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EDITORIAL

Functional imaging and neuropsychiatry[1]

Non-invasive physiological measures of *in vivo* brain function, derived from positron emission tomography (PET) and functional magnetic resonance (fMRI), are now standard tools in cognitive neuroscience. These techniques provide a powerful context for addressing critical questions regarding both the localization and mechanisms of higher brain functions. A general overview of the history and development of imaging techniques in relation to cognitive science is that of Posner & Raichle (1994). The conceptual background and methodological approaches available for neurobiological based psychiatric research, in conjunction with functional imaging, provides the focus for the present review.

Major psychiatric disorders, such as schizophrenia and depression, represent disturbances at the highest level of brain function. Providing a neurobiological account of these conditions presents the most formidable problem in clinical neuroscience. Questions posed by neurobiological perspectives on psychiatric disorders are necessarily embedded in theoretical assumptions about how we think that the brain works. From this, it follows that an important limiting factor in any neurobiological account of psychiatric disease is the stage of development and theoretical conceptualization of brain function in general.

CONCEPTUAL ISSUES IN UNDERSTANDING BRAIN FUNCTION

Two dominant themes inform current concepts of higher brain function. One view emphasizes processing in discrete modules, often anatomically circumscribed and referred to as functional segregation. A contrasting, and more holistic, view is that higher brain function cannot be strictly localized but is a property of interactions between functionally specialized, and anatomically separate, brain regions.

Functional segregation is strongly identified with the theorizing of Franz Joseph Gall (1758–1828) who believed that distinct psychological mechanisms were associated with a specific neural apparatus. Observations based upon the effects of localized brain lesions on distinct components of language provided irrefutable support for this, often derided, viewpoint (Broca, 1865; Wernicke, 1874). This, and other empirical data in man and animals, gave rise to the dominant 'lesion deficit model' where loss of function is used to infer that a specific brain region mediates a particular cognitive process (Ferrier, 1875). Evidence of functional segregation within the human brain is now overwhelming with the most striking examples being from studies of the effects of lesions on visual perception and memory function (Scoville & Milner, 1957; Zihl *et al*. 1983; Zeki *et al*. 1991). Functional segregation is distinct from the closely related concept of functional specialization which is neutral as regards a strictly circumscribed or modular localization of function. An example of non-modular functional specialization is the network of brain regions that mediate visuospatial attention (Posner & Petersen, 1990).

From an anatomical perspective the brain is a highly interconnected structure with few regions separated by more than three synaptic gaps. Furthermore, with a few notable exceptions, anatomical connections between brain regions are reciprocal. The realization of the dense anatomical interconnectivity of the brain has led to the re-emergence of a connectionist view, first espoused in the last century, that higher brain functions result from co-operative interactions

[1] Address for correspondence: Professor R. J. Dolan, Wellcome Department of Cognitive Neurology, Institute of Neurology, Queen Square, London, WC1N 3BG

between brain regions (Wernicke, 1906; Goltz, 1881). The rediscovery of connectionism in this century is attributed to the work of McCulloch & Pitts (1943) and derives its appeal from the likelihood that segregated brain regions must be integrated during normal perception and action. A number of mechanistic accounts of how integration is realized have provided the focus for the elaboration of a range of connectionist theories (Eckhorn *et al.* 1988; Gray *et al.* 1989; Singer, 1990). Although conceptually dichotomous functional segregation and integration are not necessarily mutually antagonistic and their complementarity is underlined by attempts at a unified framework (Tononi *et al.* 1994).

FUNCTIONAL SPECIALIZATION AND FUNCTIONAL IMAGING

The question can be posed as to how concepts of brain function relate to functional imaging? Functional imaging studies, of normal and pathological groups, are generally predicated on a perspective of functional specialization. Within this framework a number of experimental strategies have been adopted each with their own implicit assumptions. A selective consideration of this literature, with an emphasis on the specific methodologies adopted, illustrates these two general approaches.

Categorical approaches

Studies of normal and pathological groups predicated on functional specialization generally involve group comparisons or activation studies based upon cognitive subtraction. Categorical experimental designs are applied either within or across groups and a typical example is the comparison of a pathological with a normal reference group. Differences in brain activity, based upon this type of comparison, are then used to infer local pathophysiology. An example of this type of study is the comparison of regional cerebral blood flow (rCBF) in depressed patients and normal controls which identified regional dysfunction in the depressed patients in the left anterior cingulate, dorsolateral prefrontal cortex and angular gyrus (Bench *et al.* 1992). This approach is limited by the assumption that the pathological group, usually defined on the basis of clinical diagnostic criteria, has a single pathophysiology.

