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Commentary

Fractionating Handedness in Mental Retardation: What is the Role of the Cerebellum?

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INTRODUCTION

Handedness is at first sight a straightforward phenomenon. Most people prefer to use their right hand and are more skilled with their right hand, whereas a minority prefer to use their left hand and are more skilled with their left hand. However, as is often the case, a more detailed examination reveals that in theoretical terms the situation is potentially more complex. The consequence is that several studies have now looked at separable components of atypical handedness in groups of individuals with specific conditions and have found that different components of handedness are affected. In this issue of *Laterality* is a further such study, by Cornish, Pigram, and Shaw which suggests atypical handedness in children with the Fragile-X syndrome. It therefore seems an appropriate moment for a brief review of some studies that together suggest dissociable components of handedness, and therefore its fractionation, and to ask how damage to different parts of the brain may be affecting handedness differently.

DESCRIBING HANDEDNESS

Traditionally handedness has been measured using preference tests which typically ask a subject about the hand they use for a range of different tasks, most usually in the form of a questionnaire, but in the case of young children or adults or children with learning difficulties (mental retardation) by asking them

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to perform the various activities. A laterality index can be calculated, using some formula such as 100.(R–L)/(R + L + B), where R is the number of activities carried out using the right hand, L the number of activities using the left hand, and B the number of activities carried out using both hands, or giving mixed responses. Conventional statistical analysis of laterality indices has severe statistical problems (McManus, 1983) and therefore it is preferable to divide measures of handedness into *direction of lateralisation*, according to whether the laterality index is greater or less than zero, corresponding to the everyday usage of ''handedness'', and *degree of lateralisation*, which is the absolute value of the laterality index (i.e. removing the sign), a measure of strength of handedness. In the 1980s Satz and his colleagues (Satz, Soper, & Orsini, 1988; Soper & Satz, 1984; Soper et al., 1986) realised that additional measures of handedness could be obtained if subjects repeated measurements on two or more occasions. Two subjects could, say, have an identical laterality index and yet one would use exactly the same hand on each occasion for each task, whereas the other would use different hands on the two occasions. The latter is referred to as *ambiguous handedness*, and an index can be calculated straightforwardly. It has also been noted (McManus, 1996) that in principle ambiguous handedness can be divided into *ambiguous direction of handedness* and *ambiguous degree of handedness*, although as yet no-one has published such results. A further descriptive measure of handedness came with the study of McManus, Murray, Doyle, and Baron-Cohen (1992b) of children with autism, in which they found that although most children with autism showed relatively normal preference for the right hand, there was no concomitant skill difference between the hands. About half of the children with autism showed *inconsistent handedness*, being more skilled on a pegboard task with the non-preferred hand than the preferred hand. In their present paper that same pattern of inconsistent handedness is reported by Cornish et al. (this issue).

FRACTIONATING HANDEDNESS IN LEARNING DISORDERS

Detailed handedness test results using comparable measures are now available in three groups of children with learning disorders (Down's syndrome, Fragile-X syndrome, and autism), as well as in age-matched controls from several studies (McManus et al., 1992b; Cornish & McManus, 1996; Cornish et al., this issue). Table 1 summarises those results in simplified form.

Of great interest in Table 1 is that each of the syndromes seems to have its own particular profile of abnormalities. Down's syndrome is characterised not only by an increased incidence of left-handedness, which has been reported elsewhere (Batheja & McManus, 1985), but also by an overall reduction in speed on the pegboard task which seems not to occur in the other syndromes and therefore cannot readily be explained as a simple correlate of intellectual ability. The reduction in speed is also characterised by a retention of the same pattern of

TABLE 1
Handedness Test Results

	Control	*Down's Syndrome*	*Autism*	*Fragile X*
Preference				
Left hand preferred	← →	↑	↑	?
Degree of hand preference	← →	← →	↓	← →
Ambiguous handedness	← →	← →	↑	← →
Skill				
Overall speed	← →	↓	← →	← →
Better vs Worse hand	← →	← →	← →	← →
Inconsistent skill-preference	← →	← →	↑	↑

