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SELECTIVE OLFACTORY DEFICITS IN CASE H.M.

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SUMMARY

A variety of olfactory capacities were evaluated in H.M., a patient with bilateral medial temporal lobe resection. He demonstrated normal performance on a battery of tests of odour detection, discrimination of intensity, and adaptation. In striking contrast, H.M. was unable to discriminate or identify odours in same-different discriminations and in matching-to-sample tasks. Although he could name common objects using visual or tactile cues, he could not identify them by smell. These results indicate that the perceptual phenomena of odour detection and discrimination are dissociable by cerebral damage, and that structures in the medial temporal lobe play a critical role in odour discrimination.

INTRODUCTION

An increasing body of evidence indicates the involvement of both the frontal and temporal lobes in odour perception. Impairments in odour quality discrimination have been observed in rats and monkeys with lesions of the orbitofrontal cortex or its associated mediodorsal thalamic nucleus (Tanabe *et al.*, 1975*b*; Eichenbaum *et al.*, 1980; Sapolsky and Eichenbaum, 1980; Slotnick and Kaneko, 1981), and in monkeys with bilateral ablation of the anterior parts of the temporal lobe (Brown *et al.*, 1963). Olfactory disorders have also been described in several neurological conditions, including Korsakoff's disease, which damages the mediodorsal thalamus (Victor *et al.*, 1971), lesions of the orbitofrontal cortex (Jones *et al.*, 1975; Potter and Butters 1980), and unilateral temporal lobectomy (Rausch and Serafetinides, 1975; Eskenazi *et al.*, 1981). These behavioural observations parallel recent revisions in the delineation of primate olfactory pathways. The olfactory tract projects centrally by three routes: (1) the medial olfactory stria, which contains no afferent fibres but does support a centrifugal pathway; (2) the lateral olfactory stria, which projects to the pyriform, periamygdaloid, and entorhinal cortices of

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the uncus of the temporal lobe; and (3) fibres that terminate in the olfactory tubercle and pyriform cortex in the frontal lobe (Rosene and Heimer, 1977; Turner *et al.*, 1978). Secondary olfactory projections reach the orbitofrontal cortex directly from intracortical afferents (Krettek and Price, 1977; Potter and Nauta, 1979), and indirectly through connections of the olfactory tubercle and pyriform cortex to the mediodorsal thalamus (Heimer, 1972). In the temporal lobe, secondary olfactory projections heavily invade the amygdala and entorhinal cortex (Krettek and Price, 1977). Electrophysiological studies have identified areas in the primate orbitofrontal and temporal cortex and mediodorsal thalamus that are responsive to olfactory stimuli (Benjamin and Jackson, 1974; Tanabe *et al.*, 1975*a*, *b*; Yarita *et al.*, 1980).

The present investigation assessed a variety of olfactory functions in a patient who had undergone extensive bilateral medial temporal lobe resection, a procedure that is believed to have eliminated both the primary and secondary olfactory areas in the temporal lobe. The purpose of this study was to measure the functional capacities of the frontal olfactory system in the absence of the pathways to the temporal lobes.

SUBJECTS

The subjects of this report are the amnesic patient, H.M., and five groups of normal subjects. All gave informed consent to participate in the investigations.

Case H.M.

H.M., a 55-year-old man, was operated upon when aged 27 years following a 16-year history of cerebral seizures that had been uncontrolled by medical treatment. The surgical resection involved bilateral removal of the amygdala, uncus and anterior two-thirds of the hippocampus and parahippocampal gyrus (Scoville *et al.*, 1953). The excision probably included most of the pyriform cortex in the uncus, but other components of the first nerve projection, specifically the olfactory tubercle and adjacent pyriform cortex on the basal surface of the frontal lobe, might have been partially or completely spared. The olfactory bulbs or tracts could have been damaged by retraction of the frontal lobes, although the patient is not anosmic. In animals, anosmia occurs only after total disruption of the primary olfactory afferents or extensive destruction of the anterior pyriform cortex (*see* Sapolsky and Eichenbaum, 1980). In H.M., retraction of the frontal lobes might also have produced damage to the orbitofrontal cortex, but he demonstrates none of the more salient clinical features of frontal lobe disease (Hécaen and Albert, 1975; Blumer and Benson, 1975).