Cognitive subtraction is the most powerful type of categorical experiment used in functional activation studies. The basic idea can be traced to Donders (1868) who developed the subtraction method to measure stages of psychological processing. Reaction times on two tasks are compared where the tasks involve an equal number of processing stages plus an additional stage for the second task. Differences in reaction times are interpreted as reflecting the duration of processing for the additional stage. In the context of functional imaging the typical cognitive subtraction experiment addresses questions such as what brain regions mediate a particular cognitive processes. In the experimental setting the cognitive task is fractionated into a number of separate components. The serial subtraction of brain activity acquired while subjects perform each of the stages identifies the functional anatomy associated with the components of interest. An example of cognitive subtraction is that of a study which sought to identify the brain regions involved in the generation of words in response to letter cues. Subtracting the activity associated with a control sensorimotor condition, involving hearing and repeating words, from that in the fluency condition identifies brain regions involved in the generation of words (Frith *et al.* 1991). Using this general strategy the functional anatomy of a diverse range of cognitive processes have been identified that include motor, visuo-spatial, language and attentional systems (Posner & Petersen, 1990; Corbetta *et al.* 1991, 1993; Deiber *et al.* 1991; Wise *et al.* 1991; Jenkins *et al.* 1994; Stephan *et al.* 1994).

Functional imaging studies based upon cognitive subtraction have provided an extremely powerful experimental tool. A critical weakness is the assumption that the addition of a new cognitive component has no effect on the implementation of a previously added component. These reservations were extensively discussed in relation to psychological studies by Sternberg (1969) who advocated factorial designs where the interaction term was specifically evaluated and which eschewed a dependence on assumptions of non interacting stages of processing or 'pure insertion'.

The relevance of this critique to the design of functional imaging studies will be considered below in the context of factorial experimental designs.

Parametric experimental designs

An alternative approach to categorical based experiments that avoids many of the assumptions associated with cognitive subtraction is that of parametric experimental designs. The basic principle in a parametric study is the evocation of a physiological response (dependent variable) by a systematic variation in an independent variable which can be as diverse as a sensoriomotor, behavioural or cognitive manipulation. This approach can be used to reveal relationships between dimensions of psychopathology and brain pathophysiology in schizophrenia and depression. Here experimental variance rests upon endogenous variability, across key dimensions of psychopathology, of subjects selected upon the basis of a diagnostic category. In depression and schizophrenia striking relationships emerge when ratings of psychopathology, for example psychomotor slowing, are correlated with underlying brain physiology (Friston *et al*. 1992; Bench *et al*. 1993). The close relationship between symptom profile and brain physiology points to an absence of a unitary pattern of brain activity associated with diagnostic categories and implies that abnormalities of brain function are better predicted by symptoms (Dolan *et al*. 1993). A corollary of this position is that some experimental approaches, such as resting state categorical and parametric approaches, are likely to be ineffective in revealing core pathophysiology.

Parametric experiments are much more powerful when there is direct experimental control over the independent variable. This can be achieved by taking a single variable, such as frequency of word presentation, which is then systematically manipulated across a series of scans and the associated brain response determined. Studies of normal subjects using parametric designs have addressed a range of cognitive questions such as the relationship between increasing memory load and hippocampal activation (Grasby *et al*. 1993), the effects of frequency of word presentation on auditory and periauditory cortices (Price *et al*. 1992) and the relationship between motor learning and underlying plastic brain changes (Grafton *et al*. 1992). An assumption in most parametric designs is that the brain response to the experimental manipulation is linear. However, the brain response to an increase in a stimulus parameter cannot always be predicted in advance and the assumption of linearity may not always be warranted. Non-linear models are increasingly seen as more appropriate in certain circumstances. An example of the use of a non-linear regression model is that of a study of the effect of the frequency of word presentation on the physiological response in auditory specialized brain regions (Buchel *et al*. 1996).

