THE INFLUENCE OF BIOLOGICAL SEX ON COGNITION AND HEMISPHERE SPECIALIZATION: A STUDY OF TURNER SYNDROME

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ABSTRACT

The primary focus of this research was to investigate the possible influence of biological sex, specifically the sex chromosomes and hormones, on level of cognitive abilities and pattern of hemisphere specialization in humans. Normal males and females are known to differ in level of cognitive abilities, with males typically having a higher level of spatial ability than females, and females achieving higher scores on tests of several aspects of linguistic ability. A growing body of research indicates that the sexes may also differ in degree of hemisphere specialization, with males being more lateralized than females. It has been suggested that degree of hemisphere specialization for spatial and linguistic processing may be related to the level of these cognitive abilities. The specific hypothesis of this research was that since the sexes differ in cognitive abilities and perhaps in hemisphere specialization, then perhaps the sex chromosomes and hormones may play a role in determining patterns of neural organization and cognitive abilities.

This hypothesis was explored by comparing a group of eight Turner syndrome subjects to normal control groups of both females and males. Turner syndrome individuals were studied because they do not have a normal second

X chromosome as do normal females or the Y chromosome of normal males. Thus they are genetically different from both normal males and females. Nor do Turner syndrome individuals have normal sex hormone production. Thus the possible role of these biological variables could be studied. However, on the basis of this syndrome alone, the relative importance of these factors cannot be disentangled. The study of Turner syndrome also allows one to rule out environmental factors since Turner syndrome individuals phenotypically resemble normal females. Previous research has indicated that TS individuals have a deficit in spatial ability compared to normal females.

Male and female control subjects were matched with the Turner syndrome subjects on aspects of both Verbal and Performance IQ. Each group had a mean age of approximately 17 years.

A battery of tests measuring spatial ability, linguistic ability and hemisphere specialization was administered to the eight subjects in each of the three groups. A trend toward bilateral representation for linguistic processing was observed in the Turner syndrome group. Right hemisphere specialization for the processing of nonverbal stimuli appeared to be normal.

With regard to cognitive abilities, the Turner syndrome subjects were found to perform at a normal level on many tests such as a phonetic reading test, tests of verbal intelligence, and tests of some aspects of spatial ability, compared to normal males and females. However, their performance was found to be deficient on some aspects of a test of three-dimensional perception, a word recognition reading test, a written word fluency test and a coding or digit symbol test. It is suggested that a common element required in the performance of these tests on which Turner syndrome individuals were deficient may be some aspects of visuospatial perception and memory which become particularly deficient when there are time constraints.

Given the cognitive differences and the tendency toward a difference in hemisphere specialization between the Turner syndrome and normal subjects, it is suggested that either the lack of a second X chromosome or the lack of normal sex hormones, or both, play a role in determining the level of cognitive abilities and pattern of hemisphere specialization in normal humans. The evidence from this and previous studies suggests that the absence of a normal second X chromosome alone may underlie the differences between Turner syndrome subjects and normal females.

Some of the methodological problems encountered in this type of research are also discussed.

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CHAPTER 1

INTRODUCTION

Throughout history, differences between the sexes have been a subject of compelling interest to students of human behaviour. One finds constant references to sex differences in myths and proverbs detailing the behaviour of males and females. For example, men are believed to be more aggressive, women more emotional; women are talkers while men are doers. Such attempts to categorize behaviour as typically male or female contain varying degrees of truth but they are of interest in that they illustrate the ways in which man has conceived of man, woman, and the differences between them.

Originally the study or, more accurately, the contemplation of human sex differences was predominantly the domain of philosophers, poets and novelists. However, since about the beginning of the twentieth century this subject has come under more careful scrutiny by scientists who, for the most part, have confirmed the prevailing myths or biases, reporting that indeed males are more aggressive and independent and females more passive and emotional. It has also commonly been assumed that sex differences were biologically determined and this assumption led to the notion that since males were considered to be biologically superior they must also be intellectually superior (Parlee, 1978). Later, with the advent of feminism, the prevailing theory was that sexually dimorphic behaviour, outside the realm of reproduction, reflected differences in child-rearing practices, cultural influences and expectations, and different environmental and experiential factors. Recently, however, numerous and more careful studies have been reported which cast serious doubt on the hypothesis that environmental factors are the only ones.

Sex Differences in Cognitive Abilities

In the last few decades a considerable body of research has accumulated indicating that the sexes do indeed differ in cognitive functioning. The two most consistently reported findings are that girls perform better than boys on some tests of verbal ability and that boys perform better than girls on tests of visual-spatial and mathematical ability (for reviews see Eliot & Fralley, 1976; Harris, 1977; 1978; Maccoby, 1966; Maccoby & Jacklin, 1974; Terman & Tyler, 1954).

It has been found repeatedly that in early childhood girls acquire the phonemes (basic sound units) of the English language, speak their first word and begin putting words together at an earlier age than do boys. In terms of articulation, which requires precise motor control of the vocal apparatus, girls begin to improve at a faster rate than boys by three to four years of age. The early superiority of females on these aspects of language ability persists for a time and then begins to decrease. This is the reverse of what would be expected if environmental factors were of prime importance in the development of sex differences. Female superiority in other areas of linguistic ability, however, persists at least into adulthood. During the school years and beyond girls perform better than boys on tests of reading achievement, grammar, spelling and word fluency.

Normal males and females differ much more markedly in their ability to perform visual-spatial tasks involving visualization, manipulation and recall of spatial configurations. This difference has been found on a wide variety of tests of spatial ability as measured by accuracy or time. Unlike the sex difference in linguistic ability, however, this difference often is not found in young children. Male superiority tends to become evident at about 10 to 12 years of age and to persist throughout adulthood (for reviews see Eliot & Fralley 1976; Harris, 1978; Maccoby, 1966; Maccoby & Jacklin, 1974; Terman & Tyler, 1954). Studies typically find that males perform more accurately or more rapidly than females on a variety of tasks involving such skills as left-right orientation, a sense of direction and recognizing a three-dimensional object from a two-dimensional pattern. On such tasks only 20 to 25 percent of normal females achieve scores equal to or higher than the average score for males.

One factor that may in some way be related to sex differences in cognitive abilities is a sex difference in the rate of physical maturation. For example, on the average, girls begin puberty 16 months earlier than boys, and reach their maximum physical growth 38 months earlier (Nicolson & Hanley, 1953). It may be that neurological development also proceeds at a faster or different rate in girls than in boys. Such a difference, if it exists, could be related to the earlier onset of some aspects of speech and language in girls compared to boys. But boys catch up in some, but not all, areas of linguistic ability. With regard to spatial ability, however, once the sex difference has emerged, it persists unchanged. Girls do not catch up. Therefore, if a sex difference in rate of maturation is related to the sex differences in cognitive abilities, the relationship must be a very complex one.

Other factors that may affect a given individual's performance and pattern of cognitive abilities are environmental factors. However, differences in the way boys and girls are brought up and treated and differences in the environments that are created for them, also cannot account for all the data. If these were they only factors involved, one would expect the magnitude of the sex differences in cognitive abilities to increase with age rather than to stay the same, as is the case with spatial ability, or to decrease as is the case with some linguistic abilities.

Sex Differences in Neural Organization

Recent research has uncovered sex differences in biological or neurological variables which possibly may underlie behavioural sex differences. Studies of cerebral organization have shown that in the majority of people, language is mediated primarily by the left cerebral hemisphere and that spatial and nonverbal ability is mediated primarily by the right hemisphere. This evidence comes from studies of the behavioural and cognitive deficits in individuals with lateralized brain lesions (e.g. Dimond & Beaumont, 1974; Heilman & Valenstein, 1979; Lansdell, 1962; Mountcastle, 1962; Penfield & Roberts, 1959) and individuals who have undergone cerebral commissurotomy (severing of the neural fibres connecting the two cerebral hemispheres) for relief of epileptic seizures (e.g. Gazzaniga, 1970).

There are, however, problems involved in generalizing from the study of neurologically abnormal individuals to the functioning of the intact brain (for a detailed discussion of this issue see Witelson, 1977). Fortunately techniques have been developed which allow the study of cerebral lateralization in neurologically intact individuals.

The most widely used of these techniques involve the examination of asymmetries in tests of perception. Such tests are based on the fact that information arriving at a sense organ is initially transmitted primarily to the contralateral hemisphere. These tests involve either simultaneous or unilateral presentation of different stimuli to the left- and right-sensory fields. Any difference in the accuracy of perception of the stimuli presented to the two sensory fields is thus inferred to mean that the hemisphere contralateral to the more accurately perceived field plays the major role in the processing of that information. In the auditory modality the dichotic listening procedure originally developed by Broadbent (1954) was first noted by Kimura (1961) to be a measure of hemisphere specialization in normal adults. Since Kimura first used this technique, similar tasks based on the same principle have been developed for use in the visual modality (Kimura, 1966; Levy and Reid, 1976) and the haptic or active touch modality (Witelson, 1974). By varying the stimuli and the difficulty of the task it is possible to study hemisphere specialization for various types of information processing and in different age groups.

Hemisphere specialization has also been studied in neurologically intact individuals by testing motoric asymmetries and electrophysiological responses to different stimuli (for a review of such studies in children see Witelson, 1977; and in adults Anderson, 1977; Donchin, Kutas & McCarthy, 1977).

These methods are particularly useful in the study of hemisphere asymmetries in children since the responses measured are within an infant's behavioural repertoire. Such studies have found evidence for the existence of hemisphere asymmetries in infancy (Entus, 1977; Molfese, 1977).

Recent studies have found evidence of sex differences in hemisphere specialization and it has been suggested that these differences may be related to the sex differences in spatial and linguistic ability. Evidence from both clinical studies of patients with unilateral brain damage and non-invasive studies of neurologically intact individuals suggest that females are less strongly lateralized than males. Studies of patients with unilateral brain lesions have found that, in adults, males with left-sided lesions experience more frequent and more severe language deficits than males with right-sided lesions or females with either left-or right-sided lesions (McGlone, 1977; 1978). In females, on the other hand, left-and right-sided lesions result in verbal performance decrements equally frequently and these deficits are relatively mild compared to those found in males with left-sided damage (McGlone, 1977). With regard to right hemisphere specialization for spatial processing, similar studies have found evidence that only men show specific nonverbal deficits subsequent to right hemisphere damage (McGlone, 1978;

McGlone & Kertesz, 1973). The results of many studies of normal adults also provide evidence suggesting that both verbal and nonverbal processing appears to be more bilaterally represented in females than in males (Kimura, 1969; Lake & Bryden, 1976; Levy & Reid, 1976; McGlone & Davidson, 1973; Tucker, 1976).

Sex differences in hemisphere specialization have also been observed in children. For example, Witelson (1976) found evidence for right hemisphere specialization for nonverbal and spatial processing in boys but not in girls. Knox and Kimura (1970), on the other hand, found no difference in degree of lateralization for the processing of either verbal or nonverbal material in boys and girls. As is the case with studies of adults, some studies fail to find a sex difference in hemisphere specialization, but in those that do, the evidence suggests that females are less lateralized than males (for a review see Witelson, 1977).

Neuroanatomical studies have found evidence of asymmetries in the brain itself and this finding has led to the speculation that these anatomical asymmetries may be a neural substrate for hemisphere specialization. There is considerable evidence that the planum temporale, an area of the brain known to be of major importance for speech and language, is larger on the left than on the right in both adults (Geschwind & Levitsky, 1968; Wada, Clarke & Hamm, 1975) and in infants (Chi, Dooling & Gilles, 1977; Wada <u>et al</u>, 1975;

Witelson & Pallie, 1973). This asymmetry is recognizable even in fetal brains as early as 31 weeks gestation (Chi *et al*, 1977). One neuroanatomical study has even found some evidence of a sex difference in neuroanatomical asymmetry that is in the same direction as that in functional asymmetry, that is, suggesting greater lateralization in male than female brains (Wada *et al*, 1975).

However, it has yet to be proven that these asymmetries in hemishphere specialization and neuroanatomy are related to each other, or to the sex differences in cognitive abilities, or whether the relationship, if it exists, is a casual one. Thus far, the most direct evidence in support of the notion that sex differences in the function of some neural areas underlie sex differences in cognition stems from studies of rhesus monkeys (Goldman, Crawford, Stokes, Galkin & Rosvold, 1974). In this study Goldman *et al* (1974) found that bilateral lesions of the orbital prefrontal cortex in infancy resulted in impaired performance on a task involving discriminating between objects differing in colour, size and shape. When tested at 2½ months of age the performance of the operated male monkeys was impaired compared to that of the unoperated males. Operated female monkeys, on the other hand, showed no performance decrement compared to unoperated females. This finding indicates that there may be a sex difference in the function of frontal neural tissue, at least at this stage in development. In subsequent studies, male monkeys operated in infancy and tested at 12 months of age were impaired compared to unoperated males and operated females. The operated females however began to show similar impairments by 15 months of age and by 18 months they performed as poorly as the operated males and both sexes were impaired equally compared to their controls. These studies indicate that some relevant factors here are sex and age at testing. Goldman et al (1974) interpret these results as evidence that the functions of the orbital cortex develop earlier in male than in female rhesus monkeys.

Possible Mechanisms Underlying Sex Differences

As the above discussion has indicated a variety of methods of research on both clinical and normal populations of different ages strongly suggest the existence of sex differences in cognitive functioning, and, to a lesser extent, in hemisphere specialization. One study has even found some slight evidence that there may be a sex difference in neuroanatomical asymmetry. The mechanisms determining the manifestation of such differences are as yet unclear and it is still uncertain that these differences are related. As has already been discussed, different rates of physiological maturation and different environmental influences cannot adequately account for the complexity of the evidence.

Genetic Hypothesis

Much recent research has tended to focus on the relationship between various physiological and behavioural variables. It has been suggested that the sex difference in spatial ability has a genetic basis. More specifically, it has been proposed that spatial ability is related to an X-linked recessive gene (Stafford, 1961). The inheritance of recessive genes on the X chromosome follows a distinctive pattern and it is possible to determine whether a given trait has this pattern of inheritance by investigating its distribution among family members, between the sexes, and by demonstrating a lack of transmission from male to male (Childs, 1965). Such a trait will be manifested in all males who carry the gene but only in females who have received the gene from both parents. Since males inherit their X chromosome from their mothers, with respect to X-linked characteristics, they are more like their mothers than their fathers. Fifty percent of males will manifest the characteristic compared to only 25 percent of females. In addition, greater variability will be found among females than males for any characteristic carried by genes on the X chromosome, with females being less frequently represented at the extremes of a distribution.

This difference in variability is easily understandable in terms of basic genetics. In humans, the Y chromosome appears to carry only the genetic information necessary for masculine sexual differentiation while the X chromosome, which is considerably larger, carries genes which are unrelated to sex determination, in addition to those responsible for sexual differentiation. Therefore, in a two allele situation designated by 'A' and 'a', there will be three populations of females (AA, Aa, aa) compared to two populations of males (A and a).