The most obvious consequence of the operation is the patient's persistent anterograde amnesia. Numerous studies revealed a nearly complete inability to form long-term memories (Scoville and Milner, 1957; Milner *et al.*, 1968; Corkin *et al.*, 1981); notable exceptions are certain motor, perceptual and cognitive skills (Milner, 1962; Corkin, 1968; Nissen *et al.*, 1981; Cohen and Corkin, 1981). H.M.'s performance on short-term memory, perceptual, motor and cognitive tasks is essentially normal (Milner *et al.*, 1968; Wickelgren, 1968; Corkin, 1982) although his perception of the affective qualities of certain stimuli is diminished (Hebben *et al.*, 1981). Since the operation, his neurological symptoms have remained stable and include ataxia of gait and polyneuropathy; recently there was a reduction in the Wechsler IQ rating from the bright normal to the average range (Corkin *et al.*, 1981).

Normal Control Subjects

H.M.'s performance on the olfactory tests was compared to that of five normal control groups that had previously been examined or were concurrently tested with the same methods used with H.M. Different control groups were used for different tasks, depending upon the time and location of the experiments, and the availability of subjects. The five groups were (1) 3 men aged 45 to 58 years (mean age, 54.0 years) tested in detection and discrimination tasks; (2) the 10 normal control subjects from Potter and Butters' (1980) study, who had a mean age of 55 years; (3) 15 female college students, aged 18 to 20 years (mean age, 19.3 years) tested in detection tasks; (4) 2 female research assistants, aged 24 and 25 years, tested in discrimination tasks; and (5) 3 men aged 23, 48 and 55 years, tested in adaptation tasks.

OLFACTORY TESTS: METHODS AND RESULTS

In order to evaluate a wide range of olfactory perceptual functions, tests were designed to measure detection of different odours, discrimination of different intensities of the same odour, adaptation to a strong odour, and discrimination of different odours by quality. Because of H.M.'s severe amnesia, the memory component of the tasks was minimized. Cue cards were present during testing to remind him of the instructions, and no test, except the naming tasks, required him to remember a stimulus for more than a few seconds. The stimuli consisted of various common food flavourings and reagent grade chemicals used without further purification. All odours were presented to both nostrils simultaneously, using open bottles or specially constructed sniff chambers, except in the internasal adaptation test, where stimulation was unilateral.

Detection: Methods

Two tests of odour detection were administered, each based on a different psychophysical procedure. One used the method of limits and the other the method of signal detection.

Methods of limits. The stimuli for this test consisted of 10 sequential twofold water dilutions of each of four stock odorants; almond (McCormick), ethanol (180 proof), lemon (McCormick) and acetone. Each 1 ml stimulus was matched against a blank sample (distilled-deionized water) in 100 mm test-tubes. For each of the 10 odour and blank pairs, starting with the highest odour concentration, the subject was allowed one sniff each of the odour and blank samples, offered randomly in rapid succession, and then asked to identify which of the two tubes contained odorant. The intertrial interval was 30 s. Based on the assumption that an initial error in this test indicated proximity to sensitivity threshold, the threshold score for each odour was quantified as the highest dilution for which detection up to and including that dilution was errorless.

H.M. was tested four times on each odour. His mean threshold for each was compared with those of 3 age-matched male and 15 younger female normal control subjects, all of whom were tested once with each odour.

Method of signal detection. Odour-detection performance was also assessed by the signal-detection method using apparatus and procedures identical to those of Potter and Butters (1980). The stimuli were 1.3 mM *n*-butanol (MCB, reagent grade) in distilled-deionized water, and water alone, presented in specially constructed constant volume and vapour pressure sniff chambers (Engen *et al.*, 1975; Mair *et al.*, 1978). Single stimuli were presented successively in random order on 30 trials. On each trial the subject was allowed a single sniff and then was required to identify the stimulus as odour ('signal') or blank ('noise'). Feedback on the accuracy of the response was provided immediately and followed by a 30 s intertrial interval. A d′ measure was calculated from the observed 'hit' and 'false alarm' rate probabilities (Elliot, 1964). H.M. was tested twice; his scores were compared with the results of 10 normal adults with a mean age of 55 years, who had been given the identical test (Potter and Butters, 1980).

Detection: Results

When tested using the method of limits, H.M. correctly detected dilutions of each of four odorants that were approximately as high or higher than those detected by a larger group of younger normal adults (Table 1). With the signal-detection paradigm, H.M. correctly identified a weak stimulus 75 per cent of the time; he erroneously identified the blank as a stimulus only 25 per cent of the time. His consequent d′ of 1.22 was at least as good as that of the 10 normal adults (mean d′ = 1.10) tested by Potter and Butters (1980).

