Diminished Ability to Interpret and Report Internal States After Bilateral Medial Temporal Resection: Case H.M.

Nancy Hebben, Suzanne Corkin, Howard Eichenbaum, and Karen Shedlack
Department of Psychology and Clinical Research Center
Massachusetts Institute of Technology

These experiments centered around H.M., a 54-year-old man who became amnesic 27 years ago after a bilateral resection in the medial temporal lobe region for epilepsy. In order to document the clinical reports that he rarely comments on such internal states as pain, hunger, and thirst, his thermal pain perception was examined in relation to his other somatosensory capacities, and his reports of hunger and thirst were assessed before and after meals. In order to investigate the effect of limited memory ability on the reporting of internal states, H.M.’s performance was compared with that of 5 other subjects with global amnesia. The results provided evidence that H.M.’s information about internal states is less available or less accessible than normal and that his impairment is not attributable to his well-documented memory deficit. Instead, it is believed that the bilateral resection of the amygdala accounts for H.M.’s poor appreciation of his internal states.

Lesions of certain limbic system structures in primates are known to influence affect, personality, motivation, olfaction, sexual behavior, and response to pain (Foltz & White, 1962; Klüver & Bucy, 1939; Valenstein, 1973). In addition, discrete limbic system lesions can disrupt memory functions selectively and produce material-specific as well as global amnesia (Whitty & Zangwill, 1977). In the population of patients with limbic system lesions, the most thoroughly studied case is H.M., who at age 27 underwent bilateral resection of the uncus, amygdala, anterior hippocampus, and parahippocampal gyrus for severe and intractable epilepsy (Scoville & Milner, 1957). This patient’s 30-year history of memory disorders has been documented extensively both clinically and in the laboratory, where recall and recognition procedures have been applied to a wide variety of stimulus materials (Corkin, Cohen, & Sagar, 1983; Gabrieli, Cohen, & Corkin, 1983; Milner, Corkin, & Teuber, 1968). Little attention, however, has been paid to behaviors other than memory that are under limbic system control. An exception is a recent study of olfaction in H.M., which demonstrated a dissociation between an intact ability to detect odors and to discriminate them by intensity and a total inability to recognize or discriminate odors by quality (Eichenbaum, Morton, Potter, & Corkin, 1983). Interest in H.M.’s capacity to perceive pain and to appreciate hunger and thirst grew out of observations that he almost never comments on such internal drive states as hunger, thirst, pain, and fatigue. Milner et al. (1968) pointed out in their 14-year follow-up study that “H.M. rarely mentions being hungry, even when his meals have been somewhat delayed; however, when food is put before him, he eats in a normal manner” (p. 216). He occasionally complains of physical pain, such as toothache, but has endured other
presumably uncomfortable conditions, such as hemorrhoids, without comment. In 1962, Kimura attempted to elicit galvanic skin responses in H.M., using electric shock. Milner et al. (1968) described this study and stated that “H.M. appeared to notice the shocks but did not complain at all of being subjected to this procedure” (p. 223). The systematic studies described here were intended to evaluate these claims concerning H.M.’s appreciation of pain, hunger, and thirst. His thermal pain perception was examined in relation to other somatosensory capacities in order to determine whether pain perception was differentially affected. His reports of hunger and thirst before and after meals were also assessed. A related goal was to establish whether H.M.’s reluctance to report pain, hunger, and thirst is secondary to the memory disorder or whether it is an independent deficit. Accordingly, H.M.’s responses were compared with thermal pain perception and reports of hunger and thirst in 5 other patients with chronic global amnesia.

**Experiment 1**

The purpose of the first experiment was to examine H.M.’s thermal pain perception in relation to other somatosensory capacities. We assessed pain perception, two-point discrimination, position sense, and thermal discrimination not involving pain. Each test was administered on four occasions to H.M., on one occasion to each of the other 5 amnesic patients, and on two occasions to 15 normal control subjects.

