Developmental dyslexia

W A Lishman

The term developmental dyslexia ("specific reading retardation") refers to an unexpected difficulty in reading in children and adults who otherwise possess the intelligence, motivation, and schooling considered necessary for accurate and fluent reading.¹ The concept has had a chequered career, with debates about its definition, origin, and causes, and indeed about its validity as a distinct entity. Increasingly, however, psychological and epidemiological investigations have lent it respectability and there are strong indications that genetic influences are at work.² It is thought to affect between 4 and 7% of children, usually equivalent to a retardation of some 18–24 months in reading relative to expectation.³

A growing consensus highlights problems with phonological processing as a core deficit in the disorder, hence the focus on phonology in the majority of remedial programmes. The phoneme is the smallest identifiable unit of spoken or heard language, individual phonemes being assembled together in the construction of words. An important task in learning to read appears to consist in appreciating the correspondence between such phonemes and their equivalent representations ("graphemes") in written language.

A search is now afoot for possible physiological underpinnings to the condition, and in this, brain imaging has come to make a major contribution, as outlined below.

ADULT SUBJECTS

For obvious reasons, brain imaging was first explored in adults with a history of reading difficulties in childhood, even though by adulthood the problem may have ameliorated. In such subjects, a variety of imaging protocols have shown problems with activation of the language cortex during the performance of reading tasks. Thus, in a ground-breaking positron emission tomography (PET) study, Paulesu *et al* examined five young men who, although ultimately succeeding academically, had had marked dyslexia in childhood.⁴ In this sense they were "compensated" dyslexics. Appropriate normal reading controls were used for comparison.

During performance of a visually presented phonological rhyming task, the dyslexics activated severely restricted areas of the language cortex, in fact Broca's area alone, whereas the controls showed widespread activations from Wernicke's area posteriorly to Broca's area anteriorly plus the tissues of the insula in between. On a phonological memory task, by contrast, the dyslexics activated the posterior language areas, including Wernicke's area and the supramarginal gyrus, but Broca's area only weakly. In neither task did the dyslexics activate posterior and anterior language areas in concert with one another. This suggested a degree of "disconnection" between components of the language apparatus, with obvious consequences for ease of translation between different language codes.

Shaywitz *et al* used functional magnetic resonance imaging (fMRI) on a larger group of dyslexics and controls.⁵ They employed a hierarchical series of tests that made increasing demands on phonological functions, and the scans were analysed to see which brain areas responded with a corresponding progressive increase in activation.

Among the controls, brain activation increased systematically in posterior cortical areas as the phonological demands increased; in Wernicke's area, the angular gyrus and the visual cortex. The dyslexics failed to show such an effect. This again pointed to an imperfectly functioning system for segmenting words into their phonological constituents. By contrast, in frontal regions around Broca's area, the dyslexics showed relative overactivation in response to phonological demands, which was thought to reflect the increased effort they expended on attempts at performing the tasks.

Further studies dealing with whole word reading have shown additional differences between dyslexic readers and controls. Brunswick *et al* monitored the brain activity produced on PET scans when compensated dyslexics and controls read words presented one at a time on a screen.⁶ During word reading, all subjects activated the visual cortex, the left temporoparietal language areas, and the articulatory cortex of Broca's area,

but the dyslexics differed from the controls in certain respects. Firstly, when reading silently they showed diminished activation of the left temporoparietal region generally. Secondly, they showed increased activity in the region of Broca's area when reading aloud, but not when reading silently, which perhaps reflected compensatory efforts to decode print successfully for explicit reading. Thirdly, and perhaps most interestingly, they consistently showed decreased activation of area BA37 in the posterior part of the inferior temporal lobe.

Area BA37 appears to play a critical role in the retrieval of the names of words and objects.⁷ When damaged, for example after a stroke, the patient cannot find the name for an object he is shown even though he is clearly aware of its identity ("word selection anomia"). Any impairment in the functioning of such an area would clearly contribute to the reading difficulties of dyslexic individuals.