Factorial experiments

As discussed cognitive subtraction assumes that fractionating a cognitive process provides a basis for determining how it is represented in the brain. A framework that circumvents the assumptions inherent in this approach is that of a factorial experimental design that can subsume both categorical and parametric approaches. The basic issue in a factorial design is to determine the effect of a second factor on the effect of a primary factor. In physiological terms this reduces to assessing the effect of a second task on the neural activation evoked by the first task. In this context no assumptions are made about additivity and the strength of factorial approaches is their highly flexible range of application that includes cognitive/cognitive or cognitive/pharmacological manipulations.

An example of a factorial experiment is a study that sought to determine the brain regions involved in episodic memory encoding. The two factors were encoding (and its control) and an interference task (and its control). Encoding consisting of either listening to a series of 15 word-paired associates while subjects were being scanned. The second factor was an interference task, chosen because it interferes with effective encoding, involving moving a cursor to either sequentially cued or randomly cued locations on a screen. The brain regions activated by the encoding task which were specifically attenuated by the introduction of the second factor can be

inferred to be specific to the encoding process. The regions attenuated were the left dorsolateral prefrontal cortex and the retrosplenial cortex (Shallice *et al.* 1994).

Psychopharmacological experiments are a special case of factorial layouts and provide a means to determine the functional implications of a change in a neurochemical state on brain networks that mediate cognitive processes. The first use of this type of factorial experiment was to study of the effects of dopamine manipulation on brain regions involved in episodic memory where a specific effect of the drug was seen on the cognitive evoked physiological response in the prefrontal cortex (Friston *et al.* 1991; Grasby *et al.* 1992). The application of conjoint cognitive/pharmacological approaches have particular relevance in the study of psychiatric disorders. In the case of schizophrenia an important issue is the functional consequences of an alteration in central dopaminergic tone. In unmedicated acute schizophrenic patients a failure of verbal fluency activation, relative to controls, in the anterior cingulate cortex was reversed by apomorphine (Dolan *et al.* 1995). This finding is open to a number of interpretations. At the dosage given apomorphine has a predominant presynaptic effect resulting in a decrease in dopminergic tone. Seen in this context the data are consistent with the suggestion of a regional dopaminergic overactivity involving the anterior cingulate in acute schizophrenia. This study also illustrates the type of approach that can be used in order to identify core deficits.

FUNCTIONAL IMAGING STUDIES AND FUNCTIONAL INTEGRATION

In normal brain function the specialized processing, for example that involved in processing object identity and location, must be integrated to enable coherent perception and action. Critical questions related to integration of function are of considerable theoretical importance in the study of the psychoses where abnormal integration has been proposed as a fundamental mechanism (Wernicke, 1906). An important issue therefore is whether functional imaging can be extended to address questions related to integration. Two generic approaches have been described that provide a framework within which questions of functional integration can be addressed (Friston *et al.* 1993*a*, 1995). These approaches, based upon the analysis of functional and effective connectivity, are similar to those used in electrophysiological studies based upon coherence analysis of multi-unit recordings of separable neuronal spike trains (Gerstein & Perkel, 1969; Gerstein *et al.* 1989).

Functional connectivity

The simplest approach to integration is the analysis of how brain activity in different brain regions, evoked by a particular cognitive task, covaries as a function of time. Distributed responses of this nature can be captured by measures of functional connectivity which is formally defined as the temporal correlation between two or more regions of task related neural activity. In simple terms it provides a description of correlated patterns of activity in the brain in relation to a particular behavioural state. A number of mathematical approaches, using techniques such as singular value decomposition or recursive principal components analysis, can extract this type information from functional imaging data (Friston *et al.* 1993*a*). The approach is essentially descriptive with the resulting eigen images or spatial modes identifying brain regions that represent different systems by virtue of their functional interactions.

The utility of approaches based upon functional connectivity can be demonstrated in the context of studies of schizophrenia. In chronic medicated schizophrenic patients an abnormal pattern of fronto-temporal connectivity, characterized by a failure of task related deactivation in the superior temporal cortex, has been demonstrated. This abnormal pattern was independent of the symptom profile of the patients which suggests that the abnormality reflects a fundamental disease related process (Frith *et al.* 1995). This finding has now been replicated in acute non-medicated schizophrenic patients, which suggests that the phenomenon is not a function of disease stage or medication status (Dolan *et al.* 1995; Fletcher *et al.* 1996). The latter findings, furthermore, illustrate the complementarity of segregated and integrated function. In this study the schizophrenic patients showed a striking task related failure of activation in the anterior cingulate cortex. This

region is itself strongly interconnected with both the dorsolateral prefrontal cortex and superior temporal cortex. Thus, while the anterior cingulate deficit could be seen to represent a segregated deficit *par excellence* a connectionist interpretation would suggest that the failure of activation in the cingulate is a consequence of its failure to be integrated into the larger system with which it is anatomically and functionally connected.