↑: Increased; ↓: Decreased; ← →: Equivalent to normals; ?: Not clear at present (insufficient evidence)

right to left hand usage as in controls. Fragile X is characterised almost entirely by its ambiguous handedness, all other measures seeming to be equivalent to the control group. Finally autism shows the same abnormality of ambiguous handedness as Fragile X, as well as an overall increased incidence of left-handedness (Boucher, 1977), but in addition there is a reduced degree of hand preference and an increased amount of ambiguous handedness (Soper & Satz, 1984; Soper et al., 1986), in each case being the only syndrome so far found to show these anomalies.

The table suggests several double dissociations, e.g. between consistency of handedness and overall pegboard speed in Down's syndrome and Fragile-X, and between degree and consistency of hand preference in autism and pegboard speed in Down's, as well as several other single dissociations. Taken together these results suggest separable neuropsychological processes. What might they be? At present only speculation is possible, although we believe that understanding these differences could well contribute to understanding the genetic and neurological basis of handedness in normal individuals, which at present is poorly understood.

THE ROLE OF THE X-CHROMOSOME

The presence of inconsistent skill and hand preference in both autism and Fragile-X is intriguing, not least because the syndromes often overlap symptomatically (Reiss & Freund, 1990) and in both cases there is a large excess of males, suggesting a similar genetic basis, which in the case of Fragile-X is known to be a defect on the X-chromosome. Sex differences in the pattern of handedness in families led McManus and Bryden (1992a) to suggest the presence of an X-linked modifier gene to explain the results, and likewise Corballis, Lee, McManus, and Crow (1996) found evidence for a pseudo-autosomal or X–Y homologous gene from the detailed pattern of handedness in siblings of opposite sex. It therefore

seems at least possible that there is a gene on the sex chromosomes which in part affects handedness. That would be further supported by the suggestion of possible atypical cerebral dominance in Turner's syndrome (Netley & Rovet, 1982b; McGlone, 1985) and Klinefelter's syndrome (Crow, 1989; Netley & Rovet, 1982a; Ratcliffe & Tierney, 1982). There is clearly a case to be made for further studies of handedness in the sex chromosome aneuploidies. Amongst other syndromes, it is worth mentioning the unusual case of Rett's syndrome, which typically affects only females, although occasional males have been reported (Christen & Hanefeld, 1995), and which may show a genetic association with Fragile-X syndrome (Alembik, Dott, & Stoll, 1995). Rett's syndrome shows a very atypical handedness (Engerstrom 1992; Nomura, Segawa, & Hasegawa, 1984; Olsson & Rett, 1986), albeit of a type that seems age-dependent, with handedness often undetermined (Nomura & Segawa, 1990), and in those in whom it is determined, a seeming predominance of left-handedness in young children, and a shift to right-handedness after the age of 7.

The other anomalies in autism, of decreased hand preference and decreased consistency of hand preference are difficult to explain but do suggest a separate origin from the increased inconsistent handedness, as the deficits are not present in Fragile-X. One possibility is that an autosomal process is involved, of which perhaps all that can be said is that it is unlikely to involve chromosome 21, as Down's syndrome does not show this pattern of abnormality. As far as the specific slowing in Down's syndrome is concerned, it is important to confirm that this is not present in other trisomies, and if that is the case then there may well be a specific cause on chromosome 21.