In addition, according to the Lyon hypothesis (Lyon, 1962), very early in embryonic life, any X chromosomes in excess of one are completely, or at least partially, inactiviated. Moreover, in approximately one half of the cells the maternal X is inactivated and in the other half the paternal X is inactivated. All daughter cells of any given cell retain the same active X chromosome. Thus, all normal females are actually mosaics (having two cell lines, derived from a single zygote, which differ in genotype). Since in females three genotypes are possible and they have different active X chromosomes in different cells, the expression of any X-linked trait will be more variable than in males. For the same reasons, more males than females will be found at the extremes of the distribution for any X-linked trait.

Several researchers have studied intrafamilial correlations for spatial ability and found that father-daughter and mother-son correlations were higher than those for father-son and mother-daughter respectively (Bock &

Kolakowski, 1973; Hartlage, 1970; Stafford, 1961). These correlations are consistent with an X-linked recessive mode of inheritance.

Yen (1975) studied sibling correlations and within-sex score distributions on a variety of spatial tests. The correlations among parents and offspring and among offspring were consistent with the X-linkage hypothesis. However, the scores of the females were lower than predicted. This finding was interpreted as evidence that sex-limitation is also occurring and lowering the female scores through either environmental or genetic processes.

However, more recent family studies using a variety of tests of spatial ability have failed to find patterns of family correlations that would clearly indicate X-linkage for spatial ability (DeFries, Johnson, Kuse, McClearn, Polovina, Vandenberg & Wilson, 1979; Loehlin, Sharon & Jacoby, 1978; Guttman & Shohan, 1979).

Goodenough, Gandini, Olkin, Pizzamiglio, Thayer and Witkin (1977) have taken a different approach to the investigation of X-linkage of spatial ability. They have used a genetic paradigm for studying X-linkage that is based on the fact that the characteristics of two gene loci close together on the same chromosome tend to be associated in transmission. Two known marker variables located far apart on the X-chromosome are red-green colour blindness and the Xg blood group (Xg) refers to a red blood cell antigen). Thus by studying the association of these two marker variables with spatial abilities it may be possible to determine if spatial ability is carried by a gene on the X chromosome. Goodenough et al (1977) studied this association in 67 families each having three brothers. In such families there are four possible patterns: 1) all three sons are normal with regard to one or other of the marker variables; 2) all three sons are abnormal; 3) two sons are normal and one is abnormal; 4) two sons are abnormal and one is normal. Only the latter two family patterns can provide any information regarding the association between spatial ability and one or other of the marker variables and therefore about the proposition that the spatial ability is X-linked. The subjects were administered a battery of tests of spatial ability which are known to elicit sex differences. The results of this study suggest that spatial ability is transmitted in association with the Xg locus. Such an association is difficult to account for without appealing to an X-linked model. However, the authors point out that given the small number of informative families these results are merely suggestive and that more studies of this nature would be valuable.

The inconsistency of the findings of the intrafamilial correlation studies and the inconclusiveness of the one study of the association of spatial ability and marker variables clearly indicate that the hypothesis that sex differences in spatial ability are related to an X-linked gene or genes has yet to be proven. These studies have used a wide variety of tests presumed to measure spatial ability and it is possible that these tests tap different cognitive skills or are mediated by different cognitive processes. It may be that 'spatial ability' is too broad a term and it might be profitable to define more precisely the cognitive processes being tested.

Hormonal Hypothesis

If it is the case that spatial ability is not directly related to, or completely determined by, specific genes carried on the X chromosome, it may be that the sex chromosomes exert their influence by determining the hormonal environment in which an organism develops. There is a considerable body of literature which indicates that the presence of steroid hormones during fetal life or during a short period after birth has profound and prolonged effects not only on sexual behaviour but also on many sexually dimorphic behaviours unrelated to reproduction.

In the mammalian embryo, the Y chromosome causes the primordial gonad to develop into testes which then begin to synthesize testosterone. From this point on the development of the reproductive system depends entirely on the hormonal environment of the fetus. The presence of androgens (masculinizing hormones) and an XY chromosome complement results in the differentiation of a normal male. The presence of an XX chromosome complement and the absence of androgen results in a normal female. In the absence of androgen, even if the XY chromosome complement is present, a typically feminine morphology results.

In addition to its effects on morphology, androgen also appears to influence the physiological functioning of the central nervous system as it relates to sexual hormone secretion and behaviour. It is now accepted that androgen affects the hypothalamus, which is responsible for the pattern of gonadotropin release from the anterior pituitary, which in turn is responsible for gonadal hormone secretion. Again it is the presence or absence of androgen that determines whether the hypothalamus differentiates the acyclic pattern of gonadotropin release typical of the male or the cyclic pattern of the female (for a more detailed review see Gorski, 1973; Reinisch, 1976).

The effects of early gonadal hormones on the sexual behaviour of various species of animals at maturity are well documented (Gorski, 1971; 1973; Goy & Goldfoot, 1975; Money & Ehrhardt, 1972; Reinisch, 1974). With animals, research into the effects of steroid hormones in early life on adult sexual behaviour involves various combinations and sequences of gonadectomy and hormone injections. The results of such studies indicate that both the presence and utilization of androgen are essential for the development of sexually normal behaviour in the male and the absence of androgen, rather than the presence of estrogen, for a sexually normal female. Hormonal influences on sexual behaviour are presumably mediated by neural regions which have been influenced by early hormone levels.

These effects of the presence or absence of fetal androgen on neural tissue appear to be irreversible. For example, ovulation in genetic female rats can be permanently suppressed by a single injection of testosterone propionate in the first days of life (Gorski, 1973). Also, neonatally castrated male rats exhibit a high degree of feminine behaviour at maturity that cannot be completely suppressed by testosterone injections (Reinisch, 1974). These two facts strongly support the notion of a critical period during which the neural structures involved in sexual behaviour are extremely sensitive to androgen.

In contrast relatively little work has addressed the issue of hormonal influences on nonsexual behaviour. However, it is known that in rats such sexually dimorphic behaviours as aggression, open-field behaviour, emergence behaviour, running schedules, sleep patterns, avoidance behaviour and threat and play behaviour are affected by early hormone levels (Gorski, 1971; 1973; Reinisch, 1974). In addition, Dennis (1972), in a study of reactivity to electric footshock in neonatally castrated adult male rats and their gonadally intact adult female littermates, observed a relationship between early testosterone levels and the degree of behavioural change subsequent to lesions of the ventromedial hypothalamic nucleus. By birth, male rats are sufficiently masculinized to maintain the typical male pattern of higher thresholds for electric footshock compared to their female littermates, even after neonatal castration. After lesioning, however, the male rats, but not the females, showed significant threshold changes. This finding indicates that the role of the ventromedial hypothalamic nucleus in regulating this behaviour is much greater in males than in females. In addition, neonatally castrated male rats that were not given early testosterone replacement showed a smaller degree of behavioural change than did the neonatally castrated male rats that had been given early testosterone replacement. These results indicate that different levels of testosterone early in life resulted in different degrees of behavioural change in adulthood in response to removal of the same brain tissue.

It is now known that there are sex differences in fetal hormone production in humans as well as in other species. It has recently been found that in humans, the male fetus begins to synthesize testosterone as early as eight to 10 weeks post conception (Siiteri & Wilson, 1974). Male fetal testosterone production peaks between 11 and

17 weeks gestation and some male fetuses have testosterone levels well within the range for normal adult males (Reyes, Boroditsky, Winter & Faiman, 1974). During all stages of gestation male fetuses have significantly higher testosterone levels than do females whose only source of endogenous androgen is from the adrenal gland (Warne, Faiman, Reyes & Winter, 1977). During the period of genital and hypothalamic differentiation (approximately 12 to 20 weeks gestation), male levels are nine times those of females (Reinisch, 1976).

To date, it is still unknown whether female fetuses produce any estrogen. However, on the basis of the large sex difference in fetal testosterone levels during what could well be a critical period, one could speculate that perhaps male gonadal hormones are to some extent responsible for sex differences in human cognitive functioning. It may be that androgens influence the development or function of cortical areas that are involved in cognitive processing and, by this mechanism, underlie the sex differences in human cognition.

Studies of Turner Syndrome

In view of the evidence indicating that sex hormones affect both sexual and nonsexual behaviour in animals, and that there are sex differences in lesion effects in both animals and humans, and in hemisphere specialization in humans, it is reasonable to speculate that, to some extent, sex differences in human behaviour may be hormonally or chromosomally determined. Needless to say, in humans it is impossible to study the effects of chromosomes and hormones on behaviour and neurological development in the systematic experimental manner used with other species. This issue, however, has been approached by studying the behaviour of various clinical populations whose chromosome complement or endocrinological status has in some way been atypical or incongruent. It is within this theoretical framework that hemisphere specialization and level of cognitive abilities will be studied in one such abnormal group, Turner syndrome.

Studies of newborn infants indicate that chromosome abnormalities occur in one half to one percent of the newborn population and that approximately one half of these involve abnormalities of the sex chromosomes (Eller, Frankenberg, Puck & Robinson, 1971; Evans, 1977). It is well documented that the autosomal abnormalities, for example, Down's syndrome which involves trisomy for chromosome 21, almost invariably result in mental retardation and morphological abnormalities of the central nervous system (Polani, 1968; Thompson & Thompson, 1973). The psychological and neurological correlates of sex chromosome abnormalities are not as firmly established but the finding of a much higher incidence of individuals with sex chromosome abnormalities in institutions for the intellectually subnormal or psychiatrically disturbed than in the newborn population suggests that such abnormalities may be associated with various kinds of cognitive disorders (for reviews see Court Brown, 1967; German, 1971; Nielsen, 1969).

The cognitive abilities of individuals with Turner syndrome (TS) (45,X) have been studied more extensively than those of individuals with any other type of sex chromosome abnormality. The chromosome abnormality associated with TS is the absence of one X chromosome or a deletion which almost always involves a portion or all of the short arm of one of the X chromosomes. In addition, approximately 30 percent of individuals with TS have X chromosome mosaicism, that is, different sex chromosome complements in different cell lines. The cause of Turner syndrome is unknown. TS individuals generally have only streak gonads and therefore produce no gonadal hormones. In some cases, however, there may be some estrogen production and some development of secondary characteristics (McDonough, 1972). There are several somatic abnormalities or stigmata such as short stature, various skeletal anomalies, webbing of the neck, coarctation of the aorta and horseshoe kidney that are sometimes associated with this syndrome which occurs approximately once in every 5,000 births (Thompson & Thompson, 1973).

There are three ages at which problems may occur which lead to the diagnosis of TS. At birth, TS individuals may be small for dates (smaller than expected for gestational age), have redundant skin folds at the back and the side of the neck, and dorsal lymphedema of the hands and feet. During middle to late childhood short stature or, less frequently, trouble in school with mathematics may lead to diagnosis. In adolescence TS individuals are often diagnosed because of a failure to develop secondary sex characteristics, and primary amenorrhea. Occasionally TS individuals miss being diagnosed at one of the ages mentioned above and turn up in fertility clinics even later in life.

TS individuals have been raised as normal females and have developed a normal female gender identity (Ehrhardt, Greenberg & Money, 1970; Money & Ehrhardt, 1972; Money & Mittenthal, 1970). At the time when puberty should occur, if the condition has been diagnosed by that time, these girls are routinely given estrogen replacement therapy which results in the development of secondary sex characteristics.

The level and pattern of cognitive abilities in girls with TS has been studied quite extensively. In 1962, Shaffer first proposed a specific cognitive deficit in space-form perception associated with this syndrome. This proposal was based on his finding that the Performance IQ (PIQ) of his subjects was significantly lower than their Verbal IQ (VIQ). This finding has since been replicated many times (Buckley, 1971; Garron, 1977; Garron, Molander, Cronholm & Lindsten, 1973; Kolb & Heaton, 1975; Money, 1964; Money & Alexander, 1966; Netley, 1977; Rovet & Netley, 1979; Silbert, Wolff & Lilienthal, 1977; Waber, 1979). This lowered PIQ has typically resulted in the finding that the Full Scale IQ (FSIQ) is also lower compared to the general population (Buckley, 1971; Garron et al, 1973; Garron, 1977; Waber, 1979). However, even though TS subjects show a pattern of lower PIQ than VIQ and lower FSIQ than either groups of control subjects or the samples on which Wechsler standardized the tests, there is no evidence of an increased incidence of either moderate or severe mental retardation in TS individuals (Garron, 1977; Garron et al, 1973; Money, 1964). The lowered FSIQ is attributable to a shift of the PIQ scores toward the lower end of the normal range, although a normal distribution is maintained, rather than to an overall lowering of intelligence. The VIQ scores for these subjects are normally distributed around the normal mean (Garron, 1977; Money, 1964).

In addition to examining overall IQ levels in TS individuals, many invesigators have also looked at the intelligence test scores in terms of individual subtests and of three factors suggested by Cohen (1957; 1959).

These three factors are based on groupings of the Wechsler Intelligence Test subtests. The Verbal Comprehension factor is based on the Information, Comprehension, Similarities and Vocabulary subtests; the Freedom from Distractibility factor on the Arithmetic and Digit Span subtests; and the Perceptual Organization factor on the Block Design and Object Assembly subtests. Typically the Verbal Comprehension score is significantly higher than the Perceptual Organization score in individuals with TS (Buckley, 1971; Money, 1964; Waber, 1979). The Freedom from Distractibility score which is generally considered to be a measure of numerical ability has also been found to be lower than the Verbal Comprehension score in TS subjects (Money, 1964; Waber, 1979).

One of the limitations involved in these studies is that the scores of TS subjects are generally compared to the test norms or intraindividual comparisons of different scores are made. Only three studies have reported IQ comparisons using normal control groups and in all cases only female controls were used. Silbert <u>et al</u> (1977) matched their 13 TS subjects to normal female controls on the basis of age, race, grade level, socioeconomic status and FSIQ (within six points). The TS subjects in this study achieved a significantly lower PIQ than did the matched control subjects. Garron (1977) tested 67 TS subjects and control subjects matched for age, race, socioeconomic status and years of schooling. He found that the older TS subjects (those 16 years of age and over who were given the Wechsler Adult Scale) compared to their control subjects achieved lower VIQ, PIQ and FSIQ scores as well as lower scores on both the Freedom of Distractibility and the Perceptual Organization factors. The results for the younger TS subjects (those under 16 years of age given the Wechsler Intelligence Scale for Children) compared to their controls were the same as for the older subjects compared to their controls with the exception that in the case of the younger groups there was no difference in VIQ. Garron (1977) also compared IQ results in the younger versus the older subgroups and found no differences in either VIQ or PIQ in the TS or control subjects. Nor was there evidence of any difference between those TS subjects who had a 45,X karyotype and those who were mosaics or had an isochromosome X.

