Simulating Amnesic Symptoms in Normal Subjects

Abstract. *Patients with organic brain damage resulting in anterograde amnesia cannot recall a list of words, but when given the first three letters of each word, they complete these word stems with words from the list. We simulated this phenomenon in normal subjects who examined the list words for vowels while ignoring their semantic component. The subjects produced the list words when completing the word stems although they could not recall the words.*

The ability to remember new information is severely impaired in patients with anterograde amnesia (*1, 2*). The amnesia seems incomplete, however, because although amnesics are unable to recall a list of words, they use information from the list when given the first three letters of each word (for example, *def*) with instructions to complete these word stems to form English words. The patients are inferior to normal control subjects on a recall test, but they are equal to normals on the completion test (*3, 4*). Although the patients produce the words on the completion test they often do not remember having studied the list or any list of words. We found the same disjunction of performance on the recall and completion test with college students who searched words for specific vowels while ignoring their semantic component.

Warrington and Weiskrantz originally argued (*3*) that amnesics store new information as normal controls do, but that their ability to access and retrieve information is impaired (*5*). A retrieval deficit could be overcome by providing additional cues for the memory test (as in the completion test). Thus, the amnesics' completion test performance seems to support a retrieval interpretation. However, this argument assumes that memory tests access a single unidimensional trace and that various kinds of tests of memory are differentially effective in accessing that trace (*6*).

The dual process model (*7*), originally proposed for recognition memory, suggests an alternative explanation for these findings. This model distinguishes between elaborative processing, in which the target event is related to other mental contents, and integrative processing, in which the internal features of the event are related to each other and a perceptual representation of the target event is constructed. Integrative activity facilitates performance on a memory test to the extent that the processing of a test event activates the representation of a previously stored target event. However, retrieval of a memory trace (as in recall) requires access to the other mental contents that have been related to it through elaboration.

The completion test provides strong evidence for the availability of a target event by activation of the integrated representation since the subject who is unable to give the list word *defend* on a recall test can complete the stem *def* . . . more frequently than expected by chance. The disjunction of performance on recall and completion tests suggests that amnesics have a deficit in elaborative processing although their integrative processes are preserved. The recall-completion disjunction should be demonstrable with normal subjects when they are exposed to words in such a way that integration can take place, but elaboration is prevented.

We tested two groups of normal subjects; one group was required to process the words elaboratively, and the other group was given a task that allowed construction of an integrated representation but prevented elaborative processing. The participants were 24 undergraduate students, 12 randomly assigned to each of two experimental groups. Both groups studied a list of 20 words, each of which was typed on an index card. The elaborative processing task required subjects to rate their liking for each word on a seven-point scale (liking group). Subjects proceeded through the deck of cards at their own pace while recording their liking ratings. Since the liking judgment involves an appreciation of the meanings of each word, it ensures that the target word become related to other mental contents. We prevented elaborative processing in the second group by requiring subjects to decide whether a word shared any of its vowels with the word preceding it in the deck of cards (vowel group). This speeded vowel-search task required subjects to look briefly at each word but to ignore its semantic component and its relationships with other mental contents (*8*). The 20 list words were preceded by 8 filler words to acquaint subjects with the task and followed by 4 filler words to prevent extensive rehearsal of the last few list words. After studying the list of 20 words, each subject first received the completion test and then the recall test.

The 20 list words were drawn from a pool of 40 critical words that shared the following properties. (i) Each word contained either five or six letters. (ii) Although each of these critical words had a different stem (the first three letters), Webster's Pocket Dictionary listed at least four alternatives for completing each stem to form a word of the same length. (iii) A critical word was never the most common completion of the stem. The completion test form listed all 40 word stems—the 20 presented in the study list and the other 20 stems. Consequently, one half of the test items measured completion performance on words that were included in the study list, and the other half provided an indication of chance completion performance on these words. Each critical word was included equally often in the study list. The completion test was administered with instructions to complete each word stem to form any English word except proper nouns (*9*). The free recall test was given with instructions to write the words from the study list in any order.

