Human Neuroplasticity and Education
Pontifical Academy of Sciences, Scripta Varia 117, Vatican City 2011
www.pas.va/content/dam/accademia/pdf/sv117/sv117-vargha.pdf

Extent and Limits of Speech and Language Organization after Early Left Hemisphere Injury

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Background

A commonly held view is that the adverse consequences of brain injury are far less severe if the damage is sustained early in life when neural plasticity and reorganizational capacity are at their peak. Whilst this principle generally holds, as demonstrated by the early studies of Margaret Kennard, a pioneer in the field of plasticity (e.g. Kennard, M.A. 1936; 1938; 1940), there are long-recognized limits and costs to reorganizational processes in the immature brain (e.g. Schneider, 1974; 1979; Isaacson, 1975) with some compensational processes leading to permanent functional deficits (Goldman-Rakic, 1980; Giza and Prins, 2006; Lidzba *et al.*, 2006).

The parade-case for plasticity in humans is the remarkable rescue of speech and language after early left hemisphere injury (e.g. Vargha-Khadem *et al.*, 1985; 1991; Ogden, 1998; Bates *et al.*, 2001; Liegeois *et al.*, 2008a). Here, the typical explanation is that the non-committed right hemisphere assumes speech and language functions after sufficiently early damage to the left hemisphere, consequently sacrificing its own later-developing specialization for nonverbal and visuospatial abilities, thus giving rise to the 'crowding' of two domains of cognitive function in one single hemisphere (Teuber, 1975).

Development of hemispheric specialization for language

Reports on infants' and children's language networks and their lateralization patterns during different stages of development (Dehaene-Lambertz and Baillet, 1998; Dehaene-Lambertz, 2000; Dall'Oglio *et al.*, 1994;) coupled with brain imaging studies of language activation during infancy and childhood (Dehaene-Lambertz, Dehaene, and Hertz-Pannier, 2002; Gaillard *et al.*, 2000; Liegeois *et al.*, 2008b), and molecular studies of genes specifically associated with speech and language (Lai *et al.*, 2001), all point

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to a genetic predisposition in the vast majority of humans to accommodate orovocal communication skills in the left hemisphere. Language ability appears to unfold as a function of age and experience during normal brain development. This predisposition is realized through interactions between neural activity which becomes progressively non-redundant, and neural plasticity which gradually declines with increasing age (Vargha-Khadem *et al.*, 1994). The former process reflects the gradual establishment of crystallized hemispheric specialization by adolescence, whilst the latter explains the selective and chronic dysphasic symptoms that appear after left hemisphere insults sustained in late childhood and adolescence (e.g. Patterson *et al.*, 1989).

Thus, early unilateral brain injury changes the balance between age- and experience-dependent neural activity and neural plasticity by counteracting the emergence of the division of labour between the two cerebral hemispheres and increasing plasticity to rescue at-risk functions in the remaining viable neural space (Vargha-Khadem *et al.*, 1994). The extent to which the normal trajectory of hemispheric specialization is thrown off its course is dependent on a number of interacting variables including: (i) age at onset of the injury, (ii) presence or absence of progressive damage (e.g. intractable epilepsy), (iii) hemispheric side of damage, (iv) extent of injury as indicated by the number of lobes involved, and whether the lesion is predominantly cortical or subcortical, (v) presence or absence of damage in the opposite hemisphere, (vi) stage of cognitive development at the time of injury, (vii) elapsed time since onset of injury to age at assessment, (viii) and age at test. To account for this number of independent variables and evaluate their effects on different aspects of speech and language requires a very large and relatively homogenous population of patients, an endeavour that is currently beyond the resources of even the largest of paediatric centres worldwide. To counter this requirement that large group studies cannot address at this time, a fruitful approach is to examine unique patients whose detailed case studies can provide answers to critical questions about the extent and limits of plasticity and reorganizational capacity of the young brain. This approach will be adopted here to examine speech and language representation in the single right hemisphere of a young adult who has undergone surgical resection of his left hemisphere in childhood to treat his intractable epilepsy. Patients who have undergone hemispherectomy during childhood provide a unique model to test the extent and limits of plasticity in the context of speech and language organization in the isolated right hemisphere (Boatman *et al.*, 1999; Devlin *et al.*, 2003; see also Battro, 2000; Immordino-Yang, 2007; Liegeois *et al.*, 2008a).

