Tone probe event-related potential differences during a face recognition task in prepubertal children and Turner Syndrome girls

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Summary Hormones have been shown to play a role in both cerebral development and neurocognitive function. Turner Syndrome (TS) provides the opportunity to study the effect of the lack of estrogen on neurocognitive development. In this study, event-related potential (ERP) differences were examined among 12 TS girls, 20 prepubertal control girls, and 20 prepubertal control boys during a face recognition memory task. Stage of puberty was determined by Tanner Scale rating and hormonal assay. ERPs to pairs of auditory probe stimuli were recorded from eight scalp sites while participants performed a face recognition memory (FRM) task. For the N2 component of the ERP (which has previously been associated with evaluation of stimulus information, categorization difficulty, and attention), control boys displayed greater right versus left hemisphere amplitude, control girls displayed greater left versus right hemisphere amplitude, and there was no amplitude asymmetry for TS girls. Further, control girls had greater left hemisphere N2 amplitude than control boys and TS girls, and greater right hemisphere N2 amplitude than TS girls. The results suggest more right hemisphere activation during face recognition in boys, while the opposite pattern was present in control girls. In contrast, TS girls displayed no asymmetry, indicative of more uniform involvement of the left and right hemispheres during face recognition. These findings are consistent with differences in cortical organization related to face recognition memory processing among prepubertal control boys, girls, and...
1. Introduction

It is well established that the cerebral hemispheres are specialized for processing different types of information. Areas of the left hemisphere are specialized for language production and comprehension, and analytic processing, while areas of the right hemisphere are specialized for spatial and holistic processing (Shucard et al., 1977; Heinze et al., 1998; Springer and Deutsch, 1998). Aside from these functional differences between the hemispheres, studies have also demonstrated the presence of sex-related differences in neurocognitive function. For instance, males tend to perform better on certain tasks requiring spatial skills, while females perform better on measures of verbal skills (see for example, Maccoby and Jacklyn, 1974; McGee, 1979; Kimura, 1992; Caplan et al., 1997; Collins and Kimura, 1997; Postma et al., 1998; Gur et al., 1999).

These neurocognitive differences noted in males and females are thought, in part, to be attributable to differences in hormone exposure both early in development and following puberty. More specifically, the presence of the sex-related neurocognitive differences early in development suggests an important role of prenatal and perinatal exposure to hormones (Shucard et al., 1981b, 1992; Shucard and Shucard, 1990; Johnson and Ross, 1994). For example, early electrophysiological studies in our laboratory found that infant girls showed evidence of processing both verbal (e.g., verbal passages) and nonverbal (e.g., music) stimuli relatively more with the left hemisphere than right, while infant boys showed the opposite pattern (Shucard et al., 1981b). Further, it was shown that this pattern of asymmetry began to change in six-month-old infant girls, but remained the same in six-month-old boys as in three-month-old boys (Shucard and Shucard, 1990). Specifically, in contrast to three-month-old infant girls, six-month-old infant girls showed a higher left hemisphere response for the verbal condition and a higher right hemisphere response for the nonverbal condition. Following puberty, menstrual cycle effects on spatial memory have been demonstrated, with women performing better on such tasks during the nonmenstrual phase (Postma et al., 1999). In addition, estrogen replacement therapy has been effective in improving some aspects of neurocognitive function such as working memory, and testosterone supplements have been associated with improved performance on working memory tasks among men (Janowsky et al., 2000). Also, cross-sex hormone treatment among transsexuals has resulted in reliable changes in cognitive function (Slabbe-koom et al., 1999).

Of relevance to the present study, we recently demonstrated prepubertal sex-related differences in event-related potentials (ERPs) during a face recognition memory (FRM) task (Everhart et al., 2001). Specifically, boys displayed greater right versus left ERP amplitude for the NZ component to auditory tone probes during the task, while girls displayed the opposite pattern. The greater right versus left hemisphere ERP amplitude was interpreted to indicate relatively greater right hemisphere activation in boys during face recognition. In contrast, girls demonstrated a different pattern of asymmetry suggesting relatively more left hemisphere involvement during face recognition. The findings are of particular interest given that substantial evidence suggests right hemisphere superiority for face processing in general (for more extensive review see Everhart et al., 2001), similar to other spatial tasks.

