cre | 0.044 | -0.76 |
| | Right ST total | Cre AI | 0.023 | 0.86 |
| | Right ST total | Cre AI | 0.032 | 0.69 |
| | Right ST grey | Semantic fluency | 0.035 | 0.75 |
| | Right ST total | | 0.029 | 0.77 |

All correlations were measured using Spearman’s rank coefficient ($R_\xi$). Cho, choline-containing compounds; Cre, creatine-containing compounds; NA, N-acetyl compounds; AI, asymmetry index; ST, superior temporal; MT, middle temporal.
likely to display temporal lobe abnormalities than a group of mixed cell karyotype. Although the number of subjects is smaller than in some previously published studies of the brain in Turner syndrome, our subject group is tightly uniform in having non-mosaic karyotype, absence of oestradiol supplementation and a narrow age range. Further, all of our findings are based on rejection of the null hypothesis, suggesting that lack of statistical power (type 2 error) is not an issue. However, we would advise conservative interpretation of these data from just nine subjects and caution in generalizing the finding across the Turner population.

Our finding of decreased NA in the left temporal lobe is compatible with the decreased FDG uptake reported previously (Murphy et al., 1997) as levels of NA have been shown to correlate with glucose use (Horska et al., 2002). The finding of significant asymmetry in temporal lobe Cho is suggestive of asymmetry in cell/dendrite density in either temporal lobe. The Cho resonance has been shown to relate to total membrane density (Miller et al., 1996).

Quantitative volume analysis of the temporal lobe in Turner syndrome compared to controls (Fig. 2), showed significant volume differences in the temporal lobe which increased along the inferior–superior axis but which were largely uniform along the anterior/posterior axis (i.e. enlargement was not confined to the front or back of the temporal lobe; Fig. 3). By contrast, another area involved in verbal processing, Broca’s area, showed no volume differences. The temporal lobe volume difference was confined to the grey matter and correlated negatively with the area of the temporal Cho resonance (Table 3). This suggests that the larger temporal lobes seen in Turner syndrome arise due to increased cell size (larger cell bodies), or decreased density of dendrites (more, smaller cells, but with greatly decreased dendrites) as the Cho resonance has been shown to relate to total membrane density (Miller et al., 1996). In addition, the size of the temporal gyri correlates negatively with performance on cognitive tests such as auditory rhyme and semantic fluency. In controls, these correlations are much weaker and, where present, lie in the opposite direction (Table 3). This is in agreement with previous reports of positive correlations between brain size and mental performance (Rushton and Ankney, 1996) and between grey matter volume and cognitive performance (Gur et al., 1999).

While no difference between Turner subjects and controls was seen on performance on auditory rhyme, Turner subjects performed significantly worse than controls on semantic fluency tasks. Semantic fluency tasks have been shown to activate the left medial temporal lobe (Pihlajamaki et al., 2000) and also to correlate with relative 2-deoxyglucose uptake rates in both the left and right temporal cortex (Bovin et al., 1992). This suggests that the temporal lobe MRI and MRS changes are related to functional deficits.

Turner subjects have previously been reported to have significantly smaller cerebral hemisphere volumes than female controls (Murphy et al., 1995) although others have reported no group differences in overall cerebral volume (Reiss et al., 1995). Cerebral volume differences are therefore unlikely to account for the relative increases reported here in temporal lobe grey matter in Turner syndrome although these inconsistent findings (Murphy et al., 1993) suggest that caution should be used in extrapolating from other studies. The lack of relative volume difference reported here in Broca’s area and in the inferior temporal lobe also suggests that the finding of larger superior and middle temporal lobes is not due to any overall brain volume difference.

Previous MRI studies of Turner syndrome have reported no difference in total temporal lobe volumes (Murphy et al., 1993) in older (mean age 30 years) mixed karyotype (both mosaic and non-mosaic) subjects, or in a group of 30 (27 non-mosaic, three mosaic) younger (range 6–17, mean 10 years) subjects (Reiss et al., 1995) compared to age matched 46X,X controls. A more recent study (Brown et al., 2002) using 25 non-mosaic subjects (mean age 13.2 ± 4.3 years) also reported no significant change in temporal lobe volume. The present study may differ from that of Murphy et al. (1993) in that the subjects in this study were significantly younger and all non-mosaic. In the case of the Reiss et al. (1995) study, the brain was divided into 16 segments after placement of five planes through the brain, such that the temporal lobe was not defined by the same anatomical borders as were used in this study. The study of Brown et al. (2002) included the hippocampal formation as part of the temporal lobe parcellation. The hippocampus was previously reported to be significantly smaller in Turner syndrome (Murphy et al., 1993), offering a possible confound to comparison between temporal lobe volumes reported in this study and those reported by Brown et al. The findings of temporal lobe enlargement may also be age-related and temporary. In autism, for example, it has been reported that brain volumes are larger than in control subjects under the age of 12, but not significantly different above that age (Aylward et al., 2002).