THE CEREBELLUM IN AUTISM, FRAGILE-X AND RETT'S SYNDROME

The neurological correlates of autism and Fragile-X are also not as well understood at present as they might be, but still provide some interesting clues as to the possible mechanism for atypical handedness. Most prominent in the recent literature is the clear demonstration of abnormalities of the cerebellum in autism (Courchesne et al., 1994a; Courchesne, Townsend, & Saitoh, 1994b; Hashimoto et al., 1995; Lotspeich & Ciaranello, 1993; Murakami et al., 1989)—and possibly also Aspberger's syndrome (El-Badri & Lewis, 1993)—and in Fragile-X (Hinds et al., 1993; Reiss, Patel, Kumar, & Freund, 1988; Reiss et al., 1991a; Reiss, Freund, Tseng, & Joshi, 1991b). That the phenomenon is not a general correlate of low IQ is shown by the control groups in some of the studies (e.g. Reiss et al., 1991a), and by the *increased* cerebellar volumes in Williams' syndrome (Jernigan & Bellugi, 1990; Wang et al., 1992). There is also some evidence of cerebellar pathology in Rett's syndrome (Bauman, Kemper & Arin, 1995; Jellinger & Seitelberger, 1986; Murakami et al., 1992; Oldfors et al., 1990), although not all studies have reported it (Casanova et al., 1991; Nihei &

Naitoh, 1990; Suzuki, Hirayama, Sakuragawa, & Arima, 1989). Of relevance to any genetic understanding of these syndromes is that children with autism show an increased frequency of a polymorphism of a human homeogene involved with cerebellar development (Petit et al., 1995), and that the M6A gene which affects cerebellar neurones in cell culture is located in humans on the X-chromosome close to the loci for Rett's syndrome and X-linked mental retardation (Olinsky et al., 1996).

Although autism and Fragile-X are associated with both inconsistent handedness and with cerebellar abnormalities, that does not of course mean that the two phenomena are necessarily causally linked. Evidence to support a more direct link comes from an otherwise difficult observation for handedness, that children with spina bifida (myelomeningocoele) show an increased incidence of left-handedness, a result replicated in several studies (Lonton, 1976; Hetherington & Dennis, in press; Wassing, Siebelink, & Luyendijk, 1993), although a possible confounding influence is a very brief report suggesting that the parents of children with neural tube defects themselves have an increased incidence of left-handedness (Fraser, 1983). The link between spina bifida and the cerebellum comes from the observation that neural tube defects result in an abnormal posterior fossa, the so-called Arnold–Chiari malformation, seemingly due to mechanical tethering of the developing spinal cord. As a final link in the chain of implication that points suspicion at the cerebellum, there is a recent report that MRI abnormalities of the cerebellum are related to handedness (Snyder et al., 1995), and there is also recent evidence in a group of right-handers of greater blood flow in the right dentate nucleus than the left dentate nucleus (Gao et al., 1996). The latter study is one of a number of ''revisionist'' interpretations of the functioning of the cerebellum (Barinaga, 1996; Leiner, Leiner & Dow, 1989, 1991) which have suggested that its classical role as merely concerned in motor control should be changed to recognise that it is central to classical conditioning, to the processing of sensory information, and perhaps to the control of timing—in short that it acts as a ''neuronal learning machine'' (Raymond, Lisberger, & Mauk, 1996, p. 1196).

This is a strong link to handedness indeed, first because, as many studies have shown, timing differences are implicated in cerebral dominance, with the dominant hand being characterised precisely by faster tapping times (Peters, 1980), and also by the left cerebral hemisphere being capable of making better temporal discriminations (Nicholls, 1996). It may also not be coincidence that in dyslexia, where abnormalities of handedness are frequently found (Eglinton & Annett, 1994), there also seems to be evidence of problems in timing and other cerebellar functions (Nicolson, Fawcett, & Dean, 1995). More extreme still is the provocative suggestion by Bickerton (1996) that the neo-cerebellum, via its direct links with the pre-frontal language areas (Fiez, Peterson, & Raichle, 1997; Leiner et al., 1989, 1991), may be the neuronal substrate responsible for syntax, that quintessentially left-hemisphere activity, with damage or developmental

failure resulting in the much less effective ''protolanguage''; and in support of that position we note cases of agrammatism occurring after cerebellar damage (Silveri, Leggio, & Molinair, 1994).