As discussed above, hormones have been shown to play a role both in cerebral development and neurocognitive function. Turner Syndrome (TS), a genetic disorder involving a missing X chromosome, provides the opportunity to study the effect(s) of reduced perinatal/postnatal estrogen exposure on neurocognitive development. Because TS females are hypogonadal, they lack the ability to produce estrogen. A variety of physical anomalies and cognitive deficits exist among TS females (see Pennington et al., 1985; Rovet, 1991; Shucard et al., 1992). The cognitive deficits that are particularly noteworthy are relative decrements in Performance IQ, and poor visuomotor skills, visuospatial processing, and visuospatial memory. In contrast, verbal skills are relatively intact (Buchanan et al., 1998; Ross et al., 1995, 1998,
2. Method

Twelve right-handed TS girls and 40 prepubertal controls (20 boys and 20 girls) were included in the final sample. The participants were recruited through advertisements in local community newspapers and they were paid for their time. Parents signed informed consent agreements. A preliminary phone screening of parents of potential participants assisted in the recruitment only of those participants who met the criteria for participant selection. With regard to prepubertal controls, participants had to be right-handed and free of chronic illness, neurologic problems, learning disability, and mental retardation. Prepubertal participants also had to have normal (or corrected normal) vision, normal hearing, and normal height and weight (between 5th and 97th percentile for age and sex).

All participants were examined by a pediatric endocrinologist at the Buffalo Children’s Hospital. Prepubertal status was determined with Tanner staging of pubertal development (Tanner, 1962). Tanner staging of pubertal maturation is the accepted method for documenting pubertal development and it is a routine part of an endocrine examination. Additionally, blood was drawn at the time of examination and stored for assay of testosterone and estradiol to provide further documentation of pubertal status. All the boys were determined to be in Tanner Stage 1. Fourteen girls were in Tanner Stage 1, and six were in Tanner Stage 2. For the TS girls, six were determined to be in Tanner Stage 1, one was in Tanner Stage 2, two in Tanner Stage 3, two in Tanner Stage 4, and one in Tanner Stage 5. Demographic information and IQ variables for TS girls and prepubertal controls are reported in Table 1. Karyotype was determined from cultured lymphocytes: nine TS participants had karyotype 45X; two participants had mosaicisms, and one had karyotype 46XiXq.

2.1. Electrophysiological recording during the face recognition memory task (FRM)

Participants were seated in a comfortable chair in front of a rear-projection screen in a sound-attenuated electrically shielded room. Gold-plated electrodes (Grass Instruments) were affixed to the participant’s head at F3, F4, C3, C4, T3, T4, T5, T6, P3, P4, Fz, Cz, Pz, A1 and A2 electrode sites.
according to the International 10–20 System. The A1 and A2 electrodes were placed on the left and right mastoids and were electrically linked and used as a reference. A ground electrode was placed on the participant’s forehead. In addition, electrodes were placed on the outer canthus of each eye so that eye movement recordings could be obtained. Electrode impedance was maintained below 5000 Ω and checked and recorded at the beginning and end of the experimental session.

The EEG and eye movements (horizontal and vertical) were recorded with a Grass Instruments Model 78 polygraph with a bandpass of 1 and 100 Hz and a sensitivity of 7.5 μV/mm for EEG recordings. The Grass amplifiers were interfaced with the Neuroscan System, which was responsible for data collection, and off-line ERP waveform analysis. A Digital Equipment Corporation PDP 11/44 computer was used for stimulus control. Data collection began only when the participant was quiet and alert. Continuous EEG from all the amplifier channels was recorded and stored on the Neuroscan System and backed up on digital tape. Epochs associated with the presentation of each trial were extracted from the continuous EEG and stored for averaging and generation of the ERPs. Prior to generation of the ERPs, epochs were digitally filtered with a low-pass cutoff frequency of 25 Hz.