In the third study, Waber (1979) matched 11 TS subjects to normal female control subjects on the basis of chronological age and Cohen's Verbal Comprehension factor and found no differences in the PIQ of the two groups. Also, unexpectedly, she found that the VIQ scores of the TS group were significantly lower than those of the control group. This is surprising in view of the fact that the groups were matched on the Verbal Comprehension factor which is based on four Verbal subtests. Since VIQ was lower in the TS group, it is not surprising that the FSIQ of the TS group was also found to be lower than that of the control group. Both the TS and the control group did, however, have a higher VIQ than PIQ. Both groups also had higher scores on the Verbal Comprehension factor than on the Perceptual Organization factor. However, only the TS group had higher scores on the Verbal Comprehension factor than the Freedom from Distractibility factor. Therefore, one might expect that the two subtests from which the Freedom of Distractibility score is derived (Arithmetic and Digit Span) to be largely responsible for both the lower VIQ and FSIQ in the TS subjects. And in fact, careful examination of the data indicates that this is the case. Waber reports that the TS subjects did have significantly lower scores on the Digit Span subtest and examination of the *t*-values in Waber's tables reveals that the Arithmetic subtest scores were almost significantly lower in the TS group.

It is often stated that TS individuals have a deficit in numerical ability but these statements are based on their generally lowered scores on Cohen's Freedom of Distractibility factor which is based on the Arithmetic and Digit Span subtests. However, when scores on these two subtests are examined separately, one sees that a low Digit Span score is a consistent finding but that only one study has reported lower scores on the Arithmetic subtest, and then only in the adult subjects (Garron, 1977).

A similar situation exists with the Perceptual Organization score (based on the Block Design and Object Assembly subtests). In this case lowered Object Assembly scores are often found among TS subjects but less frequently for the Block Design subtest. Neither Waber (1979) nor Silbert et al (1977) found a difference between TS subjects and control subjects on the Block Design test.

When considering other subtests that are not included in Cohen's factors the findings are even less consistent. The only Verbal subtest, other than Arithmetic and Digit Span, on which TS subjects have been found to have significantly lower scores than normal control subjects is the Comprehension subtest (Garron, 1977). Of the Performance subtests, other than Block Design and Object Assembly, TS subjects have been found to be significantly worse than control subjects on the Digit Symbol or Coding subtest (Garron, 1977; Silbert et al, 1977) and the Picture Completion subtest (Silbert et al, 1977).

Clearly, the intelligence profile of the TS subjects that emerges from these studies is less than definitive. The picture changes slightly from study to study and depending on the group to which the TS subjects are compared.

The inconsistency in these findings has caused many investigators to attempt a more thorough examination of just what it is that TS subjects have difficulty doing. The primary focus of recent research has been the investigation of the spatial deficit in TS individuals. Thus, a variety a tests measuring different aspects of spatial ability have been administered to groups of TS and control subjects. The results of these studies, as with the IQ studies, are by no means definitive. However, most of the evidence would indicate that TS individuals do have a cognitive deficit in spatial ability, or at least some aspects of it. Serra, Pizzamiglio, Boari and Spera (1978) found that TS subjects had a lower level of field independence than matched control groups of fertile and sterile females. Tests of field independence measure the ability to ignore dominant visual cues and to abstract and organize parts from an embedding configuration and are frequently used as a measure of spatial ability. Serra et al (1978) also found that the TS group had lower scores on tests of spatial visualization and orientation compared to the control groups. Alexander and Money (1966) and Money (1973) in a study of the possibility of a deficit in skills mediated by the parietal lobe of the brain, concluded that TS subjects have difficulties with extrapersonal space and form perception and in visual-constructional ability.

The Road Map Test of Direction Sense has been administered to TS subjects, and they have performed less well than normal females (Alexander, Walker & Money, 1964; Waber, 1979). Silbert et al (1977) administered a battery of tests of spatial ability, sensory-motor sequencing, and memory for series of digits and musical patterns. They concluded that the deficit in TS individuals is limited to tasks requiring the integration of spatial elements into wholes and remembering total configurations. They suggest that perhaps this reflects a deficit in cognitive functions typically lateralized to the right cerebral hemisphere.

Waber (1979), on the other hand, interpreted her results as providing no clear evidence of a deficit in spatial ability in TS individuals. She proposes that the problem lies with visual memory regardless of the type of material being processed. Careful examination of Waber's data indicates that these two interpretations may be unwarranted.

First of all, Waber (1979) bases her conclusion that there is no deficit in spatial ability solely on the facts that the scores of the TS group on the Perceptual Organization factor and the Spatial Ability test of the California Mental Maturity Test (which involves reporting whether pictures of hands and feet are of a left or right hand or foot in each case) were not significantly lower than those of the normal control group. However, aside from the Block Design and Object Assembly subtests which are the two tests which comprise the Perceptual Organization factor, the TS group tended to show impaired performance on all of the other Performance IQ subtests.

Waber's (1979) interpretation appears even more unwarranted in view of the fact that she administered several other tests that are considered to be tests of spatial ability, for example; the Road Map Test of Direction Sense, the Rey-Osterrieth Complex Figure Design Copying Test, and a Face Recognition test. On all of these tests the TS group performed significantly less well than the control group. Given all of these findings, it is difficult to understand how Waber can interpret her results as indicating that there is no evidence of a spatial deficit in individuals with TS. Surely, the Perceptual Organization factor and the Spatial Ability test of the California Mental Maturity Test are not the definitive measures of spatial ability.

A similar interpretational difficulty is evident on examination of Waber's (1979) proposal that TS subjects have a visual memory deficit. This hypothesis is based on the lower performance of the TS group on the visual part of the Consonant tri-gram test and the Face Recognition test. In the Consonant tri-gram test, the three letters are presented to the subject either aurally or visually. The subject is then asked to count backwards for zero to 18 seconds before reporting the letters. This methodological condition forces the subject to use visual memory rather than a verbal strategy. In the Face Recognition test the subject is shown photographs of unfamiliar faces and houses, in either an upright or inverted orientation. The subject is then required to select from a pair of photographs the one that had been presented previously. These two tests tap both visual perception and memory. A deficit in this function could account for the impaired performance of the TS group. The TS group differed from the control group only when the photographs were presented in the upright condition. Why the groups did not differ for the inverted condition, which one would intuitively assume to involve as much visual memory as the upright condition, is difficult to understand.

Waber (1979) also attributes the poor performance of the TS group on the Digit Span subtest to a visual memory deficit. This test is composed of two parts. In the first, the subject is asked to repeat increasingly longer series of digits, and in the second, to repeat the series backwards. It was the backwards condition that presented problems for the TS group. It may be that in order to perform this task successfully it is necessary to first visualize the digit series and then to read them off backwards.

The poor performance of the TS group on the Consonant tri-gram test, the upright condition of the Face Recognition test, and the Digit Span test does suggest that TS individuals may have a visual memory deficit. However, these same findings could also be used in support of the notion that TS individuals have a deficit in spatial ability since, by its very nature, vision must involve spatial processing to some extent. It is difficult to imagine how visual memory could be totally divorced from spatial memory. Therefore, Waber's (1979) conclusion that the fundamental problem associated with TS is a specific deficit in visual memory would seem to be premature.

In contrast to spatial abilities, verbal abilities in TS, other than VIQ, have received scant attention. On the basis of the normal distribution of the VIQ scores around the normal mean, and the consistent finding of higher VIQ than PIQ, it has been assumed that TS individuals have normal linguistic abilities. This notion is further supported by the finding of normal ability on a reading test (Alexander & Money, 1965) and a test of verbal comprehension (Serra _et al_, 1978). However, two studies have used a Word Fluency test, which involves generating as many words in a given category as possible within a specified time period, and have found that TS subjects perform poorly compared to control subjects (Money &

Alexander, 1966; Waber, 1979).

The bulk of the evidence suggests that cognitive differences do exist between TS and normal individuals. Certainly a considerable body of information has been gathered regarding this particular syndrome. Of more relevance to the issue of this research, however, is the possibility that sex chromosomes or hormonal variables may underlie individual differences in cognition.

In view of the fact that sex differences have been found in cognitive abilities in normal individuals and the possibility that these differences may be related to a sex difference in pattern of hemisphere specialization, one could speculate that the spatial ability deficit in TS individuals may be related to an atypical pattern of hemisphere specialization. If this is the case, then the study of TS may shed some light on the mechanisms underlying sex differences in patterns of hemisphere specialization in normal individuals.

Only three studies have addressed themselves to this issue and all have examined only left hemisphere specialization for verbal material and all have used the dichotic listening technique and normal female control subjects. Netley (1977) compared 14 TS subjects to 18 normal female subjects, of the same age range and ability, on a verbal dichotic listening task in which the stimuli were spoken digits. On this test most normal subjects would be expected to show a right-ear advantage. Only 16 percent of the normal subjects failed to show the expected right-ear superiority while 57 percent of the TS subjects showed this atypical pattern. This was a significant difference. Netley (1977) suggests, on the basis of this finding, that the absence of an X chromosome is associated with a tendency towards right hemisphere processing of verbal material. Waber (1979) got similar results when she compared 10 TS subjects to 10 matched female control subjects on a dichotic listening test in which the stimuli were consonant-vowel (CV) syllables. In this study, 40 percent of the TS subjects showed a left-ear superiority compared to zero percent of the control group, again a significant difference. Weiss (1976) also found evidence, on the basis of a verbal dichotic listening test, that the functions normally attributed to the left hemisphere are less lateralized in TS subjects.

Clearly the issue of the mechanisms that may underlie sex differences in cognitive abilities and pattern of hemisphere specialization is very complex. There are a number of possible relationships among chromosomes, hormones, neuroanatomy, hemisphere specialization and the level and pattern of cognitive abilities. Since TS individuals have an abnormality of the sex chromosomes and hormones, the investigation of this syndrome may provide some information regarding the mechanisms underlying normal sex differences. Unfortunately such a study cannot provide enough information to disentangle the relative influence of sex chromosomes and sex hormones since TS involves an abnormality of both.

TS individuals differ from both normal males and females in sex chromosome complement. However, they resemble normal males in that both have only one X chromosome and it is the same one in all cells,at least in those TS individuals with a 45,X karyotype. Therefore, one would expect TS individuals to resemble males for any X-linked characteristics. In fact, colour-blindness, which is known to be an X-linked recessive trait, has the same incidence in TS individuals and normal males, that is, higher than in normal females as would be expected for known X-linked traits (Polani, Lessof & Bishop, 1956). If spatial ability is also an X-linked recessive characteristic one would expect TS individuals to resemble males in this respect also, yet there is considerable evidence that they do not. However, the evidence for the X-linkage of spatial ability is equivocal.

In terms of gonadal hormones, TS individuals resemble males with regard to estrogen production. With regard to fetal exposure to maternal estrogens and androgens, TS individuals resemble both males and females. In terms of androgen production, TS individuals most closely resemble normal females.

On the basis of the results of most previous studies of cognitive abilites in individuals with TS, their cognitive pattern could be described as ultra-feminine. Their level of spatial ability appears to be lower than that of normal females which in turn is lower than that of normal males. TS individuals also appear to show an even greater degree of right hemisphere involvement in language functions than do normal females. To date, nothing is known about right hemisphere specialization in TS individuals. Moreover, they have never been compared to normal males on any measure.

The aim of this study is to examine the level and pattern of cognitive abilites and both left and right hemisphere specialization for some verbal and nonverbal stimuli in individuals with TS compared to both normal female and normal male control groups. Theoretically, this investigation will provide information regarding the question of whether sex chromosomes and hormones play a role in sex differences in level and pattern of cognitive abilities and hemisphere specialization in normal individuals.

CHAPTER II

METHOD

Subjects

Eight individuals with Turner syndrome participated in this study. The age range of the subjects was from 11 to 24 years (mean age = 17.9 years, median = 17.2 years, see Appendix A). All of the subjects lived in central Ontario which is the area serviced by the Regional Cytogenetics Laboratory at the McMaster University Medical Centre.

The subjects were selected from the cases of Turner Syndrome that had been karyotyped at the Regional Cytogenetics Laboratory. Initially an attempt was made to recruit an adequately sized sample from among those individuals with a 45,X karyotype. This, however, proved to be impossible. The first step in subject recruitment involved receiving the permission of the individual physicians involved in these cases to contact their patients. Of the sixteen 45,X patients on file, such permission was denied in five cases. In these particular cases the physician agreed to contact the patients, but the patients themselves refused to participate. Of the remaining 11 possible subjects, four could not be located. Of the seven patients actually contacted by the author two refused to participate. Thus, five of a possible 16 (31.25%) patients with

45,X karyotype were recruited.

In order to increase the sample size, an identical procedure was followed with patients having TS as a result of deletion of the short arm and duplication of the long arm of one X chromosome (isochromosome X). A total of 13 such patients were on file with the Cytogenetics Laboratory. Eight of these patients were excluded as possible subjects because their chronological age was too far outside the range of the five subjects already recruited, or because they had an inappropriate karyotype. Of the remaining five isochromosome X patients, one could not be located and one refused to participate. Thus, a total of eight TS subjects were tested. Five of the subjects had a 45,X karyotype. Two subjects had an isochromosome X, the karyotype being 46,X,i(Xq) which indicates the presence of 46 chromosomes, one being a normal X and the other being an isochromosome X. The last patient was a mosaic with karyotype 46,X,i(Xq)/45,X indicating that in some cells both a normal X and an isochromosome X were present and in other cells only one X chromosome was present.

At the time of testing five of the subjects were receiving estrogen replacement therapy, one began estrogen therapy halfway through the testing and two were too young to require estrogen replacement.

A group of 40 potential control subjects (20 females and 20 males) was recruited from grades 12 and 13 of a suburban Hamilton Catholic High School. Right handed students with grade averages between 55 and 75 were asked by the Guidance Counsellor to volunteer to participate in the study. This range of grades was selected since a pool of potential control subjects was required whose intelligence would be similar to that of the TS subjects, that is, neither very high nor very low. Only those students whose parents signed a Consent Form were tested. The female control subjects ranged in age from 16 to 18 years (mean = 17.6, median = 17.8). The ages of the male control subjects ranged from 16 to 19 years (mean = 17.8, median = 17.5).

After some preliminary testing, the eight girls and the eight boys whose intelligence most closely matched that of the TS subjects were selected for further testing.

Medical Information

The karyotypes of all the TS subjects who agreed to participate in the study were made available by the Regional Cytogenetics Laboratory (see Appendix A). Karyotyping was done using white blood cells and, in cases of suspected mosaiciam, skin fibroblasts. In addition, information regarding the medical treatment of these subjects was obtained from their individual physicians.

