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Is developmental dyslexia a disconnection syndrome?
Evidence from PET scanning

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Summary
A rhyming and a short-term memory task with visually presented letters were used to study brain activity in five compensated adult developmental dyslexics. Their only cognitive difficulty was in phonological processing, manifest in a wide range of tasks including spoonerisms, phonemic fluency and digit naming speed. PET scans showed that for the dyslexics, a subset only of the brain regions normally involved in phonological processing was activated: Broca's area during the rhyming task, temporo-parietal cortex during the short-term memory task. In contrast to normal controls these areas were not activated in concert. Furthermore the left insula was never activated. We propose that the defective phonological system of these dyslexics is due to weak connectivity between anterior and posterior language areas. This could be due to a dysfunctional left insula which may normally act as an anatomical bridge between Broca's area, superior temporal and inferior parietal cortex. The independent activation of the posterior and anterior speech areas in dyslexics supports the notion that representations of unsegmented and segmented phonology are functionally and anatomically separate.

Keywords: dyslexia; functional brain imaging; insula; phonology; perisylvian regions

Abbreviations: BA = Brodmann's area; IFG = inferior frontal gyrus; rCBF = regional cerebral blood flow; SMA = supplementary motor area; WRAT = Wide Range Achievement Test

Introduction
Between 2 and 10% of the population of the English speaking world have great difficulty with learning to read in spite of adequate educational resources, a normal (or even above normal) IQ and no obvious sensory defects (Rutter and Yule, 1975; Miles and Haslum, 1986). This disorder is commonly called developmental dyslexia and has long been believed to have a neurological basis (Morgan, 1896; Hinshelwood, 1917; Critchley, 1970). It is also increasingly clear from investigations of twins and families that dyslexia is a developmental disorder with a genetic origin (Stevenson *et al.*, 1987; Olson *et al.*, 1989; DeFries, 1991; Cardon *et al.*, 1994).

The existence of a specific problem with learning to read, alongside normal development of other abilities, suggests damage to a specific cognitive component which is essential to the development of word recognition (Shankweiler and Crain, 1986; Anderson, 1992; Morton and Frith, 1995). Conversely, the existence of hyperlexia in people who are otherwise mentally handicapped shows that the component underlying word recognition can remain functionally intact despite impairments in other cognitive functions (Frith and Snowling, 1983). The anatomical basis for this specific component is still unknown.

The authors of most reviews of the field have concluded that developmental dyslexics have an underlying problem in the domain of phonology (e.g. Frith, 1981, 1985; Snowling

1981; Wagner and Torgesen, 1987; Brady and Shankweiler, 1991). Phonological problems are seen particularly in a relative failure to read and spell non-words (Rack *et al.*, 1992). They are seen outside reading and spelling activities in tasks that assess phonological awareness (Liberman *et al.*, 1974; Bradley and Bryant, 1978; Manis *et al.*, 1993), verbal short-term memory (Nelson and Warrington, 1980; Jorm, 1983; Johnston, *et al.*, 1987), word and non-word repetition (Brady *et al.*, 1983; Kamhi and Catts, 1986; Snowling *et al.*, 1986), rapid automatic naming (Denckla and Rudel, 1976; Wolf, 1986; Bowers and Swanson, 1991) and phoneme perception (Brandt and Rosen, 1980). Developmental dyslexia is often associated with other speech and language impairments (Kamhi and Catts, 1986). Early manifestations of dyslexia can be seen already at age 2.5 years, where deviant speech patterns and impairments of productive syntax have been reported (Scarborough, 1990). Dyslexics can achieve reading and spelling skills that are sufficient for academic success. However, a number of studies (Campbell and Butterworth, 1985; Felton *et al.*, 1990; Pennington *et al.*, 1990; Bruck, 1992; Elbro *et al.*, 1994) have shown that an underlying deficit in phonology persists through adulthood.

While there may be cases in which there is a prominent visual problem (e.g. Livingstone *et al.*, 1991), the prevailing opinion is that, for the most part, the difficulties in learning to read and write that are typical of dyslexia, are caused by a fundamental problem with speech processing. Exactly what this fundamental problem consists of is less clear. Speech processing is highly complex and involves many different representations from the acoustic signal associated with heard words to the sequence of articulations associated with spoken words (Levelt, 1989). These different representations must be encoded in the nervous system. We shall refer to them as codes in order to emphasize the requirement that they are equivalent and that they can be converted from one to another. An analogy is Morse code, which involves the representation of letters of the alphabet in a novel form.

In order to read and write, children have to learn how to map the sound of the heard word, the sight of the written word and the articulatory sequence of the spoken word on to each other (Ehri, 1992). Additional codes have to be learned concerning segments of word sounds and word spellings, specific sequences of letters and their relation to speech sounds. Thus, both whole word and segmented codes are involved in the acquisition of written language, and the child needs to learn to relate these codes correctly to each other. Suggestions of how the mapping from one code to another might be learned have been proposed in connectionist terms by Seidenberg and McClelland (1989) and Shallice and Plaut (1992) amongst others.

In the skilled language user, the mapping between all these different codes will occur rapidly and automatically. In the case of dyslexics, this high level of skill may never be reached. Phonological codes appear to be less well specified (Snowling and Hulme, 1994) and translation from one code to another remains difficult. For example, Snowling (1980) found that dyslexic children were worse than normal controls of the same reading age in cross-modal matching (visual–auditory) of non-words, but were not impaired when matching stimuli presented in the same modality. Furthermore, with increasing sight vocabulary the dyslexic sample showed no such increase in their cross-modal matching ability. The idea that weak connections between different linguistic codes may be critical in dyslexia, is reminiscent of earlier suggestions that there is a more general failure of cross-modal associations (in particular auditory–visual integration) (Birch and Belmont, 1964; Critchley, 1970). Nevertheless, this difficulty does not appear to prevent the acquisition of a large sight word vocabulary (Snowling *et al.*, 1994).

