Multiple-trace theory and semantic dementia: Response to K.S. Graham (1999)

We are indebted to Graham for raising the issue of semantic dementia and its implications for multiple-trace theory (Graham, K.S. (1999) Semantic dementia: a challenge to the multiple-trace theory of memory consolidation? Trends Cognit. Sci. 3, 85–87). Investigating people with semantic dementia to study hippocampal function and episodic memory is an innovative departure from the typical strategy of studying people with amnesia who have lesions to the medial temporal lobe and diencephalon. By capitalizing on the observation that the medial temporal lobes are spared in the early-middle stages of semantic dementia, one can evaluate their contribution to episodic and semantic memories.

In response to Graham’s (1999) response, we would like to restate our theory of episodic memory in semantic dementia. In our most recent study (Garrard, P., Hodges, J.R. and Patterson, K., in press), we have extended this more extensive lesion model to accommodate people with semantic dementia. The resulting semantic memory framework is one in which more remote memories are multiply-represented and widely distributed. Because each of the subregions of the hippocampal complex is significantly damaged, the resulting memory framework is one in which each of the subregions is significantly damaged.

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that are the more crucial, will lead to the most extensive retrograde amnesia for autobiographical details. This hypothesis was consistent with the data we reviewed in 1997 and accurately predicted findings that have been reported since then. For example, of the four new cases of amnesia reported by Reed and Spours, two with restricted hippocampal formation lesions had a temporally graded RA that was not extensive whereas the cases whose lesions encompassed most or all of the hippocampal complex had a more extensive RA, which in one case covered a lifetime.

Graham's critique of multiple-trace theory

In developing our model and formulating its predictions, we focused almost exclusively on the medial temporal lobes and neglected to consider what effects neocortical lesions would have on episodic autobiographical memory. The only exception was prompted by Graham and Hodges' report of a 'reverse' temporal gradient in episodic memory in semantic dementia that appeared as we were writing our paper.

Because there was so little evidence about episodic memory loss in this disorder, we suggested that the frontal-lobe degeneration often accompanying semantic dementia could lead to strategies for episodic remembering, a hypothesis that we speculated might affect remote memory more than recent memory. We agree with Graham that the evidence now available on this score does not support this idea, but we also agree with her that the nature of the evidence, a report of a small patient, warrants caution in interpreting the data.

As episodic autobiographical memory for encasing caution should be extended to all the recent studies on episodic memory in semantic dementia. A small number of patients have been studied, and for most of them the level of performance on episodic memory tests is very poor at all but the most recent time period, when it rises but still remains below control levels. This performance contrasts with that of controls who are virtually ceiling at all time periods tested. It is against the background of the flat-gradient of control performance, and in comparison with amnestic performance, that the temporal gradient, or more properly the step-function, in semantic dementia appears to be 'reversed' and unusual.

How deficient is episodic memory in semantic dementia?

Before we attempt to see if our model can account for the data from semantic dementia, we think it necessary to have a better appreciation of the nature of the deficit than is provided in the few published studies. The 'reversed' pattern that is meant to characterize semantic dementia resembles what is typically observed in controls when the test is not too easy that performance is at ceiling.

The reader may be satisfied on this point by trying to describe in detail a recent vacation and one that was taken between the ages of 6–10, or even in high school. If one assumes that the degeneration typical of semantic dementia causes a severe reduction in all available memories, then the ones that will be preserved best, or at all, will be the most recent. We will return to this point in a moment.

Our own examination of a single case of semantic dementia led us to believe that remote memories may be better preserved than Graham and her colleagues believe, at least in some, if not all patients, with the disorder. Most tests of autobiographical memory are verbal both in the cues used to elicit memories and in the response demanded of the participant. Although semantic dementia is characterized by loss of verbal and non-verbal knowledge, the deficit is most severe in the verbal domain, a fact consistent with the locus of degeneration in the left temporal lobe. Indeed, as Graham notes, one of the hallmarks of the disorder is that non-verbal problem solving and good visual-spatial abilities are relatively preserved, and sometimes normal. In response to verbal questioning, our participant, who was in his mid-sixties, was able to recollect some facts about his early life such as where he was born, where and how he emigrated to Canada, where he got married, what his education was, how many children he had, and so on. It was difficult for us to elicit any autobiographical episodes until they appeared serendipitously in response to cues on other tests. When shown a picture of Hitler, he became animated, identifying him vaguely as a leader during a war a long time ago. He then gave as detailed an account as was possible with his limited vocabulary of his life in England during the German bombing raids, of the time a bomb leveled the house next door to him, and of his having spent much time underground. When shown a van on a semantic classification test, he said 'I had one of those, long time ago' (a phrase he repeats) and then recounted a vacation trip he and his family took down south (we assume to Florida). When shown a map, he became animated and pointed to Brazil and then described the job and life he had there in his twenties. We are now planning to conduct systematic tests of his remote memory and devise others that may allow us to tap into these memories using non-verbal cues or verbal ones that he grasps well. There is no doubt, however, that rich remote memories do exist in at least some cases of semantic dementia. Gaining access to them, however, may prove problematic.