Second, it provides an explanation of why there should be inconsistency in skill and preference for handedness, as the original study of McManus et al. (1992b) suggested that hand preference is prior to skill asymmetry, and that skill asymmetry normally occurs because the dominant hand is used more frequently, and therefore becomes more skilled. If conditioning and other forms of cerebellar learning are abnormal in autism and Fragile-X then it becomes possible both to have a preferred hand (due to some prior, non-learned, mechanism) but for the additional experience acquired due to being preferred not subsequently influencing the learning of motor skills. It may also explain why mature patterns of handedness begin to develop at about 2 years of age, precisely when children progress from protolanguage to language.

OTHER BRAIN AREAS LINKED TO HANDEDNESS

This review began by suggesting that handedness could be fractionated into separable components by looking at atypical patterns of handedness, but has concentrated on the possible role of the cerebellum in the particular anomaly of ambiguous handedness. Much could also have been written about the role of fluctuating asymmetry in increasing the overall incidence of left-handedness in retarded populations (Batheja & McManus, 1985; Livshits & Kobyliansky, 1991; Malina & Buschang, 1984). However, little could have been written about other putative brain areas that may determine atypical patterns of handedness. It seems unlikely that cerebral cortex is not in some way involved in aspects of determining handedness, although other areas of the brain may also be important in some anomalies—and a crucial role may well be played by the hippocampus, given the important recent finding of Lipp et al. (1996) that both direction and degree of paw preference in mice is correlated with asymmetry in the size of the intra-/infrapyramidal mossy fibre projections.

CONCLUSIONS

In a recent review, Peters (1995, p. 194) wrote ''In the literature on handedness, the cerebellum does not normally enter the discussion. However there are good reasons to focus some attention on this structure''. Neither has the study of handedness normally looked at the wide range of syndromes associated with mental retardation and learning disability. It is perhaps time now to start looking systematically at other syndromes such as foetal alcohol syndrome, William's syndrome, Joubert syndrome (autosomal cerebellar vermis agenesis) (Holroyd, Reiss, & Bryan, 1991), cri-du-chat syndrome, and the wide range of autosomal and sex chromosomal aneuploidies, particularly if there is evidence of cerebellar

abnormality. Therein may lie the clue to unravelling the neural basis of handedness.

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REFERENCES

Alembik, Y., Dott, D., & Stoll, C. (1995). Rett-like syndrome in fragile X syndrome. *Genetic Counseling*, *6*, 207–210.

Barinaga, M. (1996). The cerebellum: Movement coordinator or much more? *Science*, *272*, 482–483.

Batheja, M., & McManus, I.C. (1985). Handedness in the mentally handicapped. *Developmental Medicine and Child Neurology*, *27*, 63–68.

Bauman, M.L., Kemper, & Arin. (1995). Pervasive neuroanatomic abnormalities of the brain in three cases of Rett's syndrome. *Neurology*, *45*, 1581–1586.

Bickerton, D. (1996). *Language and human behaviour*. London: UCL Press.

Boucher, J. (1977). Hand preference in autistic children and their parents. *Journal of Autism and Childhood Schizophrenia*, *7*, 177–178.

Casanova, M.F., Naidu, S., Goldberg, T.E., Moser, H.W., Khoromi, S., Kumar, A., Kleinman, J.E., & Weinberger, D.R. (1991). Quantitative magnetic resonance imaging in Rett syndrome. *Journal of Neuropsychiatry and Clinical Neurosciences*, *3*, 66–72.

Christen, J.H., & Hanefeld, F. (1995). Male Rett variant. *Neuropediatrics*, *26*, 81–82.

Corballis, M.C., Lee, K., McManus, I.C., & Crow, T.J. (1996). Location of the handedness gene on the X and Y chromosomes. *American Journal of Medical Genetics (Neuropsychiatric Genetics)*, *67*, 50–52.

Cornish, K.M., & McManus, I.C. (1996). Hand preference and hand skill in children with autism. *Journal of Autism and Developmental Disorders*, *26*, 597–609.

Cornish, K.M., Pigram, J., & Shaw, K. (this issue). Do anomalies of handedness exist in children with Fragile-X syndrome? *Laterality*, *2*.