Handedness

The preferred hand of each subject was initially checked by noting the hand with which the subject wrote. As a more sensitive measure of handedness, the Annett Handedness Questionnaire as modified by Briggs and Nebes (1975) was also administered. The subjects were given a list of 12 common activites, such as brushing teeth, and asked to indicate for each one whether they always used their right hand, usually used their right hand, had no preference, usually used their left hand or always used their left hand.

Although a sample consisting of only right handed subjects would have been desirable, the one left handed TS subject was not excluded in view of the small sample size.

Materials

Intelligence Tests

The age appropriate Wechsler Intelligence Scale was administered to all subjects -- the Wechsler Intelligence Scale for Children (WISC) (Wechsler, 1949) to those subjects under 16 years of age and the Wechsler Adult Intelligence Scale (WAIS) (Wechsler, 1955) to those 16 years of age and over. Both of these tests are scaled for age, allowing for the comparison of the IQ scores of individuals of different ages. The Wechsler Intelligence Scales are composed of several subtests which yield a Verbal IQ, a Performance IQ and a Full Scale IQ.

The Verbal subtests are: Information; Comprehension; Arithmetic; Similarities; Vocabulary and Digit Span. On the WISC the Digit Span subtest is optional and is not used in the calculation of IQs, but for the purpose of this study it was administered as an additional test. The Performance subtests are: Picture Completion; Picture Arrangement; Block Design; Object Assembly and Digit Symbol (called Coding on the WISC). The WISC also includes an optional Mazes subtest which was not used in this study. The recommended order of administration of the Performance subtests of the WISC and WAIS is slightly different and for both tests the recommended order was used.

Tests of Hemisphere Specialization

Four tests to investigate hemisphere specialization were used in this study, a nonverbal and a verbal test in each of the auditory and haptic modalities. These tests consisted of two dichotic tape recordings in which two different stimuli are presented simultaneously to the two ears, and two dichhaptic tests in which the subject's hands simultaneously feel two different shapes.

Auditory Tests

Since individuals with Turner syndrome are reported to have an increased incidence of hearing impairment (Andersen, Filipsson, Fluur, Koch, Lindsten and Wedenberg, 1969) the subjects were first screened for pure tone hearing thresholds.

For those subjects whose thresholds were above the normal range or whose thresholds for the two ears differed by 5 dB or more on three or more of the seven frequencies tested, the volume at which the dichotic tapes were presented was adjusted accordingly.

Volume adjustments were done by establishing a comfortable listening level for the ear with the highest threshold and then adjusting the volume to the other ear until the subject reported that the sound seemed to be localized in the centre of the head, which was interpreted as indicating equal perception in each ear. The 1,000 Hz tones at the beginning of each tape were used for these adjustments.

Volume adjustments were necessary for four of the TS subjects but for none of the control subjects. Three TS subjects required adjustments for both of the dichotic listening tests and one for only the dichotic Melodies test which was presented at a lower intensity than the dichotic CV test. After adjustments were made, the volume settings used for each subject were measured to determine the intensity at which the stimuli on each channel were delivered. Although this method of adjustment depended on each subject's judgment of sound localization, the two subjects who had a bilateral but equal hearing impairment and who therefore required only a volume increase, balanced the two channels to within 2 dB in one case and to within 4 dB in the other. For the two subjects whose hearing was unequal in the two ears the volume to the two ears was rebalanced until the subjects reported that the sound seemed to come from the centre of the head. The difference between the two channels never exceeded 10 dB and the tapes were never presented at more than 80 dB for any subject.

On the verbal dichotic tape the stimuli used were six naturally voiced consonant-vowel (CV) syllables: pa; ta; ka; ba; da; ga. These stimuli were of approximately 400 milliseconds duration. The test consisted of 60 trials in which two different syllables were presented simultaneously to the subject's two ears.[1] After each pair the subject was required to report verbally the two syllables that had just been heard. This tape was constructed so that each syllable was paired with each other syllable an equal number of times and occurred on each channel an equal number of times. After 30 trials, the earphones were reversed for each subject and the same 30 trials were repeated.

Before beginning this test each subject was given several monaural practice trials for each ear in order to be

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1. This tape was made at the Kresge Hearing Research Laboratory of the South and was courteously furnished to S. Witelson by C.I. Berlin.

certain that the syllables could be accurately discriminated. Monaural practice was discontinued for each ear after each subject had correctly reported each syllable. The number of practice trials varied among the subjects. In addition, each subject was given several trials of dichotic practice. Dichotic practice continued until the subject reported two syllables after each trial for at least five trials, with at least some of them being correct.

The stimuli used on the nonverbal dichotic tape were solo violin melodies taken from Gordon's Musical Aptitude Profile (1965). Two different melodies of 2 seconds duration were presented simultaneously, one to each ear. After a 5 second interval the dichotic pair was followed by a binaurally presented recognition stimulus also of 2 seconds duration. The test consisted of 48 such trials.[2] Each dichotic pair was preceded by a spoken digit which served as a ready signal for the subject and which also identified the next stimulus pair. After each binaural recognition stimulus the subjects responded by placing a check mark in either the YES or NO column of a record form according to whether they thought the recognition stimulus was a member of the preceding dichotic pair. On one half of the trials the recognition stimulus was neutral, that is, it had not been a member of the dichotic pair, on

2. This tape was made at the University of Victoria and was kindly supplied to S. Witelson by O. Spreen.

one quarter the recognition stimulus had been presented to the right ear and on the remaining quarter it had been presented to the left ear. The position of the earphones was counterbalanced across subjects.

These tapes were presented on either a Tandberg 1200X tape recorder with Sharpe HA 10MKII earphones, or on an Akai GX365 or Technics RS-1500US stereophonic tape recorder with TDH-39 earphones. Three different tape recorders were used due to difficulties in scheduling time in the available laboratories. The Tandberg tape recorder and Sharpe earphones were used for those TS subjects tested at the Chedoke-McMaster Child and Family Centre and, because the Tandberg is relatively portable, for those subjects tested in their homes. The Akai tape recorder and TDH-39 earphones were used for those TS subjects tested at the McMaster University Medical Centre. For all control subjects, who were tested in their school, the Technics tape recorder and TDH-39 earphones were used.

The beginning of each tape recording contained 1,000 Hz tones that were used as reference calibration signals. The tape recordings were calibrated for use with each combination of tape recorder and earphones using a B&K Sound Level Meter. For the dichotic CV tape, the output at the level of the earphones was set at a sound pressure level of 70 dB, except for those subjects whose hearing necessitated a volume adjustment. This intensity was selected because it is the one that has most frequently been used in other studies. The dichotic Melodies tape was presented at a sound pressure level of 50 dB, again, except when a volume adjustment was necessary. This tape was presented at 50 dB because it is at this intensity that the largest differences between ears are observed. (Spreen, Spellacy & Reid, 1970).

Haptic Tests

Both of the dichhaptic tests are adaptations of existing tests which were originally designed for use with children. The original tests were altered in such a way as to make them appropriate for use with older subjects. Before being administered to the TS subjects, pilot testing was done with groups of male and female volunteers from McMaster University and Mohawk College.

The dichhaptic Shapes test used in this study was a modification of that originally devised by Witelson (1974) as a test of right hemisphere specialization. Since the test was originally designed for use with children, and most of the subjects who participated in this study were older than those in Witelson's (1974) study, the original test was made more difficult. The test was also made longer in order to obtain a larger sample of the behaviour being investigated. This test required the subject to feel simultaneously two different nonsense shapes which could not readily be labelled, one with each hand. After feeling the two shapes the subject was shown a display of six shapes and was asked to point, with the left hand, to the shapes that had just been felt (the target shapes). The shapes were felt, out of view for 5 seconds, using the index and middle fingers of each hand. The 5 second presentation was followed by a 5 second delay after which a display of six shapes was presented.

In a further attempt to prevent the possibility of the subjects using a verbal strategy, a verbal interference condition was used. Before presentation of the two shapes, the subjects were told to perform aloud some simple verbalizations such as repeating their own name, counting, or spelling a familiar word such as 'Mississippi'. These verbalizations then continued throughout the 5 second presentation and the 5 second delay.

Before administration of the actual test, the subjects were given four practice trials. The test itself consisted of 20 trials with each of 10 pairs of target shapes (see Appendix B) being presented twice so that each shape was felt by each hand. A different verbal interference condition was used with each of the 20 trials. The six shapes on the recognition display card for any given trial consisted of the two target shapes, two other shapes which were used as targets in other trials, and two distractor shapes which were never used as targets. The shapes were arranged on the display cards in a staggered circular fashion (see Appendix C) and each target shape occurred in each position an equal number of times. The shapes were approximately one and one quarter inches square and were cut from one eighth inch thick styrofoam.

A similar strategy was used to test left hemisphere specialization. The dichhaptic Words test used in this study was an adaption of that designed by Khadem (1977). The stimuli used in this test were plastic upper case letters forming pairs of three letter words. Two letters, one from each word, were presented simultaneously so that the subject would first feel the first letters of each word, one with each hand, then the second letters and then the third letters. That is, one hand would feel the first, then the second and then the third letters of one word while the other hand simultaneously felt, in sequence, the three letters of the other word. The same letter never occurred in both words. In this case only the index fingers were used since the letters were somewhat smaller than the shapes (one inch high and three quarters of an inch wide) and the use of two fingers caused the subjects to miss internal details which were essential to the identification of the letters. These letters were one quarter inch thick.

Each letter was felt for 3 seconds. After feeling all of the letters, the subject was shown a display card containing six words printed in upper case letters, the same size as the plastic letters they had felt, and asked to say which were the target words. The recognition display was composed of the two target words and four distractors. Two of the distractors began with the same letters as the target words and two ended with the same letters as the target words. The middle letters of the distractors were never the same as the middle letters of either target word. As with the Shapes test, each target word appeared in each position an equal number of times. The test consisted of 10 trials, preceded by four practice trials, with each word being presented to each hand.

Tests of Spatial Ability

The Space Relations subtest (Form T) of the Differential Aptitude Tests (DAT) (Bennet, Seashore and Wesman, 1973) was administered to each subject. This test is designed to measure the ability to visualize a three dimensional object from a two dimensional pattern and then to imagine it rotated in space (see Appendix D). The subject is given 25 minutes to do as many of 60 questions as possible. This test was designed for use with individuals in Grade 8 or above but in this study it was given to the two youngest subjects as well. These two subjects were both in Grade 6 at the time they were tested. However, these subjects were also given the Scientific Research Associates (SRA) Spatial Relations subtest (Thurstone, 1962) appropriate for their grade. This test consists of 30 questions in which the subject must recognize geometric figures which have been rotated. The subject is asked to complete as many questions as possible in seven minutes.

The Road-Map Test of Direction Sense (Money, Alexander and Walker, 1965) was also done by each subject. This test requires the subject to follow a route marked on a map and to indicate at each turn whether he would turn to his right or his left. Turning of the map was not allowed. The score on this test was the number of errors. The time taken to complete the test was scored as an additional measure since Tapley and Bryden (1977) have reported a sex difference using this measure in normal adult males and females.

The Draw-a-Man Test (Harris, 1963) which is untimed, was also administered to each subject. This test simply consists of asking the subject to draw a man and was given as a measure of visual memory and because it involves production of a drawing.

Tests of Linguistic and Mathematical Ability

The Reading subtest of the Wide Range Achievement Test (WRAT) (Jastak & Jastak, 1965) was administered to all subjects. Like the Wechsler Intelligence Scales, the WRAT is provided at two levels designed for use with individuals under 12 years of age and for those 12 years of age and over. The test scores are also scaled for age so that scores can be compared over a wide age range. The WRAT Reading subtest involves reading aloud, with correct pronunciation, a list of words of increasing difficulty. The subject is allowed 10 seconds for each word. The test is discontinued when the subject has made 12 consecutive errors.

The Reading of Symbols subtest of G-F-W Sound Symbols Tests (Goldman, Fristoe and Woodstock, 1974) required the subject to read 70 nonsense words ranging from one to three syllables in length and containing all the major spelling combinations found in the English language. The test was designed to measure the ability to read phonetically.

The Word Fluency Test from the SRA Primary Mental Abilities Test for ages 11-17 (Thurstone and Thurstone, 1947) was also done by each subject. On this test the subject is told to write as many words that begin with the letter 's' as he can think of in 5 minutes.

The WRAT Arithmetic subtest was also included in the test battery. This test simply requires the subject to complete as many written computations as possible within 10 minutes.

Procedure

Each Turner Syndrome subject was tested individually. Seven of the eight TS subjects were tested in two separate sessions, each of about 3 hours duration. One subject required a third session. Four of the subjects who lived farthest from McMaster University were tested in their homes and the others were tested either at the McMaster University Medical Centre or at the Chedoke-McMaster Child and Family Centre. At the beginning of the first testing session the subject or the subject's mother signed a Consent Form and a Release of Information Form. The following tests were administered during the first session: audiological screening; dichhaptic Shapes test; Wechsler Intelligence Scale; the dichotic Melodies test; Road-Map Test of Direction Sense; and the SRA Word Fluency Test. During the second session the subjects did the WRAT Reading and Arithmetic subtests, the dichotic CV test, the dichhaptic Words test, the DAT Space Relations test, the Draw-a-Man Test, the PMA Spatial Relations subtest (only in the case of the two youngest subjects), the G-F-W Reading of Symbols Test and finally the handedness questionnaire. The tests were given in the same order to all of the TS subjects. All of the standardized tests were given in accordance with the instructions in their respective manuals. The dichhaptic Shapes test was given before the dichhaptic Words test because Witelson (1974) observed a stronger left-hand advantage when shapes were administered before letters.

The order of testing varied somewhat for the control subjects. Since two of the tests in the battery -- the dichhaptic Shapes and Words tests -- had been used relatively little in precisely the form used in this study it was necessary to administer these tests to a fairly large control group. Initially, therefore, these two tests were administered to all 40 potential control subjects. They were administered in the same order as to the TS subjects, that is, Shapes first. At the same time, all 40 subjects were also given the handedness questionnaire in order to verify handedness, which at this point was known only by self report, and a short form of the WAIS so that a smaller sample could be selected which was matched for intelligence with the TS subjects. The short form of the WAIS consisted of three Verbal subtests, Comprehension, Similarities, and Vocabulary, and two Performance subtests, Block Design and Object Assembly. These subtests are the ones most highly correlated with Verbal and Performance IQ respectively (Wechsler, 1955).

In order to select matched controls, the mean Scaled Score for the three Verbal subtests and the mean Scaled Score for the two Performance subtests were calculated for each of the 40 control subjects and each of the Turner Syndrome subjects. Then, the one female and the one male control subject who were most closely matched to each TS subject were selected. Priority was given to the Verbal match since the existing literature indicates that TS individuals do not have lower Verbal IQ scores, but do show indications of lower Performance IQ scores, compared to normal females. However, since the range of Performance IQ scores overlapped considerably between the TS subjects and the two groups of control subjects, it seemed reasonable to match for Performance IQ also. This comparison is different from that made in all previous studies and allows the investigation of the degree of the spatial deficit in TS subjects compared to control groups with similar Performance IQ scores. It was possible to match the mean Verbal score within two points for the female controls and within one point for the male controls. For the Performance score, matching was within three points for the female controls and within four points for the male controls.