The hemispherectomy procedures

Hemispherectomy – complete or partial removal or disconnection of one cerebral hemisphere – is one of the most common forms of pediatric neurosurgery for the relief of epilepsy (Devlin *et al.*, 2003). When children are assessed for hemispherectomy, critical questions that inform surgical decision making relate to neurological status (i.e. presence or absence, and severity of motor and/or visual field deficits), status of intellectual function, the pattern of language lateralization on fMRI, identification of risk factors for the removal of a language dominant hemisphere, and the long term consequences of surgery on speech and language development. Candidates for surgery usually present with a unilateral structural lesion and seizures, the origins of which date to neurodevelopmental pathologies of congenital or early acquired events, although some children are diagnosed with later acquired disorders such as Rasmussen's syndrome that can develop from about 1 year of age through adolescence (Freeman, 2005).

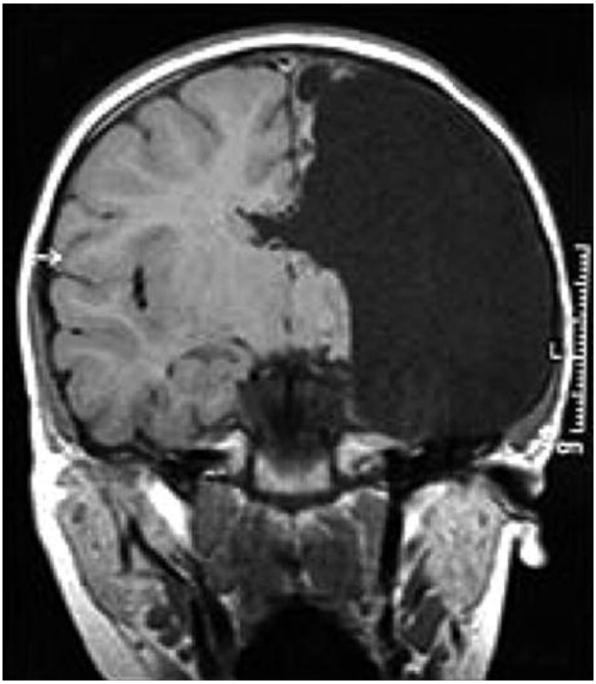

Figure 1. A total hemispherectomy illustrating the disconnection line from the right hemisphere, the large extra dural space created by the removal of the entire left hemisphere and the basal ganglia, and the spared thalamus on the left.

Is there a critical period for speech and language development in the isolated right hemisphere? The case of Alex

A remarkable feature of normal human development is that virtually all healthy children acquire the grammar and vocabulary of their mother tongue within the first few years of life. Failure to achieve this significant milestone in the absence of hearing impairment, social deprivation, or severe intellectual disability, signals lifelong oro-vocal communication deficits leading many language theorists and linguists to hypothesize that there is a 'critical period' for the development of different aspects of speech and language (e.g. Shriberg *et al.*, 1994; Doupe and Kuhl, 1999), with this time window closing around the age of five or six (e.g. Grimshaw *et al.*, 1998).

A robust test of the 'critical period hypothesis' is provided by the case of Alex (Vargha-Khadem *et al.*, 1997), a young boy who was diagnosed at birth with Sturge-Weber syndrome, a rare congenital neurological and cutaneous disorder that is often associated with port-wine stains of the face, glaucoma, seizures, and profound intellectual restriction. Consistent with this diagnosis, within the first few months of life Alex developed infantile left hemisphere seizures, a right-sided hemiplegia, and right hemianopia. By the age of two years, he was diagnosed with severe developmental delay and hyperactivity, and a notable absence of speech, leading his physician to conclude that in his case, Sturge-Weber disease had affected the neural substrates of speech and language on both sides of the brain, thereby permanently precluding the development of this function.