STUDIES IN CHILDREN

Attention has now turned to studies in children to see how far such findings may already be present during the period of literacy acquisition or whether they largely reflect long-term changes as the person matures. The results to date strongly support the former view.

Temple *et al* examined fMRI scans during a visual phonological rhyming task in 24 dyslexic children aged 8–12 years (mean 10.7) and controls.⁸ The normal reading controls activated both the left inferior frontal gyrus and the left temporoparietal area. The dyslexics activated the inferior frontal region well (though in a somewhat more anterior location), but temporoparietal activity was virtually absent. Additionally, on a parallel test of orthographic processing (judgements as to whether two visually presented letters were the same) the dyslexic children activated a greatly reduced area of the extrastriate occipital cortex.

Shaywitz *et al* examined a larger and rather older group of 70 dyslexic children aged 7–18 years (mean 13).⁹ Rhyming tasks during fMRI were again employed. In this sample, activations were apparent in left hemisphere posterior sites (both temporoparietal and occipitotemporal), although significantly reduced in degree compared with controls. Left frontal activation was also reduced in the dyslexic children. Thus, support was again obtained for the view that disruptions in important language regions of the brain are already present in childhood dyslexics. Significant correlations were observed between the extent of activation in the posterior

brain regions and a measure of reading skill across the full cohort of dyslexic and control children.

Shaywitz *et al* comment on the contrast between the impaired frontal activity in their childhood dyslexics and the increased frontal activity observed in some adult samples. An age analysis on their cohort showed that the older dyslexic children engaged the frontal systems to an increasing extent as the phonological demands of the tasks increased, suggesting therefore that this represents a compensatory process.

Finally, Simos *et al* have applied magnetoencephalography (MEG) to the problem, examining 10 dyslexic children (mean age 12.6 years) and 8 normal reading controls during performance of a visual word reading task.¹⁰

The results were striking. The left basal temporal cortex in the vicinity of the fusiform and lingual gyri was activated first in all subjects (within 200 ms), presumably representing the pre-lexical analysis of print. Normal readers then activated the left temporoparietal language regions of the brain (superior temporal, angular and supramarginal gyri) within some 300 ms, whereas the dyslexics in the main activated the corresponding regions of the right hemisphere. Only one of the dyslexic children showed reliable left temporoparietal activity, and this was delayed and weak in comparison with the right-sided activity.

Simos *et al* thus concluded that there are marked and consistent differences in the patterns of brain activation between young dyslexic and normal readers during the first half second after reading the printed word. Aberrant patterns of functional connectivity between the basal temporal cortex and the key language areas of the left hemisphere appear to be responsible.

STUDIES OF REMEDIATION

A crucial question concerning the primacy or otherwise of the brain changes observed in dyslexia must lie in whether they are reversible in some degree with remediation. Rather surprisingly, this issue has already been tackled, and both Temple and Simos report encouraging results.

Temple *et al* have reported a move towards normalisation of fMRI scans in 20 dyslexic children after an intensive 8 week course of therapy.¹¹ This consisted of a computerised battery of exercises (*Fast ForWord Language*) including, for example, practice in auditory discrimination, phoneme identification, and language comprehension. After treatment, the left temporoparietal cortex showed activation when this had not been present before. The left frontal

activation had moved more posteriorly to the area seen in controls. Moreover, significant correlations could be observed between the magnitude of increased left temporoparietal activation and improvements on certain measures of language ability and phonological awareness.

Other brain regions, not active in controls, also showed activation post-treatment, including right hemisphere areas homologous to the language areas on the left. This may have reflected compensatory processes. It was also clear that the new left temporoparietal activation was in a region near to, but not identical with the focus seen in normal controls, indicating that the return towards normality was as yet incomplete. More could scarcely be expected after so brief an intervention.