Thus, for each TS subject there was one matched female control subject and one matched male control subject. The matched female controls were 16 to 18 years of age (mean = 17.5, median = 17.4) and the matched male controls were 17 to 19 years of age (mean = 18.1, median = 17.9).

Two of the matched control subjects, a boy and a girl, had originally been left handed but at an early age had switched to right hand preference. This was fortuitous since one of the TS subjects was also left handed.

The two matched control groups each consisting of eight subjects, then performed the remainder of the test battery including those subtests of the WAIS which had not yet been done. Time constraints and scheduling difficulties made it impossible to preserve the same order of testing as that used with the TS subjects. However the original testing order was maintained as far as possible and the four tests of hemisphere specialization were given in the same order as to the TS subjects. Most of the testing of the control subjects was done individually but some of the tests which did not demand individual testing were administered to groups of two to three subjects at a time. These tests were the DAT Space Relations subtests, the WRAT Arithmetic subtest, the SRA Word Fluency Test, and the Draw-a-Man Test.

CHAPTER III

RESULTS

Hemisphere Specialization

The scores for each of the four tests of hemisphere specialization were the number of stimulus items correctly identified for each sensory field. Tests of significance for differences in sample variances were done in all cases in which the variances may have been different. None of the differences were found to be significant. Thus for each test a two-factor mixed-design analysis of variance was performed with Group as the between subjects variable (the three groups being Turner syndrome subjects (TS), normal matched females (NMF) and normal matched males (NMM), and Sensory Field (left versus right) as the within subject variable. Results were considered significant only if the probability was .05 or less. However, if the probability was .2 or less, it has been indicated in the Tables for the purpose of giving a more complete picture and indicating trends.

The mean accuracy scores and standard deviations for the dichotic CV test are presented in Table 1. Analysis of variance for this test showed no main effects for Group or Ear which indicates that the three groups did not differ in total (left plus right) accuracy and that there was no overall difference in accuracy between the two ears. The Group by Ear interaction was not significant, indicating that the relationship between left- and right-ear scores

TABLE 1

Mean Accuracy Scores and Standard Deviations for the Dichotic CV Test

Group	Ear					
	Left		Right		Total	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
TS (n=8)	34.6	10.3	32.0	9.8	66.6	11.9
NMF (n=8)	34.8	4.9	37.0	7.6	71.8	10.5
NMM (n=8)	31.6	4.8	36.6	6.3	68.3	7.6

Maximum possible score for each ear is 60.

Summary of Analysis of Variance

Main factors and interaction terms:

Group	F = 0.53	df = 2/21	p = NS
Ear	F = 0.44	df = 1/21	p = NS
Group x Ear	F = 0.92	df = 2/21	p = NS

did not differ among the groups. A right-ear advantage was expected on this test. The lack of a significant ear effect was unexpected but may be attributable to small differences between the groups which, although insignificant, may have been large enough to eliminate an overall ear effect. However, both the NMF group and the NMM group showed a tendency toward the expected right-ear superiority while the TS group showed a tendency toward a left-ear superiority. In order to test whether the control subjects by themselves would yield the expected significant right-ear advantage, a t-test for related measures was done for the right-versus left-ear accuracy scores of the two control groups combined (n=16, mean left-ear score = 33.2, mean right-ear score = 36.2). This combined group did show a small but significant right-ear advantage ($t = 1.88$, $p < .05$, one-tailed test).

If one looks at the proportion of individuals in each group who had a larger right- than left-ear score, one sees that the majority of subjects in both normal control groups showed a right-ear advantage (75% and 62.5% for the NMF and NMM groups, respectively). In contrast only 25% of the TS group showed a right-ear advantage on this test. In order to assess these differences χ^2 tests were performed on these data and were not significant even at the 0.1 level for the TS versus the NMF group ($\chi^2 = 2.25$, $p < .2$) or for the TS group versus the two normal groups combined ($\chi^2 = 2.54$, $p = <.2$). There was very little difference for the TS versus the NMM comparison.

In view of the small sample size (n=8), the lack of a significant right-ear advantage in each of the two control groups, and the absence of significant differences between the TS group and the normal subjects, the above results must be interpreted with caution. The possibility that individuals with Turner syndrome may more frequently have an atypical pattern of hemisphere specialization in respect to some aspects of cognitive processing compared to normal subjects appears worthy of consideration. On the basis of the consistency of the distribution results of this study with those of similar studies by Netley (1977) and Waber (1979), both of which showed a significantly more frequent left-ear advantage in TS subjects compared to normal females (40% vs 0%, n = 14; and 57% vs 16%, n = 10, respectively; see Table 2), it might be fruitful to consider the hypothesis that this atypical pattern of ear advantage may reflect a tendency toward a more frequent, or greater than normal, participation of the right hemisphere in the processing of at least some aspects of speech and language in individuals with Turner syndrome.

TABLE 2

Verbal Dichotic Listening: A Comparison of Ear Advantages in Studies of Turner Syndrome Subjects and Control Subjects

	Turner Syndrome				Control Subjects				
	Ear Advantage (% of Cases)				Ear Advantage (% of Cases)				
	N	R>L	L>R	R=L	N	Sex	R>L	L>R	R=L
Netley (1977)	14	43	57	0	18	F	67	16.5	16.5
Waber (1979)	10	60	40	0	10	F	100	0	0
Swallow (1980)	8	25	75	0	8	F	75	25	0
					8	M	62.5	25	12.5

For the dichotic Melodies test (see Table 3) a similar analysis of variance showed no main effect for Group, indicating that, on this test too, the groups did not differ in overall accuracy. There was a significant main effect for Ear which indicates a left ear superiority on this task for all groups combined. The Group by Ear interaction was also significant indicating that group or sex is relevant to the relationship between left- and right-ear scores. Individual comparisons using the Duncan Multiple Range Test (Duncan, 1955) showed that for the NMF group the mean left-ear score was significantly greater than the mean right-ear score ($p < .05$, $df = 20$). The ear difference was not significant for the NMM or the TS group. A t-test for related measures for the two normal control groups combined, as with the CV test, ($n = 16$, mean left-ear score = 9.8, mean right-ear score = 8.3) did not show the expected significant left-ear advantage ($t = 1.39$, $p < .2$, one-tailed test).

The percentage of each group showing a left-ear advantage for this test was also examined (100%, 62.5% and 62.5% for the NMF, NMM and TS groups respectively). χ^2 tests performed on these data were not significant for any comparison. This suggests that, in terms of the frequency of a particular pattern of hemisphere specialization for the processing of such nonlinguistic material, the TS group does not differ from either control group.

TABLE 3

Mean Accuracy Scores and Standard Deviations for the Dichotic Melodies Test

Group	Ear					
	Left		Right		Total	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
TS (n=8)	9.6	2.3	7.1	2.8	16.8	3.5
NMF (n=8)	10.9	1.1	7.0	2.7	17.9	3.1
NMM (n=8)	8.8	2.9	9.6	2.2	18.4	2.8

Maximum possible socre for each ear is 12

Summary of Analysis of Variance

Main factors and interaction terms:

Group	F = 0.56	df = 2/21	p = NS
Ear	F = 6.01	df = 1/21	$p < .025$
Group x Ear	F = 3.56	df = 2/21	$p < .05$

To further assess any possible differences in hemisphere specialization among the three groups on these two tests, χ^2 tests were performed for each group on the number of individuals showing a right- or left-ear superiority on the dichotic CV test versus a right- or left-ear advantage on the dichotic Melodies test. Thus, χ^2 tests for paired samples were performed for each group separately. The χ^2 for the NMF group just failed to reach significance at the .05 level ($\chi^2 = 3.63$, $p < .1$) indicating that a right-ear advantage occurred more frequently on the CV test than on the Melodies test and, conversely, that a left-ear superiority occurred more frequently on the Melodies than on the CV test but not significantly so. Such a reversal of ear advantage on the two tests did not even approach significance for the NMM or the TS group ($\chi^2 = 1.25$, p = NS and .625, p = NS, respectively).

Analysis of variance similar to that done for the two dichotic listening tests was done for the dichhaptic Shapes test and the dichhaptic Words test. Mean hand scores and standard deviations for these two tests are presented in Tables 4 and 4a. No significant main effects or interactions were found for either test. Although it was not significant, a trend toward lower overall accuracy for the TS group was observed on the Shapes test.

TABLE 4

Mean Accuracy Scores and Standard Deviations for the Dichhaptic Shapes Test

Group	Hand					
	Left		Right		Total	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
TS (n=8)	9.4	2.7	8.4	1.8	17.8	3.4
NMF (n=8)	10.5	2.2	10.0	1.9	20.5	2.4
NMM (n=8)	10.5	2.6	10.0	2.0	20.5	4.1

Maximum possible score for each hand is 20

Summary of Analysis of Variance

Main factors and interaction terms:

Group	$F = 1.75$	$df = 2/21$	$p < .2$
Hand	$F = 1.31$	$df = 1/21$	$p = NS$
Group x Hand	$F = 0.08$	$df = 2/21$	$p = NS$

TABLE 4a

Mean Accuracy Scores and Standard Deviations for the Dichhaptic Words Test

Group	Hand					
	Left		Right		Total	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
TS (n=8)	7.3	1.5	7.8	1.4	15.0	2.6
NMF (n=8)	7.6	1.4	8.0	2.8	15.6	4.1
NMM (n=8)	8.1	1.5	7.8	1.7	15.9	2.7

Maximum possible score for each hand is 10

<u>Summary of Analysis of Variance</u>

Main factors and interaction terms:

Group	F = 0.16	df = 2/21	p = NS
Hand	F = 0.29	df = 1/21	p = NS
Group x Hand	F = 0.79	df = 2/21	p = NS

It was hoped that these tests would elicit more consistent left- and right-hand advantages respectively in these young adults than did the original versions when administered to adults. Initial pilot testing suggested that this would be the case but unfortunately it was not. These tests were given to larger groups of 20 males and 20 females which included the 16 matched control subjects. However, this testing could only be done concurrently with the testing of the TS subjects so further adaptations of the tests for the present study were impossible. Although these results shed little light on hemisphere specialization for cognitive processing, they do indicate that the performance of the TS group does not differ either in overall accuracy or left- and right-hand performance compared to normal controls.

Level of Cognitive Ability

For all tests of cognitive abilities, tests of significance for differences in sample variances were done. When the variances were equal, a one-way analysis of variance was performed on the data. In those cases in which the variances were found to be different (Similarities, Vocabulary, Picture Arrangement and Digit Symbol subtests of the IQ test, Word Fluency test and WRAT Arithmetic subtest) the logarithmic transformation was applied. If this transformation equalized the variances, a one-way analysis of variance was performed on the transformed data (Picture Arrangement and Word Fluency). When the variances were still unequal, a nonparametric test, the Kruskal-Wallis one-way analysis of variance by ranks (Siegel, 1965), was performed on the untransformed data (Similarities, Vocabulary, Digit Symbol and WRAT Arithmetic). The Kruskal-Wallis test yields the H statistic.

Intelligence Tests

Since control subjects were selected who were matched to the TS subjects on three Verbal subtests (Comprehension, Similarities and Vocabulary) and two Performance subtests (Block Design and Object Assembly), differences in overall IQ scores were not expected. One-way analysis of variance performed separately on the Verbal, Performance and Full Scale IQ scores for the three groups failed to reveal any differences on any score (see Table 5). However, given that the groups were matched on only five of 11 subtests, differences among the groups may exist on those subtests for which the subjects were not matched. Accordingly the appropriate one-way analysis of variance was performed on the Scaled Scores of the three groups for each of these subtests (see Table 5). Only on the Digit Symbol subtest did the groups differ significantly. The Wilcoxin test for two matched samples showed that the TS group performed significantly less well than the NMF group ($p < .02$, two-tailed

TABLE 5

IQ Tests

Mean Scaled Scores and Standard Deviations

	TS		NMF		NMM		F	H	P
	Mean	S.D.	Mean	S.D.	Mean	S.D.			
Full Scale IQ	98.5	9.9	106.9	6.5	104.1	9.6	1.86		p< .2
Verbal IQ	100.9	11.5	107.1	9.0	107.3	8.5	1.12		NS
Performance IQ	96.0	7.3	105.8	10.3	99.1	12.1	1.95		p< .2
Verbal Subtests									
Information	10.4	3.4	10.3	2.4	11.3	2.2	0.23		NS
Comprehension	9.8	3.0	10.1	1.9	10.0	1.6	0.06		NS
Arithmetic	7.8	2.7	9.6	2.2	10.3	2.5	2.32		p< .2
Similarities	11.3	3.7	11.9	1.3	10.8	2.0	——	1.36	NS
Vocabulary	10.9	0.8	10.3	2.9	10.6	2.3	——	1.66	NS
Digit Span	8.6	2.4	10.0	2.5	10.8	3.1	1.29		NS
Performance Subtests									
Picture Completion	8.6	1.9	9.6	1.2	10.5	3.5	1.24		NS
Picture Arrangement	10.1	0.8	10.8	3.4	9.9	1.6	0.17**		NS
Block Design	10.1	3.0	9.0	2.0	8.0	1.9	1.65		NS
Object Assembly	8.4	2.1	10.4	3.4	9.6	2.1	1.94		p< .2
Digit Symbol/Coding	9.6	0.7	13.5	2.5	10.5	2.4	——	8.73	p< .005

F = value of F-statistic for one-way analysis of variance
df for each analysis of variance = 2/21
H = H-statistic for the Kruskal-Wallis test
p = probability level
** = logarithmic transformation applied

test). They did not, however, differ from the NMM group. Nor was there any difference between the two control groups.

Tests of Spatial Ability

Mean scores and standard deviations for all the tests of spatial ability are presented in Table 6.

One-way analysis of variance of the raw scores of the three groups on the DAT Space Relations test indicates that the groups do not differ in overall accuracy. In terms of the raw scores, the NMF and NMM groups are nearly identical, while the TS group scored approximately eight points lower. Since the percentile scores for this test are standardized for males and females separately, the percentile scores were also analyzed, using the female norms for the TS group. Again, there was no significant difference among the groups. The mean percentile score for the NMM group was approximately 10 points lower than the mean percentile of the NMF group which, although it was not significant, was unexpected.

The lack of significant differences among the three groups was somewhat surprising in view of the facts that (1) this particular test generally elicits a sex difference, with males scoring higher than females, and (2) that TS individuals are presumed to have particular difficulty with this type of cognitive task.