Courchesne, E., Saitoh, O., Yeung Courchesne, R., Press, G.A., Lincoln, A.J., Haas, R.H., & Schreibman, L. (1994a). Abnormality of cerebellar vermian lobules VI and VII in patients with infantile autism: Identification of hypoplastic and hyperplastic subgroups with MR imaging. *AJR: American Journal of Roentgenology*, *162*, 123–130.

Courchesne, E., Townsend, J., & Saitoh, O. (1994b). The brain in infantile autism: Posterior fossa structures are abnormal. *Neurology*, *44*, 214–223.

Crow, T.J. (1989). Pseudoautosomal locus for the cerebral dominance gene. *Lancet*, *ii*, 339–340.

Eglinton, E., & Annett, M. (1994). Handedness and dyslexia: A meta-analysis. *Perceptual and Motor Skills*, *79*, 1611–1616.

El-Badri, S.M., & Lewis, M.A. (1993). Left hemisphere & cerebellar damage in Asperger's syndrome. *Irish Journal of Psychological Medicine*, *10*, 22–23.

Engerstrom, I.W. (1992). Rett syndrome: The late infantile regression period—a retrospective analysis of 91 cases. *Acta Paediatrica*, *81*, 167–172.

Fiez, J., Peterson, S.E., & Raichle, M.E. (1997). Impaired habit learning following cerebellar haemorrhage. A single case study. *Society for Neuroscience Abstracts*, *16*, 287.

Fraser, F.C. (1983). Association of neural tube defects and parental nonrighthandedness. *American Journal of Human Genetics*, *35*, 89A.

Gao, J., Parson, L.M., Bower, J.M. Xiong, J., Li, J., & Fox, P.T. (1996). Cerebellum implicated in sensory acquisition and discrimination rather than motor control. *Science*, *272*, 545–547.

Hashimoto, T., Tayama, M., Murakawa, K., Yoshimoto, T., Miyazaki, M., Harada, M., & Kuroda, Y. (1995). Development of the brainstem and cerebellum in autistic patients. *Journal of Autism and Developmental Disorders*, *25*, 1–18.

Hetherington, R., & Dennis, M. (in press). Motor function profile in children with early onset *hydrocephalus*. *Developmental Neuropsychology*.

Hinds, H.L., Ashley, C.T., Sutcliffe, J.S., & et al. (1993). Tissue specific expression of FMR-1 provides evidence for a functional role in fragile-X syndrome. *Nature Genetics*, *3*, 36–43.

Holroyd, S., Reiss, A.L., & Bryan, R.N. (1991). Autistic features in Joubert syndrome: A genetic disorder with agenesis of the cerebellar vermis. *Biological Psychiatry*, *29*, 287–294.

Jellinger, K., & Seitelberger, F. (1986). Neuropathology of Rett syndrome. *American Journal of Medical Genetics, Supplement*, *1*, 259–288.

Jernigan, T.L., & Bellugi, U. (1990). Anomalous brain morphology on magnetic resonance images in Williams syndrome and Down syndrome. *Archives of Neurology*, *47*, 529–533.

Leiner, H.C., Leiner, A.L., & Dow, R.S. (1989). Reappraising the cerebellum: What does the hindbrain contribute to the forebrain? *Behavioral Neuroscience*, *103*, 998–1008.

Leiner, H.C., Leiner, A.L., & Dow, R.S. (1991). The human cerebro-cerebellar system: Its computing, cognitive and language skills. *Behavioral Brain Research*, *44*, 113–128.

Lipp, H., Collins, R.L., Hausheer-Zarmakupi, Z., Leisinger-Trigona, M., Crusio, W.E., Nosten-Bertrand, M., Signore, P., Schwegler, H., & Wolfer, D.P. (1996). Paw preference and intra-infrapyramidal mossy fibres in the hippocampus of the mouse. *Behavior Genetics*, *26*, 379–390.