An investigator remained in the shielded room with the participant throughout the recording session. Instructions were presented for the experimental conditions, and several practice trials were administered to assure that the participant understood the tasks. During all of the conditions of the experiment, the state of the participant was continuously monitored by the investigator seated in the shielded room with the participant and by observation of the ongoing EEG and eye movement recordings. Eye movement recordings were used to correct for the presence of eye movement artifact in the ERPs and to determine which trials should be excluded from averaging. Individual trials that contained excessive artifact (±50 μV of EOG) associated with body and eye movements were discarded during off-line processing and prior to averaging.

ERPs were obtained from participants while they performed a face recognition memory task (FRM) developed in our laboratory. The faces used in this condition were adapted from Ekman and Friesen’s (1978) standardized pictures of facial affect; happy, sad, fear, angry, surprise, disgust, and neutral faces were used. The ERPs were recorded to task-irrelevant tones, with two tones presented during each condition of the FRM. Each tone was 70 dB, 600 Hz, and 100 ms in duration (90 ms plateau; 5 ms rise/fall time). A 2-s inter-tone interval for probe stimuli was used to ensure no interference with slide onset/offset. Each trial of the FRM consisted of three slides. For each slide, stimulus duration was 5000 ms, and tone probe pairs were presented 1500 and 3500 ms after stimulus onset.

**Fig. 1** provides a visual display of one trial of the face matching task. The first slide for each of the trials was the fixation slide, with an "X" located in the center. This slide was considered to be a baseline. The second slide (target) of each trial had one face located in the center and it was presented 1000 ms following the offset of slide one. One pair of tone probes was presented while the participant studied the face. The third slide (recognition) occurred at 3000 ms following the offset of slide two. This slide showed three different faces. Here, the participant was asked to select the particular face (using vocal response) that matched the face of the person in the previous

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**Table 1** Demographic and IQ variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Boys (n = 20)</th>
<th>Girls (n = 20)</th>
<th>TS girls (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Age (year)</td>
<td>9.90</td>
<td>1.25</td>
<td>9.35</td>
</tr>
<tr>
<td>Grade</td>
<td>4.80</td>
<td>1.36</td>
<td>4.10</td>
</tr>
<tr>
<td>Full-scale IQ</td>
<td>112</td>
<td>11</td>
<td>107</td>
</tr>
<tr>
<td>Verbal IQ</td>
<td>112</td>
<td>13</td>
<td>106</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>110</td>
<td>12</td>
<td>105</td>
</tr>
</tbody>
</table>

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**Fig. 1.** One sample trial of the face recognition memory (FRM) task.
slide, regardless of the emotional expression on the face. During a practice series that preceded testing, participants were trained to associate the positions of the three faces on the recognition slide as positions one, two, and three. They then stated out loud the number associated with the face that matched the target face at the end of each trial. An experimenter recorded the participant’s responses. One pair of probe tones also occurred during the presentation of the third slide. A total of 36 trials were presented to each participant. For further details pertaining to the stimulus conditions, see Everhart et al. (2001).

3. Results

3.1. Behavioral data

No group differences were observed for accuracy scores on the face recognition memory task \((F_{2, 50} = 2.77, \text{ ns})\). This finding indicates that control boys (mean = 28.86, SD = 1.23), control girls (mean = 29.57, SD = 0.65), and TS girls (mean = 28.38, SD = 1.19), performed equally well on the task.

