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 lobes and diencephalon. By capitalizing on the observation that the medial temporal lobes are spared in the early to middle stages of semantic dementia, one can evaluate their contribution to episodic (and semantic) memory when the lateral inferotemporal cortex, which supports semantic memory, is damaged. In their investigations, Graham and Hodges confirmed and extended Snowden et al.'s initial observations that episodic and semantic memories based on recent experiences are relatively spared in semantic dementia, whereas remote memories are deteriorated or lost. Graham and Hodges concluded that these results provided evidence for traditional consolidation theory, which states that the medial temporal lobes or hippocampal complex play only a time-limited role in memory. By this view, once memories are consolidated, they are retrieved directly from the neocortex and other structures in which the memory or engram is represented. Because semantic dementia results from neocortical degeneration, only these remote, consolidated memories would be lost. More recent memories would be spared because they had not yet been consolidated and could still be recovered via the medial temporal lobe structures that are intact. We believe this interpretation is neither the only, nor the best, available for data from these intriguing cases.

We recently offered an alternative to traditional consolidation theory, the multiple-trace theory, which Graham believes faces less well than the traditional view in accounting for the evidence from semantic dementia. In order to respond to her criticisms, we first would like to restate our theory briefly because we believe that Graham may have misinterpreted some aspects of it. For example, Graham quotes us out of context when she says we proposed that ‘consolidation processes last on the order of decades, or indeed the entire lifetime’ (p. 221). That statement referred not to our theory but to what the traditional theory would have to conclude based on reports of retrograde amnesia that lasts decades or even a lifetime. Also, she refers only to the hippocampus whereas we explicitly stated that our theory also includes the adjacent structures in the medial temporal lobe, one of which comprises what we called the hippocampal complex.

The multiple-trace theory

According to our theory, during consolidation the neural elements involved in cortex and elsewhere mediating a particular conscious experience are bound into a cohesive unit by the hippocampus and adjacent medial temporal lobe structures (the hippocampal complex). The resulting memory trace or engram consists of a cohesive medial temporal-neocortical ensemble. The medial temporal component, which may provide the spatial context of the experience, acts as a pointer or index to the neocortical components needed to provide the detailed content of the experience. The medial temporal lobe units are an integral part of the episodic memory trace and are needed to recover it as long as it exists. Over time, as an episodic memory is recovered, it is recoded so that multiple, related memory traces are formed and dispersed over wider areas of the hippocampal complex. Because we believe that semantic memories can be acquired or retained without the medial temporal lobes (see Ref. 8), we confined our model only to episodic, autobiographical memories.

By virtue of the multiple-trace aspect of the model, more extensive lesions to the hippocampal complex are required to expunge more remote memories that are multiply-represented and widely distributed. Because each of the subregions of the hippocampal complex has a distinct function, and because autobiographical, episodic memories are multifaceted and rich in detail, it is likely that each of these subregions is in storing or recovering some aspect of a remembered experience. Incomplete lesions to the complex will lead to a temporally-graded retrograde amnesia (RA). Damage to all the subregions, or to those...
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, the four new cases of amnesia reported by Reed and Squire, 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 strategic processing deficits which, 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 report, but we also agree with her that the nature of the evidence, a report about a single patient, warrants caution in interpreting the data.

Graham's recommendation for exercising caution should be extended to all the recent studies on episodic memory in semantic dementia. A small number of patients has been studied, and for most of them the level of performance on episodic memory tests is very low 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 at 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 believe 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 is what is typically observed in controls when the test is not so 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 leads us to believe that recent 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 recount some facts about his early life such as where he was born, where and how he emigrated to Canada, when 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 his house was bombed and the time he had to leave the house next door to his, and of his having spent much time underground. When shown a van on a semantic classification test, he said: 'I had one of those a long, 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 them with 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, but basically similar, pattern to that observed in normal controls when performance on tests of autobiographical memory is not at ceiling. This pattern differs from the classic 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 remote memory 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 intact subjects (if tested accurately) 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 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 the level, of performance of 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 either be forgotten or would have benefited from the formation of multiple traces in the hippocampal complex and neocortex' (Ref. 4, p. 223). Because the vast majority of experiences are forgotten, the benefit would accrue only to a relatively small number of memories. Earlier, we argued that the model is better overall for recent than for remote experiences in neurologically-normal controls, with the pattern being reversed in people with amnesia caused by partial damage to the hippocampal complex, as predicted by the model. When damage primarily affects the neocortex, as it does in semantic dementia, multiple trace theory would predict a pattern of remote and recent memory loss that depends very much on the type of information represented by the structures that are 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 the neocortex is based on similarity, 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 medial-temporal component is sparse, distributed, and neurally separate from the memory trace which was reactivated, but whose neocortical component shares many of the same memory elements that encode the features of that trace. Put another way, the reactivated traces have minimal neural overlap in the medial temporal lobe but extensive overlap in neocortex. If a region of the brain coding for a particular type of information is damaged, those memory traces dependent 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 retrograde amnesia in a person with loss of visual imagery associated with inferior temporal cortex damage. Because our experience of remembering autobiographical events is highly visual, Ogden speculated that the loss of visual 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 extensive 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, anterograde amnesia is moderate or mild, so that these people acquired new memories but, presumably, ones that were no longer strongly visual. In terms of our theory, the visual, neocortical component of old memory traces was lost so that even if the medial temporal component was retained, the memories could not be recovered easily. In two of the cases, remote memories for songs were preserved though it is not clear that these memories included specific episodes.

Our theory predicts that retrograde amnesia in semantic dementia will be evident to the extent that the semantic information that is lost is either a part of the memory representation 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. It is reasonable to assume, on this basis, that semantic information is an important part of the memory trace and is needed to gain access to it. It is no surprise, therefore, that neural degeneration that leads to semantic memory loss, as it does in semantic dementia, will also lead to loss of old memories that had a semantic component. Those memories that were not as semantically-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 neural activity is exceeded) will 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 conceptual, representations, and neurons that support right-hemisphere functions. As a result, the recent memories that are spared in semantic dementia should be more perceptual than conceptual 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 degenerative process will affect even those newly-created memories so that only the most recent ones are viable. This might account for the step-function that Graham observed.

Conclusion: the multiple-trace theory vindicated

Investigations of episodic memory loss in semantic dementia address the question of the role that neocortical semantic processes play in episodic memory. We have argued that the pattern of deficits observed is at least as consistent with the multiple-trace theory of memory as with the traditional consolidation model. Indeed, we believe the evidence favors our theory. Predictions based on the multiple-trace model can account for the fact that memories formed within the very recent past, that is within the last one or two years, are easiest to recover, at least via verbal cues. According to Graham and Hodges' interpretation of traditional consolidation theory, this occurs because during this time period memories are still being consolidated and dependent on medial temporal lobes which are used to recover them. Once the two years are past, consolidation is complete and memories are dependent exclusively on neocortex, making them vulnerable to the ravages of the disease. If, following the logic of Graham and Hodges' account, we take two or so years as the time needed for consolidation, traditional theory would then be unable to explain why retrograde amnesia extends well beyond that time in patients with extensive medial temporal damage. This inability to deal with variations in RA is the central weakness of traditional consolidation theory, and the evidence from semantic dementia does nothing to mitigate it.

References