**Method**

**Subjects**

*Case H.M.* H.M. is a right-handed man with a high-school education, who was 54 years old at the time of this study. The neurological examination revealed ataxia of gait, polyneuropathy, and a left ulnar neuropathy. The CT (computerized tomography) scan showed evidence of tissue loss in both medial temporal regions, and marked cerebellar atrophy (from chronic Dilantin therapy; Corkin, 1984). Between 1977 and 1983, H.M.’s Verbal and Performance IQ ratings dropped 10 and 11 points, respectively. The current Verbal IQ is 97, and the Performance IQ is 115. The evidence of slight deterioration in overall intelligence coupled with the clinical observation of a mild anemia, which had not been apparent earlier, suggests that the manifestations of normal aging may be occurring prematurely in H.M. The mechanism of this modest decline may involve an interaction of the normal aging process with any or all of H.M.’s other neural abnormalities (Corkin, 1984).

*Control subjects with global amnesia.* The 5 control patients with global amnesia ranged in age from 22 to 49 years and had a mean age of 40.6 years. Of the 5 patients, 2 had amnesia following closed head injury, 2 following ruptured anterior communicating artery aneurysm, and 1 following herpes simplex encephalitis. The duration of the amnesias ranged from 1 to 24 years (M = 8 years), and the severity from mild in 1 case to moderate in 4 cases; in no patient, however, was the memory deficit as profound as in H.M. (Table 1). On the Wechsler Memory Scale, Patient No. 5919 obtained a Memory Quotient of 152. This test is not a particularly sensitive measure of memory capacities, and the patient was familiar with the material, having taken the test several times prior to the current assessment. He did well on all the subtests, especially Information, Orientation, Mental Control, and Digit Span; nevertheless, his impaired recall of the material after a 1-hr delay showed him to be mildly amnesic (Corkin et al., 1983). Their education in years ranged from 12 to 19 years (M = 14.8 years), and all were right-handed.

**Table 1**

*Patients With Global Amnesia: Wechsler Intelligence and Memory Scale Scores*

<table>
<thead>
<tr>
<th>Patient</th>
<th>Verbal IQ</th>
<th>Performance IQ</th>
<th>Full-Scale IQ</th>
<th>Wechsler Vocabulary (Scaled Score)</th>
<th>Memory Quotient</th>
<th>Delayed recall</th>
</tr>
</thead>
<tbody>
<tr>
<td>5335</td>
<td>110</td>
<td>73</td>
<td>94</td>
<td>11</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>5246</td>
<td>90</td>
<td>96</td>
<td>92</td>
<td>9</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>4624</td>
<td>105</td>
<td>123</td>
<td>114</td>
<td>12</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>5919</td>
<td>123</td>
<td>112</td>
<td>118</td>
<td>12</td>
<td>132</td>
<td></td>
</tr>
<tr>
<td>4599</td>
<td>107</td>
<td>127</td>
<td>116</td>
<td>11</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>H.M.</td>
<td>97</td>
<td>108</td>
<td>104</td>
<td>12</td>
<td>64</td>
<td></td>
</tr>
</tbody>
</table>

* Memory Passages score plus number of Associate Language pairs recalled after a 1-hr delay.

b Visual Reproductions score after a 1-hr delay.
Normal control subjects. The normal control subjects were 7 men and 8 women, aged 22–74 years. Their educational levels ranged from 10 to 20 years, and all were right-handed.

Behavioral Assessment

Pain perception test. In the pain perception test, radiant heat stimuli were presented by a hand-held Hardy-Wolff-Goodell dolorimeter (Hardy, Wolff, & Goodell, 1952), a gun-like projector that housed a 100-W bulb. The stimuli were presented for 3 s unless subjects withdrew the projector from their skin before that time. The 2-cm-diameter heat stimuli were presented sequentially to six patches of India ink applied to the volar surface of each forearm. During the test, 144 stimuli (24 at each of 6 intensities, 0, 90, 180, 270, 320, and 370 mcald were presented pseudorandomly with respect to intensity. The patient was instructed to assign each sensory experience to one of the categories on a scale ranging from absolutely nothing to very painful and withdrawal. Throughout the test, a scale showing the 11 labels was placed before the subjects. H.M.’s pain perception was evaluated on four occasions. On one of them, the stimuli were applied to H.M.’s chest, because of the possibility that the results for his forearm had been affected by his known peripheral neuropathy, presumably resulting from the use of Dilantin and other anticonvulsant medications for 40 years.

