MECHANISMS IN 'PURE RETROGRADE AMNESIA': FUNCTIONAL, PHYSIOLOGICAL OR PATHOPHYSIOLOGICAL?

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The topic of 'pure' or 'focal' retrograde amnesia is one that is both complex and controversial. Sellal et al. (2002, this issue) present a case of dense retrograde amnesia following an apparently minor head injury. Their case is similar to other cases of relatively isolated, dense retrograde amnesia following minor or apparent absence of cerebral pathology. The reader is referred to recent papers that have reviewed such cases (Parkin, 1996; Kopelman, 2000a,b; Kapur, 1999, 2000) for an overview of their clinical, neuropsycholological and neuroimaging features. In this commentary, I will provide some specific comments on the paper by Sellal et al. and also more general comments on attempts to document neural correlates of memory loss.

Specific comments. In their case report, Sellal et al. note that their patient 'had no past history of psychiatric disorders and at the time of the examination there were neither any psychiatric nor psychological disorders'. These observations are of course important in this type of case, but as Kopelman (2000a) has pointed out it is important that such observations are based on detailed psychiatric assessment, including background information from family/relatives and medical practitioners who have treated the patient in the past. It is not possible to infer whether such a detailed assessment was in fact carried out in this particular case.

While it seems likely that their case falls into the same category as other cases in the literature where a dense retrograde amnesia follows an apparently minor head injury, two other possibilities are worth considering. Firstly, it is possible that their case was one of transient global amnesia (TGA) induced by minor trauma, a possibility that the authors note in their Discussion. The occurrence of TGA following minor trauma has been well documented, and a review of trauma-induced TGA has been provided by Haas (1990). There is no reported evidence in the paper by Sellal et al. that there was a dense TGA-type anterograde amnesia in the immediate aftermath of the patient's head injury, although there is mention of the fact that 'he had no recollection of the 24 hours following the trauma'. Clinically, the presence of TGA is very striking, so it would seem unlikely that such amnesia was present but was not recorded. In addition, it would be very unusual for the retrograde amnesia associated with TGA to persist for several days or weeks. A second possibility is that the case reported by Sellal et al. was one of epilepsy-related amnesia. There is no

reported evidence of clinically obvious seizure activity in this case, but it is worth bearing in mind that memory loss may arise in association with the occurrence of subclinical seizure activity (Binnie, 2001). While marked retrograde amnesia has been associated with episodes of transient epileptic amnesia (Corridan et al., 2001; Zeman et al., 1998), such patients eventually show clinical and other evidence of the presence of temporal lobe epilepsy. The apparent absence of such evidence and of features such as spike and wave features in the EEG would again tend to rule out this alternative diagnostic scenario.

The absence of any loss of personal identity, or any failure to recognize family members, is an important observation and would support the exclusion of any major psychiatric disturbance, though not necessarily any more discrete abnormality.

The period of retrograde amnesia appears to coincide with the period during which the patient was married, though it is not possible to discern from the report if this was a precise cut-off point. If such a discrete temporal boundary to the retrograde amnesia was present, there would of course be grounds for suspecting the operation of psychological factors. The autobiographical memory loss for events in this period seems to have been particularly marked – the patient did not know that he had a 7-year-old son, that he had built a house eight years earlier or that he had his own business. Such marked memory loss for personally-related information would be unusual in purely neurological disease without evidence of major cerebral pathology.

The actual neuropsychological tests scores relating to the patient's retrograde amnesia could be interpreted as reflecting a mild-moderate rather than marked deficit. The Autobiographical Memory Interview is subject to some degree of variability in scores, since a number of the questions may not apply to all individuals, and the actual 'abnormal' scores of the patient were generally just below the cut-off threshold. In the case of the public events scores, I note that the patient had nine years of schooling. It is unclear how often he attended to media reports of public events when they occurred, though I note that the control subjects were matched for profession and educational level. I agree that the presence of a temporal gradient to the patient's retrograde memory performance would be in keeping with what has been seen in neurological disease, and that any effects due to low media exposure would have been more general rather than temporally-specific.

The loss of 'procedural memory', where skills such as handwriting appear to have 'regressed', is somewhat unusual in neurological disease. We did make one such observation in a case of psychogenic retrograde amnesia following a minor head injury (Kapur, 1999).

In the case of the patients reported by Kapur et al. (1992) and by Stuss and Guzman (1988), to which Sellal et al. refer, both of these cases subsequently transpired to have psychogenic features that may have partly or wholly explained their retrograde amnesia (Gow et al., 1989; Kapur, 2000).