This neurodevelopmental profile prevailed until the age of eight, at which time a resting Positron Emission Tomography scan revealed normal metabolism in the right hemisphere, along with virtually absent metabolic activity in the atrophic left hemisphere. Based on this evidence, the decision was taken to proceed with surgery and Alex underwent a total hemispherectomy at the age of 8:6 years.

The surgery was successful; Alex's seizures were arrested and the pre-existing neurological impairments (i.e. the hemiplegia and the right visual field defect) were not exacerbated. The anticonvulsant regime administered as prophylactic was gradually reduced and eventually discontinued 9 months after surgery, when Alex was aged 9:3 years. Approximately one month after the withdrawal of anticonvulsant medication, Alex's parents noted that he was producing syllables and single words, gradually becoming more communicative and less hyperactive. Within several months of this dramatic breakthrough, he had progressed to producing full sentences.

By the age of 11 when he was seen for a full neuropsychological investigation, Alex was speaking intelligibly in well structured, clearly enunciated sentences and his average length of utterance had increased to 11.6 words, equivalent to the standard of a typical 6- to 7-year old. Between the ages of 9:4 and 15, Alex's linguistic and intellectual abilities were examined in detail, allowing for quantitative assessment of the development and establishment of his speech and language, and other cognitive skills (Vargha-Khadem *et al.*, 1997; Rankin and Vargha-Khadem, 2007). This report extends the follow-up investigations to about age 22 when Alex had achieved maturity as a young adult.

Intellectual development

Prior to surgery at the age of 8:2, Alex's mental age in the various domains of cognitive and behavioural function was between 1:9 and 3:11 years (Griffiths Mental Development Scales, Griffiths, 1970). After the emergence of conversational language and reaching a mental age of about 6 years, however, Alex's intellectual status up to the age of about 21 years was longitudinally assessed using the Wechsler Scales of Intelligence (see Figure 2, p. 243). With increasing age and experience, Alex's verbal and nonverbal IQs on the child version of the Wechsler Scales incrementally increased up to the age of 16:10 showing a modest advantage in verbal relative to nonverbal abilities (~ ½ SD). A switch to the adult Wechsler Scales at the age of 17:9 documented an impressive increase in both IQ scores (in the 70s range), but this was due to the change of scales from child to adult, as a repeat administration of the child scales at age 18:5 showed virtually the same level of performance as that obtained at age 16:10. The final assessment of intelligence on the adult scales at the age of nearly 22 years indicated IQ scores in the exceptionally low range. Overall, across a time span of almost 11 years, Alex's full scale IQ showed incremental, but nevertheless impressive gains of about 20 points, from the low 40s to the low 60s.

Speech and language

At the age of 11 when Alex's speech and language abilities were assessed in detail, he was speaking fluently with an English accent and without a trace of hesitation or unintelligibility. In particular, there were no dysphasic symptoms, and no word finding difficulties. Infrequent grammatical errors were noted, however, and these are underlined in the following free recall of the Bus Story (Renfrew, 1969) that had been read to him. The immediate recall of this passage indicated an age equivalent of 7 years, an increase in verbal output of 5-6 years in a matter of approximately 18 months since the onset of speech relative to his pre-hemispherectomy state of virtual mutism. The text in italics refers to embellishments that Alex introduced into his account of the story (Fig. 3).

The Bus Story
Once upon a time there was a very naughty bus. While his driver was trying to mend him, he decided to run away. He ran along the road beside a train. They made funny faces at each other and raced each other. But the bus had to go on alone, because the train went into a tunnel. He hurried into the city where he met a policeman who blew his whistle and shouted, 'Stop, bus'.

But he paid no attention and ran on into the country. He said, 'I'm tired of going on the road'. So he jumped over a fence. He met a cow who said 'Moo, I can't believe my eyes'. The bus raced down the hill. As soon as he saw there was water at the bottom, he tried to stop. But he didn't know how to put on his brakes. So he fell in the pond with a splash and stuck in the mud. When his driver found where he was, he telephoned for a crane to pull him out and put him back on the road again.