3.2. Electrophysiological data

The ERP amplitude data were analyzed for the baseline (fixation) and face recognition conditions (slides one and three, respectively). Only correct trials were used for analyses. Fig. 2 presents the grand averages of the ERPs obtained to the paired tone probes during face recognition. For each ERP, three positive and three negative peak deflections were identified based on the latency window. These peaks are indicated in Fig. 3. The mean latencies and standard deviations in milliseconds of these peaks are presented in Table 2. Peak amplitude scores (in microvolts) were obtained by computing the peak-to-peak distances in microvolts between consecutive positive- and negative-going peaks. Thus, five peak-to-peak values, identified as Peak 1 through Peak 5, were obtained for each ERP. Only the later peaks 2, 3, and 4 were considered in the analyses, as these peaks are thought to be indicative of cognitive processing (Coles and Rugg, 1995).

Inspection of the grand averages (see Fig. 2) revealed a polarity reversal for temporal sites (T3, T4) in comparison to other sites (frontal F3, F4; central C3, C4; and parietal P3, P4). Polarity reversal at the temporal sites during auditory stimulation is consistent with the literature (see for example, Ponton et al., 1993). The polarity reversal is illustrated in Fig. 3, which provides a closer view of the grand averages for temporal site T4 and central site C4. Positive- and negative-going peaks are labeled in Fig. 3. For the statistical analyses that included comparisons between temporal and other sites, the ERP peaks at the temporal sites were equated with the ERP peaks at the other sites. For example, Peak 3 (P2–N2) of the temporal sites is equal to Peak 2 (N1–P2) of frontal, central, and parietal sites, and Peak 4 (N2–P3) of the temporal sites is equal to Peak 3 (P2–N2) of the frontal, central, and parietal sites.
on ERP amplitude data for baseline separately for Peaks 2, 3, and 4. No main effect for group and no interactions including group were present. Thus, control boys’, control girls’, and TS girls’ responses to tone probes presented during the baseline condition did not differ for any of the peak amplitudes: Peak 2 \( (F_{2,39} = 1.2, \ ns) \); Peak 3 \( (F_{2,39} = 0.211, \ ns) \); Peak 4 \( (F_{2,39} = 0.06, \ ns) \). This finding suggests that control boys, control girls, and TS girls processed tones in a similar fashion during the baseline condition.

### 3.4. Group ERP amplitude differences during face recognition

#### 3.4.1. Peak-to-peak analyses

To test the hypothesis pertaining to sex-related differences in ERP amplitude during the FRM, Group \( \times \) Hemisphere \( \times \) Site ANOVA were performed separately for Peak 2 (N1–P2), Peak 3 (P2–N2), and Peak 4 (N2–P3) on the ERP amplitude measures obtained from tone probes (collapsed across tone 1 and tone 2).

For Peak 2, there was a significant Hemisphere \( \times \) Site interaction \( (F_{3,147} = 3.9, \ p < 0.05) \). No other significant interactions or main effects were observed. For Peak 3, there was a significant main effect for site \( (F_{3,147} = 38.4, \ p < 0.001) \). No other main effects or interactions were observed. Peak 4 (N2–P3) showed a significant Group \( \times \) Hemisphere interaction \( (F_{2.49} = 3.84, \ p < 0.05) \), and significant main effects for group \( (F_{2.49} = 7.08, \ p < 0.01) \) and site \( (F_{2.98} = 16.8, \ p < 0.001) \). The Group \( \times \) Hemisphere interaction indicates that peak-to-peak amplitude differences were present between the hemispheres but that this hemispheric asymmetry differed amongst the groups (boys, girls, TS girls). This finding is of particular relevance to the hypotheses of interest. These data are presented in Fig. 4.

#### 3.4.2. Baseline-to-peak analyses

In order to determine the specific component(s) (positive or negative) associated with the Group \( \times \) Hemisphere interaction noted above, the same Group \( \times \) Hemisphere \( \times \) Site ANOVAs were performed separately for baseline-to-peak amplitude measures for the P2, N2, and P3 ERP components obtained for auditory tone probes collapsed across tone pairs. Of note, for these analyses, the “baseline” portion of the “baseline-to-peak” measure refers to the ERP amplitude immediately prior to stimulus delivery.