TABLE 1. DETECTION OF COMMON ODORANTS: MEAN DILUTION AT THRESHOLD

		Odour			
Subjects	*Mean age*	*Almond*	*Ethanol*	*Lemon*	*Acetone*
Normal control					
Females (n = 15)	19.3	—	4.8	3.7	—
Males (n = 3)	54.0	5.7	3.3	2.7	5.1
H.M.		5.0	4.6	5.5	5.2

Discrimination of Intensity: Methods

Threshold for discrimination of intensity difference was tested using the same four odorant dilution series as in the first detection test. In the intensity discrimination task, however, subjects were asked to choose the stronger stimulus in 10 odour pairs, each composed of an odorant in its lowest dilution (i.e., highest concentration) and the same odorant in a higher dilution (i.e., lower concentration). On successive trials presented at 30 s intervals, the lowest dilution (strongest stimulus) was paired with the weakest and then successively stronger stimuli until, on the last of the 10 trials, the two samples were identical. Threshold for intensity difference discrimination was defined as the lowest dilution sample for which identification up to and including that dilution was errorless. H.M. was tested twice with each of the four odorants; his scores were compared with those of 3 age-matched normal control subjects.

Discrimination of Intensity: Results

H.M.'s capacity to distinguish odour intensities is also normal. For each of the four common odorants, H.M. could successfully discriminate among odours of the higher concentrations used (Table 2).

TABLE 2. INTENSITY DIFFERENCE THRESHOLD FOR COMMON ODORANTS: MEAN DILUTION AT THRESHOLD

		Odour			
Subjects	*Mean age*	*Almond*	*Ethanol*	*Lemon*	*Acetone*
Normal control					
Males (n = 3)	54.0	8.2	8.3	7.3	1.3
H.M.		2.0	6.5	6.5	2.0

Adaptation: Methods

Using the same apparatus and signal detection-with-feedback procedure as described for the intensity-discrimination test, H.M. was tested on detection of 10 mM aqueous *n*-butanol (MCB in pH 7 buffer and 1.3 mM β-phenethyl alcohol (Aldrich Gold Label) in pH 7 buffer during adaptation to the same odour, to the other odour, or to a blank pH 7 buffer diluent presented in equilibrium sniff chambers (*see* Method of signal detection, *above*). On each adaptation test, he first sniffed continuously for 100 s either the blank or a strong solution of *n*-butanol (500 mM) or of β-phenethyl alcohol (17 mM) in open 250 ml Erlenmeyer flasks. Then he sniffed a sample either of one of the test odorants or of the blank and stated whether a smell was present. During the subsequent 10 s intertrial interval, he sniffed the adapting stimulus. The 6 combinations generated from the 3 adapting and 2 test odorants were each presented in 40 trial blocks. In order to allow sufficient time for equilibration of odour concentration in the sniff chambers, each stimulus was contained in four chambers, which were used in rotation. The entire series of tests was administered to H.M. twice. On separate days, he was tested in the control (blank 'adapting' stimulus), adaptation and cross-adaptation conditions with only one test odour, and the order of conditons was varied (*see* Table 3 *below*). Each condition with *n*-butanol as the test stimulus was administered to two normal male subjects on one day.

Internasal adaptation was also investigated. H.M. and a normal male subject aged 55 years were adapted unilaterally to 50 mM *n*-butanol by covering the left nostril with the right thumb and sniffing with the right nostril for 10 s. Immediately following, the subject covered his right nostril with his left thumb and sniffed with his left nostril either 10 mM *n*-butanol or a blank.

Adaptation: Results

Prior adaptation to a stong intensity of the stimulus odorant decreased H.M.'s ability to detect odours in the normal way (Table 3). He demonstrated significant detection of *n*-butanol and β-phenethyl alcohol when the 'adapting stimulus' was only the buffered diluent water. When the adapting stimulus was a stronger concentration of the test odour, detection fell to chance for both stimuli. In the

TABLE 3. ADAPTATION AND CROSS-ADAPTATION: d′ FOR CASE H.M.