Immediate recall of The Bus Story
"*Once on up a time*... there was a nice bus and he decided to run away. He made funny faces at each other. He went through the country knocking down the people and the policeman blewed his whistle so loud. He couldn't stop and he rode through the countryside and he jumped over the fence and rushed through the fields. And the cow said 'moo' and he said '*good gracious, goodness me*' and he went roaring down the hill. He fell into the water with a big splash. *The end*".

Figure 3. Text of the Bus Story and Alex's immediate recall of the same story (Adapted from Vargha-Khadem *et al.*, 1997, Appendix 2).

Between the ages of 14:2 and 17:9, Alex's listening comprehension and oral expression skills were evaluated on the Wechsler Objective Language Dimensions (Rust, 1996), a test of everyday language use (see Figure 4, p. 243). While his listening comprehension remained stable in the low range (i.e. standard scores in the high 70s), his oral expression skills showed impressive gains, rising from just below the standard score of 60 (i.e. exceptionally low range) to 82 (i.e. low average range).

Phonological abilities

It is well recognized that phonological awareness emerges early during development, manifesting itself as sensitivity to rhymes, sound blending, and phonological imitation, and serving as a reliable predictor of subsequent reading ability in normally developing children (Goswami and Bryant, 1990; Carroll *et al.*, 2003), as well as in cases with various neurodevelopmental or acquired disorders of language, such as developmental dyslexia (Hulme and Snowling, 2009) and *deep dyslexia* (Patterson *et al.*, 1989). Recent evidence suggests that the left dorsolateral prefrontal cortex may play an important role in subserving phonological awareness for spoken language (Kovelman *et al.*, 2011). Thus, the integrity of this brain region in the left hemisphere may be critical for acquisition of reading skills.

To explore Alex's phonological awareness, the Phonological Awareness Protocol devised by Muter (1994a, b) was administered between the ages of 14:11 and 16:10. This protocol comprises tests of rhyme detection, rhyme production, syllable and phoneme identification and segmentation, phoneme deletion and sound blending. Also administered was a test of non-word reading, which is particularly sensitive to detecting difficulties with phonological processing and phoneme to grapheme transcription (Non-word Reading Test, Snowling *et al.*, 1996). Results indicated that whilst Alex's phonological awareness skills at age 14:11 were at the level of a 5- to 6-year-old (i.e. ~2 SDs below the mean) with deficits being much more pronounced on the phoneme than on the syllable subtests, there was evidence of improvement in every domain with increasing age and training experience. By the age of 16:10, the most challenging aspects of phonological processing were non-word reading (Snowling *et al.*, 1996), and sound blending (Muter, 1994b) which showed resistance to significant improvements (Table 1).

Phonological Abilities

	Age		
Test	**14:11**	**15:11**	**16:10**
	%	%	%
Rhyme Detection	40	40	70
Phoneme Completion	62	75	100
Phoneme Deletion - start	12	50	100
Phoneme Deletion - end	0	25	87
Sound Blending	53	75	72
Non-word Reading	0	5	35

Table 1. Development of phonological processing skills during adolescence.

Acquisition and development of literacy skills

Assessed for reading and writing skills (Wechsler Objective Reading Dimensions – WORD; Wechsler, 1993) at the age of 14:11 years, when he had completed four academic terms receiving formal literacy training, Alex had achieved an age equivalent of 6:0 years (i.e. floor level) for both single word reading and spelling. His significantly restricted sight vocabulary had precluded his scoring any points on the reading comprehension subtest of WORD.

Between the ages of 14:11 and 16:10 when Alex's phonological abilities were also being assessed, only limited improvements in literacy skills were achieved, although the acquisition of some sight vocabulary did result in a standard score for reading comprehension that was somewhat above the floor level. Thus, the improvements in certain aspects of phonological processing that took place over the span of two years (i.e. between the age of 14:11 and 16:10 years – see Table 1 above), did not appear to translate to marked changes in the level of reading.

Re-assessed on the same tests at the age of 17:9 years, Alex's scores did not reveal a significant change from when he began to acquire literacy skills at the age of 14:2 years. This, despite the fact that between the ages of 15 and 18 years, Alex was placed in an intensive cognitive and motor rehabilitation programme including literacy training for several hours per day. Yet, his literacy skills failed to improve beyond a basic sight vocabulary for reading and single word spelling (see Figure 5, p. 244).