The anatomy of the phonological system is known in broad terms. The available anatomical evidence stems from the study of pathological correlates in aphasic patients with phonological defects in speech production or in speech comprehension (e.g. conduction aphasics and Wernicke's and Broca's aphasics; for review, *see* Lecours and Lhermitte, 1970). All of these studies emphasize the importance of the perisylvian structures of the dominant hemisphere for phonological processing (Cappa *et al.*, 1981). In particular, the areas that have been consistently implicated are Broca's area (Gainotti *et al.*, 1982), Wernicke's area (Selnes *et al.*, 1985; Lund *et al.*, 1986), the insula (Damasio and Damasio, 1980), the supramarginal gyrus and the arcuate fasciculus (Warrington *et al.*, 1971; Benson *et al.*, 1973; Kertesz et al., 1979; Mazzocchi and Vignolo, 1979). Additional convergent evidence on the role of the perisylvian structures in phonology has now been provided by PET (Démonet *et al.*, 1992, 1994; Sergent *et al.*, 1992; Zatorre *et al.*, 1992; Paulesu *et al.*, 1993) and functional MRI activation experiments (Paulesu *et al.*, 1995; Shaywitz *et al.*, 1995)

In the speech processing system, specific roles for Broca's area and Wernicke's area have been suggested: Broca's area being involved in an output code (Mohr *et al.*, 1978; Démonet *et al.*, 1992; Zatorre *et al.*, 1992; Paulesu *et al.*, 1993), and Wernicke's area (the superior temporal gyrus) in some form of input code (Zatorre *et al.*, 1992). Further evidence (Paulesu *et al.*, 1993: Price *et al.*, 1995), however, shows that Wernicke's area is not only activated by auditory language input, but also by language tasks which do not involve auditory stimulation. Thus, Wernicke's area may be involved in modality independent phonological representations. However, the role of a number of other components of the phonological system (e.g. insula) remains unknown.

The psychological evidence for a phonological deficit in dyslexia is supported by some anatomical evidence. Most of the pathological and the neuroimaging evidence has pointed to anomalies of the perisylvian regions (Galaburda *et al.*, 1985; Humphreys *et al.*, 1990; for a review, *see* Galaburda, 1992). One important question is whether, in dyslexics, the perisylvian areas have preserved phonological competence. Functional imaging techniques seem well suited to explore this question. Indeed, a recent PET activation study (Rumsey *et al.*, 1992) has shown that developmental dyslexics failed

to activate the region of the left temporo-parietal cortex during a rhyming task, a result that complements pathological and structural imaging evidence.

In the present study we have combined cognitive and biological investigations and compared normal and abnormal phonological processing. We used a PET paradigm which has already been shown to give robust activation, highly consistent over individual normal subjects, in brain areas associated with phonological processing (Paulesu *et al.*, 1993). This paradigm consists of a rhyming task and a phonological short-term memory task in which verbal material is presented visually. Most of the main components of the phonological system are engaged by these tasks. Segmented phonology is vital for the rhyming task (the sub-syllabic components onset and 'rime' have to separated, e.g. b/ee); short-term phonological storage is vital for the memory task. Unsegmented phonology may be important in both tasks since visual stimuli have to be translated into names. Comparison of the two tasks permits separation of some of these components. The developmental dyslexics who volunteered for this study were all tested on a range of psychological tasks and all exhibited phonological problems. These problems could derive from defects in any or all of the components of the phonological system and their interactions.

Methods

Subjects

Right-handed males who had completed secondary or tertiary education in spite of a clear history of developmental dyslexia were identified from the records of a dyslexia clinic. Four were university students or postgraduates and the fifth was running a family business. All were succeeding in life in spite of their problems. Five right-handed males matched for educational level, but with no history of reading or phonological problems acted as controls for the PET study. All volunteers underwent 12 consecutive regional CBF (rCBF) measurements (three for each of four psychological tasks described below). Volumetric MRI scans were performed on all the dyslexics to make sure that there were no gross structural abnormalities. Details of the MRI scanning procedure are described elsewhere (Watson *et al.*, 1993).

Each volunteer gave written informed consent. The studies were approved by the Hammersmith Hospital Medical Ethics Committee and permission to administer radioactivity was obtained from the ARSAC, UK.

Psychological assessment

The dyslexic volunteers and controls received a detailed psychological assessment with emphasis on phonological skills. Standard reading and spelling tests were included to document attainment level relative to the general population [Wide Range Achievement Test (WRAT); Jastak and Wilkinson, 1984]. Reading and spelling of non-words was included to test knowledge of grapheme–phoneme correspondences. An extensive battery of short-term memory tests was given with visual and auditory presentation of different types of stimuli. A Spoonerism test (based on Perin, 1983) was used to detect persistent difficulties with segmenting and manipulating phonemes. In this task, subjects have to exchange the beginning sounds of two words, so that John Lennon becomes 'lon jennon'. Verbal fluency tasks were used to test access to the lexicon via phonemic cues (predicted to be impaired) in contrast to semantic cues (Frith *et al.*, 1995). Articulation rate was measured since this is known to affect short-term memory (Hulme and McKenzie, 1992). The tests and results are listed in Table 1.

Activation tasks

The two tasks were chosen because they give highly consistent results in normal volunteers and activate all the left perisylvian language areas. The first required rhyme judgements for the names of English letters and the second short-term memory for the same English letters. Stimuli for control conditions were line drawings derived in part from the Korean alphabet. Stimuli were presented visually and subjects were instructed not to speak. For subjects who do not know Korean, Korean letters are unfamiliar visual symbols. In this case they are not processed via a phonological code as has been demonstrated in a previous experiment (Paulesu *et al.*, 1993). A graphical representation of the tasks is presented in Fig. 1. The simplicity of the tasks was such that the dyslexic volunteers could perform them well in spite of their phonological problems.

Similarity judgement tasks

Phonological similarity task (rhyming). Subjects were asked to make rhyme judgments about consonants appearing on a computer screen at a rate of one per second. They moved a joy-stick towards a 'yes' symbol every time a letter appeared that rhymed with the letter 'B' which was always present on the screen. Rhyming letters occurred at a frequency of one in seven.

Shape similarity task. Subjects were asked to judge whether a Korean letter looked similar to a Korean target letter. This target letter was always present on the screen.

Short-term memory tasks

Phonological short-term memory task. Randomized sequences of six phonologically dissimilar consonants were presented on a computer screen at the rate of one per second. Subjects were instructed to rehearse the stimuli silently and to remember the consonants. Two seconds after each sequence, a probe consonant appeared and subjects judged if it was present in the previous sequence. Subjects responded by pointing with a joy-stick to yes/no symbols.