Condition	*Order of conditions*[a]	*Adapting stimulus*	*Test stimulus*[b]	*Hits/ false alarms*	*d′*	*P value*[c]
Control	1	Blank	BuOH	17/5	1.72	< 0.001
	2	Blank	BuOH	15/5	1.20	0.003
Adaptation	1	BuOH	BuOH	6/8	−0.27	0.318
	2	BuOH	BuOH	8/6	0.27	0.318
Cross-adaptation	1	PeOH	BuOH	16/5	1.52	< 0.001
	2	PeOH	BuOH	20/15	0.96	0.077
Control	3	Blank	PeOH	10/2	1.41	0.003
	2	Blank	PeOH	13/8	0.38	0.215
Adaptation	3	PeOH	PeOH	9/9	0.00	0.563
	2	PeOH	PeOH	10/9	0.13	0.437
Cross-adaptation	3	BuOH	PeOH	10/2	1.04	0.019
	2	BuOH	PeOH	11/8	0.64	0.077

[a] 1. Control, then adaptation, then cross-adaptation. 2. Cross-adaptation, then control, then adaptation. 3. Control, then cross-adaptation, then adaptation. [b] BuOH = *n*-butanol; PeOH = β-phenethyl alcohol. [c] Exact probability calculated from Bernoulli Trials (Apostol, 1962).

cross-adaptation paradigm, where the adapting stimulus was a strong odour that differed in quality from the test odour, H.M.'s detection of the test odour was well above chance, though lower than when the 'adapting stimulus' was water. While overall performance varied in different test sessions, variations in the order of control, adaptation and cross-adaptation conditions had no effect on relative scores for the three conditions. When the combined adaptation scores for the two sessions were compared to the combined scores for the control conditions, H.M.'s correct answers were lowered after adaptation by 3.10 and 5.52 standard deviations for β-phenethyl alcohol and *n*-butanol, respectively. His combined correct answers after cross-adaptation were lowered by only 0.95 and 1.31 standard deviations, respectively. By comparison, when two normal male subjects, aged 23 and 48 years, were adapted to *n*-butanol (80 trials each), their number of correct answers was lowered by 11.0 and 5.0 standard deviations, respectively. In contrast, cross adaptation to β-phenethyl alcohol did not affect detection in one control subject and reduced the performance of the other control subject by only 1.4 standard deviations.

In the internasal adaptation condition, the single normal control subject lost sensitivity (Table 4). Similarly, H.M. significantly detected *n*-butanol unilaterally before adaptation, but his performance fell to near chance after internasal adaptation. The difficulty of maintaining patency of both nostrils during this procedure precluded the running of a more complete series of experiments. H.M.'s contralateral adaptation was not as profound as that of the normal control subject, nor as his own bilateral adaptation (Table 3). Moreover, in a separate experiment (Table 4), when the initial 100 s adapting sniff was omitted, bilateral adaptation was less profound than when it was given. Although H.M.'s performance using his left nostril alone did not differ significantly between nonadapted and adapted conditions ($P = 0.12$), there is no evidence to suggest that he did not experience contralateral adaptation.

TABLE 4. INTERNASAL ADAPTATION: d' FOR DETECTION OF *n*-BUTANOL

Subject	*Adaptation condition*	*Adapting stimulus*	*Hits/ false alarms*[a]	*d'*	*P value*[b]
Normal control (n = 1, aged 55 yrs)	Control	Blank	16/5	1.52	0.001
	Adaptation	BuOH[c]	5/2	0.60	0.215
H.M.	Control	Blank	9/2	1.15	0.019
	Adaptation	BuOH	8/5	0.42	0.215
	Control (bilateral)	Blank	14/6	1.05	0.008
	Control (bilateral)	BuOH	11/6	0.66	0.077

[a] Out of 20 possible for each. [b] Exact probability calculated from Bernoulli trials (Apostol, 1962).
[c] BuOH = *n*-butanol.

Discrimination of Odour Quality: Methods

H.M.'s ability to discriminate odours was measured with three tests that differed both in the mode of stimulus presentation and in response requirements.