Conclusions

The remarkable emergence and subsequent development of articulate speech and everyday communication abilities during Alex's second decade of life clearly indicates that the isolated right hemisphere can develop such skills well beyond the 'critical period' of five or six years, thus raising the age for effective learning of a first language to the first decade of life, and possibly up to puberty. Whilst after the emergence of speech, language *comprehension* remained relatively stable within the upper limits of the standard Low range (i.e. 70-79), there was genuine improvement in language *expression* over the late adolescence period (see Figure 4, p. 243). Thus, Alex's standard scores increased at age 14:2 from the Exceptionally Low range (i.e. < 60) to the low average range (i.e. 80-89) at age 17:9. This is an impressive gain indeed given that during this period and beyond, Alex's intellectual abilities remained stable (see Figure 2, p. 243), within the same restricted range (i.e. < 60; Exceptionally Low range). The remarkable development of expressive language over an eight-year period from a baseline of virtual mutism suggests that everyday communication skills are of high priority and are rescued despite restricted intellectual standards.

However, the rescue of verbal communication has not been achieved without costs to other domains of function. For example, deficits have persisted in important aspects of phonological abilities and literacy skills, and in those areas previously reported, such as intelligence, particularly nonverbal intelligence, working memory, formal aspects of language processing and grammar, and visuo-perceptual skills (Vargha-Khadem *et al.*, 1997). This plethora of cognitive deficits prevailed over the period extending to early adulthood. Moreover, systematic training in certain skills, such as reading and writing, did not generalize to improve literacy standards. This pattern of a domain-specific rescue of everyday verbal communication against the background of widespread cognitive impairment raises the intriguing possibility that the right hemisphere has the same capacity as the left only for the high priority function of 'listening and speaking'. Effective development of other cognitive domains, including those involving higher order language processing, appear to require the specialized potential of the left hemisphere, with the impetus provided by intellectual capacity.

Acknowledgements

Thanks are extended to Alex and his family for participation in our research. The UCL Institute of Child Health received funding as a National Institute for Health & Research Specialist Biomedical Research Centre. This research was supported by a grant from the Epilepsy Research Foundation, UK.

References

Bates, E., Reilly, J., Wulfeck, B. *et al.* (2001). Differential effects of unilateral lesions on language production in children and adults. *Brain and Language*. 79(2), 223-265.

Battro, A. (2000). *Half a Brain is Enough: The Story of Nico*. Cambridge, UK: Cambridge University Press.

Boatman, D., Freeman, J., Vining, E., Pulsifer, M., Miglioretti, D., Minahan, R., Carson, B., Brandt, J. & McKhann, G. (1999). Language recovery after left hemispherectomy in children with late-onset seizures. *Annals of Neurology*. 46(4), 579-586.

Goswami, U. and Bryant, P. (1990). *Phonological Skills and Learning to Read*. Lawrence Erlbaum Associates. London.

Carroll, J.M., Snowling, M.J., Stevenson, J., Hulme, C. (2003). The development of phonological awareness in preschool children. *Developmental Psychology*. 39(5), 913-923.

Dall'Oglio, A.M., Bates, E., Volterra, V., Di-Capua, M. & Pezzini, G. (1994). Early cognition, communication and language in children with focal brain injury. *Developmental Medicine and Child Neurology*. 36, 1076-98.

Dehaene-Lambertz, G. & Baillet, S. (1998). A phonological representation in the infant brain. *Neuroreport*. 9(8), 1885-1888.

Dehaene-Lambertz, G. (2000). Cerebral specialization for speech and non-speech stimuli in infants. *Journal of Cognitive Neuroscience*. 12(3), 449-460.

Dehaene-Lambertz, G., Dehaene, S. & Hertz-Pannier, L. (2002). Functional neuroimaging of speech perception in infants. *Science*. 6, 298(5600), 2013-5.

Dehaene-Lambertz, G., Hertz-Pannier, L. & Dubois, J. (2006). Nature and nurture in language acquisition: Anatomical and functional brain-imaging studies in infants. *Trends in Neurosciences*. 29(7), 367-73.