For P2, there were significant main effects for hemisphere \( (F_{1,34} = 4.88, \ p < 0.05) \) and site \( (F_{3,147} = 37.00, \ p < 0.001) \). For N2, significant
findings suggest that it is the negative aspect of control boys, control girls, and TS girls. These the mean amplitudes for N2 at each scalp site for N2 collapsed across electrode sites. Table 3 lists Peak 4 (N2

Fig. 4. Group × Hemisphere interaction (p < 0.05) for Peak 4 (N2–P3).

Group × Hemisphere \((F_{2,49} = 8.38, \ p < 0.001)\) and significant Group × Site interactions \((F_{6,147} = 3.05, \ p < 0.01)\) were obtained, as was a significant main effect for site \((F_{3,147} = 18.82, \ p < 0.001)\). Fig. 5 illustrates the Group × Hemisphere interaction for N2 collapsed across electrode sites. Table 3 lists the mean amplitudes for N2 at each scalp site for control boys, control girls, and TS girls. These findings suggest that it is the negative aspect of the Peak 4 component (N2–P3) that is largely responsible for the Group × Hemisphere interaction seen for Peak 4. For P3, only a significant Hemisphere × Site interaction \((F_{2,98} = 3.90, \ p < 0.05)\) was obtained.

To evaluate the Group × Hemisphere interaction at N2 more closely, post hoc comparisons were performed in two ways. First, N2 ERP amplitudes were compared among the groups for the left and right hemispheres separately (collapsed across intrahemisphere electrode sites). Control girls showed greater left hemisphere ERP amplitude for N2 than control boys \((t_{38} = 2.99, \ p < 0.01)\) and TS girls \((t_{30} = 4.20, \ p < 0.01)\). In addition, control girls demonstrated greater ERP amplitude in the right hemisphere than TS girls \((t_{30} = 3.74, \ p < 0.01)\), but not control boys \((t_{38} = 1.38, \ ns)\). Second, left and right hemisphere amplitude differences were compared for each group separately, again collapsed across intrahemisphere electrode sites. Control boys showed significantly greater right than left hemisphere amplitude \((t_{19} = 2.94, \ p < 0.01)\), control girls showed significantly greater left versus right hemisphere amplitude \((t_{19} = 2.43, \ p < 0.05)\), and TS girls showed no hemisphere amplitude differences \((t_{11} = 0.642, \ ns)\).

We examined amplitude differences among the groups at each site (Group × Site interaction) for the N2 component with separate analyses collapsed across hemispheres at frontal (F3, F4), central (C3, C4), temporal (T3, T4), and parietal (P3, P4) sites. Control girls demonstrated greater ERP amplitude at frontal sites (F3, F4), central sites (C3, C4), and parietal sites (P3, P4) than TS girls [frontal \((t_{30} = 3.79, \ p < 0.001)\); central \((t_{30} = 3.62, \ p < 0.001)\); parietal \((t_{30} = 2.79, \ p < 0.01)\)]. ERP amplitude at the same sites for control boys did not significantly differ from control girls [frontal \((t_{30} = 1.60, \ ns)\); central \((t_{30} = 1.85, \ ns)\); parietal \((t_{30} = 0.69, \ ns)\)] or TS girls [frontal \((t_{30} = 1.80, \ ns)\); central \((t_{30} = 1.31, \ ns)\); parietal \((t_{30} = 1.94, \ ns)\)]. No group differences were observed for temporal scalp sites (T3, T4). These findings are illustrated in Fig. 6.

As reported above, five TS girls had exceeded Tanner Stage 2 due to hormone replacement therapy (HRT). Given that a major emphasis of this study was to examine prepubertal differences in cortical organization during a face recognition task, baseline-to-peak components P2, N2, and P3 were reanalyzed using only TS girls in Tanner Stages 1 and 2 \((N = 7)\). No significant group interactions or main effects were present for P2 or P3. However, as with the previous analyses, a significant Group × Hemisphere interaction \((F_{2,44} = 7.95, \ p < 0.001)\).
the mean amplitudes for N2 at left and right hemisphere scalp sites for this sample. Post hoc comparisons revealed that the findings for the entire group were replicated in this reduced sample that included only Tanner 1 and 2 TS girls. An additional analysis was also conducted to determine whether the age difference between the controls and TS girls influenced the findings for N2. A Group × Condition × Site ANCOVA, using age as a covariate, was performed with all participants included in the analysis. The group by hemisphere interaction remained significant after controlling for age ($F_{2, 44} = 8.11, p < 0.001$).