Method of signal-detection. One technique was based on the signal-detection method. The stimuli, apparatus and procedure were identical to that used by Potter and Butters (1980). On each of 32 trials, a pair of suprathreshold stimuli were presented in succession with a 15 s silent interval separating the two presentations. On half of the trials, the two stimuli were different, the condition defined as the 'signal'; on the other half of the trials, they were identical, the condition defined as the 'noise'. After presentation of the stimulus pair, the subject was asked whether the odours were the same or different. Each trial was followed by a 30 s intertrial interval. Discrimination was tested with three odour pairs: methylsalicylate *versus* guaiacol (easiest for normal control subjects to discriminate), eugenol *versus* guaiacol and allyl caproate *versus* amyl proprionate (most difficult for normal control subjects to discriminate). For each odour pair d' was determined by relating H.M.'s correct identifications of different stimuli to incorrect identifications of the same stimuli as being different. His d' scores were compared to the scores of 10 normal adults as reported by Potter and Butters (1980).

Triangle match-to-sample-test. This test involved a matching-to-sample procedure in which the subject was asked to match a weak sample odour to one of two choices, either a stimulus of identical quality and the same or stronger intensity, or a distractor that differed from a sample in quality and from the other match stimulus in both quality and strength. The subject was instructed to match the sample by odour and not by strength. On half of the trials, the sample and the correct match stimulus were the same both in quality and intensity, whereas on the other half the sample and the correct match were the same in quality but not in intensity. The stimuli included 1.7 mM (weak) and 8.3 mM (strong) β-phenethyl alcohol and 10 mM (weak) and 50 mM (strong) *n*-butanol all diluted in pH 7 buffer and presented in open 250 ml Erlenmeyer flasks. During each of the two testing sessions, H.M. was given 10 trials with each of the four sample and match combinations, the presentation order of sample and match stimuli was randomized. On each trial, a 5 to 10 s sniffing of the sample was followed immediately by a 5 to 10 s sniffing of each match stimulus.

Matching and naming of common odours. In this task, the subject was asked to match a sample odour stimulus or blank (distilled-deionized water) to one of 9 common odours or a blank each presented in a 3 ounce brown bottle. The odours were coconut (McCormick), mint and peppermint (McCormick), almond (McCormick), vanilla (McCormick), orange (McCormick), cloves (McCormick), raspberry aldehyde (Givaudan) and β-phenethyl alcohol ('rose,' Eastman). On each of 10 trials involving a different sample odour, the subject was given the sample and 10 potential match stimuli, and instructed to sniff each bottle and find the one that contained the same odour as the sample. Repeated sniffing of sample and match stimuli was allowed. After the match choice was made, the subject was asked to identify the stimulus by name or, if no name was given, to make a verbal association. H.M.'s percentage of correct responses for matching and naming on two completions of the test was compared to those of 3 age-matched normal males and 2 younger adults.

Two modifications of this procedure were also administered. In one, H.M. was asked to match a sample to one of only two match stimuli. He performed this task three times with each of the 10 sample stimuli. In a recognition version of the task, H.M. and a normal male subject were presented in successive trials with one of the 10 sample stimuli and asked to identify the name of the odour from a written list of five odour labels. In the 10 lists, the labels of the 10 sample stimuli occurred with equal frequency.

As a control for modality of stimulus presentation, H.M. was asked to name four common foods separately by odour, touch, and sight. Thus, in separate presentations, he tried to identify orange, onion, lemon and banana, under three conditions: (1) when allowed only to sniff the crushed food, (2) when allowed only to handle the food in an opaque paper bag, and (3) when allowed only to see the food.

Discrimination of Odour Quality: Results

In contrast to a normal capacity to detect odours, make intensity discriminations and adapt to odours, H.M. demonstrated no ability to discriminate the quality of odours. In the signal-detection testing of quality discrimination, H.M. could not reliably identify a pair of different odours as different, even when the odour pair was one that normal control subjects found easy to differentiate (Table 5).

TABLE 5. ODOUR-QUALITY DISCRIMINATION: MEAN d'

Subjects	*Mean age*	*Amyl proprionate vs. allyl caproate*	*Eugenol vs. guaiacol*	*Guaiacol vs. methyl salicylate*
Normal control (n = 10)[a]	55.0	1.8	2.4	3.3
Case H.M.		0.0 (14/14)[b]	0.5 (14/12)	0.0 (14/14)

[a] From Potter and Butters (1980). [b] (Hits/False alarms) out of 16 possible for each.

In the triangle match-to-sample test, H.M. could not reliably match an odour stimulus to an identical quality-matched stimulus or to an odour of a different quality and strength. Although he could match a weak β-phenethyl alcohol sample perfectly to the same stimulus paired with strong *n*-butanol, he scored at chance in matching that sample to strong β-phenethyl alcohol paired with *n*-butanol. H.M. scored at chance on both tasks where he was required to match a weak *n*-butanol sample (Table 6).