The pain perception data were analyzed by the methods of nonparametric sensory decision theory (Clark, 1974). This analysis generated a measure of sensory discriminability, P(A), and a measure of response criterion, B. A low P(A) meant that stimuli of different intensities were confused with one another, a result suggesting that the subject’s appreciation of them was impaired. A low B reflected many reports of pain.

Somatosensory control tests. The somatosensory control tests included two-point discrimination, position sense, and thermal discrimination on the hand. H.M. received additional somatosensory testing in order to measure pressure sensitivity and two-point discrimination thresholds on both sides of the chest. In the two-point discrimination test, a two-point aesthesiometer (Corkin, Milner, & Rasmussen, 1970) was used to assess the smallest distance between two probes at which they were appreciated as two. In the position sense test (Corkin et al., 1970), subjects were asked to discriminate small downward from small upward movements of the distal phalanx of the individual fingers of both hands. Thermal cutaneous sensation was measured by the Minnesota Thermal Disks (Dyck, Curtis, Bushek, & Offord, 1974), which consisted of four cylinders with a copper, stainless steel, glass, or polyvinyl chloride disk embedded at one end. The copper disk was the reference for cold; the steel, glass, and polyvinyl chloride disks felt progressively less cold. The copper disk was paired sequentially with each of the other three in random order for 50 trials. The stimuli were applied alternately to two blackened areas on the palm of the dominant hand, and subjects were required to identify one stimulus as cold and one as warm.

Results

Pain Perception Test

Sensory decision theory analysis of the pain perception data revealed that the discriminability, P(A), scores of the control patients with global amnesia were approximately equal to the discriminability scores of the normal control subjects (Figure 1). In contrast, H.M. had poorer discriminability scores than subjects in both groups at all levels of intensity at all three stimulus sites (right and left arms and chest). H.M.’s scores, however, were relatively far from 0, which indicates that he could appreciate differences between intensities, albeit less well than the normal subjects and control patients.

Examination of response criterion, B, showed that scores for the control patients with global amnesia and the normal control subjects decreased significantly as thermal intensity increased: As intensity increased, there were more reports of pain (Figure 2). In addition, the control patients with global amnesia and the normal subjects had similar response-bias scores. Both groups tended to label 0 mcal as “nothing” or “maybe something,” 90 mcal as “faintly warm” or “warm,” 180 mcal as “hot” or “very hot,” 270 mcal as “very faint pain,” 320 mcal as “very painful,” and 370 mcal as “withdrawal.” When given the three highest intensities, subjects usually withdrew the projector before the maximum stimulus duration of 3 s had elapsed. Withdrawal occurred between 2 and 3 s for 270 mcal, between 1 and 2 s for 320 mcal, and at 1 s or less for 370 mcal. H.M., however, had higher response-bias scores than subjects in both groups, especially at the more intense stimulus values. Unlike the control patients with global amnesia and the normal subjects, H.M. did not label any stimuli painful no matter how intense they were, nor did he withdraw the stimulus gun before the 3-s interval ended. Stimulation of H.M.’s chest resulted in abnormal findings comparable to those for his arms.
Somatosensory Control Tests

On the two-point discrimination, position sense, and thermal discrimination tasks, all 5 control patients with global amnesia achieved normal scores except Patient 5919, who had a slight defect on his left hand in two-point discrimination (score = 13; slight defect = 12.82; Corkin et al., 1970) and position sense (score = 56/60 correct; defect = 57; Corkin et al., 1970; see present Table 2). H.M. achieved scores on all three tests that were consistent with a mild to moderate deficit on both hands (greater on the left than on the right), reflecting a mild peripheral neuropathy. It was not expected, but the pressure sensitivity thresholds on the chest were also mildly elevated bilaterally, and both two-point discrimination thresholds were markedly abnormal.

Discussion

On a thermal pain perception test, H.M. had significantly poorer discriminability scores for all intensity levels than did the other amnesic subjects or the normal control subjects. He also had higher criterion scores than subjects of both groups, particularly at the more painful stimulus levels.