Simos *et al* have repeated MEG studies on eight dyslexic children (mean age 11.4 years) after an 8 week period of therapy.¹² This consisted of approximately 80 hours of one to one instruction focused on the development of phonological processing and decoding skills. On this occasion, they employed a visual rhyming task in conjunction with the MEG recordings

Before the intervention, all of the dyslexic children had shown little or no activation in the left temporoparietal regions, in sharp contrast to the controls, and the predominant activity had been in the homologous regions of the right hemisphere. After treatment, all showed dramatic changes in regional activation profiles; activation in the left superior temporal gyrus now exceeded that on the right, with non-significant trends in the same direction for the supramarginal and angular gyri. All children showed significant gains in reading skills, and a strong correlation was observed between improvement in response accuracy on the rhyming task and the degree of increased activation in the left superior temporal gyrus.

Again, however, there were indications that the restoration towards normality was incomplete, in that the time to peak development of left superior temporal gyrus activity was longer in the treated dyslexics than among the normal reading controls (at 800 ms and 600 ms respectively).

CONCLUSIONS, IMPLICATIONS, AND FURTHER QUESTIONS

These relatively recent investigations give strong support for the validity of the concept of developmental dyslexia along with evidence of its neurobiological basis. The results are impressive, not least in revealing dysfunctions in areas where one would expect to find them; in brain regions known to be involved with

language generally and with phonological processes in particular. Such dysfunctions appear to be present from an early age, at least from the period of learning to read, yet they have proved to be amenable in some degree to modification with training. This reinforces the importance of identifying vulnerable children at the earliest opportunity and engaging them in appropriate remediation.

Several questions follow on from these findings, such as possible origins for the disturbed brain physiology, its cerebral substrate, and its universality among poor readers generally. In this last regard, it may also be asked how broadly it applies to languages other than English.

With regard to its origins, the obvious contenders lie with genetics and/or adverse intrauterine events, but these may not be the whole answer. Brain development continues through childhood and possibly adolescence, and becomes "fine tuned" in relation to environmental influences. Those connections that are activated appropriately become strengthened and endure, while others are pruned and discarded. When the child becomes involved with language, such modifications no doubt affect the language systems of the brain to a substantial degree. Thus, both genetic and environmental influences may contribute in varying degrees to the final shaping of the dyslexic brain.

The cerebral substrate underlying the dysfunction also remains mysterious. Galaburda and colleagues have reported cortical dysplasias and ectopias in occasional dyslexic subjects at autopsy,¹³ sometimes in the language cortex itself, but it is impossible to gauge how common these may be. A relative underdevelopment of the left temporal lobe has been suggested by Eliez *et al*, who found a 12% reduction in volume on magnetic resonance images among dyslexic men, affecting the grey matter predominantly.¹⁴ Klingberg *et al* have found evidence on diffusion tensor imaging (DTI) pointing to microstructural abnormalities of the temporoparietal white matter in adults with reading difficulties, the relevant axons being mainly anteroposterior in orientation.¹⁵ DTI is a development of MRI that reflects the integrity of axonal membranes and myelin sheaths, and the coherence of axonal orientation. Significant correlations were observed between reading scores and the severity of the changes in the left white matter tracts that contain the connections between posterior and anterior language areas. However, all such findings rest to date on the investigation of very small numbers of cases.

With regard to the entire spectrum of poor readers, it is noteworthy that brain imaging research has so far been carried out exclusively on subjects with severe and well-diagnosed dyslexia, leaving uncertain the status of the long tail of "other impaired readers". In some, the reading difficulties may appear to have derived from lack of sufficient educational opportunity, or deprivation from an early age of adequate encouragement and stimulation. The question arises whether they too would show abnormal patterns of brain activation when processing written language, or whether this is the prerogative of a small subsample alone. Thus, it remains to be determined how far brain imaging will ultimately reveal differences between those who labour with dysfunctional brains from the outset, and those whose reading difficulties have social rather than innate biological causes.

The question also arises whether English, with its so-called "deep orthography", is unique in leading to dyslexic difficulties in association with this particular neurobiological background. English uses 1120 graphemes to represent the 40 phonemes of the language; Italian, by contrast, uses 33 graphemes to suffice for its 25 phonemes. The prevalence of dyslexia across different languages appears to be related to the depth or shallowness of their orthographies. Paulesu *et al* have nevertheless found that English, Italian, and French dyslexics all show equivalent reductions in activation of the key brain regions known to be affected in English-speaking dyslexics when PET

scans are carried out during word reading.¹⁶ Whether or not there is a universal brain basis for developmental dyslexia in yet other languages remains to be determined.