A Larger Temporal Lobe in Turner Syndrome; Why Might This Be So?

Given that Turner syndrome subjects lack genetic material possessed by both 46,XY and 46,XX subjects, Turner subjects might conceivably lack genetic material responsible for pruning areas of the temporal lobe. For example, one might argue that the brains of those with Turner syndrome fail to develop normally during gestation, perhaps because of a lack of normal cellular pruning associated with appropriate developmental neurobiology prenatally during brain development time windows. During specific weeks of gestation the brain undergoes normal apoptosis (cell death) and specifically loses cells so that normal cell patterns emerge. These cellular
patterns enable normal cellular functioning such as in cells clustered as columns or raindrop patterns found in the primary and secondary speech processing regions. Without appropriate pruning an increased volume would eventuate. The strong correlations between temporal lobe Cho and temporal lobe volumes indicates that the histology of the temporal lobe in Turner syndrome is altered such that, for example, cells may be larger or have fewer dendrites, consistent with a developmental abnormality.

An X-chromosome effect on temporal lobe development is supported by a study of men with non-mosaic Klinefelter’s syndrome (47,XXY; Patwardhan et al., 2000) Decreased superior temporal gyrus grey matter on the left and right was reported, although the difference was more marked on the left. There was also a trend for the decreased volume to be associated with reduced verbal fluency, measured using the controlled oral word association test. However, the authors reported that, in five cases where Klinefelter subjects were taking testosterone supplements, the superior temporal gyrus abnormalities were not present and suggested that they may be associated with testosterone, although they cautioned against drawing this conclusion too forcefully on such a small subject group. It would be of interest to know whether the temporal lobe enlargement seen in Turner subjects in this study survives later oestrogen replacement therapy.

Subjects with Turner syndrome have been shown to display different cognitive profiles depending on the parental origin of the X-chromosome (Skuse et al., 1997; Donnelly et al., 2000; Larizza et al., 2002). Subjects in whom the X-chromosome was inherited from the mother are more likely to have enhanced verbal forgetting compared to controls, while those with a paternal X-chromosome are more likely to have reduced visuospatial memory (Bishop et al., 2000). The incidence of maternally derived X-chromosome (74%) in live Turner births is higher than paternal (Jacobs et al., 1997); this is attributed to imprinting of genes on the paternal X-chromosome which make the 45,XP offspring less viable (Jamieson et al., 1999). Subjects in this study were not classified according to parental origin of X-chromosome as parental DNA samples were not available. However, given the relatively high incidence of 45,Xp and the relatively low number of Turner subjects in this study (n = 9) it must also be considered that the temporal lobe abnormalities seen here may occur only in 45,Xp subjects. Subjects in this study displayed no deficit in visuospatial memory as might be expected in 45,Xp subjects. It has recently been reported that there were no significant differences in brain volumes between Turner subjects with 45,Xp and 45,Xq karyotypes (Brown et al., 2002) making parent of origin effects unlikely, although we note that the temporal lobe parcellation in Brown et al. (2002) differed from that in this study.

In conclusion, young subjects with Turner syndrome have been found using MRS to have temporal lobe biochemical deficits. These subjects also display enlarged superior and middle temporal lobes compared to 46,XX controls. The degree of enlargement correlates negatively with functional performance on temporal-lobe associated tasks, suggesting that it may be a compensatory mechanism, or possibly causative in the case of semantic fluency performance.

Notes
This work was presented previously (Rae et al., 2002b). It was supported by the APEX Foundation for Research into Intellectual Disability, by a Macquarie University Research Grant, by the Australian National Health and Medical Research Council (fellowship to C.R.) and by the Department of Radiology at the Children’s Hospital at Westmead. The MRUI software package was kindly provided by the participants in the EU Network programmes: Human Capital and Mobility, CHRX-CT94-0432 and Training and Mobility of Researchers, ERB-FMRX-CT970160. The authors gratefully acknowledge the professional assistance of Ms Peggy Chan, Dr Bogdan Chapman, Mr Malcolm Hayden, Ms Bin Moore, Ms Sally McEwan and Mr William Lowe. The authors would like to thank those who generously volunteered their time to take part in this study, and thank the Turner Syndrome Association of Australia for their support.

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