In fact, H.M. never gave reports of pain for the most intense stimulus applied either to his forearms or chest, and, in contrast to most other subjects, he did not withdraw the stimulus gun before the end of the 3-s stimulus duration. The decreased discriminability scores and elevated response bias on the pain perception test may simply reflect the abnormal sensory state of H.M.'s hands and chest. Nevertheless, his inability in this experiment to identify and respond to painful stimuli as such suggests that the capacity for pain detection was disproportionately compromised relative to the capacity to detect light touch (pressure sensitivity).

Experiment 2

The purpose of Experiment 2 was to document H.M.'s sparse reporting of the internal states of hunger and thirst and to establish whether this deficit was secondary to the amnesic syndrome or independent of it.

Method

Subjects

The participants in this study included H.M., 4 of the 5 amnesic patients who served as control subjects
in Experiment 1, and 4 normal men, aged 30–56 years, whose educational levels ranged from 10 to 14 years. All subjects were right-handed.

**Behavioral Assessment**

Assessment of hunger and thirst with a visual analogue scale. Extent of hunger and thirst was assessed with a visual analogue scale. Subjects were asked to indicate how hungry and thirsty they were by marking two 5-in. lines whose only labels were very hungry and very thirsty, respectively, on the left end, and very full and not at all thirsty, respectively, on the right end. Ratings were quantified by measuring the distance in inches from the 0 point, dividing by 5 in. (the maximum possible score), and multiplying by 100; this calculation yielded a number between 0 and 100. Assessments were made six times per day: 20 min before and after breakfast, lunch, and dinner. On the last 2 days, the control patients also recorded what they ate and drank throughout the day, and the Clinical Research Center dietitians recorded the same information for H.M. In this way we could be sure that the patients were consuming normal amounts of food and fluids. Only the records from the final 2 days of monitoring were used; the initial 3 days of record keeping served to desensitize the patients to the procedure and to reduce the bias that may have accompanied self-recording (Kanfer, 1970).

**Dinner experiment with H.M.** Initially, H.M. was asked to rate his hunger on a scale from 0 to 100, where 0 is famished and 100 is too full to eat another bite before and after meals. On one occasion an at-

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Two-point discrimination (0–60 mm)</th>
<th>Position sense (0–60 correct)</th>
<th>Thermal discrimination (0–150 correct)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>Normal control</td>
<td>15</td>
<td>7.3</td>
<td>6.6</td>
<td>59.7</td>
</tr>
<tr>
<td>Global amnesic patients</td>
<td>5</td>
<td>9.0</td>
<td>5.8</td>
<td>58.8</td>
</tr>
<tr>
<td>H.M.*</td>
<td></td>
<td>18.0</td>
<td>13.0</td>
<td>57.0</td>
</tr>
</tbody>
</table>

*Mean of three tests.
tempt was made to influence his reports of hunger by supplying him with as much food as he could eat at one sitting. One evening after he had eaten one full dinner, his empty tray was removed and without explanation replaced within 1 min by another tray containing a meal just like the one he had eaten. He was again asked to rate his hunger 20 min after he had finished the second meal.

Results

Examination of the self-reports of hunger and thirst indicated that both the normal control group and the amnesic group showed a greater amount of change in their feelings of hunger and thirst from before to after meals than did H.M. (Figure 3). Further, the patients with global amnesia showed a greater difference in their ratings of both hunger and thirst from before to after meals than did either the normal subjects or H.M. Three of the four normal subjects and three of the four amnesic patients indicated the expected decreases in hunger and thirst after all meals. The fourth normal subject indicated an increase in hunger after one breakfast, no change in hunger after one lunch, and decreases in hunger and thirst at the other meals. The fourth amnesic patient, the postencephalitic case, showed either no change or an increase in hunger and thirst after four of the six meals.

When asked to rate his hunger, H.M. consistently reported 50, whether he was about to eat or had just eaten. Moreover, in 5 of his 9 reports of thirst and in 2 of his 9 reports of hunger, H.M. rated himself as less thirsty and more full before the coming meal than 20 min after it despite having consumed an adequate amount of food and drink for a man of his age and weight. The attempt to alter his report of hunger with a greater than normal amount of food at one meal had little effect. H.M. consumed the first dinner and then ate the second one at his normal, fairly slow but steady pace until only the salad remained. When questioned about why he had not finished the meal, he did not state that he was "full" but only that he had "finished." The second tray was removed. After 20 min had elapsed, he was asked to rate his hunger from 0 to 100; he rated it at 75. At that time, he could not remember what he had eaten.