Finally, this work on dyslexia may be viewed in the context of other forms of learning disability such as difficulties with numeracy or fine manipulative skills. These too may prove to have distinctive correlates in functional brain changes if carefully examined by modern techniques. It is probable that research in dyslexia has at the moment simply taken the lead because problems with reading are so damaging and disabling in present day society.

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REFERENCES

- 1 Shaywitz SE. Dyslexia. *New Engl J Med* 1998;338:307–12.
- 2 Grigorenko EL. Developmental dyslexia: an update on genes, brains, and environments. *J Child Psychol Psychiatry* 2001;42:91–125.
- 3 Snowling M. Reading and other learning difficulties. In: Rutter M, Taylor E, eds. *Child and*

adolescent psychiatry, 4th edition, chapter 40. Blackwell Science, 2002.

- 4 Paulesu E, Frith U, Snowling M, *et al*. Is developmental dyslexia a disconnection syndrome? Evidence from PET scanning. *Brain* 1996;119:143–57.
- 5 Shaywitz SE, Shaywitz BA, Pugh KR, *et al*. Functional disruption in the organisation of the brain for reading in dyslexia. *Proc Natl Acad Sci USA* 1998;95:2636–41.
- 6 Brunswick N, McCrory E, Price CJ, *et al*. Explicit and implicit processing of words and pseudowords by adult developmental dyslexics. A search for Wernicke's Wortschatz? *Brain* 1999;122:1901–17.
- 7 Benson DF. *Aphasia, alexia, and agraphia*. New York: Churchill Livingstone, 1979:154.
- 8 Temple E, Poldrack RA, Salidis J, *et al*. Disrupted neural responses to phonological and orthographic processing in dyslexic children: an fMRI study. *Neuroreport* 2001;12:299–307.
- 9 Shaywitz BA, Shaywitz SE, Pugh KR, *et al*. Disruption of posterior brain systems for reading in children with developmental dyslexia. *Biol Psychiatry* 2002;52:101–10.
- 10 Simos PG, Breier JL, Fletcher JM, *et al*. Cerebral mechanisms involved in word reading in dyslexic children: a magnetic source imaging approach. *Cereb Cortex* 2000;10:809–16.
- 11 Temple E, Deutsch GK, Poldrack RA, *et al*. Neural deficits in children with dyslexia ameliorated by behavioral remediation: evidence from functional MRI. *Proc Natl Acad Sci USA* 2003;100:2860–5.
- 12 Simos PG, Fletcher JM, Bergman E, *et al*. Dyslexia-specific brain activation profile becomes normal following successful remedial training. *Neurology* 2002;58:1203–13.
- 13 Galaburda AM. Neurology of developmental dyslexia. *Curr Opin Neurol Neurosurg* 1992;5:71–6.
- 14 Eliez S, Rumsey JM, Giedd JN, *et al*. Morphological alteration of temporal lobe gray matter in dyslexia: an MRI study. *J Child Psychol Psychiatry* 2000;41:637–44.
- 15 Klingberg T, Hedehus M, Temple E, *et al*. Microstructure of temporo-parietal white matter as a basis for reading ability: evidence from diffusion tensor magnetic resonance imaging. *Neuron* 2000;25:493–500.
- 16 Paulesu E, Démonet J-F, Fazio F, *et al*. Dyslexia: cultural diversity and biological unity. *Science* 2001;291:2165–7.

Ruptured intracranial aneurysms

Surgical treatment of ruptured intracranial aneurysms

D W J Dippel

The paper by Lafuente and Maurice-Williams on p 1680–1684 describes a well documented, consecutive, personal series of neurosurgically treated patients with aneurysmal sub-arachnoid haemorrhage, and it puts the finger on a sore spot.

