PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

General Discussion

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GENERAL DISCUSSION

L. Weiskrantz (*Department of Experimental Psychology, University of Oxford, South Parks Road, Oxford OX1 3UD, U.K.*). I have tried to link what we have heard from experimental studies in humans with what we have heard from experimental studies in monkeys concerning functions of the prefrontal cortex. The obvious difference is that in my experience, patients with posterior cortical lesions are often those with short-term memory deficits (such as patient KF), whereas you have to work very hard with frontal lobe lesioned patients to see profound impairments of that kind. This provides an obvious contrast with experimental studies in monkeys which suggest a role for the prefrontal cortex in just such simple short-term or working memory processes. I was wondering if any of the speakers would care to comment on this rather obvious distinction between human and monkey work that has ben presented so far?

P. Goldman-Rakic (*Section of Neurobiology, Yale University School of Medicine, 333 Cedar Street, New Haven, CT, 06520-8001, U.S.A.*). Other participants may have a better answer to the question than I. For my part, I wonder if the distinction between results in humans and experimental primates is more apparent than real. As I recall, patient KF had severe difficulty with auditory-verbal short-term memory, which would be expected from the location of the lesion in the inferior parietal lobe of the left hemisphere. The question that I would ask is whether this and other auditory-verbal memory deficits observed following tempoparietal lesions of the left hemisphere can be dissociated from perceptual deficits in the auditory domain and also whether the location of the prefrontal lesions with which parietal lesions have been compared involved auditory working memory domains of the prefrontal cortex, which would be the only meaningful comparison.

As to a difficulty in demonstrating short-term memory deficits in patients, there can be no doubt that patients with prefrontal lesions exhibit a whole host of severe short-term or working memory problems in the form of deficits of delayed-response tasks, recency memory, self-ordered tasks, etc., but also, as I have argued, in tasks which depend in part or in whole on 'on-line' processing such as the Stroop test, the Wisconsin card sorting test, verbal and graphic fluency, the Tower of London and Hanoi tests, the California verbal learning test, trials B, etc.

Finally, the fact that patients with parietal lesions may also exhibit short-term memory loss is compatible with and predicted by studies in non-human primates which show that posterior parietal and prefrontal areas are reciprocally interconnected, coativated during working or short-term memory tasks (confirmerd by PET/fMRI studies in humans), and both areas have been shown to contain neurons with similar task-related profiles of activation. The real distinction may lie in whether memory deficits can invariably be dissociated from sensory-guided performance in subjects with parietal lesions as they can be in prefrontal patients whose deficits are highly specific to memory-guided performance.

A. Baddeley (*Department of Psychology, University of Bristol, 8 Woodland Road, Bristol BS8 1TN, U.K.*). A great deal of the neuropsychological research on working memory deficits in human patients has so far concentrated on impairment to the phonological loop component of working memory, as typified by grossly reduced auditory digit span. Both lesion and PET studies implicated the temporal lobes and Broca's area as responsible for this system. Monkeys probably do not have the phonological loop, making it difficult to conduct parallel studies. It seems much more likely that there will be similarities between human and monkey studies in research on the other components of working memory. I would regard the work by Patricia Goldman-Rakic as being concerned with exploring the components of the visuo-spatial sketchpad, and producing results that are broadly consistent with lesion and PET data in humans. Finally, I would regard the work on executive processes that forms the core of much of the work described at the present symposium as being very clearly associated with the central executive component of working memory. Indeed I would regard the overall tenor of the meetings as indicating clear convergence between the monkey and human work.

T. W. Robbins (*Department of Experimental Psychology, University of Cambridge, Downing Street, Cambridge CB2 3EB, U.K.*). In terms of Baddeley's working memory model, we must obviously separate the components due to the 'visuo-spatial sketchpad' and the 'central excutive'. From our perspective the test of spatial span provides an index of the ability to hold spatial information on-line and is thus relevant to the former component. We have reported patients with frontal lobe excisions to be unimpaired in maximum spatial span attained. Recently, Owen and colleagues have shown, using a functional imaging paradigm, that a similar task activates ventro-lateral prefrontal cortex. This may correspond to evidence that frontal patients have subtle deficits in attaining the maximum span (Owen & Robbins, unpublished data). By contrast, the self-ordered spatial working memory task is highly sensitive to frontal damage and produces activations in both ventro-lateral and dorso-lateral regions of prefrontal cortex in normal volunteers. We interpret this self-ordered task as having a greater 'executive' component because the spatial information has to be updated on the basis of previous choices and there is also a specific strategy that can be followed to enhance