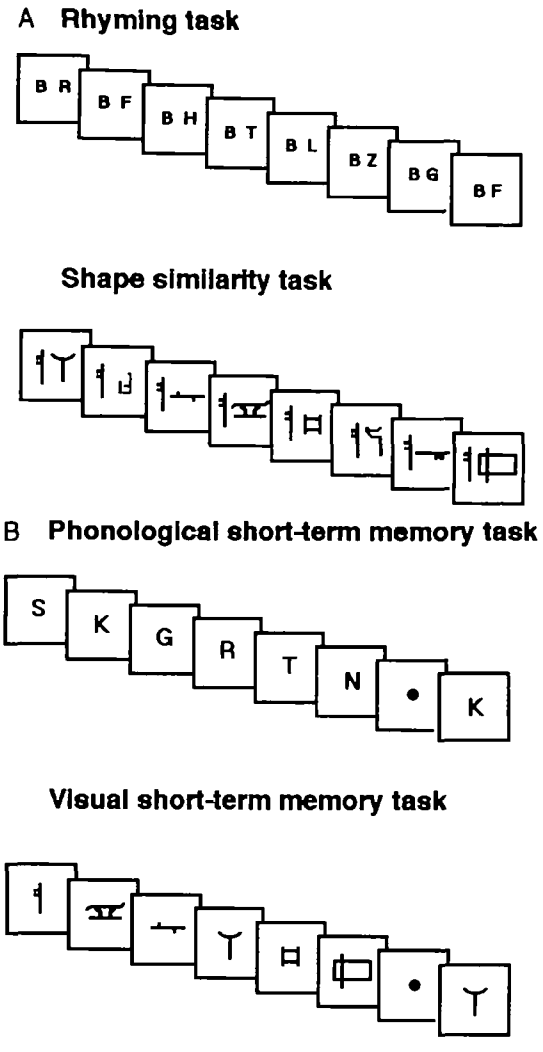

Fig. 1 (**A**) Schematic representation of the rhyming task for letter names and its control task (shape similarity judgements for Korean letters). (**B**) Schematic representation of the phonological short-term memory task and its control (visual short-term memory task for Korean letters) used during PET scanning. A full description of the tasks is given in the main text.

Visual short-term memory task. This task was identical to the previous one with the exception that Korean letters were used. Subjects were encouraged to remember the stimuli using a purely visual code.

PET scanning

Regional CBF was measured by recording the distribution of cerebral radioactivity following the intravenous injection of ^{15}O-labelled water ($H_2{}^{15}O$) with the CTI 953B PET scanner (CTI Inc., Knoxville, Tenn., USA). Data were acquired by scanning with inter-detector collimating septa retracted (3D mode) (Townsend *et al.*, 1991). Each rCBF scan was divided into two frames: (i) 30-s measurement of the background radiation; (ii) 2.45-min rCBF measurement with concurrent psychological stimulation. $H_2{}^{15}O$ infusion (10 ml/min; 55 MBq/ml) started at the beginning of the background frame and lasted for 2 min followed by a 30-s flush of non-radioactive saline. After attenuation correction (measured by a transmission scan), the data were reconstructed as 31 transaxial planes by three-dimensional filtered back projection with a Hanning filter of cut-off frequency 0.5 cycles/pixel.The resolution of the resulting images was 8.5×8.5×4.3 mm at full width half maximum (Spinks *et al.*, 1992). The integrated counts accumulated over the second PET frame, corrected for background activity, were used as an index of rCBF (Mazziotta *et al.*, 1985; Fox and Mintun, 1989).

Image analysis was performed using statistical parametric mapping (SPM) software (Frackowiak and Friston, 1994) on a SPARC 1 workstation (Sun Microsystems Inc., Surrey, UK) using ANALYZE™ version 6.2 (Robb, 1990). Calculations and image matrix manipulations were performed in MATLAB version 3.5 (Mathworks Inc., New York, USA).

Anatomical normalization of PET scans

The 31 original PET scan slices were interpolated to 43 planes in order to render the voxels approximately cubic. Head movements between scans were corrected by aligning them all with the first one using Automated Image Registration software (Woods *et al.*, 1992). PET images were then normalized to the stereotactic space of Talairach and Tournoux (Talairach and Tournoux, 1988; Friston *et al.*, 1991*a*). The stereotactically normalized images had 26 planes of 2×2×4 mm voxels. In order to increase signal to noise ratio and accommodate normal variability in functional gyral anatomy, each image was smoothed in three dimensions with a low-pass Gaussian filter (full width half maximum 10×10×6 pixels, 20×20×12 mm) (Friston *et al.*, 1990).

Experimental design

Our experiment is constructed according to a formal factorial design with one between-group factor (dyslexics versus controls) and three within-group factors; type of task (memory versus matching), type of stimuli (phonological versus visual) and three replications. The order of the conditions was counterbalanced. We first computed activations related to rhyme judgements (versus shape matching) in each group, and then computed activations related to phonological short-term memory (versus visual short-term memory). Differences in activations between the groups for each phonological task (compared with baseline) were then assessed as interactions between the between-group factor (normal controls versus dyslexics) and the relevant within-group factor (tasks).

Statistical analysis

Differences in global activity within and between subjects were removed by analysis of covariance on a pixel-by-pixel basis with global counts as covariate. This was undertaken as inter- and intra-subject differences in global activity may obscure regional alterations in activity following psycho-

Table 1 *Psychological assessments*

Variable	Dyslexics (n = 5)	Controls (n = 6)	Significance Mann–Whitney P (two-tailed)
Age (years)	25.2 (1.5)	27.2 (2.2)	n.s.
Literacy skills			
Reading WRAT, standard score (x = 100)	101.6 (13.0)	115.2 (4.7)	0.02
Spelling WRAT, standard score (x = 100)	96.8 (21.4)	121.5 (4.4)	0.01
Non-word reading (max. = 15)	11.2 (5.0)	14.3 (0.8)	n.s.
Non-word spelling (max. = 15)	12.6 (3.8)	13.8 (0.4)	n.s.
Short-term memory, auditory presentation			
Word repetition (max. = 12)	11.8 (0.4)	12.0 (0.0)	n.s.
Non-word repetition (max. = 12)	9.2 (1.5)	10.2 (1.5)	n.s.
Digit span scaled score (x = 10)	12.0 (3.1)	16.0 (2.4)	0.05
Non-confusable letters (max. = 60)	45.0 (13.0)	59.0 (1.3)	0.02
Confusable letters (max. = 60)	39.6 (4.5)	54.5 (4.4)	0.01
Short words (max. = 60)	43.6 (9.6)	56.0 (3.2)	0.09
Long words (max. = 60)	24.8 (7.4)	40.8 (6.3)	0.01
Short-term memory, visual presentation			
Non-confusable letters (max. = 60)	43.0 (13.1)	59.2 (10.0)	0.01
Confusable letters (max. = 60)	41.6 (9.2)	51.7 (6.2)	0.08
Phoneme manipulation			
Spoonerisms			
Items (max. = 12)	10.4 (1.1)	11.7 (0.5)	0.05
Time (seconds)	13.6 (12.5)	2.4 (1.9)	0.01
Word retrieval (no. words in 1 min)			
Semantic (animals, foods)	23.2 (6.5)	28.4 (3.1)	n.s.
Phonemic (words beginning with 'sh', 'f')	10.8 (3.1)	15.7 (1.5)	0.01
Speech rate			
Digit naming (50 digits)	18.4 (7.9)	13.2 (3.1)	0.10
Word pair repetition (12 times)	21.4 (1.1)	18.8 (1.5)	0.06

n.s. = not significant.

logical activations (Friston *et al.*, 1990). For each pixel in stereotactic space the analysis of covariance generated a condition-specific adjusted mean rCBF value (normalized to 50 ml/dl/min) and an associated adjusted error variance. A repeated-measures ANCOVA was used for the comparison of different tasks, each subject being studied under all conditions. The ANCOVA allowed comparison of the means across conditions using the t statistic. The resulting set of t values constitutes a statistical parametric map (SPM{t}) (Friston *et al.*, 1991*b*). Activations are reported if they reached a significance level of $P < 0.001$. This level protects against false positives (Bailey *et al.* 1991). A further Gaussian filter (8 mm full width half maximum) was applied at this stage of the computation of the statistical parametric maps. The final resolution of the statistical parametric maps was ~10 mm full width half maximum.