In the case of the imaging findings, I am impressed by the recovery of EEG and SPECT abnormalities that occurred in parallel with clinical and neuropsychological improvement. However, I am uncertain as to what

significance, if any, may be attached to the observation that EEG abnormalities appeared to be more posterior in the temporal lobes, while SPECT abnormalities were more anterior. I am also uncertain as to what weight should be put on the reported perfusion ratios in the absence of relevant normative data. It may be useful for the authors to consider registering the two sets of SPECT images on a common template, and to define common regions of interest over the temporal lobe and cerebellum. In addition, it might have been helpful to publish the second set of normal images, and to provide some reassurance that factors such as positioning artefacts were controlled for when considering changes between the two sets of scans.

General comments. It would seem that there are at least five possibilities which may explain the pattern of results reported by Sellal et al. Firstly, their findings may solely reflect the presence of an unconscious psychogenic retrograde amnesia, with the imaging data being a coincidental and random occurrence of what might be found in the normal population. Secondly, the findings may reflect the occurrence of malingering, that is conscious simulation of memory symptoms and low test scores. Thirdly, the results could be directly tied to the occurrence of a discrete neurological event, perhaps vascular, ischaemic, encephalitic, toxic or epileptic in origin. Fourthly, the observations may point to a temporary metabolic disturbance in the right hemisphere that arose from some form of abnormal psychological state. This could have been precipitated by the trauma, perhaps occurring in the context of undetected premorbid psychiatric factors, and this selective brain abnormality may somehow have resulted in the pattern of memory symptoms and memory test scores that were found. Fifthly, the clinical, neuropsychological and neuroimaging profile may reflect some combination of one or more of the above possibilities.

While it is not possible to offer a definitive judgement as to which of these explanations is more likely, the fourth and fifth explanations may perhaps be most plausible. The presence of imaging abnormalities is not inconsistent with the operation of conscious or unconscious psychological factors, as has been demonstrated in a number of recent studies which have yielded brain abnormalities on SPECT or functional imaging in a range of psychiatric conditions that have included hysteria, post-traumatic stress disorder and malingering (Tiihonen et al., 1995; Marshall et al., 1997; Markowitsch, 1999; Spence et al., 2000; Vuilleumier et al., 2001; Yasuno et al., 2000; Sachinvala et al., 2000). Although a number of these changes have been primarily in frontal lobe structures, some changes have been noted (Yasuno et al., 2000) close to the right anterior temporal region that showed an abnormality in the study by Sellal et al. One may speculate that the right temporal abnormality noted by Sellal et al. could be related to evidence that the right hemisphere is generally considered to be more specialised for attentional/emotional functions and thus more likely to underlie psychologically-based abnormalities, such as has already been shown in hysterical sensory loss (cf Joseph, 1988; Sierra and Berrios, 2001). Although there may be some overlap between the anatomical regions highlighted in the case reported by Sellal et al. and those which have been documented in functional imaging studies of autobiographical memory (e.g. Markowitsch et al.,

2000), the limited anatomical imaging resolution in their case, and the variability that has been found between functional imaging studies, makes any specific comparisons rather problematical.

The interaction of neurological and psychological variables in the same patient is important to bear in mind, and has been highlighted both in review articles (Kopelman, 2000a) and in experimental investigations that have employed functional imaging paradigms (Costello et al., 1998). As has been implied by a number of authors (e.g. De Renzi et al., 1997; Costello et al., 1998; Ron, 2001), evidence from functional imaging of psychological disorders is forcing a re-evaluation of the concepts and vocabulary that are used to describe general brain correlates and specific neural signatures of abnormalities of cognitive and emotional functioning. Perhaps there is a case for formally distinguishing between functional physiological and pathological physiological (pathophysiological) abnormalities, with the former being more susceptible to being reversed by the free will of the individual or by psychological/social variables, and the latter relatively immune to such influences and more likely to be a direct consequence of specific brain pathology, whether it be a structural brain lesion or a temporary abnormality, as in transient global amnesia, transient epileptic amnesia, toxic disturbances, etc.

As I have pointed out elsewhere (Kapur, 2000), in cases of focal retrograde amnesia one is often coming face-to-face with two scientific truisms – 'absence of evidence is not evidence of absence', and 'presence of evidence is not evidence of primacy'. The first truism is seen in situations where, for example, the apparent absence of psychiatric evidence cannot necessarily be taken as evidence for the absence of operation of psychiatric factors. The second truism may be seen in scenarios where the presence of imaging correlates to a neuropsychological profile may not necessarily indicate that such correlates represent the primary or only basis for any cognitive symptoms and deficits that have been demonstrated.

In summary, the findings reported by Sellal et al. provide memory researchers with an enigma and a paradox, and challenge us to redefine the boundaries, the overlap, and the interaction between psychologically-driven and pathologically-driven brain abnormalities.

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