On the completion test, the liking and vowel groups produced a similar proportion of the study list words in response to the three-letter stems (.31 and .28). The distribution of scores obtained on the completion test indicated that the groups interpreted the completion instructions similarly. The median proportion of words produced (.30 and .28 for the liking and vowel groups) was the same as the mean, and the scores ranged from .00 to .60 for the liking group and from .10 to .45 for the vowel group. In contrast, the recall test showed that the liking group recalled a considerable proportion of the studied words (.30), while the vowel group recalled almost none of them (.08). An analysis of variance showed a significant interaction effect between group (liking versus vowel) and test (recall versus completion) [$F(1, 22) = 7.98$, $P < .01$]. This pattern of performance replicates the results previously found with amnesic patients.

Additional analyses of the completion test data further support these findings. Completion performance was substantially better for those words whose stems were included in the study list (.29) than "correct" completion of the remaining 20 critical word stems (.06). The two experimental groups did not differ significantly in their performance on either the list word stems or the remaining word stems. Thus, subjects in both groups completed the stems with words from the study list about five times as often as would be expected by chance.

During the recall test, subjects sometimes wrote words that they had given on the preceding completion test but that were not in the study list. Such intrusions from the completion test were

0036-8075/82/1217-1243$01.00/0

more frequent for the vowel group (13 intrusions equaling .41 of all words recalled) than for the liking group (5 intrusions equaling .06 of all words recalled).

Our findings show a pattern of results with normal subjects that mirrors the performance of anterograde amnesic patients. Like amnesics, our vowel subjects gave little evidence of having seen the words that they successfully produced on the completion test. The vowel subjects explained, for example, that they "did not look at the words" or that they were "not instructed to look at the words." This dissociation of recall and completion performance is predicted by the dual process model of recognition for any group of subjects that is prevented from elaborative processing. Different and separate underlying processes are responsible for recall and for completion. The advantages of elaborative processing are not available to amnesic patients—they are unable either to construct and store or to retrieve the elaborative network necessary for recall. In the case of our vowel group, we have prevented elaborative encoding and produced similar results.

PETER GRAF
GEORGE MANDLER
PATRICIA E. HADEN
Center for Human Information Processing, University of California, San Diego, La Jolla 92093

References and Notes

1. For example, alcoholic patients with Korsakoff syndrome and patients who have received bilateral electroconvulsive therapy for the relief of depressive illness. For recent reviews of amnesics' memory deficits see L. R. Squire, N. J. Cohen, and L. Nadel [in *Memory Consolidation*, H. Weingartner and E. Parker, Eds. (Erlbaum, Hillsdale, N.J., in press)] and E. K. Warrington and L. Weiskrantz (*2*).
2. E. K. Warrington and L. Weiskrantz, *Neuropsychologia* **20**, 233 (1982).
3. ———, *ibid.* **12**, 419 (1974).
4. ———, *ibid.* **16**, 169 (1978).
5. Warrington and Weiskrantz have recently revised their retrieval interpretation of amnesics' memory deficit (*2*). They distinguish between a semantic and a mediational (retrieval) memory system. Completion test performance depends on the semantic system, which is spared in amnesia.
6. See E. K. Warrington and L. Weiskrantz [*Nature (London)* **228**, 628 (1970)] and L. R. Squire [*Neuropsychologia* **18**, 369 (1980)] for critical discussions.
7. G. Mandler, *Psychol. Rev.* **3**, 252 (1980); *Am. Sci.* **69**, 211 (1981). For general evidence for the dual process model see also R. C. Atkinson and J. Juola [in *Contemporary Developments in Mathematical Psychology*, vol. 1, *Learning, Memory, and Thinking*, D. H. Krantz *et al.*, Eds. (Freeman, San Francisco, 1974), p. 243] and G. Mandler, G. O. Goodman, and D. L. Wilkes-Gibbs [*Mem. Cognit.* **10**, 33 (1982)].
8. In several pilot studies, we had used limited exposure (100 to 200 msec) compared with 1- to 2-second exposures. However, this manipulation did not produce the dissociation between recall and completion test performance that we found with the liking rating and the vowel-search task.
9. These instructions were designed to encourage subjects to produce words that were immediately accessible; the words whose activation level had been increased during the original presentation and that also satisfied the appropriate three-letter stems should be the most likely responses in completing the stems.
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Transient Raman Study of Hemoglobin: Structural Dependence of the Iron-Histidine Linkage