4. Discussion

The purpose of this study was to examine differences in cortical organization among TS girls and prepubertal control boys and girls during a face recognition task. As shown in an earlier study with prepubertal children, sex differences in ERP hemisphere amplitude asymmetry were obtained to auditory tone probes during a face recognition task (Everhart et al., 2001). The major finding of the present study is that TS girls demonstrated no

| Table 3 | Means and standard deviations for N2 amplitude (microvolts) for left and right scalp electrodes |
|---|---|---|---|---|---|
| | Boys | Girls | TS girls |
| | Left | Right | Left | Right | Left | Right |
| Frontal | | | | | | |
| Mean | 4.20 | 4.79 | 6.07 | 5.88 | 2.60 | 2.82 |
| SD | 2.75 | 2.66 | 2.89 | 3.16 | 2.21 | 1.78 |
| Central | | | | | | |
| Mean | 3.21 | 4.23 | 5.80 | 5.46 | 2.50 | 2.70 |
| SD | 2.76 | 2.68 | 1.65 | 2.76 | 1.29 | 1.54 |
| Parietal | | | | | | |
| Mean | 2.09 | 2.34 | 3.89 | 3.31 | 1.77 | 1.69 |
| SD | 2.04 | 2.41 | 2.84 | 1.91 | 1.01 | 1.25 |
| Temporal | | | | | | |
| Mean | 2.32 | 2.56 | 2.71 | 2.38 | 2.30 | 2.32 |
| SD | 1.17 | 1.75 | 1.65 | 1.75 | 1.29 | 1.21 |

Fig. 6. Group × Site interaction ($p < 0.05$) for N2. Frontal: F3, F4; Central: C3, C4; Temporal: T3, T4; Parietal: P3, P4.

$p < 0.001$ was obtained for N2, as were significant main effects for site ($F_{3, 132} = 14.99, p < 0.001$) and for group ($F_{2, 44} = 4.11, p = 0.02$). Table 4 lists

| Table 4 | N2 amplitude (microvolts) for control boys, control girls and TS girls in Tanner Stages 1 and 2 |
|---|---|---|---|---|---|
| | Boys | Girls | TS girls ($n = 7$) |
| | Left | Right | Left | Right | Left | Right |
| Mean | 2.96 | 3.48 | 4.63 | 4.25 | 2.50 | 2.74 |
| SD | 1.80 | 2.02 | 1.72 | 1.51 | 1.67 | 1.24 |
asymmetry between the hemispheres to tone probes presented during FRM. In contrast, control boys demonstrated relatively greater overall right than left hemisphere amplitude, while control girls displayed relatively greater overall left than right hemisphere amplitude. These findings remained constant when the data were reanalyzed using TS girls in only Tanner Stages 1 and 2. Further, the age difference between the controls and TS girls did not account for the findings.

It is important to note that no group differences were observed during the baseline condition, and that differences noted during FRM were isolated to the N2 (−250 ms) component of the ERP. The absence of group differences during baseline indicates that control boys, control girls, and TS girls process auditory tone probes equivalently when not engaged in tasks that require higher cognitive functions. The presence of differences in the later ERP components and not in the earlier components during face recognition memory suggests that the groups differed during higher cognitive processing of stimuli. More specifically, ERP components that occur after 200 ms from stimulus onset are thought to reflect cognitive or psychological processes; whereas ERP components that occur prior to 200 ms have been referred to as ‘‘obligatory’’ central nervous system responses to stimulation. These earlier components are influenced primarily by the physical characteristics of the stimulus, such as the loudness of a tone (Naatanen, 1990). There is now substantial support in the literature that N2 reflects task-related evaluation of stimulus information (Naatanen, 1992) as well as categorization difficulty and attention to the stimulus (Altenmüller, 1993; Coles and Rugg, 1995).