TABLE 6

Tests of Spatial Ability

Mean Scores and Standard Deviations

Test	TS		NMF		NMM			
	Mean	S.D.	Mean	S.D.	Mean	S.D.	F	P
Space Relations								
Raw Score	24.6	5.8	33.1	7.1	32.5	12.6	2.21	$p<.2$
Percentile	46.3	25.0	58.1	16.5	47.3	28.2	0.61	NS
Percent correct of questions attempted	59.4	16.9	60.1	13.1	59.8	23.7	0.003	NS
Number attempted	43.6	13.5	56.0	8.6	55.5	7.8	3.67	$p<.5$
Road Map Test of Direction Sense								
Time	170.9	72.4	121.6	46.9	127.1	43.8	1.87	$p<.2$
Errors	5.3	6.3	3.1	3.5	4.1	5.2	0.34	NS
Draw-a-Man Test								
Standard Score	99.9	9.5	105.0	15.3	94.4	12.5	1.41	NS

F = value of F-statistic for one-way analysis of variance
df for each analysis of variance = 2/21
p = probability level

During the course of administering this test it was noted that only one TS subject answered all of the questions within the 25 minutes allowed for the test, but that many of the NMF and NMM subjects (six and five respectively) completed the test well within the allotted time. Accordingly, the percentage of correct responses for the number of questions attempted was analysed, and in this respect the three groups were nearly identical, with each group correctly answering approximately 60% of the questions attempted.

However, analysis of the number of questions attempted regardless of accuracy did reveal significant differences among the groups. Individual comparisons using the Duncan Multiple Range Test showed that the TS group attempted significantly fewer questions than either the NMF group ($p < .05$, $df = 20$) or the NMM group ($p < .05$, $df = 20$). This result is somewhat puzzling. Since the TS group attempted significantly fewer questions than either control group, but correctly answered the same percentage of those attempted, one would have expected the total number correct (raw score) to be lower for the TS group. But analysis of variance of the raw scores was not significant. However, as indicated above, there was definitely a trend toward lower raw scores for the TS group. Although it is impossible to conclude that the TS group performs less accurately, it is clear that they do perform this test more slowly than the control subjects.

Similar analysis was done for the Road Map Test of Direction Sense. Although the TS group did make a few more errors and did take approximately 50 seconds longer to complete the test than either control group, no significant differences were found for either the number of errors or the time taken to complete the test. Again, this lack of difference was unexpected in view of the existing literature.

Analysis of the Standard Scores for the Draw-a-Man Test also failed to reveal any differences among the groups.

One test considered to have a spatial component, as well as measuring other aspects of information processing, on which the groups did differ is the Digit Symbol test mentioned above. On this test the TS group performed less well than the NMF group but not the NMM group. The two control groups did not differ from each other.

Tests of Linguistic and Arithmetical Ability

Similar analyses were carried out for all of the tests of linguistic and arithmetical ability. The mean scores and standard deviations for these tests are presented in Table 7.

One-way analysis of variance of the standard scores on the Reading of Symbols Test revealed no differences among

TABLE 7

Tests of Linguistic and Arithmetical Ability

Mean Scores and Standard Deviations

Test	TS		NMF		NMM				
	Mean	S.D.	Mean	S.D.	Mean	S.D.	F	H	p
Reading of Symbols* Standard Score	46.4	5.8	48.6	7.3	48.5	6.4	0.21		NS
Word Fluency Raw Score	34.8	12.3	51.4	14.5	36.6	5.5	4.76**		p<.025
WRAT Reading Standard Score	103.9	11.6	117.3	9.0	114.3	10.2	3.70		p<.05
WRAT Arithmetic Standard Score	85.5	9.9	98.4	12.1	89.4	2.5	——	5.68	p<.1

F = value of F-statistic for one-way analysis of variance
df for each analysis of variance = 2/21 except * where df = 2/18 as this test was not administered to three subjects
H = H-statistic for the Kruskal-Wallis test
p = probability level
** = logarithmic transformation applied

the groups. Nor did the Digit Span test, mentioned above, elicit any differences among the groups.

Differences, however, did exist for the PMA Word Fluency test. The Duncan Multiple Range Test indicated that the TS and NMM groups, while not differing from each other, both generated significantly fewer words than the NMF group ($p < .05$, $df = 20$, for both comparisons).

The three groups also differed on their Standard Scores on the WRAT Reading Test. Individual comparisons indicated that on this test the TS group performed significantly less well than the NMF group ($p < .05$, $df = 20$). The TS group also performed less well than the NMM group but not significantly so ($p < .1$, $df = 20$). The two control groups did not differ from each other. This result is, once again, inconsistent with the existing literature.

Analysis of the Standard Scores for the three groups on the WRAT Arithmetic Test fell just short of significance.

Matched Control Groups versus Pilot Groups

As has already been noted, the performance of the eight males selected as matched control subjects was not always what would be predicted for a group of normal males. Rather than having better spatial ability than the NMF group, the NMM group scored lower, although not significantly, on the DAT Space Relations Test and the

Road Map Test of Direction Sense. In order to examine the possibility that the NMM group might represent a subgroup of normal males having poor spatial ability, the IQ scores of the NMM group were compared to those of the 12 remaining male pilot subjects who were not selected as matched controls. Accordingly, t-tests for the difference between two independent means were performed on the mean scaled scores for the five subtests that were administered to the entire pilot group. The NMM group had a significantly lower mean scaled score for the Block Design subtest than did the 12 male pilot subjects (means = 8.0 and 11.8 respectively, $t = -3.68$, $df = 18$, $p < .01$, two-tailed test). The NMM group also performed less well on the Object Assembly subtest, although this difference was not significant (means = 9.6 and 11.7, $t = -1.63$, $p < .2$).

Similar analysis for the NMF group compared to the remaining 12 female pilot subjects showed no difference on any of the five subtests.

Comparisons Within the Turner Syndrome Group

The TS subjects who participated in this study were far from a homogeneous sample (see Appendix A). Five subjects had a 45,X karyotype, two had an isochromosome X, and one was a mosaic. Five subjects were receiving estrogen replacement therapy at the time of testing and one began midway through the testing. For purposes of this analysis this subject was considered not to be receiving estrogen replacement. The age range of this group was also quite large (11 to 24 years of age). In an attempt to determine whether any of these factors contributed to the test results, the data for the 45,X group were compared to that for the non-45,X group (isochromosome X and mosaic subjects). Similar comparisons were made for those subjects who were receiving treatment at the time of testing and those who were not. The results of comparisons of these variables cannot easily be interpreted since there is considerable overlap among the subgroups. Two of the three non-45,X subjects were untreated at the time of testing and were also two of the youngest subjects. These same two subjects also had the highest IQ scores. Thus it would be impossible to sort out whether any possible differences are due to age, treatment or genotype, or intelligence. Given the small sizes of these groups statistical comparisons were not feasible. However, mere examination of the mean IQ scores shows that the 45,X group (n = 5) compared to the non-45,X group (n = 3) had lower Verbal (97.0 vs 107.3), Performance (94.4 vs 98.7) and Full Scale IQ scores (95.4 vs 103.7). The treated (n = 5) versus the untreated (n = 3) comparison yielded a similar picture, with the untreated group achieving higher scores. This is not surprising since two of the non-45,X subjects were also not receiving treatment. Whether these differences are related to circulating hormone levels, genotype or some other factor entirely remains open to question.

When these subgroups were compared on the tests of cognitive ability, it was observed that on the Word Fluency Test, the Test of Direction Sense and the Draw-a-Man Test, the non-45,X and the untreated groups performed at a somewhat lower level than the 45,X and treated groups respectively. The non-45,X and untreated groups, however, performed slightly better than the 45,X and treated groups, respectively, on the WRAT Reading and Arithmetic subtests, the Reading of Symbols Test and the DAT Space Relations Test.

Similar comparisons were made for the two dichotic listening tests. There were no differences on any comparison for the dichotic Melodies test for either overall accuracy or ear asymmetry. On the dichotic CV test, however, it would appear that although overall accuracy did not differ, the non-45,X and untreated groups had slightly larger left- than right-ear scores compared to the 45,X and treated groups who tended to show no difference between ears.

Although these differences do exist among the TS subgroups, it is unlikely that they influenced the pattern of results that emerged from the comparisons of the TS group as a whole and the matched control groups.

Again, because of the small sizes of the subgroups, statistical comparisons were not feasible. However, examination of the mean scores of each of the four TS subgroups compared to the mean scores of the NMF and NMM groups showed that the pattern for each test was the same as it had been when the entire TS group was compared to the control groups.

CHAPTER IV

DISCUSSION

The results of this study present a picture that is both consistent and inconsistent with that of previous studies. The lack of significant differences on certain tests between the normal females and males was somewhat surprising in view of the fact that such differences have previously been found. However, the lack of significance is likely largely attributable to the small sample size and perhaps to different and more stringent matching procedures than those used in other studies. Furthermore, a failure to find significant results does not necessarily prove that such differences do not exist. It merely means that no strong evidence has been found on which to reject the null hypothesis. As Armitage (1971) so engagingly states it:

> To draw an analogy with a court of law, the null hypothesis is rather like a presumption of the innocence of an accused person. A significant result is then like a verdict of guilty, but a non-significant result is more like the Scottish verdict of 'not proven' than the English verdict of 'not guilty' (p. 103).

One must, of course, exercise extreme caution in interpreting non-significant results. However, in a study of this nature with a small sample and using psychological tests that are not perfectly reliable, one must also interpret the finding of significance with equal caution. In such cases it is of value to examine the consistency of the results in comparison with those of other similar studies.

Methodological Considerations

Before discussing the results of this research it seems appropriate to first discuss some of the methodological problems involved in the study of Turner Syndrome individuals. Such a discussion is important because the manner in which these problems are dealt with may have considerable bearing on what results are obtained and how they are interpreted.

The first problem is that of selecting appropriate control subjects. Many previous studies of the level of intellectual functioning in TS patients did not use control groups. Rather they compared the IQ level of TS subjects to the test norms or made intraindividual comparisons of performance on different subtests. This procedure has revealed that TS patients function within the normal range of intelligence but that their PIQ is typically lower than their VIQ. However, a more valid comparison may be possible when the IQ scores of TS patients are compared to those of a group of normal individuals of similar age, race, educational level and socioeconomic status.

The situation becomes more complex, however, when the aim of the study is to investigate specific cognitive abilities in a clinical population compared to normal groups. Generally such studies attempt to use a control group that is matched to the clinical group for intelligence as well as other variables. Matching for IQ makes it more possible to determine whether any impairment that may be found in the clinical population is a specific cognitive deficit associated with the problem rather than a generally lower level of intellectual functioning.

In the case of Turner syndrome, the use of control groups matched for IQ presents logical problems. Since TS subjects appear to have normal VIQ, but a lowered PIQ compared both to their own VIQ and to the PIQ of normal individuals, and also have difficulty with many spatial tasks, it is difficult to decide whether to match TS subjects with control subjects on the basis of FSIQ, VIQ, PIQ or some combination of the three. To the extent that VIQ and PIQ may be correlated with the particular cognitive tests being used, each of these possibilities presents some problems in interpreting the results.

If the two groups are matched for FSIQ, a control group inadvertently could be selected which differed from the TS group in their pattern of performance. For example, to have the same FSIQ as the TS subjects, a control group could have any one of three patterns: a) VIQ equal to PIQ, making their VIQ lower and their PIQ higher than those of the TS subjects; b) VIQ lower than PIQ, again making VIQ lower and PIQ higher than those of the TS group but to an even greater degree than in the first case; c) VIQ higher than PIQ, which would make all three IQ scores roughly equal in the two groups. The first two possibilities would result in a control group whose pattern of performance was the reverse of that usually found in TS could in interpreting the results of comparisons on tests of either linguistic or spatial ability. The third possiblilty would result in a control group with the same pattern of performance as the TS subjects and might appear to present the fewest interpretational problems. However, a control group with a large difference between VIQ and PIQ, regardless of the direction of the difference, might possibly represent a distinct subgroup of the normal population. Matching for either VIQ or PIQ alone will present similar interpretational difficulties.

In this study the groups have been matched on the basis of both Verbal and Performance scores as this seemed to be the least problematic solution. This method of matching clinical and control subjects has the advantage of being more rigorous because it most clearly allows the interpretation that differences on other tests of cognitive abilities, if such differences are found, are not due to differences in VIQ or PIQ.

A second problem inherent in finding appropriate control subjects is that of age. Given the relative infrequency of Turner syndrome, it is necessary to test whatever subjects are available and agreeable to participating in research. Samples of TS subjects, therefore, are almost invariably quite small and span a wide age range. The similarity of the age ranges tested in different groups of TS patients is remarkable. They almost without exception fall between the ages of

11 and 24 and have a mean age of 15 to 17 years. The absence of older individuals is understandable because once the condition has been diagnosed and treatment has been initiated, it is not necessary for patients to remain in close contact with the clinic where they were diagnosed. Since it is only at such clinics that groups of patients are on file, many older patients are difficult to locate because they have moved and are no longer in touch with the clinic. The absence of younger children in these studies is not surprising since it is often only by about the time of puberty that this syndrome is diagnosed. It has also been my experience that when younger children have been diagnosed, the parents are often very reluctant to expose the child to testing. Given the nature of the condition, they are fearful that the experimenter may say something to upset the child or something not consistent with the way in which the parents have chosen to cope with the problem. Also the very fact of participating in a study does emphasize the fact the the child is in some way different which is a situation the parents usually wish to avoid.

Thus the wide age range of TS subjects is unavoidable but it does present problems in terms of obtaining matched control subjects. It also presents problems in terms of the tests that can reasonably be administered. Tests that have norms for different ages and cover the age range of the sample are [illegible] there are often two or more levels for different age groups, for example, the WISC and the WAIS for those under 16 years of age and those 16 years of age and over, respectively, The WRAT also has two levels one for subjects under 12 years of age and one for subjects 12 years and over. In both cases the format of the two levels is identical but the actual questions are not. Therefore, test scores are often combined that may not be strictly comparable.

These problems are unavoidable but must be taken into consideration when analysing and interpreting the data. It is possible that in some cases, if scores on a test are particularly sensitive to the effects of age and are not corrected to rule out age effects, that the scores of the younger TS subjects may lower the mean score for the group as a whole. This is especially problematic in studies which do not use control subjects of the same age. The interpretation of the results of such studies must be approached with caution. For example, Alexander _et al_ (1964) found that a group of 13 TS subjects, ranging in age from 13 to 26 years, made significantly more errors on the Road Map Test of Direction Sense than a group of 40 nursing students. Even though the mean ages of the two groups were 19.4 and 19.8 respectively, it is highly questionable whether these two groups are comparable with regard to the range of ages tested. It is also likely that the nursing students had higher IQ scores although these were not reported. The IQ scores of the TS group were: VIQ = 102; PIQ = 83; FSIQ = 92.5.