One technique that may be useful is to ask someone close to the participant to supply what they believe are significant incidents and see if there are pictures or other cues that can be used to elicit them.

To summarize, the 'reverse' gradient or step-function that is observed in semantic dementia may be a severely depressed or reversed pattern to that observed in normal controls when performance on tests of autobiographical memory is not at ceiling. This pattern differs from the classical temporal gradient observed in amnesia with restricted medial temporal damage in which remote memories are remembered better than recent ones. In addition, performance on tests of retrieval in semantic dementia may be improved if non-verbal cues are used.

Multiple-trace theory and episodic memory in semantic dementia

What would our model predict about the effects of neocortical lesions on episodic memory? Graham states that we would predict that 'neurologically normal subjects (if tested appropriately) should show better retrieval of older episodic memories compared to those of their more recent past' and 'that patients with semantic dementia should show a similar pattern of performance to control subjects on tests of autobiographical memory', with the proviso that memory will be impaired overall. Although Graham is correct in assuming that the pattern, but not level, will be impaired in semantic dementia patients resembles that of controls, we do not believe that in either case the model predicts that older memories should be retrieved better than recent ones. As we stated earlier, 'as episodic memories age, they would call the forgrtgradually beneitted from the formation of multiple traces' (Ref. 4, p. 223). Because the vast majority of experience are forgotten, the benefit would accrue to only a relatively small amount of memory.

As noted earlier, in general, memory is better overall for recent than for remote events. If we assume a neocortical normal control, with the pattern being preserved for both recent and remote memory, then the model predicts that partial damage to the hippocampal complex, as predicted by the model. When damage primarily affects the neocortex, as it does in semantic dementia, then the model predicts a pattern of remote memory loss that depends very much on the type of information represented by the structure that is damaged. Recall that according to our model the memory trace for an experienced event consists of a medial temporal–neocortical ensemble, with the neocortical component representing the feature information about the event. Whereas representation in the hippocampal complex is sparse and distributed, with little or no relation between neuronal coding and event similarity, representation in neocortex is based on similar ity, with similar features being represented in close proximity to each other. According to the multiple-trace theory,
reactivation of a memory trace results in the creation a newly encoded trace whose mediatis-material component is spared, dissociation and neurally separate from the memory trace which was reactivated, but whose neuronal component shares many of the neural elements that encode the features of that trace. Put another way, the reacti-
vated traces have minimal neural overlap in the medial temporal lobes but extensive overlap in neocortices. If a re-
region of neocortex coding a particular type of information is damaged, those remote memory traces depend on them will be lost, whereas those that are not will be spared.

With this framework in mind, let us first examine some interesting cases of focal retrograde amnesia that can serve as models of the type of deficits to be expected in semantic dementia. Ogden reported a case of extensive retro-
grade amnesia in a person with loss of visual imagery associated with infer-
striatal cortex damage. Because our experience of remembering auto-
bihographical events is highly visuall, Ogden speculated that the loss of vi-
ual imagery would deprive memories of a major source of their information content and of access to other aspects of the memory trace. In a recent review of the literature, Rubin and Greenberg reported 11 other similar cases with loss of long-term visual memory and extended retrograde amnesia and named the syndrome visual memory deficit amnesia. What makes these cases relevant for semantic dementia is that in some of them, the hippocampus and related structures are relatively spared. Despite extensive RA, antero-
bradiate thalamus, the auditory cortex, and the inferior parietal lobule are relatively spared, so that these people acquired new memo-
ories but, presumably, ones that were no longer strongly visual. In terms of our theory, the visual, neocortical com-
ponent of old memory traces was lost so that even if the medial temporal component was spared, the memo-
ries could not be recovered easily. In two of these cases, remote memory for songs were preserved though it is not clear that these memories included specific episodes.

Our theory predicts that retro-
grade amnesia in semantic dementia will be evident to the extent that the semantic information that is lost is either part of the memory trace or is needed to access it. It is known that the more semantically-encoded information is the better it is remembered and the better it serves as a retrieval cue. If it is reasonable to assume, on this basis, that semantic information is an impor-
tant part of the memory trace and is needed to gain access to it. It is no sur-
prise, therefore, that neural degener-
ation that leads to semantic memory loss, a loss in semantic dementia, will also lead to loss of old memories that had a semantic component. Those memories that were not as semanti-
cally-based, or could be accessed via visual cues, as they were in our patient, should be retained and recovered.

The question remains as to whether remote memories will be affected more than recent ones. One possibility is that the gradient (or step-function if a threshold needs to be exceeded) would resemble that of controls on tests in which controls also show the typical gradient. On the other hand, the model also allows for the possibility that remote memories will be more severely affected. Because the medial temporal lobes are intact, they are free to form new memory traces by binding those neocortical neurons that did not succumb to the degenerative process. Presumably, these will be neurons that support perceptual, rather than con-
tceptual, representations, and neurons that support right-hemisphere func-
ctions. As a result, the recent memories that are spared in semantic dementia should be more perceptual than con-
tceptual in nature, and more reliant on non-verbal right hemisphere processes than verbal (left-hemisphere ones). Moreover these new memories will be relatively short-lived since the degen-

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