Since the early 1960s, not more than two randomised controlled trials of surgical interventions in aneurysmal subarachnoid haemorrhage have been published. As a result, we are still not sure whether patients should be operated early, whether it would be safe

enough to operate in the 4–10 day period when risks of ischaemia are high, and whether surgery in patients with a lowered level of consciousness should be postponed, or not. It was therefore virtually impossible to make a surgical management strategy that fits the risk profile of the individual patient and base it on firm evidence.

Before these questions concerning aneurysm surgery have been answered, the new therapeutic possibility of endovascular coiling is gaining acceptance. The International Subarachnoid Aneurysm Trial (ISAT),² which compared endovascular treatment with aneurysm surgery in more than 2000 patients had several characteristics not seen often in neurosurgical trials: it was randomised, large, and pragmatic. Neurosurgeons with limited experience

(at least 30 aneurysm treatment procedures) were allowed to participate. Such a pragmatic study provides pragmatic, global results and conclusions: 76% of the patients who underwent endovascular treatment were independent after 1 year, whereas 69% of the patients who were allocated to neurosurgical treatment were independent (difference: 7%, 95% confidence interval (CI): 3 to 11%). Interestingly, a similar difference was found in the proportions of patients who had no symptoms at all after treatment, suggesting that neuropsychological disturbances may be more common after neurosurgical treatment.

The ISAT results should be considered as preliminary, as long term follow up results are lacking. The low rate of rebleeding after 1 year of follow up (0.2%) in ISAT are reassuring, but who knows how endovascular coils will behave after 3, 5, or 10 years? Other questions remain to be answered with regard to timing of the procedure and to the shape, size, and site of aneurysms that will be more suitable for coiling than for surgery.

The results of Lafuente and Maurice Williams are impressive: overall mortality in their series is 17.1%, and the mortality in operated patients was 5 out of 190 (2.6%). Should these figures be taken at face value? There are at least four potential sources of error here. Firstly, the favourable baseline

characteristics compared with population studies³ suggests referral selection, although its effects may be limited because surgery was late.⁴ Secondly, authorship bias, as reported by Rothwell in carotid endarterectomy, should be considered, but is probably not applicable.⁵ Thirdly, publication bias may play a role; would other experienced neurosurgeons with somewhat less favourable results also publish such a study? Fourthly, there is the role of chance itself, note that the 95% CI for surgical mortality ranges from 1 to 6%. Because of the above, and because prognostic factors in ISAT were less favourable, a direct comparison with the neurosurgical results in this study is not possible.

However, we all want to make evidence based treatment decisions for our aneurysm patients. We therefore need large randomised studies that compare treatment strategies. These studies should allow for detailed scrutiny of subgroups and types of treatment. Where multicentre randomised studies cannot provide this because of their inherent heterogeneity, we will have to resort to well described single centre and population based studies with long follow up. I would not be surprised if neurosurgery should remain the treatment of choice for a rather large subset of patients with aneurysmal SAH. Meanwhile, the challenge to neurosurgeons will be to use and preserve

their common expertise. The standard for late surgery has been set.

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REFERENCES

- 1 Lafuente J, Maurice-Williams R. Ruptured intracranial aneurysms: The outcome of surgical treatment in experienced hands in the period prior to the advent of endovascular coiling. *J Neurol Neurosurg Psychiatry* 2003;74:1680-4.
- 2 Molyneux A, Kerr R, Stratton I, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. *Lancet* 2002;360:1267-74.
- 3 Hackett ML, Anderson CS. Health outcomes 1 year after subarachnoid hemorrhage: An international population-based study. The Australian Cooperative Research on Subarachnoid Hemorrhage Study Group. *Neurology* 2000;55:658-62.
- 4 Whisnant JP, Sacco SE, O'Fallon WM, et al. Referral bias in aneurysmal subarachnoid hemorrhage. *J Neurosurg* 1993;78:726-32.
- 5 Rothwell PM, Slattery J, Warlow CP. A systematic review of the risks of stroke and death due to endarterectomy for symptomatic carotid stenosis. *Stroke* 1996;27:260-5.