Effective connectivity

Effective connectivity, in contrast to functional connectivity, is mechanistic and is a measure of the influence one brain region exerts upon another. Measures of effective connectivity rely upon a theoretical model which may be linear or non-linear (Friston *et al.* 1993*b*). In assessing effective connectivity the question being asked is what is the effect on a brain region of one or more extrinsic inputs to that region. This is modelled in terms of the changes in a region as a linear sum of changes at all other points in the brain. The weighting of any target region to the one in question is a measure of the strength of that connection or its effective connectivity. It is important to bear in mind that these influences, and the consequent measures, are dynamic and change with time. The potential applications of effective connectivity are extremely wide ranging and include assessing changes in the interaction between brain regions that may occur as a function of learning or as a consequence of alteration in a modulatory neurotransmitter input to that region. This type of approach is still in development but a pertinent example is the analysis of the mutual influence of V1 and V2 in human subjects based upon data from fMRI (Friston *et al.* 1995). The application of measures of effective connectivity is likely to be of major importance in studies of the psychoses where abnormal connectivity provides a compelling theoretical perspective on these conditions (Friston & Frith, 1995). The ability to assess the functional effects of pharmacological agents on patterns of connectivity is an unexplored area for future research.

CONCLUSION

Rather than an exhaustive overview of the published functional imaging literature in psychiatry this review has focused on fundamental methodological approaches. These approaches are generic and not limited to a particular technology. It is clear that all methodological approaches using functional imaging are predicated on a set of assumptions as to how the brain works. In psychiatric studies there is no *a priori* reason for favouring approaches that assume functional segregation or integration. However, the perspective of functional segregation may be more relevant to understanding the relationships between components of psychopathology (i.e. symptoms) and underlying brain function. This is illustrated by the predictive power of symptoms in determining patterns of regional brain function that is independent of diagnostic category (Dolan *et al.* 1993). An integrationist perspective may be more relevant to understanding fundamental disease mechanisms. This assertion gains support from studies of patients with schizophrenia where abnormal fronto-temporal patterns of activity are independent of symptoms and stage of illness. What is now clear is that imaging techniques and the associated experimental methodologies have reached a level of sophistication that provide a powerful means of addressing questions that relate to fundamental disease processes in psychiatry. The prospects for significant advancement in knowledge of the fundamental biological mechanisms in psychiatric disorders have never seemed brighter.

R. J. DOLAN AND K. J. FRISTON

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REFERENCES

Bench, C. J., Friston, K. J., Brown, R. G., Scott, L., Frackowiak, R. S. J & Dolan R. J. (1992). The anatomy of melancholia. Abnormalities of regional cerebral blood flow in major depression. *Psychological Medicine* **22**, 607–615.

Bench, C. J., Friston, K. J., Brown, R., Frackowiak, R. S. J & Dolan, R. J. (1993). Regional cerebral blood flow (rCBF) in depression measured by positron emission tomography (PET): the relationship with clinical dimensions. *Psychological Medicine* **23**, 579–590.

Broca, P. (1865). Sur le siège de la faculté du langage articulé, suives

d'une observation d'aphemia. *Bulletin et Mémoires de la Société anatomique de Paris* **62**, 330–357.

Buchel, C., Wise, R. J. S., Mummery, C. J., Poline, J-B & Friston, K. J. (1996). Non-linear regression in parametric activation studies. *Neuroimage* **4**, 60–66.

Corbetta, M., Miezin, F. M., Dobmeyer, S., Shulman, G. L. & Petersen, S. E. (1991). Selective and divided attention during visual discriminations of shape, colour, and speed: functional anatomy by Positron Emission Tomography. *Journal of Neuroscience* **11**, 2383–2402.