performance. It is these aspects of the task which we believe make it particularly susceptible to frontal lobe damage. Overall, these results are entirely compatible with observations that patients with posterior cortical damage such as patient KF can have severe impairments in short-term memory, whereas frontal lesions impair those aspects of performance requiring some higher order manipulation of the information, which may correspond to certain functions of a hypothetical 'central executive'. In comparison to the studies with monkeys, our data are compatible with the deficits found by Petrides and by Passingham using different tests of self-ordered memory analogous to those we have employed in humans. Based on evidence cited by Diamond, I presume that the delayed response task also has some executive components (including response inhibition) which, together with its memorial requirement, make it such a sensitive task for detecting deficits produced by lesions of the dorso-lateral prefrontal cortex.

M. Petrides (*Montreal Neurological Institute, 3801 University Street, McGill University, Montreal, Quebec, Canada, H3A 2B4*). I am in complete agreement with your statement that, in patients, short-term memory deficits are most clearly seen after posterior cortical lesions. In patients with lateral frontal lesions, deficits emerge only under certain testing conditions that tax executive processing. It is possible to show that the patient with lateral frontal lesions performs well under certain conditions of testing short-term memory, but not under others. It is for this reason that I prefer to talk of monitoring within working memory in trying to characterize the specific functional contribution of the mid-dosolateral frontal cortex and active retrieval or judgements on certain aspects of mnemonic information for the ventrolateral frontal cortex. The processes that we subserve under the term working memory are the result of complex interactions between frontal with poterior cortical areas, as well as several subcortical areas. In the monkey, although posterior cortical lesions do impair short-term memory, as for instance, lesions of the anterior inferotemporal cortex for visual short-term memory and the superior temporal cortex for auditory short-term memory, thinking has been so dominated by the delayed response deficits after prefrontal lesions that we have tended to neglect the posterior cortical contribution. As I have tried to show in my presentation, the impairments in delay tasks after lateral frontal lesions in the monkey, when analysed more closely, appear to be in line with those observed in work with patients.

R. E. Passingham (*Department of Experimental Psychology, University of Oxford, South Parks Road, Oxford OX1 3UD, U.K.*). I do not agree that the data on monkeys show that the role of the prefrontal cortex is in 'just such simple short-term or working memory processes'. It is true that the delayed response tasks require that the monkeys remember the side that was baited, but the animals also have to discriminate between recent memories. Dr Diamond has shown that monkeys with dorsal prefrontal lesions succeed if the reward remains on the same side for two trials; they fail when it changes from one trial to the other because they fail to suppress routine responses to the side that was previously rewarded. These data suggest that the dorsal prefrontal cortex is not a simple mechanism for short term retention. There are now many PET studies that support the view that the area plays a role when an operation has to be performed on information in memory.

A. Diamond (*Department of Brain and Congitive Sciences, Massachusetts Institute of Technology, Building E10-044, Cambridge, MA, U.S.A.*). An obvious difference between findings from humans and monkeys is that patients with posterior cortical lesions have STM deficits, whereas you have to work hard with frontal lobe patients to see a profound memory impairment. Yet in monkeys, prefrontal cortex seems to be important for short term or working memory processes.

I think that the findings in monkeys correspond well with what Professor Weiskrantz describes in human patients. Monkeys with lesions of dorsolateral prefrontal cortex do not tend to show deficits on tasks that rely principally on short term or working memory processes, such as delayed nonmatching to sample. It is necessary to tax both working memory and inhibitory control, or to complicate the task in some other way, before deficits are seen in monkeys following bilateral removal of dorsolateral prefrontal cortex. This is quite consistent with the human literature, I think. More ventral lesions in monkeys have been associated with impairments on delayed nonmatching and matching tasks, but it is not clear why animals with such lesions fail, as they do not succeed even at the shortest delays tested. That is, there is no evidence that they learned or understood the task.

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