Devlin, A.M., Cross, J.H., Harkness, W., Harding, B., Vargha-Khadem, F. & Neville, B. (2003). Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. *Brain*. Vol. 126, No. 3, 556-566.

Doupe, A.J., and Kuhl, P.K. (1999). Birdsong and human speech: Common themes and mechanisms. *Annual Review of Neuroscience*. 22:567-631.

Freeman, J.M. (2005). Rasmussen's syndrome: progressive autoimmune multi-focal encephalopathy. *Pediatric Neurology*. 32(5):295-299.

Gaillard, W.D., Hertz-Pannier, L., Mott, S.H., Barnett, A.S., LeBihan, D. & Theodore, W.H. (2000). Functional anatomy of cognitive development: fMRI of verbal fluency in children and adults. *Neurology*. 54(1), 180-185.

Giza, C.C., and Prins, M.L. (2006). Is being plastic fantastic? Mechanisms of altered plasticity after developmental acquired traumatic brain injury. *Developmental Neuroscience,* 28: 364-379.

Griffiths, R. *The abilities of young children* (1970). London: Child Development Research Centre.

Grimshaw, G.M., Adelstein, A., Bryden, M.P. & MacKinnon, G.E. (1998). First-language acquisition in adolescence: Evidence for a critical period for verbal language development. *Brain and Language*. 63, 237-255.

Goldman-Rakic, P.S. (1980). Morphological consequences of prenatal injury to the primate brain. *Progress in Brain Research*. 53: 3-10.

Hulme, C. and Snowling M.J. (2009) *Developmental Disorders of Language, Learning and Cognition*. Oxford: Wiley-Blackwell. pp. 37-89

Immordino-Yang, M.H. (2007). A tale of two cases: Lessons for education from the study of two boys living with half their brains. *Mind, Brain and Education*. 1, 66-83.

Isaacson, R.L. (1975). The myth of recovery from early brain damage. In: N.R. Ellis (Ed.). *Aberrant Development in Infancy: Human and Animal Studies*. Lawrence Erlbaum Associates, Hillsdale, NJ. 1-25.

Kennard, M.A. (1936). Age and other factors in motor recovery from precentral lesions in monkeys. *American Journal of Physiology*. 115, 138-146.

Kennard, M.A. (1938). Reorganization of motor function in the cerebral cortex of monkeys deprived of motor and premotor areas in infancy. *Journal of Neurophysiology*. 1, 477-496.

Kennard, M.A. (1940). Relation of age to motor impairment in man and in subhuman primates. *Archives of Neurology and Psychiatry*. 44, 377-397.

Kovelman, I., Norton, E.S., Christodoulou J.A., Gaab N., Lieberman, D.A., Triantafvllou, C., Wolf, M., Whitfield-Gabrieli, S., Gabrieli, J.D. (2011). Brain basis of phonological awareness for spoken language in children and its disruption in dyslexia. *Cerebral Cortex*. E-Pub ahead of publication.

Lai, C.S.L., Fisher, S.E., Hurst, J.A., Vargha-Khadem, F. and Monaco, A.P. (2001) A novel forkhead-domain gene is mutated in a severe speech and language disorder. *Nature*. 413, 519-523.

Lidzba, K., Staudt, M., Wilke, M., Grodd, W. & Kraggeloh-Mann, I. (2006). Visuospatial deficits in patients with early left-hemispheric lesions and functional reorganization of language: Consequence of lesion or reorganization? *Neuropsychologia*. 44(7), 1088-1094.

Liegeois, F., Cross, J.H., Polkey, C., Harkness, W., & Vargha-Khadem, F. (2008a). Language after hemispherectomy in childhood: Contributions from memory and intelligence. *Neuropsychologia*. 46, 3101-3107.

Liegeois, F., Connelly, A., Baldeweg, T. & Vargha-Khadem, F. (2008b). Speaking with a single cerebral hemisphere: fMRI language organization after hemispherectomy in childhood. *Brain and Language*. 106(3), 195-203.

Muter, V (1994a). *Phonology and learning to read in normal and hemiplegic children*. (Ph.D. Thesis). University of London.