Corbetta, M., Miezin, F. M., Shulman, G. L. & Petersen, S. (1993). A PET study of visuospatial attention. *Journal of Neuroscience* **13**, 1202–1226.

Deiber, M.-P., Passingham, R. E., Colebatch, J. G. & Frackowiak, R. S. J. (1991). Cortical areas and the selection of movements: a study with positron emission tomography. *Experimental Brain Research* **84**, 393–402.

Dolan, R. J., Bench, C. J., Liddle, P. F., Friston, K. J., Frith, C. D., Grasby, P. M. & Frackowiak, R. S. J. (1993). Dorsolateral prefrontal cortex dysfunction in the major psychoses; symptom or disease specificity. *Journal of Neurology, Neurosurgery and Psychiatry* **56**, 1292–1298.

Dolan, R. J., Fletcher, P., Frith, C. D., Friston, K. J., Frackowiak, R. S. J. & Grasby, P. J. (1995). Dopaminergic modulation of an impaired cognitive activation in the anterior cingulate cortex in schizophrenia. *Nature* **378**, 180–182.

Donders, F. C. (1868). In *Attention and Performance* (ed. W. G. Koster), vol. 2, pp. 412–431. North Holland: Amsterdam. 1969.

Eckhorn, R., Bauer, R., Jordan, W., Brosch, M., Kruse, W., Munk, M. & Reitboek, H. J. (1988). Coherent oscillations: a mechanism of feature linking in visual cortex? *Biology and Cybernetics* **60**, 121–130.

Ferrier, D. (1875). Experiments on the brains of monkeys. *Proceeding of the Royal Society London* **23**, 409–430.

Fletcher, P. C., Frith, C. D., Grasby, P. M., Friston, K. J. & Dolan, R. J. (1996). Local and distributed effects of apomorphine on fronto-temporal function in acute unmedicated schizophrenia. *Journal of Neuroscience* **16**, 7055–7062.

Friston, K. J. & Frith, C. D. (1995). Schizophrenia: a disconnection syndrome? *Clinical Neuroscience* **3**, 89–97.

Friston, K. J., Grasby, P., Frith, C. D., Bench, C. J., Dolan, R. J., Cowen, P. J., Liddle, P. F. & Frackowiak, R. S. J. (1991). The neurotransmitter basis of cognition: psychopharmacological activation studies using positron emission tomography. In *Exploring Brain Functional Anatomy with Positron Tomography* (ed. D. J. Chadwick and J. Whelan), pp. 76–92. Wiley: Chichester.

Friston, K. J., Frith, C. D., Liddle, P. F., Hirsch, S. R., & Frackowiak, R. S. J. (1992). The left medial temporal region and schizophrenia: a PET study. *Brain* **115**, 367–382.

Friston, K. J., Frith, C. D., Liddle, P. & Frackowiak, R. S. J. (1993*a*). Functional connectivity: The prinicipal component analysis of large (PET) data sets. *Journal of Cerebral Blood Flow and Metabolism* **13**, 5–14.

Friston, K. J., Frith, C. D. & Frackowiak, R. S. J. (1993*b*). Time-dependent changes in effective connectivity measured with PET. *Human Brain Mapping* **1**, 69–79.

Friston, K. J., Ungerleider, L. G., Jezzard, P. & Turner, R. (1995). Characterizing modulatory interaction between areas V1 and V2 in human cortex: a new treatment of functional MRI data. *Human Brain Mapping* **2**, 211–224.

Frith, C. D., Friston, K. J., Liddle, P. F. & Frackowiak, R. S. J. (1991). A PET study of word finding. *Neuropsychologia* **29**, 1137–1148.

Frith, C. D., Friston, K. J., Herold, S., Silbersweig, D., Fletcher, P., Cahill, C., Dolan, R. J., Frackowiak, R. S. J. & Liddle, P. F. (1995). Regional brain activity in chronic schizophrenic patients during the performance of a verbal fluency task. *British Journal of Psychiatry* **167**, 343–349.

Gerstein, G. L. & Perkel, D. H. (1969). Simultaneously recorded trains of action potentials: analysis and functional interpretation. *Science* **164**, 828–830.

Gerstein, G. L., Bedenbaugh, P. & Aersten, A. M. H. J. (1989). Neuronal assemblies. *Transactions in Biomedicine and Engineering* **36**, 4–14.