The age problem does exist in this thesis. The mean ages of the two groups are the same but the age range for the TS group is much wider. However, the scores of the three youngest TS subjects were examined to see whether they could have had the effect of lowering the mean scores for the entire group. This was not found to be the case. In addition, for most tests the scores of the TS group were not found to differ significantly from those of the control subjects.

A third issue of particular importance for control groups for TS individuals is that of sex. To date, the control subjects in every study investigating Turner syndrome that has reported sex, have been female. Garron (1977) did not mention the sex of his control group. It is reasonable to compare TS subjects to normal females since TS individuals are phenotypic and legal females, have been raised as females, and have a feminine gender identity. However, TS individuals are not genetic females. Therefore, it is also reasonable to compare them to normal males. Since the primary aim of this study is to investigate the mechanisms which may underlie sex differences in cognitive functioning and hemisphere specialization in normal males and females, and since TS individuals are neither genetic males nor females but are biologically similar to both sexes in some respects, control subjects of both sexes may be appropriate.

The use of male and female control groups also helps to unravel to some extent the role of environment in cognition in general. If differences are found between the TS group and the normal females, they cannot be attributed to environmental factors since the two groups share similar environments with regard to variables related to sex. By inference, then, any differences between normal males and females cannot readily be attributed solely to environment, as some theorists would have it. If biological variables are found to be associated with differences in cognitive functioning or hemisphere specialization between TS patients and normal females, then it is certainly possible that these same variables may be associated with the differences between normal males and females.

In addition to the methodological problem of selecting control subjects and matching them on appropriate variables there is also a problem in comparing the results of the different studies in this area. On careful examination of the data, when they are presented, it becomes apparent that in those studies using t-tests for matched samples one-tailed tests are sometimes used and other times two-tailed tests are used. This is an important issue and will be discussed in relation to the three recent studies of Turner syndrome that have used matched control groups.

First, though, a discussion of the relative merits of one- and two-tailed tests is in order. There is considerable controversy surrounding this question. One aspect of this issue on which there is agreement is that the decision to use a one-tailed or a two-tailed test should always be made on the basis of the original question and never after examination of the data. There has also been considerable discussion of the circumstances in which it is appropriate to use a one-tailed test. For example, Alder and Roessler (1968) state that:

> If the interest in the problem is restricted to the fact that either a very low or a very high result was obtained (but not both), a one-tailed test is called for; otherwise a two-tailed test should be used. In case of doubt, a two-tailed test is recommended (p. 124).

This position is stated even more strongly by Armitage (1971) who states that one-tailed tests should be used

> . . . only if it is quite certain that departures in one particular direction will always be ascribed to chance, and therefore regarded as non-significant however large they are. This situation rarely arises in practice, and it will be safe to assume that significance tests should almost always be two-sided (p. 104).

This reluctance to use one-tailed tests is, in part, based on the commonly held assumption that one-tailed tests are less stringent than two-tailed tests since it is twice as easy to get a significant result when using a one-tailed test. However, in a discussion of the relative power of one- and two-tailed tests, Hays (1973) points out that:

> If a one-tailed test is used, and the true alternative is in the direction of the rejection region, then the one-tailed test is more powerful than the two-tailed test... In a way we get a little statistical credit in the one-tailed test for asking a more searching question.

> On the other hand, if the true alternative happens to be in the tail opposite the rejection region in a one-tailed test, the power is very low . . . If you will, we are penalized for framing a stupid question (p. 373).

Hays continues his discussion by pointing out that if the original question is one of what happens in certain situations, two-tailed tests are used. In psychological research many questions are of this nature.

Within the theoretical framework of this thesis, the question being asked is whether individuals with Turner syndrome perform differently on certain tasks than do normal males and females. This is essentially the same question being asked in the studies of Waber (1979), Silbert *et al* (1977) and Garron (1977). Thus the finding of any difference, regardless of direction, is of importance.

Waber (1979) and Silbert *et al* (1977) have each compared TS patients to one matched control group of normal females and Garron (1977) to a matched control group of unreported sex. All, therefore, have used t-tests for matched samples in analysing their data. Garron (1977) has used two-tailed tests for all comparisons. Waber (1979) and Silbert et al (1977) have made use primarily of one-tailed or directional tests. Waber (1979) used one-tailed tests in analysing the results of all the tests administered except the IQ data for which two-tailed tests were used. The rationale behind this approach was not explained. However, one might assume that Waber (1979) used one-tailed tests in analysing the results of the cognitive tests on the basis of the observation of a spatial deficit in TS individuals in previous studies. Silbert et al (1977) have used both directional and non-directional tests with no given rationale nor even any apparent pattern.

In both of these studies the t-values have been presented in the tables and it is possible to determine what the results would be had two-tailed tests been used consistently. For purposes of this discussion the results of these two studies will be considered significant only if they are so for a two-tailed test at the .05 level. In many cases, what have been reported as significant differences fail to reach significance when these criteria are applied. Specifically, Waber (1979) reported that the TS subjects performed significantly less well on the Stroop Color-Word Interference Test, on a test of left-right orientation in relation to another person, and on the Wisconsin Card Sorting Test. Using two-tailed tests, these differences fail to reach significance. In the Silbert et al (1977) study, the same situation exists with regard to the Graham-Kendall Memory for Designs Test and to the Auditory Figure-Ground Test. A second interesting feature of this latter study is that the TS and control subjects were matched on the basis of FSIQ and yet the authors do not mention the fact that the control subjects tended to have a higher mean FSIQ than the TS group (significant with a one-tailed test). Nor do they point out that mean VIQ and PIQ scores tended to be higher for the control subjects (significant with a one- and a two-tailed test, respectively).

However, even with two-tailed tests Waber's (1979) TS group performed less well than the control group on the upright condition of a Face Recognition test, the visual presentation of a Consonant tri-gram test, a word fluency test, the Road Map Test of Direction Sense, the Rey-Osterreith Complex Figure Design Copying Test and a rhythmic sequencing test. With two-tailed tests, Silbert's et al (1977) TS group performed less well than the control group on the Wechsler Digit Span, Picture Completion and Digit Symbol/Coding subtests, and the testsof spatial ability.

In comparing the results of such studies it is also important to note the level of significance being applied. For example, Waber (1979) states that the control subjects had a higher mean VIQ and a higher Digits backwards score on the Wechsler Digit Span subtest than did the TS group, but the probability levels were .08 and .07 respectively, which are generally not considered to be significant. With this background, the results of the present study will be discussed.

Hemishpere Specialization

The results of the tests of hemisphere specialization, for the most part, did not show significant differences between the TS group and the control groups. For the dichotic CV test the expected right-ear advantage did not emerge for either control group separately, but for the two control groups combined there was a significant right-ear superiority. In contrast, for the TS group, there was a slight trend toward a higher mean left- than right-ear score. This specific test, although it consistently elicits a right-ear advantage in groups of normal adults (eg. Berlin, Hughes, Lowe-Bell, Cullen, Thompson, & Loovis, 1973; Berlin & McNeil, 1976) and children (Berlin, Hughes, Lowe-Bell & Berlin, 1973), does so in only about 80% of individuals (Berlin & McNeil, 1976). The other 20% show either a left-ear advantage or no difference between ears. Therefore, it is of interest to look at the percentage of individuals showing a right- or left-ear advantage as well as at the mean left- and right-ear scores. In this study, as in the studies of Netley (1977) and Waber (1979), a higher percentage of TS subjects showed an atypical left-ear superiority than did matched control subjects, although the percentage of TS subjects showing reversed laterality is quite variable. In this study, comparisons of the number of TS subjects versus the number of NMF and NMM subjects showing the typical right-ear advantage were not significant. The failure of these comparisons to reach significance in this study is probably due to the small sample sizes since, with somewhat larger groups, both Netley and Waber found a significant difference. The current results in conjunction with those of previous studies would seem to suggest that Turner syndrome may be associated with an increased incidence of a reversed pattern of functional asymmetry for linguistic processing, that is, a tendency toward greater right hemisphere processing of verbal material.

To date, no studies of right hemisphere specialization in TS individuals for nonverbal or spatial information have been done. The dichotic Melodies test used in this study has repeatedly been found to elicit a left-ear superiority in normal individuals (Dee, 1971; Spellacy, 1979; Spreen, Spellacy & Reid, 1970). In contrast to the dichotic CV test, the Melodies test did elicit a significant left-ear advantage for the three groups combined, for the female control group when the groups were considered separately, but not for the two control groups combined. The TS group showed a trend toward a higher left- than right-ear score. The NMM group, however, had a slightly higher mean right- than left-ear score. Comparisons of the percentage of individuals showing a left- or right-ear advantage revealed no differences among the groups. Thus it, would appear that the right hemisphere of TS individuals is as specialized for the processing of at least this type of nonverbal material as it is in normal males and females.

The results of the two dichhaptic tests failed to provide any evidence either in support of or in disagreement with the picture that emerged from the two dichotic listening tests. Both the dichhaptic Shapes test and the dichhaptic Words test failed to elicit any hand difference in the normal groups, making the results somewhat difficult to interpret. However, the performance of the three groups was quite similar on both tests in terms of overall accuracy, left- versus right-hand accuracy and the percentage of each group showing a left- or a right-hand superiority. One possible explanation of these results may be that these two tests involved equal participation of both hemispheres and that the combined contributions of the two hemispheres resulted in equal accuracy of the two hands.

The failure of these two tests to elicit any hand asymmetry in normal individuals was unexpected in view of the fact that several studies, using similar tests have observed differences in accuracy between the hands in normal individuals. A significant left-hand superiority on dichhaptic shapes tests has been found in both children (Cioffi & Kandel, 1979; Witelson, 1974) and adults (Gardner, English, Flannery, Hartnett, McCormick & Wilhelmy, 1977; Oscar-Berman, Rehbein, Porfert & Goodglass, 1978). However, some studies using various modifications of the dichhaptic task, have failed to find a left-hand superiority (e.g. LaBreche, Manning, Goble & Markham, 1977).

The results of studies using the dichhaptic procedure with verbal stimuli are quite consistent but present a more complex picture. Using pairs of individual letters, Oscar-Berman <u>et al</u> (1978) observed a significant right-hand superiority in adults. With children, Witelson (1974) observed a right-hand advantage that fell just short of significance. LaBreche et al (1977), however, found no hand asymmetry for the perception of letters in adolescents. When words have been used, a significant right-hand advantage has been observed in both children (Cioffi & Kandel, 1979) and adolescents (Khadem, 1977).

The two dichhaptic tests used in this study were variations of the shapes test originally designed by Witelson (1974) and of the words test developed by Khadem (1977). The tests were altered in ways intended to make them more difficult and more clearly dependent on nonverbal and verbal processing, and therefore more likely to elicit a hand asymmetry. Unfortunately this effort was not successful. It may be that these two tests are particularly sensitive to many variables such as the nature of the stimuli, the information processing required, the duration of the presentation of the stimuli and the method of response, and that the ways in which the tests were altered decreased rather than increased their ability to tap the processes lateralized to the two hemispheres. For example, on the dichhaptic Words test, the words felt and the words on the recognition display were all composed of upper-case letters. Therefore, it may have been possible to use a spatial strategy to perform this task. Thus the test may not have necessitated linguistic processing. The lack of a hand asymmetry. especially in the normal groups, on the dichhaptic Shapes test remains a mystery.

Cognitive Abilities

In this study, since the control groups were matched on three Verbal and two Performance subtests, no differences in overall IQ scores were expected. None were found. Of the six subtests for which the three groups were not matched, the TS group performed less well only on the Digit Symbol/Coding subtest and only in relation to the NMF group. The almost complete absence of differences among the three groups may be largely attributable to the fact that they were matched on both Verbal and Performance subtests. However, the lack of significant differences could also possibly be due to the small sample size, since there was a trend toward lower scores for the TS group on both PIQ and FSIQ and on the Arithmetic and Object Assembly subtests and most of these differences have been observed in previous studies. The finding of some significant differences in other studies could be due not only to larger samples but also to the different selection criteria used for the control subjects in which PIQ was not matched.

The only statement that can be made with any degree of certainty regarding the intelligence of TS individuals is that it is within the normal range. It is now well documented that Turner syndrome is not associated with overall intellectual impairment or retardation. It may be true that many TS individuals achieve higher VIQ than PIQ scores but this does not necessarily distinguish them from normal individuals of either sex.

The results of the tests specifically selected to tap aspects of spatial ability present a picture similar to that which has emerged from previous studies, that is, a somewhat lower level of spatial ability in TS subjects than in normal females. These results differ from those of previous studies only in degree and not in direction. There were no statistically significant differences among the three groups on the DAT Space Relations Test, the Road Map Test of Direction Sense or the Draw-a-Man Test, although there was a trend toward poorer performance of the TS group on the raw score of the DAT Space Relations Test and the time score of the Road Map Test. In addition, it was found that the TS group attempted significantly fewer items than either control group on the DAT Space Relations Test. Although these results provide no definite evidence of poorer spatial ability in TS subjects compared to normal females and males, given the small sample size and the trends toward poorer performance, it is difficult to completely reject the possibility of poor spatial ability in TS subjects.

It is also noteworthy that both of the tests of spatial ability on which the TS group tended to perform less well involved a time factor. As has been pointed out, on the DAT Space Relations Test, the TS subjects did attempt significantly fewer questions than either control group even though they did not differ significantly on the number of questions answered correctly. A similar situation exists for the Road Map test. The three groups did not differ in accuracy but the TS subjects tended to take more time to complete the test. It is unlikely that these finding are related to motivational factors since the TS group performed as well as the control groups on several other tests. In fact, the TS subjects often appeared to be trying harder than the control subjects.

Only a few previous studies have tested language abilities, other than VIQ, in TS subjects and the only test on which they have been reported to perform poorly is a Word Fluency test (Money & Alexander, 1966; Waber, 1979).

Alexander and Money (1965) and Serra et al (1978) both found average or above average reading ability and verbal comprehension in TS subjects. Thus, the finding, in this study, that the TS subjects achieved lower scores on the WRAT Reading subtest than did the normal control groups was unexpected, especially in view of the fact that the TS group performed as well as the control groups on the Reading of Symbols Test which taps the ability to read phonetically. However, the WRAT Reading subtest is essentially a test of word recognition while the test administered by Serra et al (1978) was a test of verbal comprehension and not a test of reading ability per se. The test given by Alexander and Money (1965), while it yielded scores for speed, accuracy and comprehension, involved the reading of sentences and paragraphs so that the subjects were reading meaningful material with individual words appearing in context. It may be that the poor performance of the TS subjects on the WRAT Reading subtest could be related to the fact that this is, in essence, a word recognition test and therefore involves visual memory and probably a spatial component. The lower performance of the TS group might also be related to the fact that the test allows only 10 seconds to read each word. It is also possible that they attempted to read the words on this test phonetically. However, it is unlikely that such a strategy would result in a high score since many of the words on this test, like so many in the English language, are exceptions to the rules of phonics.