Figure 3. Differences between before-meal and after-meal ratings of hunger and thirst for normal control subjects, patients with global amnesia, and H.M.

Discussion

H.M., unlike other amnesic patients and the normal control subjects of his age, showed no differences in his ratings of hunger and thirst from before to after a meal. Further, when he was provided with all the food he could consume at one sitting, nearly two dinners, his rating did not approach satiety. These findings support the claim that information about current internal states is less available or less accessible to H.M. than to others. The interpretation that H.M. simply does not like to overeat is discounted by the observation that from 1977 to 1983 his weight increased from 80.8 kg to 88.3 kg.

General Discussion

H.M.’s failure to appreciate thermal pain and his poor monitoring of appetite provide evidence of an inability to react appropriately to normal, mild homeostatic stress. This disorder may be due to involvement of the neuroanatomical or the neurochemical substrates of these behaviors, or to both. Eating, drinking, and response to pain are mediated by a number of different neural structures from cranial nerves to frontal cortex. Some of these areas, such as the amygdala and uncus, were resected in H.M.’s operation, and others, such as the orbital frontal cortex and olfactory bulbs, may have been at least partially compromised in the course of the operation. Al-
though alterations in eating and drinking are not commonly observed in patients with limbic system lesions, two instances of abnormally should be noted, bulimia and ictal drinking. Bulimia is a component of the human Klüver-Bucy syndrome (Lilly, Cummings, Benson, & Frankel, 1983), which is associated with bilateral dysfunction of temporal neocortex. Water drinking may occur as ictal behavior during temporal lobe seizures. Ictal drinking is a stereotyped behavior comparable to other epileptic automatisms, such as chewing or motor automatisms. The urge to drink is not motivated by thirst but rather by an attempt “to satisfy a motivational drive mechanism aroused inappropriately by epileptic discharge” (Lilly et al., 1983, p. 123). Possibly, this same mechanism is disturbed in H.M., which results in attenuated drives.

Information on the similarities and differences in the lesion sites between H.M. and the patient control subjects might have provided insight into the anatomical regions important for labeling internal states. The control patients, however, were selected because of their global amnesia and represented a diverse group of etiologies and lesions. Their CT brain scans did not provide information as to the precise locus of lesion, so that neuroanatomical comparisons between H.M. and the other amnesic patients are difficult. The lesions in the patient with postencephalitic amnesia probably involved medial temporal lobe structures (Adams & Miller, 1973; Drachman & Adams, 1962), and this man’s ratings of hunger and thirst, like H.M.’s, are aberrant. Deficient monitoring of internal states by these two patients, but not the others, may be due to the involvement of the amygdala in both cases, as compared with slight damage or preservation of this structure in the other subjects. The ruptures of anterior communicating artery aneurysms may have compromised basal forebrain structures but spared the amygdala (Gade, 1982).

Studies with experimental animals support the conclusion that H.M.’s aberrant reports of internal states are attributable to amygdaloid lesions. After amygdalotomy, monkeys do not show the galvanic skin response, heart rate, or respiratory rate components of the orienting reaction (Bagshaw & Benzies, 1968; Bagshaw & Coppock, 1968). With reference to pain, monkeys with lesions in the amygdala fail to respond differentially to a wide range of shock intensities despite lower stimulus thresholds than control monkeys (Bagshaw & Pribram, 1968). H.M. also showed decreased discriminability scores and elevated response bias on the pain perception test. This finding is consistent with Bagshaw and Pribram’s hypothesis that the amygdala is necessary for the appreciation of nuances in stimulus characteristics. Stimulation of the amygdala in monkeys disrupts temperature discrimination (Chin, Pribram, Drake, & Greene, 1976). Also, Frenk and Yitzhaky (1981) found that kindling in the amygdala produced a gradual increase in the pain threshold of rats, which could be attenuated with morphine or naloxone. Those investigators hypothesized that amygdaloid stimulation causes endogenous opioids to be secreted. This hypothesis is strengthened by the recent finding that neurons in the periaqueductal gray region, an opiate analgesia site, react to stimulation of the amygdala (Sandrew & Poletti, 1982). Each of these findings is consistent with the notion that the amygdala is critically involved in pain perception.