Results

Psychological assessments

As Table 1 shows, the five dyslexics performed significantly worse on standardized reading and spelling tests compared with six controls of similar education and age. Nevertheless, their scores were of an average level for their age, indicating that they are well compensated for their earlier problems. A high level of compensation is also indicated by their good performance on non-word reading and spelling and on word and non-word repetition tests.

The dyslexic subjects were, however, significantly impaired on digit span and most of the short-term memory tasks. Their memory problem was particularly striking with long words. They showed a normal confusability effect with auditorily presented letters (confusable letters being recalled less well than non-confusable ones), but not when the presentation was visual.

In our Spoonerism task (John Lennon spoonerized becomes 'lon jennon') there was a striking difference between the groups, both in terms of number correct, and in terms of time. Dyslexics were four to five times slower on this demanding phoneme manipulation task than the controls and all spontaneously commented on the difficulty of this task. Dyslexics were also impaired when generating words from an initial phoneme. This was in contrast to their normal performance when generating words in a semantic category. There was a strong trend for speech rate measures to be slower in the dyslexics than the controls.

In summary, on a range of tasks not involving reading, but involving phonological processing, the dyslexics were

Table 2 *Performance on psychological tasks during PET scanning (percentage correct)*

	Memory tasks		Matching tasks	
	Letters	Symbols	Letters	Symbols
Controls				
Mean	90	76	98	97
Range	85–100	62–87	94–100	92–100
Dyslexics				
Mean	85	67	95	98
Range	77–92	59–73	80–100	92–100

significantly impaired. The results show that our volunteers, despite good compensation in written language skills, still manifest the characteristic pattern of impairments seen in the majority of developmental dyslexics (Rack, 1992). We can therefore consider these subjects representative of dyslexics with phonological problems.

Performance in the activation tasks

During scanning subjects' performance was at an acceptably high level. There were no significant differences between the groups in any of the conditions. The short-term memory tasks were more difficult than the similarity judgement tasks which were virtually errorless (*see* Table 2).

PET results

PET results will be reported with reference to Brodmann's areas (BAs) as defined in the stereotactic space of Talairach and Tournoux (1988). Explicit reference to anatomical structures/landmarks are also given (e.g. the lower bank of the supramarginal gyrus; BA40), as BA topography cannot be precisely defined in life and may be insufficient to identify an activated area. As an aid to identifying these structures, we consulted an MRI image that had been normalized into the same stereotactic space.

Phonological similarity judgement (rhyming) task

Normal controls showed extensive activation of a number of perisylvian structures of the left hemisphere which include part of Broca's area [inferior frontal gyrus (IFG); BA 44/6], the posterior part of the superior temporal gyrus (Wernick's area; BA 21/22), and the anterior and posterior portions of the insula. The area of activation referred to as 'Broca's area' was extensive and included adjacent premotor cortex (BA 6) and the slightly more medial frontal operculum as well as Broca's area proper (BA 44). Additional activations were observed in the supplementary motor area (SMA; medial BA 6), in left premotor cortex (lateral BA 6), in the head of the left caudate nucleus and, bilaterally, in the cerebellar hemispheres. In contrast, dyslexics showed activity only in Broca's area (BA 44) and the left caudate. An illustration of the pattern of activation in both groups during the rhyming task is shown in Fig. 2.

Direct comparison of the controls and the dyslexics showed that the major difference was in the insula, which the dyslexics failed to activate. Smaller differences were observed in left lateral BA 6, and Wernicke's area (superior temporal gyrus; BA 21). The activity in Broca's area did not differ significantly from that of the controls. Stereotactic locations and the statistical magnitude of activations in the two groups as well as the differences between the two groups are shown in Table 3.

Phonological short-term memory task.

In normal controls, the short-term memory task produced a similar pattern of activation to the rhyming task with a few additional activated areas. In the left hemisphere, the supramarginal gyrus (BA 40) was strongly activated. The left lingual gyrus (BA 18) was also activated, and symmetrical

Fig. 2 Location of increases in rCBF (expressed as distribution of *Z* scores) during the rhyming task in normal controls (*upper images*) and in dyslexics. Dyslexics showed activation of Broca's area but not of the insula and of the temporal cortex. Sterotactic locations of these activation patterns and of the differences between the two are given in Table 3. Colour scaling of the *Z* scores across images is the same, allowing for direct visual comparison of the two data sets. *Left images.* These are shown as integrated projections through sagittal, coronal and transverse views of the brain. They permit the correct location of the activation patterns in three dimensions. *Right images.* To aid interpretation of the areas of activation, significant voxels are rendered onto the lateral view of the brain of an idealized model corresponding to the stereotactic space defined by Talairach and Tournoux (1988). The pattern of activation in the left hemisphere is shown.

Fig. 3 Location of increases in rCBF during the phonological short-term memory task in normal controls (*upper images*) and in dyslexics. Dyslexics showed activation of the superior temporal and inferior parietal cortex with minimal involvement of Broca's area and no involvement of the insula. Stereotactic locations of these activation patterns and of the differences between the two are given in Table 4. Images are displayed using the same conventions as for Fig. 2.