Abstract. *Low-frequency resonance Raman spectra of transient hemoglobin species were observed within 10 nanoseconds of photolysis. The Raman frequencies of the iron–proximal histidine stretching mode for transient species having either the R or the T quaternary structure are higher than in the corresponding deoxy species. The observed frequency difference in the iron-histidine mode between the R- and T-state transients indicates that there are quaternary structure–dependent protein forces on the iron-histidine bond in the liganded hemoglobins. These differences are interpreted in terms of changes in the tilt of the histidine with respect to the heme plane.*

Transient forms of hemoglobin (Hb) resulting from photodissociation of bound ligands provide a means of studying the conformational changes that initiate the events leading to the quaternary structure transition. After the photolysis of COHb, the porphyrin relaxes within picoseconds to a configuration nearly identical to that of an electronically relaxed deoxy (five-coordinate) heme (*1–6*). An important consideration in determining the mechanism for subsequent protein dynamics (such as the quaternary structure change) is the coupling mechanism between the nonequilibrium protein and the electronically relaxed deoxy heme. By comparing the resonance Raman spectrum of the deoxy heme in the transient species to that of the corresponding relaxed species, one can examine how specific degrees of freedom of the deoxy porphyrin are modified by the protein structure. The iron–proximal histidine (Fe–His) linkage is a potentially important element in models describing cooperativity in Hb. Using time-resolved resonance Raman scattering, we have determined the frequency of the Fe–His stretching mode from both high-affinity (R-state quaternary structure) and low-affinity (T-state quaternary structure) photodissociated ligand-bound hemoglobins. Compared to the relaxed deoxy species, the Raman bands associated with the transient species at 10 nsec are shifted to higher frequency by 6 to 10 cm^{-1}. In both the deoxy and the transient species, the Fe–His stretching frequency is higher in the R state than in the T state.

Transient resonance Raman spectra were generated with the output of a dye laser pumped by a nitrogen or an excimer laser operating at 10 Hz. The tunable output ($\leq$ 0.6 mJ) of the dye laser consisted of 10-nsec pulses. An excitation frequency near 4200 Å (Bis MSB) or 4350 Å (stilbene 3) was used to achieve resonant enhancement of the relevant Raman bands. The excitation light was focused (with a lens of focal length 250 mm) into a temperature-controlled cuvette at 2°C. No differences in spectra were observed between static and recirculated samples. The 90° scattered light was collected by an off-axis elliptical mirror and dispersed by a 1-m *f*/8 J. Y. Ramanor HG-23 spectrometer fitted with an RCA C313034-02HQ photomultiplier tube. The output of the photomultiplier tube was gated (1 nsec) and averaged with a PAR model 163 boxcar integrator. The resulting signal was stored and processed with a Nicolet 1174 signal averager, which allowed for repetitive scans of a spectrum (reset error < 0.2 cm^{-1}). A custom-designed interference filter for the excitation pulses was used to reduce the fluorescence background associated with the output of the dye laser.

The R-state transient was derived from photolyzed human adult COHb and NOHb and the corresponding T-state species were derived from photolyzed NOHb and from COHbK (Kansas) (700 μM, *p*H 6.5, 100 m*M* bis-tris), both in the presence of inositol hexaphosphate (IHP). The high heme concentration was necessary to ensure a sizable population of tetramers in the HbK (Kansas) sample. No spectral dependence on heme concentration (100 to 500 μM) was observed for the R-state transients.

Figure 1 shows low-frequency resonance Raman spectra of transient Hb species occurring within 10 nsec of photolysis of COHb. The upper and lower spectra are from the photolyzed carboxy derivatives of adult hemoglobin (HbA) and HbK (plus IHP, *p*H 6.5), respectively. Under the conditions used, the transients associated with HbA and HbK have the quaternary structure of the R state and the T state, respectively. From

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