Mesial temporal atrophy

Why study mesial temporal atrophy in patients with intractable temporal lobe epilepsy?

F Andermann

The paper by Bonilha *et al* in this issue (pp 1627-1630) represents yet another step in clarifying the significance of atrophy of mesial temporal structures beyond the hippocampus.¹

One of the major advances in the imaging of patients with temporal lobe epilepsy was recognition of hippocampal atrophy, now visible and quantifiable, based on high quality magnetic resonance imaging.² Measurements

of the amygdala volume, carried out in addition to volumetric studies of the hippocampus, provided insights into the significance of the clinical symptom presentation in patients who turned out to have prominent amygdaloid atrophy. Much less clear is the significance of amygdaloid enlargement present in some patients. This does not correspond to a clear neoplastic process and is still awaiting pathological

correlation. The issue of enlargement of the amygdala correlating with various behavioural states such as anxiety, depression, or an aura of fear is receiving increasing attention.

Recent studies have also focused on the volume of the entorhinal cortex, the parahippocampal cortex, the perirhinal cortex and the temporopolar cortex. The latter, coupled with an abnormal signal in the anterior temporal lobe, has been the object of recent studies by the French and Australian schools, but the role of the temporal pole in mesial temporal epilepsy is still not fully clarified.

The study by Bonilha *et al*,¹ in an attempt to resolve the differences between the results of the Montreal³ and the Kuopio schools,⁴ concludes that there is significant reduction in the volume of cortical structures closest to the hippocampus, for example, the entorhinal and perirhinal cortices, whereas the parahippocampal and temporopolar cortices are less affected. They suggest that this volumetric information may strengthen the conclusions of studies

of the hippocampus and amygdala and confirm lateralisation of seizures in patients with unilateral ictal onsets.

Despite the growing body of data describing mesial temporal atrophy, many neurosurgeons, neuroradiologists, and neurologists have not been converted to recognising the value of quantitative volumetric studies, and continue to rely solely on their visual impression of atrophy. This, in addition to signal abnormalities, is often quite clear. Volumetric studies, however, have been shown to greatly improve the yield and to provide valuable evidence for lateralisation and localisation. They also improve recognition of dual pathology—that is, mesial atrophy associated with an additional lesion. These studies require validation by correlation with the surgical results.

Hopefully, increased use of automated methods will lead to greater

utilisation of volumetric studies, which together with optimal EEG and SEEG will provide improved presurgical evaluation and surgical treatment of patients with intractable temporal lobe epilepsy. There will always remain some uncertainty in prognosis based on the effect of disconnection *v* resection, and last but not far from least, on the extent of resection as well as the experience and skill of the surgeon.

Patients with mesial temporal sclerosis and atrophy are still over-represented among individuals with intractable epilepsy. Frequently, because of residual prejudice and other reasons they are deprived of the benefits of surgical therapy, which is increasingly successful in the treatment of this form of epilepsy.

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REFERENCES

- 1 Bonilha L, Kobayashi E, Rorden C, *et al*. Mesial temporal lobe atrophy in patients with refractory temporal lobe epilepsy. *J Neurol Neurosurg Psychiatry* 2003;74:1627–30.
- 2 Cendes F, Andermann F, Gloor P, *et al*. MRI volumetric measurement of amygdala and hippocampus in temporal lobe epilepsy. *Neurology* 1993;43:719–25.
- 3 Bernasconi N, Bernasconi A, Caramanos Z, *et al*. Mesial temporal damages in temporal lobe epilepsy: a volumetric MRI study of the hippocampus, amygdala and parahippocampal region. *Brain* 2003;126:462–9.
- 4 Jutila L, Ylinen A, Partanen K, *et al*. MR volumetry of the entorhinal, perirhinal, and temporopolar cortices in drug-refractory temporal lobe epilepsy. *AJNR Am J Neuroradiol* 2001;22:1490–501.

BNA 2004 Annual Meeting

The British Neuropsychiatry Association 2004 Annual Meeting will be held at the Institute of Child Health, central London, on 26–27 February. The meeting will cover the following topics:

- language disorders
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