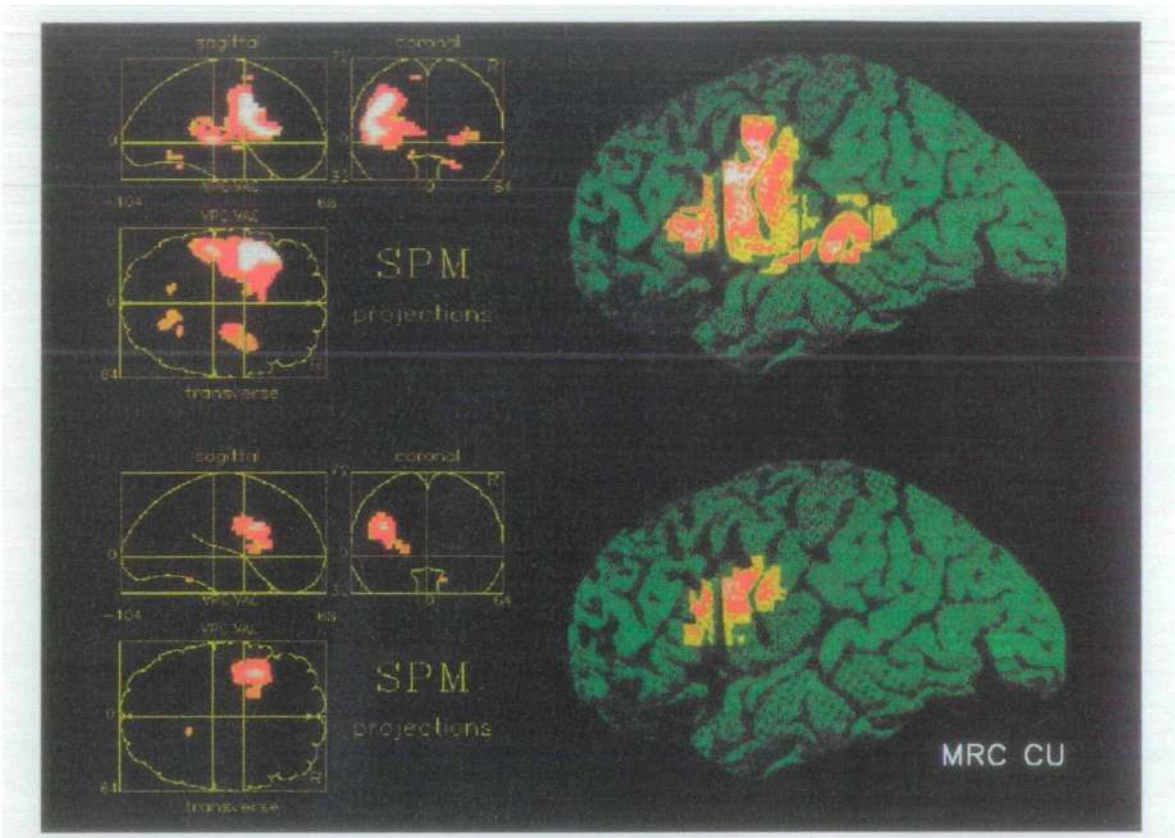

Fig. 2

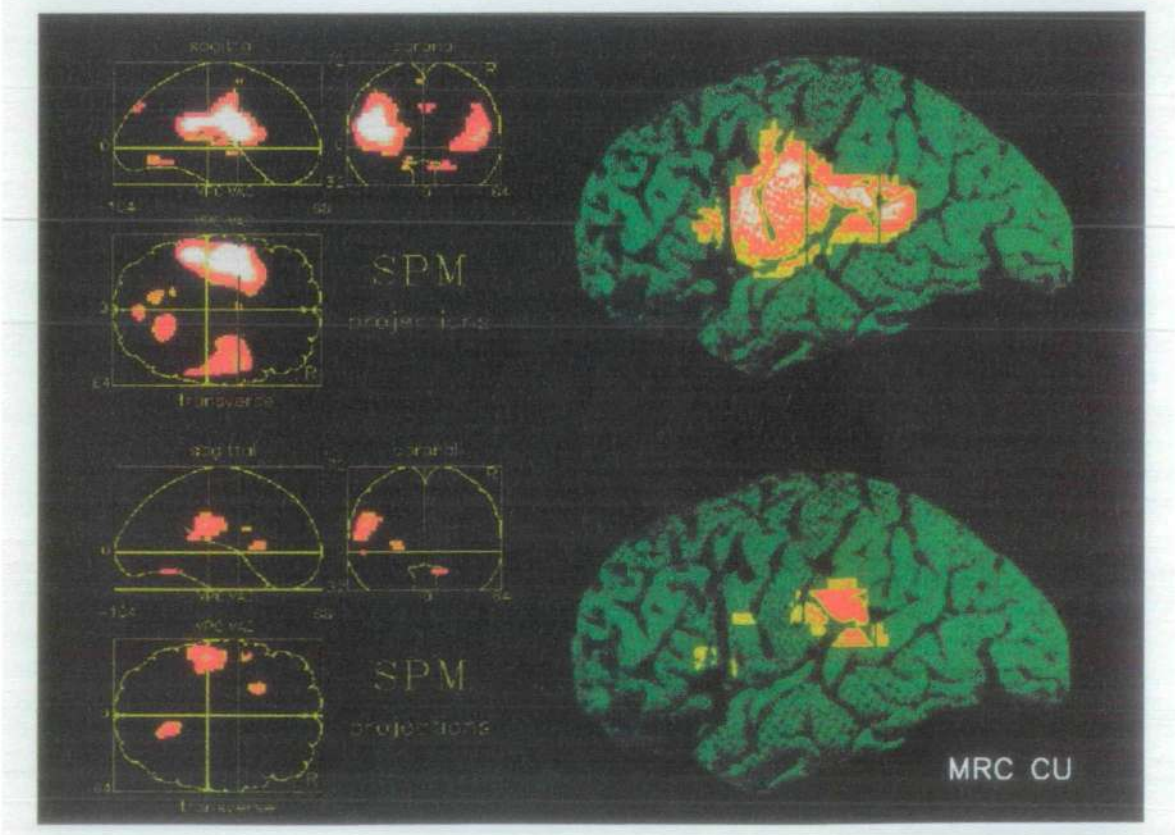

Fig. 3

Table 3 *Brain areas activated during the rhyming task*

	Normals				Dyslexics			
	x	*y*	*z*	*Z* score	*x*	*y*	*z*	*Z* score
Left hemisphere								
SMA (BA 6)	−14	8	56	3.7*				
IFG (BA 45/44/6)	−36	32	12	6.0	−34	22	12	3.8
(Broca's area)	−46	12	12	6.5	−36	10	24	5.8
PMC (BA 6)	−38	6	32	7.4*	−38	8	32	4.7
Insula	−34	−6	−4	3.3				
	−38	14	0	3.8**				
STG (BA 21/22)	−46	−26	4	6.1*				
(Wernicke's area)	−44	−32	12	3.9				
Caudate	−6	18	8	4.9	−18	8	8	3.6
	−22	22	12	2.9				
Cerebellum	−12	−58	−12	3.3				
Right hemisphere								
Insula	34	12	4	3.7				
Striatum	18	−12	4	4.5*				
Cerebellum	18	−64	−16	3.5				
Brain areas where dyslexics showed significantly less activity than controls								
SMA (BA 6)					6	−6	52	1.7
Left PMC (BA 6)					−32	2	40	2.7
Left STG (BA 21/22) (Wernicke's area)					−44	−22	4	1.9
Left insula					−34	−14	4	**3.3**
Right striatum					18	−6	8	2.4
					34	6	4	2.5

x, *y*, and *z* refer to the stereotactic co-ordinates in the three orthogonal dimensions of the atlas of Talairach and Tournoux (1988). The reference point is the junction of the vertical anterior commissural line and the intercommissural line. The reference plane is the bicommissural plane. *x* refers to millimetres left (−) and right of the reference point, *y* to millimetres anterior and posterior (−) to the reference point and *z* to planes above and below (−) the reference plane. The *Z* score indicates the significance of CBF change for each comparison, at the relevant location. STG = superior temporal gyrus. Areas where there were significant differences in extent of activation between dyslexics and controls: $*P < 0.01$; $**P < 0.001$.

activations were observed in the right hemisphere in IFG (BA 6/44) and in posterior perisylvian areas (BA 22/40). There was also activation of the cuneus (BA 19).