Muter, V., Snowling, M., Taylor, S. (1994b). Orthographic analogies and phonological awareness: Their role and significance in early reading development. *Journal of Child Psychology and Psychiatry*. 35(2): 293-31.

Ogden, J.A. (1998). Language and memory functions after long recovery periods in left-hemispherectomized subjects. *Neuropsychologia*. 26(5), 645-659.

Patterson, K., Vargha-Khadem, F., and Polkey, C.E. (1989). Reading with one hemisphere. *Brain*. 112: 39-63.

Rankin, P. and Vargha-Khadem, F. Neuropsychological evaluation – Children. (2007). In: *Epilepsy: A Comprehensive Textbook*, Engel, J. and Pedley, T.A. (eds.). Philadelphia: Lippincott Williams & Wilkins.

Renfrew, C.E. (1969). *The Bus Story*. Old Headington (Oxford): C.E. Renfew.

Rust, J. (1996). *Wechsler Objective Language Dimensions*, Psychological Corporation, London.

Schneider, G.E. (1974). Functional recovery after lesions of the nervous system: 3 developmental processes in neural plasticity. Anomalous axonal connections implicated in sparing and alteration of function after early lesions. *Neuroscience Research Program Bulletin*. 12(2): 222-227.

Schneider, G.E. (1979). Is it really better to have your brain lesion early? A revision of the "Kennard principle". *Neuropsychologia*. 17(6), 557-83.

Shriberg, L.D., Gruber, F.A., and Kwiakowski, J. (1994). Developmental phonological disorders III: Long-term speech-sound normalization. *Journal of Speech and Hearing Research*. 37(6): 1151-1177.

Snowling, M., Stofhard, S., McLean, J. (1996). *Graded Nonword Reading Test*. Bury St Edmunds (Suffolk): Thames Valley Test Company.

Teuber, H.L. (1975). Effects of focal brain injury on human behavior. In: Tower, D. (Editor). *The Nervous System*. Vol. 2, Raven Press, New York, pp. 182-201.

Vargha-Khadem, F., Watters G.V., O'Gorman, A.M. (1985). Development of speech and language following bilateral frontal lesions. *Brain and Language*. 25: 167-183.

Vargha-Khadem, F., Isaacs, E.B., Papaleloudi, H., Polkey, C.E., and Wilson, J. (1991). Development of language in six hemispherectomized patients. *Brain*. 114: 473-495.

Vargha-Khadem, F., Isaacs, E. & Muter, V. (1994). A review of cognitive outcome after unilateral lesions sustained during childhood. *Journal of Child Neurology*. 9, supplement, 2S67-2S73.

Vargha-Khadem, F., Carr, L.J, Isaacs, E., Brett, E., Adams, C. & Mishkin, M. (1997). Onset of speech after left hemispherectomy in a nine-year-old boy. *Brain*. 120(1), 159-182.

Wechsler, D. (1992). *Wechsler Intelligence Scale for Children*, Edition III. UK. Sidcup, Kent. UK. The Psychological Corporation.

Wechsler, D. (1993). *Wechsler Objective Reading Dimensions*. Sidcup, Kent, UK. The Psychological Corporation.

Wechsler, D. (1998). *Wechsler Adult Intelligence Scale*, Edition III, UK. Sidcup, Kent, UK. The Psychological Corporation.