Goltz, F. (1881). *Transactions of 7th International Medical Congress, vol* 1. Kolkmann, J. W.: London.

Grafton, S. T., Mazziotta, J. C., Presty, S., Friston, K. J., Frackowiak, R. S. J. & Phelps, M. E. (1992). Functional anatomy of human procedural learning determined with regional cerebral blood flow and PET. *Journal of Neuroscience* **12**, 2542–2548

Grasby, P., Frith, C., Friston, K. J., Frackowiak, R. S. J. & Dolan, R. J. (1993). Activation of the human hippocampal formation during auditory-verbal long-term memory function. *Neuroscience Letters* **163**, 185–188.

Grasby, P. M., Friston, K. J., Bench, C. J., Frith, C. D., Paulesu, E., Cowen, P. J., Liddle, P. F., Frackowiak, R. S. J. & Dolan, R. J. (1992). The effect of apomorphine and buspirone on regional cerebral blood flow during the performance of a cognitive task – measuring neuromodulatory effects of psychotropic drugs in man. *European Journal of Neuroscience* **4**, 1203–1212.

Gray, C. M., Konig, P., Engel, A. K. & Singer, W. (1989). Oscillatory responses in cat visual cortex exhibit inter-columnar synchronization which reflects global stimulus properties. *Nature* **338**, 334–337.

Jenkins, I. H., Brooks, D. J., Nixon, P. D., Frackowiak, R. S. J. & Passingham, R. E. (1994). Motor sequence learning: a study with positron emission tomography. *Journal of Neuroscience* **14**, 3775–3790.

McCulloch, W. S. & Pitts, W. H. (1943). A logical calculus of ideas immanent in nervous activity. *Bulletin of Mathematics and Biology* **5**, 115–133.

Posner, M. I. & Petersen, S. E. (1990). The attention system of the human brain. *Annual Review of Neuroscience* **13**, 25–42.

Posner, M. I. & Raichle, M. (1994). *Images of Mind*. Scientific American Library: New York.

Price, C., Wise, R. S. J., Ramsay, S., Friston, K. J., Howard, D., Patterson, K. & Frackowiak, R. S. J. (1992). Regional response differences within the human auditory cortex when listening to words. *Neuroscience Letters* **146**, 179–182.

Scoville, W. B. & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery and Psychiatry* **20**, 11–21.

Shallice, T., Fletcher, P., Frith, C. D., Grasby, P., Frackowiak, R. S. J. & Dolan, R. J. (1994). Brain regions associated with acquisition and retrieval of verbal episodic memory. *Nature* **368**, 633–635.

Singer, W. (1990). Search for coherence: a basic principle of cortical self-organisation. *Concepts in Neuroscience* **1**, 45–54.

Stephan, K. M., Fink, G. R., Passingham, R., Silbersweig, D., Ceballos-Baumann, A., Frith, C. D., Frackowiak, R. S. J. (1994). SMA and anterior cingulate involvement in imagining and performance of upper limb movements. *European Journal of Neuroscience* **14**, (suppl. 7) (15.03).

Sternberg, S. (1969). The discovery of processing stages: extensions of Donders method. *Acta Psychologica* **30**, 276–315.

Tononi, G., Sporns, O. & Edelman, G. M. (1994). A measure for brain complexity: relating functional segregation and integration in the nervous system. *Proceedings of the National Academy of Science, USA* **91**, 5033–5037.

Wernicke, C. (1874). *Der Aphasische Symptomenkomplex*. Breslau: Poland.

Wernicke, C. (1906). *Grundrisse der Psychiatrie*. Thieme: Leipzig.

Wise, R., Chollet, F., Hadar, U., Friston, K. J., Hoffner, E. & Frackowiak, R. S. J. (1991). Distribution of cortical neural networks involved in word comprehension and word retrieval. *Brain* **114**, 1803–1817.

Zeki, S., Watson, J. D. G., Lueck, C. J., Friston, K. J., Kennard, C. & Frackowiak, R. S. J. (1991). A direct demonstration of functional specialization in the human visual cortex. *Journal of Neuroscience* **11**, 641–649.

Zihl, J., Von Cramon, D. & Mai, N. (1983). Selective disturbance of movement vision after bilateral brain damage. *Brain* **106**, 313–340.