Dyslexics activated a subset of these areas in the left hemisphere. The supramarginal gyrus (BA 40) was strongly activated. Wernicke's area (superior temporal gyrus; BA 22) and the anterior part of the lenticular nucleus were also activated. Broca's area (BA 44) was activated, but weakly and in one plane only. An illustration of the pattern of activation in both groups during the verbal short-term memory task is shown in Fig. 3.

When activation in the groups was compared directly, we found that many of the areas activated by normal controls were significantly less active in dyslexics. However, the largest differences were observed in Broca's area (BA 44) and in the insula which again failed to show any significant activation in dyslexics. In contrast, the activity in Wernicke's area (superior temporal gyrus; BA 22) was not significantly different from that observed in controls. Stereotactic locations and statistical magnitude of activations in the two groups and of the differences in activations between the two groups for phonological short-term memory are shown in Table 4.

No differences were observed between the replications.

Discussion

Our main finding was that dyslexics, while engaged in tasks that involve phonological processing, activated the same brain areas as controls, but, unlike controls, they did not activate them in concert (*see* Figs 2 and 3). Thus Broca's area was extensively activated when deciding whether two letters rhymed, but was very weakly activated when remembering whether a particular letter had been present in a list. Wernicke's area was activated during the memory, but not during the rhyming task. In addition, there was one area, the insula (and to a lesser extent SMA and lateral premotor cortex on the left), which was not activated during either task, but which was always activated by the controls.

The only previous studies of developmental dyslexia with PET reported a lack of activation of left temporo-parietal cortex during a rhyming task, but no other differences (Rumsey *et al.*, 1992, 1994). Our results confirm this observation, but show that this same brain area was activated in dyslexics during a phonological memory task. Our use of two tasks and a voxel-by-voxel image analysis procedure (statistical parametric mapping), rather than a regions of interest approach, permitted a much more detailed investigation of the complex system of brain areas that are

Table 4 *Brain areas activated during the phonological short-term memory task*

	Normals				Dyslexics			
	x	*y*	*z*	*Z* score	*x*	*y*	*z*	*Z* score
Left hemisphere								
Anterior lenticular nucleus				–22	16	4	3.6	
SMA (BA 6)	–2	2	56	3.3*				
IFG (BA 6/44)	–46	–2	20	9.7**	–48	6	20	3.1
(Broca's area)	[*–42*	*10*	*16*	*4.3*]		(on one plane only)		
	[*–52*	*0*	*16*	*4.2*]				
PMC (BA 6)	–36	–8	36	6.1*				
Insula	–30	0	0	5.2**				
STG (BA 22)	–46	–38	16	6.5	–52	–32	12	3.8
(Wernicke's area)								
SMG (BA 40)	–44	–34	24	6.7*	–48	–26	24	5.6
LG (BA 18)	–14	–68	–8	3.5				
Cerebellum	–12	–68	–12	3.7*				
Right hemisphere								
IFG (BA 6/44)	50	2	16	5.9**				
PMC (BA 6)	46	–8	36	4.8				
Insula	38	0	4	5.5**				
STG(BA 20)/SMG(BA 40)	54	–42	20	4.3				
Cuneus (BA 19)	4	–84	32	4.8				
Cerebellum	14	–58	–16	4.7	14	–56	–16	4.2
Brain areas where dyslexics showed significantly less activity than controls								
Left hemisphere								
Left SMA (BA 6)					–8	0	56	2.2
Left IFG (BA 6/44)					–38	–4	20	**4.2**
Left PMC (BA 6)					–40	–6	32	2.2
Left insula					–34	0	12	**3.9**
Left SMG (BA 40)					–46	–44	24	2.8
Left cerebellum					–16	–48	–16	2.4
Right hemisphere								
Right IFG (BA 6/44)					44	0	12	3.3
Right insula					38	2	4	**3.8**

Stereotactic conventions as for Table 3. The stereotactic locations reported in italics represent the result of an additional analysis carried out for the normal volunteers. As the activation focus seen in Broca's area in normal volunteers appeared to incorporate both BA 6 and BA 44, a further analysis was performed where no secondary smoothing was applied to the images. Under these circumstances, it was possible to distinguish two separated peaks of activation for each of these subcomponents of Broca's area. PMC = premotor cortex; SMG = supramarginal gyrus; LG = lingual gyrus. Areas where there were significant differences in the extent of activation between dyslexics and controls: $*P < 0.01$; $**P < 0.001$.

concerned with phonological processing, whilst avoiding anatomical preconceptions. We are therefore able to provide a much richer account of the differences between dyslexic and normal readers.

There are three problems we need to consider. (i) How did the dyslexics achieve the same performance as the controls while only activating a subset of brain areas? (ii) What are the roles of the various brain areas engaged by our phonological tasks? (iii) Can the different pattern of brain activity observed in the dyslexics explain their persistent problems with the more difficult phonological tasks applied outside the scanner (*see* Table 1)?

How can dyslexics perform the tasks with only a subset of brain areas?

Since the dyslexics could comfortably perform the simple tasks used during scanning, we presume that any brain areas which they did not activate are not necessary for these tasks. By the same logic we presume that our normal controls were activating areas which were not strictly necessary for performance. It is known from both behavioural and physiological studies that presentation of words can automatically and involuntarily engage a number of different codes. For example, in the Stroop task (name the colour of the ink when the word RED is written in GREEN) the sound of the word (which does not need to be accessed) interferes with the name of the colour (MacLeod, 1991). Automatic activation of unnecessary codes can also be observed in PET studies. In a feature detection experiment on visually presented stimuli (Price *et al.*, 1995), it has been shown that many different brain areas (reflecting many different codes) are activated when normal subjects look at words, even though there is no explicit instruction to process the words. The majority of the codes used are therefore not actually necessary for the task being performed. For example, when

explicitly required simply to detect descenders in visually presented words (e.g. the p in poor), normal subjects showed activation in the left perisylvian areas observed in our study (Price *et al.*, 1995) in addition to areas associated with visual analysis (extrastriate occipital and parietal regions; Gulyas and Roland, 1991; Paulesu *et al.*, 1993).