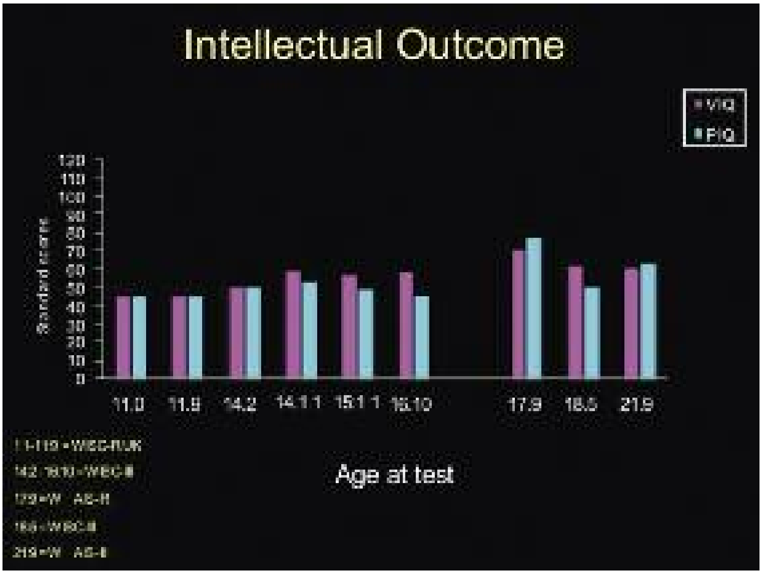

Figure 2. Alex's standardized (mean = 100, SD, 15) intelligence quotients (pink: Verbal IQ; blue: Performance IQ) between the ages of 11:0 and 21:9 years. Range of the average population intelligence quotients (green) is from 80 to 109.

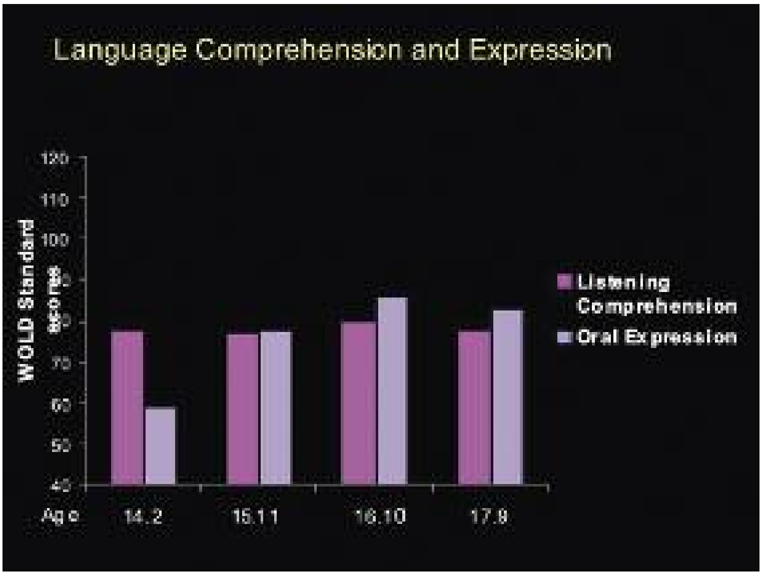

Figure 4. Everyday language comprehension and expression skills of Alex showing improvements in oro-vocal communication during adolescence.

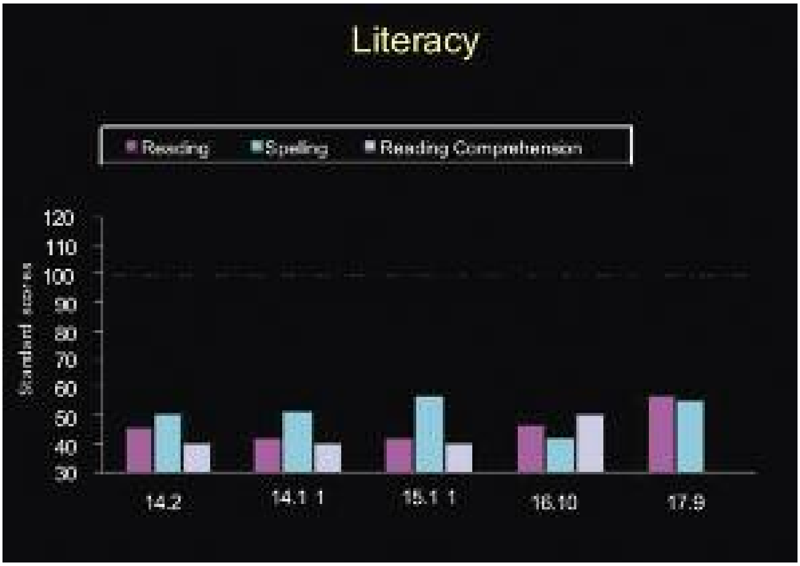

Figure 5. Development of literacy skills during adolescence.