Livshits, G., & Kobyliansky, E. (1991). Fluctuating asymmetry as a possible measure of developmental homeostasis in humans: A review. *Human Biology*, *63*, 441–446.

Lonton, A.P. (1976). Hand preference in children with myelomeningocoele and hydrocephalus. *Developmental Medicine and Child Neurology*, *18 (Supp 37)*, 143–149.

Lotspeich, L.J., & Ciaranello, R.D. (1993). The neurobiology and genetics of infantile autism. *International Review of Neurobiology*, *35*, 87–129.

Malina, R.M., & Buschang, P.H. (1984). Anthropometric asymmetry in normal and mentally retarded males. *Annals of Human Biology*, *11*, 515–531.

McGlone, J. (1985). Can spatial deficits in Turner's syndrome be explained by focal CNS dysfunction or atypical speech lateralization? *Journal of Clinical and Experimental Neuropsychology*, *7*, 375–394.

McManus, I.C. (1983). The interpretation of laterality. *Cortex*, *19*, 187–214.

McManus, I.C. (1996). Handedness. In J.G. Beaumont, P.M. Kenealy, & M.J.C. Rogers (Eds.), *The Blackwell Dictionary of Neuropsychology* (pp.367–376). Oxford: Blackwell.

McManus, I.C., & Bryden, M.P. (1992a). The genetics of handedness, cerebral dominance and lateralization. In I. Rapin & S.J. Segalowitz (Eds.), *Handbook of neuropsychology, Vol. 6, Section 10: Child neuropsychology (Part 1)* (pp.115–144). Amsterdam: Elsevier.

McManus, I.C., Murray, B., Doyle, K., & Baron-Cohen, S. (1992b). Handedness in childhood autism shows a dissociation of skill and preference. *Cortex*, *28*, 373–381.

Murakami, J.W., Courchesne, E., Haas, R.H., Press, G.A., & Yeung Courchesne, R. (1992). Cerebellar and cerebral abnormalities in Rett syndrome: A quantitative MR analysis. *AJR: American Journal of Roentgenology*, *159*, 177–183.

Murakami, J.W., Courchesne, E., Press, G.A., Yeung Courchesne, R., & Hesselink, J.R. (1989). Reduced cerebellar hemisphere size and its relationship to verbal hypoplasia in autism. *Archives of Neurology*, *46*, 689–694.

Netley, C., & Rovet, J. (1982a). Handedness in 47, XYY males, *Lancet*, *ii*, 267.

Netley, C., & Rovet, J. (1982b). Atypical hemispheric lateralization in Turner syndrome subjects. *Cortex*, *18*, 377–384.

Nicholls, M.E.R. (1996). Temporal processing asymmetries between the cerebral hemispheres: Evidence and implications. *Laterality*, *1*, 97–137.

Nicolson, R.I., Fawcett, A.J., & Dean, P. (1995). Time estimation deficits in developmental dyslexia: Evidence of cerebellar involvement. *Proceedings of the Royal Society of London, Series B, Biological Sciences*, *259*, 43–47.

Nihei, K., & Naitoh, H. (1990). Cranial computed tomographic and magnetic resonance imaging studies on the Rett syndrome. *Brain Development*, *12*, 101–105.

Nomura, Y., & Segawa, M. (1990). Characteristics of motor disturbances of the Rett syndrome. *Brain Development*, *12*, 27–30.

Nomura, Y., Segawa, M., & Hasegawa, M. (1984). Rett syndrome—Clinical studies and pathophysiological consideration. *Brain Development*, *6*, 475–486.

Oldfors, A., Sourander, P., Armstrong, D.L., Percy, A.K., Witt Engerstrom, I., & Hagberg, B.A. (1990). Rett syndrome: Cerebellar pathology. *Pediatric Neurology*, *6*, 310–314.

Olinsky, S., Loop, B.T., DeKosky, A., Ripepi, B., Weng, W., Cummins, J., Wenger, S.L., Yan, Y., Lagenaur, C., & Narayanan, V. (1996). Chromosomal mapping of the human M6 genes. *Genomics*, *33*, 532–536.