These observations raise the problem of how to distinguish areas of activation that are necessary or critical for the task in hand (thus revealing something about their function) from those areas that are activated incidentally. We believe that the comparison of normal and abnormal subject groups can throw light on this problem. Since our dyslexic volunteers could perform the two tasks (which have minimal processing requirements) while activating only a subset of areas, we were able to infer that this subset is 'necessary' (i.e. close to the minimum neural substrate) for task performance. Without this information we would not have been able to suggest that the additional areas seen in normal readers may be 'incidental'.

What are the roles of the various left perisylvian areas?

In our previous account of the articulatory loop in normal volunteers we proposed that, on the one hand, Broca's area was the major component of the rehearsal system while, on the other hand, the supramarginal gyrus (BA 40) was crucial for phonological short-term memory (Paulesu *et al.*, 1993). These suppositions are strongly supported by our findings in dyslexic subjects which suggest that these areas are necessary for certain functions. Broca's area seems necessary for making rhyme judgements about visually presented letters. For this task it is not sufficient to convert the visual appearance of the letter into a name. Producing the letter name involves whole word phonology (Besner, 1987). For rhyming, the letter name must be segmented into a consonant and a vowel part, the vowel alone contributing to the rhyme. This involves segmented phonology. Segmentation is also necessary before the name can be articulated (programming of consonant and vowel components for speech). Wernicke's area and the supramarginal gyrus (BA 40) (but only minimally Broca's area) seem to be necessary for the memory task. This task can be performed better if the visual appearance of the letter is converted into a name (whole word phonology), but segmentation is not necessary. Evidence from other PET studies broadly supports these conclusions. Wernicke's area (left superior temporal gyrus) is associated with whole word phonology (Démonet *et al.*, 1992; Zatorre *et al.*, 1992); Broca's area (IFG, operculum and premotor cortex) is associated with articulation (Petersen *et al.*, 1988; Paulesu *et al.*, 1993), and the supramarginal gyrus (BA 40) is activated whenever there is a short-term mnemonic component (Paulesu *et al.*, 1993; Démonet *et al.*, 1994).

The stereotactic coordinates of Broca's area reported in our earlier study (Paulesu *et al.*, 1993) suggested that the activation focus fell in between BAs 44 and 6. An additional analysis using a narrower spatial filter has shown that BAs 44 and 6 were both separately activated in the phonological short-term memory task (*see* Table 4). In addition, BA 44 was clearly involved in the rhyming task. Taken together, these observations confirm the role of Broca's area as classically defined (BA 44) in subvocal rehearsal.

Why do our dyslexics have persistent phonological problems?

Our dyslexics could activate Broca's area (segmented phonology), Wernicke's area (whole word phonology) and supramarginal gyrus (phonological store), but unlike the controls, they did not activate these areas in concert. In addition, there were some areas which were consistently activated less than in the controls. These were the insula, the SMA and premotor cortex. However, of these three areas only the differences in the insula reached a high level of significance. The dyslexics did not activate the insula in either task. Could this explain their persistent phonological problems? With more demanding examples of phonological tasks (Spoonerism task, short-term memory task for long words, phonemic fluency) our dyslexics performed poorly. The major behavioural problem our dyslexics have with these tasks is to go directly from the written form of a word to the associated phonology in segmented form. This makes it difficult to manipulate the sound segments of words. We know that in normal subjects the manipulation of sound segments depends strongly on inner speech, since this process is interfered with by articulatory suppression (Besner, 1987). However, manipulation of phonemes (as in the Spoonerism task) is also likely to require a short-term memory store.

Thus, at the physiological level, performance of such tasks would depend upon interaction between Broca's area and supramarginal gyrus, if our modular/anatomical assignations are correct. Indeed, in the short-term memory task (which requires inner speech and a phonological store) both structures are activated in normal subjects, as is the insula. We would suggest that the insula provides a 'bridge' between these two structures, and that the function of this bridge is a conversion between codes. This is certainly plausible on the basis of what little is known about the anatomical connections between anterior and posterior language areas (Meynert, 1865). Lesions of the left insula can cause conduction aphasia in which patients are unable to translate heard, written or self-generated words into appropriate phonemic sequences (Damasio and Damasio, 1980). The lack of activation in the insula in dyslexic subjects could underlie a disconnection between anterior and posterior speech areas (Fig. 4). This would mean, in psychological terms, a lack of support for recoding, or fewer simultaneously available codes.

Translating between different language codes

There is evidence that, in normal readers, the route from print to phonological short-term storage involves 'subvocal'

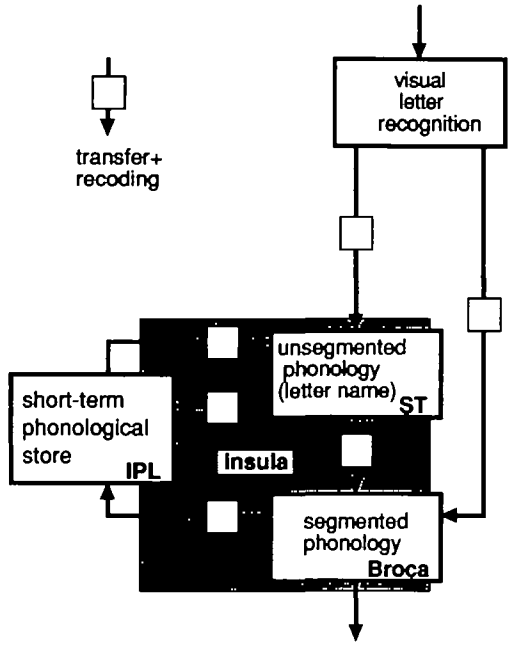

Fig. 4 Integrated information processing diagram of the phonological system based on neurophysiological findings from normal controls and dyslexics. Cognitive components are linked with brain physiology. On the basis of our results, we suggest that a (letter name) phonological code can be generated even in the presence of an inadequate rehearsal system, and that this code can access short-term storage. The insula is placed as a connection device between different brain areas representing different phonological codes/operations. ST = superior temporal gyrus; IPL = inferior parietal lobule.

articulation (Salamé and Baddeley, 1982; Vallar and Cappa, 1987) and thus, presumably, segmented phonology. This is consistent with the results of our study of normal subjects in which both Broca's area (segmented phonology) and the supramarginal gyrus (phonological store) were activated by short-term memory tasks for verbal material. This pattern was not observed in the dyslexics who activated the supramarginal gyrus in the short-term memory task with very limited activity in Broca's area.