The lower scores of the TS subjects on the Word Fluency Test may also be related to the visual memory component of the task and to the fact that this test, too, was timed. On this task the subject must write down as many words as possible beginning with the letter 's' in 5 minutes. Possibly the TS group experienced difficulty in conjuring up visualizations and then transferring the visualization of the word to script.

Taken together, the results of the cognitive tests suggest that TS individuals may have a deficit involving visual memory including at least some aspects of spatial ability. This is similar to Waber's (1979) interpretation. It would also appear that this difficulty may come into play when time is factor, that is, when there is a time limit involved or when time taken to complete the task is measured. The three tests on which the TS group performed significantly less well than the control subjects (the Wechsler Digit Symbol/Coding subtest, the WRAT Reading Subtest and the Word Fluency Test) all involve visual memory and all are timed. The time limit on the DAT Space Relations Test also influenced the performance of the TS group in that they attempted significantly fewer questions than either control group. Further evidence for this hypothesis is the tendency toward lower performance on the part of the TS group on the

Wechsler Object Assembly subtest (on which the groups were matched), the Wechsler Arithmetic subtest, and the WRAT Arithmetic subtest. All of these three tests are timed and some involve visual memory to some extent.

A few findings, however, would seem to be inconsistent with the hypothesis that a visual memory deficit and the involvement of a time factor are related to the TS group's poor performance on some tests, specifically, the backwards component of the Wechsler Digit Span subtest or on the Draw-a-Man Test, both of which involve aspects of visual memory. However, neither of these tests are timed. Nor did the groups differ on the Wechsler Picture Completion, Picture Arrangement or Block Design subtests. These three subtests are all timed but they may not depend as heavily on visual memory for successful performance as do the tests on which the TS group tended to perform less well.

In summary, one possible hypothesis which seems to emerge from these findings is that TS individuals may have difficulty on tasks which involve visual perception and memory and on tasks which require accurate performance within time constraints. The fact that the groups were so closely matched on both Verbal and Performance subtests strongly suggests that these differences were not due to differences in intelligence.

The tests used in this study, especially the

Wechsler Performance subtests are not pure tests of spatial ability. Therefore, the picture that emerges is not unambiguous and is difficult to interpret. TS individuals do not perform poorly on all tests involving spatial ability and they do perform poorly on some tests which would appear not to involve spatial ability. Therefore, although TS subjects may have a deficit in spatial ability, it does not involve all aspects of spatial ability. In order to determine more precisely what cognitive processes may be impaired in TS individuals it would be necessary to devise tests that could more clearly illuminate the specific nature of the problem.

On the basis of the results of this study and of previous studies it would appear that TS individuals do not have difficulty with language _per se_. The most parsimonious explanation of their poor performance on a Word Fluency test and the WRAT Reading subtest may be that TS individuals possibly have difficulty with only those aspects of language which involve visual memory.

The Matched Male Control Group

One other factor which is likely related to the failure to find significant differences among the groups on some tests is one aspect of the matching procedure used in this study. The decision to match the groups on the Wechsler Block Design and Object Assembly subtests, which are the two most highly correlated with PIQ, may have resulted in the selection of control groups with poorer than average spatial ability, especially in the case of the NMM group. As has been mentioned previously, the performance of the NMM group was atypical on several tests. On the DAT Space Relations test, males generally achieve higher raw scores than females. The reverse was found in this study. On the Road Map Test, males typically complete the test faster and with fewer errors than do females. In this study the NMM group took longer to finish the test and made more errors than the NMF group. It could be argued that it is the NMF group that is performing in the unexpected fashion by achieving better scores than the NMM group on the Space Relations and Road Map Tests. However, if the scores of these subjects are compared to those of the male and female college students (who may be brighter as a group) to whom Tapley and Bryden (1977) administered these same tests, it is clear that the scores of the NMF group are very similar to those of the female college students. In contrast, the scores of the NMM group are considerably lower than those of the male college students and lower even than those of the female college students.

Although the performance of the NMM group was somewhat unusual, the differences discussed above were not large and none were statistically significant. These differences do, however, raise the possibility that the male control group selected in this study may be slightly atypical in some respects. Several findings would seem to support this possibility. As has been noted, compared to the 12 remaining pilot subjects, the NMM group performed significantly less well on the Block Design subtest and there was a trend toward poorer performance on the Object Assembly subtest. Also, the mean scores of the NMM group fall between those of the NMF group and the TS group on almost every test. Furthermore, whenever analysis of variance showed that the groups differed, individual comparisons usually showed significant differences only for the NMF versus TS comparison. The atypical performance of the NMM group is likely to some extent responsible for the lack of significant differences among the groups on some tests.

In view of the possibility that the NMM group may not have been the most appropriate control group, it would be valuable to consider the alternative methods of selecting matched control groups. As has already been discussed, matching on Verbal or Performance subtests alone presents interpretational difficulties. The best solution, therefore, is to control for both Verbal and Performance IQ, which was the aim in this study. The subtests on which the groups were matched were selected because they are the ones most highly correlated with VIQ and PIQ. However, in view of the problems encountered in this study, it would appear to be more appropriate to match on VIQ and PIQ rather than on specific subtests. The 1½ to 2 hours spent administering the entire IQ test to every potential subject would be time well spent.

Possible Mechanisms Underlying Sex Differences

As has been mentioned earlier the hypothesis that spatial ability is related to an X-linked recessive gene has yet to be proven. One of the arguments often used against this hypothesis is the fact that TS individuals who should, according to the hypothesis, manifest the same level of spatial ability with the same frequency as normal males, do not. In this study the TS subjects, however, do manifest a cognitive profile more like that of the male control group than the female control group. This fact, however, cannot be used as an argument in favour of the X-linked theory of spatial ability since the male control group may have inadvertently been selected for poorer than normal spatial ability and may represent a subgroup of the normal male population.

Many attempts have been made to attribute sex differences in cognitive abilites in normal individuals to the fact that physical maturation proceeds at different rates in the two sexes. It may be that differential rates of maturation and the biological variables which determine them also influence neurological development, pattern and degree of hemisphere specialization, and pattern and level of cognitive abilities. Clearly any relationship of biological sex variables, hemisphere specialization and cognitive ability must be a very complex one and it will require considerable and sophisticated research to disentangle any interrelationships of these variables.

However, since systematic manipulation of these biological variables in humans is impossible, the study of sexually abnormal populations is the only road open to the study of this problem. It was hoped that this study of Turner syndrome would shed some light on the issue of the influence of sex variables on cognition and hemisphere specialization. In some respects, this expectation has been realized. Evidence has been found that TS individuals differ from both normal males and females on some aspects of cognitive ability and there is some suggestive evidence that they may possess a somewhat atypical pattern of hemisphere specialization. These differences cannot be attributed to different intellectual capacity since the three groups had very similar IQ scores. In addition, the fact that the TS group differed from the normal females, in this study even more than from the normal males, would suggest that environmental factors are not of primary importance since the environments of TS subjects and normal females are similar.

On the basis of these findings and those of previous studies, it would appear that sex chromosomes and/or sex hormones are likely related to cognition and hemisphere specialization. It may be that in the absence of a normal second X chromosome an individual will not develop the level of cognitive abilities or the pattern of hemisphere specialization of a normal female. Nor will the absence of a normal second X chromosome, without the presence of a Y chromosome and fetal testosterone, result in the pattern and level of cognitive abilities and hemisphere specialization of a normal male.

It is more difficult to speculate about the possible role of estrogens in the development of a normal female pattern of cognition and hemisphere specialization. Although male fetuses produce testosterone, there is, as yet, no evidence that female fetuses produce estrogen. It would appear that normal females and TS individuals have the same hormonal environment at least until the time when normal females begin ovarian estrogen production at puberty. Therefore if estrogen production were related to the development of a feminine pattern of cognition and hemisphere specialization one would expect to find differences between pre- and post-pubertal normal females and between TS subjects receiving estrogen replacement and those who were not. To date, there is no evidence that such differences exist either in normal females or in TS individuals. However, the possibility that estrogens are related to cognition and hemisphere specialization cannot be completely ruled out since it may be possible that female fetuses and children do produce estrogens in amounts sufficient to have an effect on cognition and neural organization but too small to be detected by the existing technology.

On the basis of the existing evidence it would appear that the absence of a normal second X chromosome alone could be responsible for the differences in cognition and neural organization between TS individuals and normal females. According to the Lyon hypothesis, normal females also only have one active X chromosome. If this is the case it is difficult to understand why differences should exist between TS individuals and normal females. It may be that the second X chromosome in normal females has some effect very early in fetal life before it is inactivated, or that it is not completely inactivated. Alternatively, it may be that the fact that normal females are actually mosaics, with an active paternal X chromosome in some cells an active maternal X chromosome in others, while TS individuals, at least those with a 45, X karyotype, have the same X chromosome in all cells, may be related to differences in cognition and neural organization.

It would undoubtedly be fruitful to continue these investigations with other groups having abnormal sex chromosome complements or hormonal environments. A refinement of methodology and the tests used to measure dependent variables would also appear to be in order.

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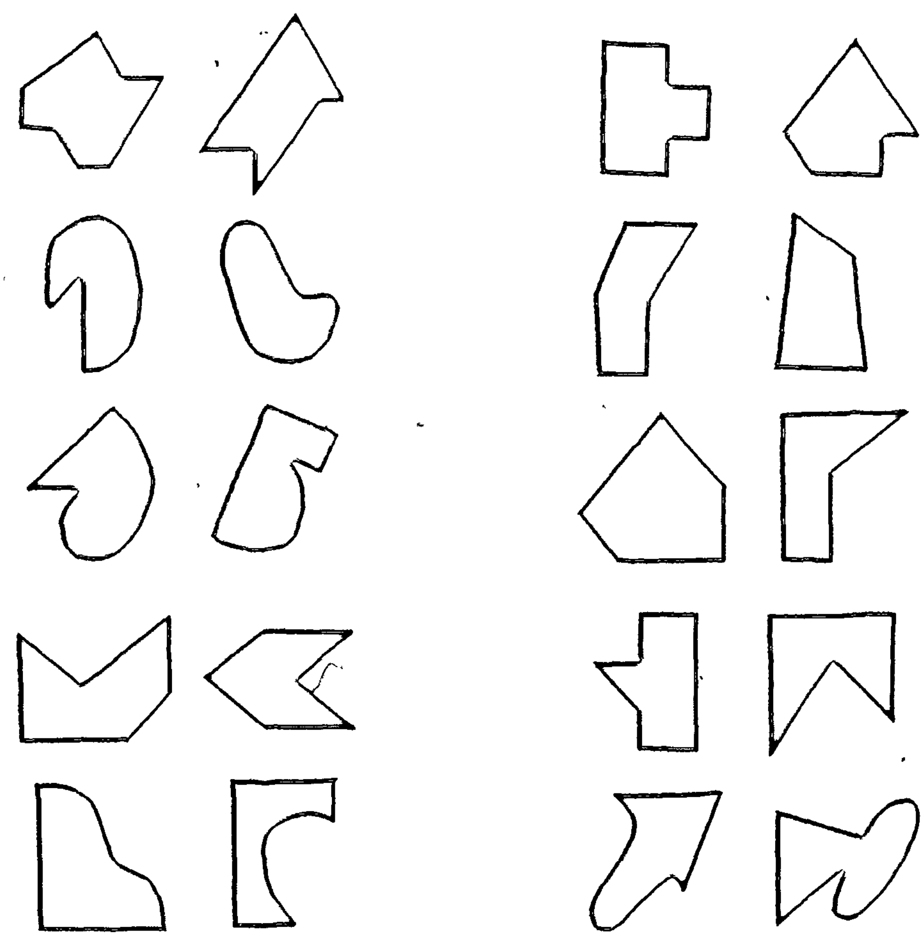
APPENDIX A

Turner Syndrome Subjects

Subject	Age(yr)	Karyotype	Estrogen Replacement	VIQ	PIQ	FSIQ
RK	12.8	45,X	No	85	94	88
CP	21.5	45,X	Yes	110	94	104
GD	24.5	45,X	Yes	100	99	99
HB	16.9	45,X	Yes	94	96	94
SB	24.3	45,X	Yes	96	89	92
SJ	17.5	46,X,i(Xq)	Yes	93	85	88
VV	14.9	46,X,i(Xq)	No/Yes	108	104	107
CG	11.0	46,X,i(Xq)/45,X	No	121	107	116

APPENDIX B

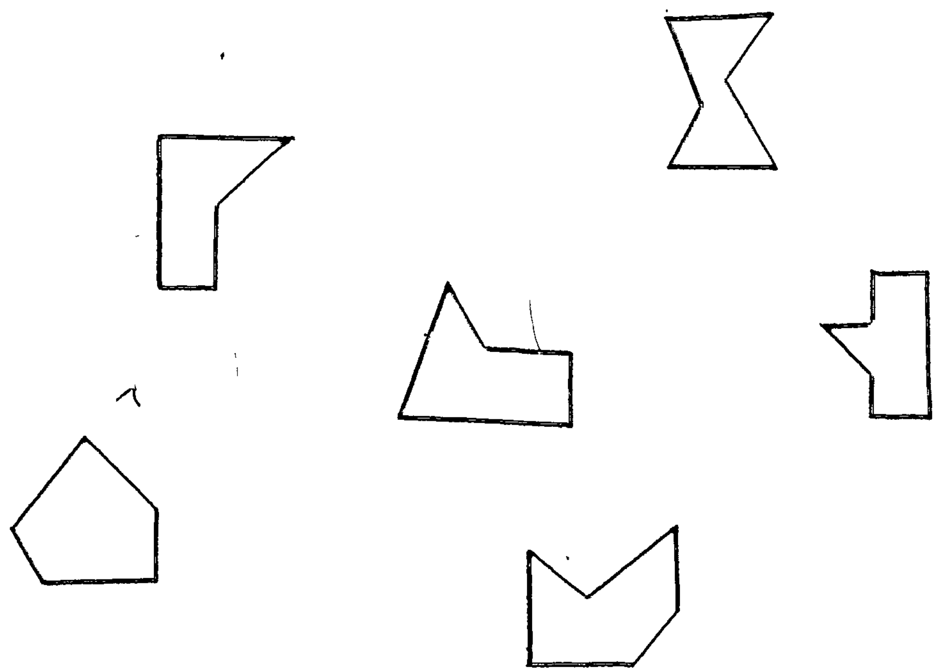
Pairs of Target Shapes Used in the Dichhaptic Shapes Test



Approximately one-half actual size

APPENDIX C

Sample Recognition Display Used in the Dichhaptic Shapes Test



Approximately one-half actual size

APPENDIX D

Sample Question from the DAT Space Relations Subtest (Form S)

Instructions to Subject: "In Example X, which one of the four figures - A, B, C, D - can be made from the pattern at the left?".