Olsson, B., & Rett, A. (1986). Shift to righthandedness in Rett syndrome around age 7. *American Journal of Medical Genetics*, *24*, 133–141.

Peters, M. (1980). Why the preferred hand taps more quickly than the non-preferred hand: Three experiments on handedness. *Canadian Journal of Psychology*, *34*, 62–71.

Peters, M. (1995). Handedness and its relation to other indices of cerebral lateralization. In R.J. Davidson & K. Hugdahl (Eds.), *Brain asymmetry* (pp.183–214). Cambridge, MA: MIT Press.

Petit, E., Herault, J., Martineau, J., Perrot, A., Barthelemy, C., Hameury, L., Sauvage, D., Lelord, G., & Muh, J.P. (1995). Association study with two markers of a human homeogene in infantile autism. *Journal of Medical Genetics*, *32*, 269–274.

Ratcliffe, S.G., & Tierney, I.R. (1982). 47 XXY males and handedness [letter]. *Lancet*, *2*, 716.

Raymond, J.L., Lisberger, S.G., & Mauk, M.D. (1996). The cerebellum: A neuronal learning machine? *Science*, *272*, 1126–1131.

Reiss, A.L., Aylward, E., Freund, L.S., Joshi, P.K., & Bryan, R.N. (1991a). Neuroanatomy of fragile X syndrome: The posterior fossa. *Annals of Neurology*, *29*, 26–32.

Reiss, A.L., & Freund, L. (1990). Fragile X syndrome. *Biological Psychiatry*, *27*, 223–240.

Reiss, A.L., Freund, L., Tseng, J.E., & Joshi, P.K. (1991b). Neuroanatomy in fragile X females: The posterior fossa. *American Journal of Human Genetics*, *49*, 279–288.

Reiss, A.L., Patel, S., Kumar, A.J., & Freund, L. (1988). Preliminary communication: Neuroanatomical variations of the posterior fossa in men with the fragile X (Martin-Bell) syndrome. *American Journal of Medical Genetics*, *31*, 407–414.

Satz, P., Soper, H.V., & Orsini, D.L. (1988). Human hand preference: Three nondextral subtypes. In D.L. Molfese & S.J. Segalowitz (Eds.), *Brain lateralization in children* (pp. 281–287). New York: Guilford Press.

Silveri, M.C., Leggio, M.G., & Molinari, M. (1994). The cerebellum contributes to linguistic production: A case of agrammatic speech following a right cerebellar lesion. *Neurology*, *44*, 2047–2050.

Snyder, P.J., Bilder, R.M., Wu, H., Bogerts, H., & Lieberman, J.A. (1995). Cerebellar volume asymmetries are related to handedness: A quantitative MRI study. *Neuropsychologia*, *33*, 407–419.

Soper, H.V., & Satz, P. (1984). Pathological left-handedness and ambiguous handedness: A new explanatory model. *Neuropsychologia*, *22*, 511–515.

Soper, H.V., Satz, P., Orsini, D.L., Henry, R.R., Zvi, J.C., & Schulman, M. (1986). Handedness patterns in autism suggest subtypes. *Journal of Autism and Developmental Disorders*, *16*, 155–167.

Suzuki, H., Hirayama, Y., Sakuragawa, N., & Arima, M. (1989). [Progression of CT scan findings in Rett syndrome.] *No To Hattatsu*, *21*, 321–326.

Wang, P.P., Hesselink, J.R., Jernigan, T.L., Doherty, S., & Bellugi, U. (1992). Specific neurobehavioral profile of Williams' syndrome is associated with neocerebellar hemispheric preservation. *Neurology*, *42*, 1999–2002.

Wassing, H.E., Siebelink, B.M.,& Luyendijk, W. (1993). Handedness and progressive hydrocephalus in spina bifida patients. *Developmental Medicine and Child Neurology*, *35*, 788–797.