How then did our dyslexic subjects achieve the conversion from print to sound, and how did they access the phonological store? In order to answer these questions it is useful to consider Morton's logogen model (Morton, 1980). This model and its many variants assume that there are many alternative routes from print to sound. In particular, there is provision for a lexical code as well as for various more peripheral sublexical codes. There is evidence that dyslexics with phonological impairments can use lexical codes proficiently, and are penalized only when having to use sublexical codes (Snowling *et al.*, 1994). This finding suggests that for the short-term memory task used during scanning, our dyslexics accessed the (unsegmented) name of the visually presented single letters via lexical codes, thus avoiding the need for segmented phonology (*see* Fig. 4). In order to perform the rhyming task they were, however, forced to use segmented phonology, and this is reflected in their activation of Broca's area.

This account at the cognitive level suggests that the role of the left insula is to convert between unsegmented and segmented codes. Such a transcoding role for the insula would be consistent with Mesulam and Mufson's (1985) suggestion that the insula provides low level integration between signals from different modalities. However, in the monkey at least, the insula has a preponderance of limbic rather than of sensori-motor inputs. Thus our proposal for the role of this structure must be considered speculative. It has also been proposed that the arcuate fasciculus is important for connecting anterior and posterior language areas (Meynert, 1865; Benson *et al.*, 1973). Given that PET assesses grey matter activity only, we cannot comment, at this stage, on the relevance of this white matter bundle to the transcoding hypothesis.

The 'perceptual' role of Broca's area

It is somewhat surprising that, when doing the rhyming task, dyslexic subjects activated Broca's area only. This result implies that this premotor area can, in certain circumstances, be used purely for perception. This finding is consistent with other observations at the cognitive and the physiological level. Cognitive psychology suggests that segmented phonology requires subvocalization, since performance during a rhyming task can be impaired by articulatory suppression but not by unattended speech (for review, *see* Gathercole and Baddeley, 1993). Broca's area, which we associate with segmented phonology, was also the most active area in our controls during the rhyming task. Other authors have observed activation in Broca's and closely adjacent areas during similar phonological tasks, no matter whether the stimuli were presented aurally or visually (Démonet *et al.*, 1992; Zatorre *et al.*, 1992). As the superior temporal cortex was activated in these experiments as well, these authors offered the interpretation that activation in Broca's area was due to covert articulation of the stimuli. Our results in dyslexic subjects provide a more appealing interpretation, namely that Broca's area contributes independently to phonological perception, since our subjects' performance in the rhyming task was virtually errorless. However, speech perception based on an 'isolated' Broca's area, as postulated in dyslexia, is probably insufficient to provide flawless performance in more demanding phonological tasks, especially those which require maintenance of segmented phonology in working memory.

Right hemisphere, phonology and dyslexia

Another difference between dyslexics and normal controls during the phonological short-term memory task was that dyslexics did not activate any brain structure in the right hemisphere. A contribution of the right hemisphere to reading has been proposed to explain residual performance in the acquired dyslexias, e.g. deep dyslexia (Coltheart, 1980; Zaidel

and Peters, 1981). Clearly, this hypothesis does not hold for our developmental dyslexics, as no activation was observed in the right hemisphere. Their success in compensating for their reading and phonological difficulties cannot be due to a relateralization of language competence.

Is developmental dyslexia a disconnection syndrome?

The idea that a disconnection between otherwise intact brain areas may explain behaviour in certain brain-damaged patients is as old as neuropsychology (Wernicke, 1874; Lichtheim, 1885; Geschwind, 1965). In its modern formulation, disconnection provides a good account in certain syndromes. Amongst these is colour anomia as interpreted by Geschwind and Fusillo (1966). The proposal is that colour anomia occurs in the presence of concurrent lesions of the left mesial extrastriate cortex and of the splenium of the corpus callosum: information from the intact right occipital cortex (by which colours can still be discriminated) cannot access the left-sided language areas, where lexical items for colour are still available.

Is it possible that similar disconnections occur, even within the same hemisphere, for phonological processing in dyslexia? We believe that such a disconnection is indicated by our observation that the major sites of the phonological system could be activated by our dyslexic subjects separately, but not together. Such a disconnection between different codes can also explain the poor performance of our subjects on the more demanding phonological tasks. As discussed earlier, these tasks (e.g. Spoonerisms) require segmentation of verbal material held in working memory. In other words, both segmented and unsegmented codes need to to be held simultaneously in working memory. However, as we observed in the pattern of brain activations, these codes are not activated at the same time in the dyslexics. Thus, both the behavioural and the physiological data are consistent with a disconnection. Using a very different approach, connectionist modellers (e.g. Seidenberg and McClelland, 1989) have proposed that the presence of weak connections in a simple artificial neural network for translating print to sound can simulate the symptoms of dyslexia.

In summary, the neuropsychological and the PET findings both point to a disconnection between different phonological codes. At a neurophysiological level this became manifest as the isolated activation of Broca's area and of Wernicke's area and the supra marginal gyrus during the different phonological tasks.

It is easy to see how such a disconnection could also account for the difficulty that individuals with this type of phonological disorder experience in learning to read. During speech development, children learn how the speech they hear maps onto the utterances they produce. The efficacy of the mapping depends on the degree of connectivity between the relevant language areas in the brain. Weak connectivity between brain areas involved in hearing words and saying words will not only cause delay in establishing different language codes, but will also cause difficulties in learning an alphabetic code. Successful use of the alphabet, in particular, depends upon precise and redundant mappings between individual graphemes, phonemes and whole word spelling and sound.

Conclusions

On the basis of the data from a small group of compensated developmental dyslexics with persistent phonological problems, we suggest that this kind of disorder arises from disconnections between the different neural codes associated with words, in particular between segmented and unsegmented phonological codes. This explanation allows us to integrate neurophysiological findings with behaviour and current theories of the mechanisms relating to normal and abnormal acquisition of reading skills. We further suggest that the left insula, which was inactive in dyslexics in contrast to normals in both our PET scanning tasks, has a major role in linking the different phonological codes. If these results can be replicated, the value of studying pathological groups for delineating the functional anatomy of normal brain systems will be confirmed. On the basis of our analysis of normal volunteers we had no convincing evidence for assigning, even speculatively, a function to the insula. Developmental dyslexia (and this probably applies to other developmental disorders as well) is of particular interest because the abnormalities are not associated with macroscopic brain lesions. It is therefore possible in such patients to avoid many of the methodological problems associated with imaging studies of acquired disorders. We now know that normal volunteers activate cortical language areas that are not strictly necessary to perform the simple tasks of rhyming and remembering letters. The comparison with dyslexics showed us which areas are sufficient to perform these tasks. This example suggests that the grand enterprise of linking cognition and brain function can be vitally enhanced by studying anomalous groups.

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