In reference to hunger, monkeys with lesions in the amygdala are hyperphagic in ad-lib feeding conditions and exhibit seemingly indiscriminate feeding behavior (Klüver & Bucy, 1938). In a series of studies, Schwartzbaum (1960a, 1960b, 1961) showed that monkeys with amygdaloid lesions have diminished sensitivity to shifts in food reward magnitude and type of food reward during operant bar pressing. These monkeys also have decreased responsiveness to either prolonged deprivation or satiation in the same test situation. These results indicate that the amygdaloid lesions alter the animal’s appreciation of food and diminish its capacity to recognize hunger and satiety.

Possible damage to orbitofrontal cortex or basal forebrain structures might have contributed to H.M.’s diminished perception of internal states. Experimental studies with animals, however, indicate a lesser
role for frontal cortical areas than for the amygdala. Thus, orbitofrontal lesions do not disrupt simple autonomic reactions (Rosenkilde, 1979). Orbitofrontal stimulation disrupts thermal discrimination, but this effect habituates, unlike the effect of amygdaloïd stimulation (Chin et al., 1976). Orbitofrontal ablations do not qualitatively affect feeding habits in monkeys (Rosenkilde, 1979), although they do reduce responsiveness to changes in food deprivation level (Butter, Mishkin, & Rosvold, 1963).

The amygdala and orbitofrontal cortex have reciprocal connections with each other and with the hippocampal formation, hypothalamus, basal forebrain, thalamus, and other limbic cortical areas (Aggleton, Burton, & Passingham, 1980; Krettek & Price, 1977a, 1977b, 1978; Porrino, Crane, & Goldman-Rakic, 1981). Effects similar to those found with lesions and stimulation of the amygdala in animals are found with lesions and stimulation of the hypothalamus. Hypothalamic stimulation produces autonomic responses (Hess, 1954), such as changes in heart rate, blood pressure, and gastrointestinal motility, all responses correlated with emotional behavior. In addition, stimulation of the lateral hypothalamus elicits feeding behaviors, whereas stimulation of the medial hypothalamus suppresses feeding behaviors (Miller, Bailey, & Stevenson, 1950). In contrast, lesions of the lateral hypothalamus result in aphagia (Marshall, Turner, & Teitelbaum, 1971) and placidity; lesions of the medial hypothalamus produce animals that are highly excitable (Malick, 1970). It would seem from these lesion and stimulation studies that the amygdala, orbitofrontal cortex, hypothalamus, and their reciprocal connections form a neural system related to the mediation of various motivational states (Turner, 1973). This system appears to be compromised in H.M., although the possible contribution of medication-induced defects in elementary sensory functions should not be overlooked.

It is unlikely that H.M.'s neglect of internal states is simply a by-product of an amnesic syndrome. First, although the other 5 amnesic subjects tested had documented long-term memory deficits, they did not have difficulty reporting pain, hunger, and thirst. Moreover, they did not show deficits on measures of internal states that were proportional to the extent of their memory deficit, results suggesting that the ability to detect and report internal drive states is not directly related to the severity of the anterograde amnesia. Patient 4624, for example, had great difficulty recalling both verbal and nonverbal information after a delay (Table 1), but he had no difficulty reporting feelings of hunger before a meal and satiation after a meal (Figure 3); his mean differences score for dinner was 75. Second, the tests used in these experiments did not appear to require the use of long-term memory. The patients merely had to judge their immediate internal sensations; therefore, not even patients like H.M. and Patient 4624, who are unable to store information once they have been distracted, were compromised by task requirements. H.M. can retain information in immediate and short-term memory (Corkin, Sullivan, Twitchell, & Grove, 1981), and he was able to comply with task directions. Despite these capacities, he failed to report changes in his internal states. Further comparisons between H.M. and other patients with well-documented lesions in various limbic system structures should help clarify the pathophysiology of the disorder.

References


Received May 30, 1984

Revision received January 10, 1985