Our previous paper (Everhart et al., 2001) posited that prepubertal boys and girls use differing, although overlapping neuronal systems for processing faces. In other laboratories, asymmetry of the N2 component has been demonstrated in the processing of ‘‘nonfacial’’ local and global targets (hierarchical stimuli) during divided attention tasks (Heinze et al., 1998). The N2 amplitude to local targets was larger over the left hemisphere and N2 amplitude to global targets tended to be larger over the right hemisphere. It was thus speculated in the present study, that boys process faces at a global level (right hemisphere), while girls process faces at a local level (left hemisphere). Others have speculated that females may use verbal strategies for processing faces, while males may rely more on spatial processing (Lewin et al., in press). Regardless of possible differences in processing strategies between the sexes, previous electrophysiological studies using three- and six-month-old infants in our laboratory demonstrated that sex-related differences for processing of verbal and nonverbal stimuli are present early in neurocognitive development (Shucard et al., 1981b; Shucard and Shucard, 1990). Infant girls had ERP data that suggested they process both verbal and nonverbal materials relatively more with the left hemisphere than the right. Infant boys showed the opposite pattern.

In the present study, it is interesting to note that TS girls displayed symmetry to auditory tone probes during face recognition memory, while prepubertal boys and girls displayed predictable, opposing patterns of asymmetry. This pattern of results occurred across multiple scalp sites of the left versus right hemisphere for the N2 component, and thus, most likely reflects group differences in intrahemispheric processing. As stated previously, TS girls lack the ability to produce estrogen and therefore provide the opportunity to study the potential influence of endogenous hormones (or lack thereof) on neurocognitive development. The symmetry among TS girls cannot be accounted for by task difficulty or attention, as statistical analyses showed that TS girls, control boys, and control girls performed equally well on the task. Rather, the differences noted in ERP amplitude to auditory tone probes are reflective of cortical functional organizational differences in processing spatial stimuli. It is possible that the lack of estrogen interferes with the development of hemispheric specialization, thus resulting in the development of differing retrieval strategies (as seen in prepubertal boys and girls). This impression is strengthened by the finding that TS girls displayed lower N2 amplitude to auditory tone probes than did control boys and control girls only during the FRM task and not during baseline. As with the asymmetry results described above, this amplitude finding was limited to the N2 component, but only at frontal and central sites. Consistent with this impression, findings from comparative studies also show a potential link between lack of estrogen exposure and differences in hemispheric specialization. For example, Fitch and Denenberg (1998) commented that removal of the ovaries of the female rat as late as Day 16 increases the cross-sectional area of the adult corpus callosum, which is integral for interhemispheric communication. In addition, Diamond et al. (1983) demonstrated that female rats ovariectomized at day one show the expected ‘‘male’’ pattern of $R > L$ cortical thickness within the visual cortex at 90 days of age.

In explaining the findings noted between TS girls and control boys and girls, it is noteworthy
that the present investigation paired an auditory probe with a visually presented face recognition task. Thus, a mixed sensory paradigm was used, which has previously been reported in the literature (see for example, Cuthbert et al., 1998; Schupp et al., 1997). In general, fluctuations in auditory probe ERP amplitudes are thought to represent modulations in the allocation of attentional resources to ongoing visual or auditory stimuli. It is our interpretation that relatively greater right versus left ERP amplitude indicates relatively greater right hemisphere activation in control boys to auditory probe tones during face recognition (FRM). In contrast, control girls demonstrated a different pattern of asymmetry than boys to tone probes, suggesting relatively more left hemisphere involvement during the face recognition task. TS girls demonstrated symmetry to tone probes during the FRM. Our interpretation stems from Kinsbourne’s “activation” hypothesis, which suggests that a higher amplitude response to probe stimuli may occur due to heightened neuronal activity produced by the ongoing tasks itself, thus increasing the responsivity of those areas of the brain to all incoming stimuli (Kinsbourne and Hiscock, 1983). This hypothesis appears to be more feasible during a mixed sensory paradigm such as that used in the present study, than when both probe (e.g., auditory probe) and ongoing stimuli (e.g., auditory task) are presented in the same modality. When probe and task stimuli are presented in the same modality (e.g., Shucard et al., 1977, 1981a,b; Shucard and Shucard, 1990), the incoming information may be competing for overlapping resources, whereas, in a mixed sensory paradigm, competition for neuronal resources may not be present. It is acknowledged that further research regarding the interpretation of mixed sensory paradigms is required. Irrespective of the details of interpretation, however, the findings support the notion that there are sex-related differences with regard to the neuronal systems involved in face processing.

Of potential relevance to the present study is a previous finding that in comparison to female controls, TS girls have a smaller proportion of gray and white matter tissue within the right and left parietal regions, and a larger proportion of gray and white matter tissue within the right inferior parietal–occipital region (Reiss et al., 1995). Sex-related differences in gray and white matter tissue distribution have also been reported for healthy adults without neuroendocrine disorder. For instance, using volumetric analysis of MRI, Gur et al. (1999) reported that healthy adult women have a higher percentage of gray matter in comparison to healthy adult men, while men have a higher percentage of white matter in comparison to women. Moreover, in the same study, intracranial volume was positively associated with performance on a verbal task for women, but not for men. The precise relationship between performance on such neurocognitive tasks, reduced hormone exposure, and the differences in neural tissue distribution noted above are currently uncertain. Prospective longitudinal studies may more clearly define the relationship between neurocognitive function, estrogen, and hemispheric asymmetry as it pertains to the regional distribution of gray and white matter.

The group differences noted in this study suggest that TS girls differ from control boys and girls in the functional organization of brain systems that involve memory for the recognition of faces. This difference in functional organization may also be related to the deficits in spatial abilities seen in TS. Given the absence of estrogen among TS girls, particularly during early development, it is reasonable to suggest that sex hormones play a role in the development of certain neurocognitive processes, and that these processes established early in development may be somewhat invariant to hormonal fluctuations (i.e., puberty) later on. Future studies should address whether HRT (e.g., estrogen replacement) for TS girls alters their neurocognitive pattern observed during face recognition memory. If estrogen therapy does not alter this observed pattern, it is possible that “critical” periods exist for the establishment of neural pathways necessary for the recognition of face-specific stimuli. This notion is possibly supported by studies of cognitive change among postmenopausal women who are prescribed estrogen (e.g., HRT). Although the notion of significantly improved cognition during HRT remains debatable, systematic reviews of the literature have noted no clinically meaningful cognitive improvements during HRT (Gupta and Aronow, 2002; Nelson et al., 2002). Although only speculative, it appears plausible to suggest that such critical periods may indeed exist. Long-term developmental study is required in order to explore these issues further.

The present investigation used facial stimuli and ERPs to examine group differences in cortical organization during a face recognition memory task. Of note, it is possible that the results obtained in the present investigation are not specific to face recognition memory. Rather, the results may be indicative of general spatial memory. The design limitations of the current study do not permit for examination of potential group differences in the processing of facial versus other (i.e., shapes, animals, vegetables) stimuli, and this remains an important area of study for future
Investigation. In addition, the present multimodal paradigm represents one of the few available studies that employs the use of visual stimuli and auditory tone probes. To date, the precise relationship between visual stimuli and ERPs recorded to auditory tone probes is unclear, and future investigations will attempt to unravel potential interactive effects.

Acknowledgements

This study was supported in part by the National Institutes of Health, US Public Health Service Grant HD25718. The authors thank Dr. Richard Clopper for his work on the development of the FAIT and Greg Cuipak for his assistance with data collection and scoring.

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