TABLE 6. ODOUR-QUALITY DISCRIMINATION: H.M.'S PERFORMANCE ON TRIANGLE MATCH-TO-SAMPLE TEST

Sample stimulus	*Match stimuli*[a]		*Mean percentage correct*
	Strong	*Weak*	
Weak PeOH	BuOH	PeOH	100
Weak PeOH	PeOH	BuOH	50
Weak BuOH	PeOH	BuOH	55
Weak BuOH	BuOH	PeOH	50

[a] BuOH = *n*-butanol; PeOH = β-phenethyl alcohol.

On the common odour-matching task, normal control subjects score between 85 and 95 per cent correct. In contrast, H.M. performed at chance level (11 per cent correct). On each of two repetitions of the test he correctly matched only one of 9 odour samples to a test odorant. He always correctly identified the blank sample and match stimuli. Even when the number of match stimuli was reduced

TABLE 7. ODOUR-QUALITY DISCRIMINATION: MEAN PERCENTAGE CORRECT ON COMMON-ODOUR MATCHING[a]

Subjects	*Mean age*	*Matching*	*Naming*
Normal control			
10 choice			
Females (n = 2)	24.5	95.0	85.0
Males (n = 3)	54.0	85.0	90.0
H.M.			
10 choice		11.0	5.6
2 choice		53.0	—

[a] Excludes trials with the blank stimulus.

to two, his score remained at chance (50 per cent) (Table 7). Normal subjects, when asked to identify these common odours, could name 85 to 95 per cent correctly, but H.M. consistently identified only the nonodorous water stimulus. He did use odour labels (for example, 'flowers', 'decaying matter', etc.) but the names bore no obvious relationship to the actual odour qualities and were not consistently applied (Table 8). H.M. sometimes repeated the same name for different odours presented in sequence but when asked if these odours smelled alike would insist not, and offered additional descriptors to clarify the differences. In two repetitions of the recognition version of the task, H.M. again identified the blank sample, but correctly identified the name of the sample only twice, resulting in a performance score no better than chance. The normal control subject correctly recognized the name of each odorant.

When asked to name four common foods by odour, H.M. failed in each case, again applying odour labels inconsistently. Yet he could easily name each food when handling it in a bag or upon brief visual examination.

TABLE 8. NAMING OF COMMON ODORANTS BY H.M.

Odour	*Test 1*	*Test 2*
Coconut	'Soap'	'Flowers'
Mint	'Flowers'	'An acid'
Almond	'A wild flower'	'An acid'
Lemon	'Flowers'	'An acid'
Vanilla	'Weak roses'	'Newly made paper'
Orange	'An acid'	'Weak perfume'
Cloves	'Fresh woodwork'	'Dead fish, washed ashore'
Raspberry	'Flowers'	'Carrion, a squirrel'
Rose	'A rose flower'	'Bad water'
Water	'I can't smell anything'	'I can't smell anything'

DISCUSSION

H.M.'s test performance demonstrates a striking dissociation of olfactory perceptual capacities. His performance on the intensity dimension is preserved, whereas his performance on the quality dimension is severely compromised. On the intensity dimension, he has a normal capacity for detection of weak odorants, for differentiation of odours by concentration, and for normal adaptation to a strong odour.

The present results show that odour quality discrimination and recognition are not necessary for detection, adaptation or intensity discrimination. Indeed, H.M. could sometimes use the intensity dimension to perform well in odour-quality matching tasks. He always matched the blank sample correctly in the common odour matching-to-sample task, and under one condition in the triangle test, H.M. could distinguish a strong *n*-butanol solution from weak *β*-phenethyl alcohol. In striking contrast, his performance on this task was consistently at chance when forced to match by odour quality when the intensities of sample and match stimuli were comparable. Other tests also revealed that H.M. is unable to differentiate or recognize odours by quality, whether tested by same-different judgements, matching, or naming. H.M. easily identified by touch or sight the same common foods that he could not name by odour.

Even though H.M.'s olfactory deficit is modality specific, it should not be termed an agnosia (Teuber, 1965; Corkin, 1978). His impairment involves not only a loss of the appreciation for the meaning of stimuli but also includes elementary functions, such as same-different judgements: H.M. is not only without the ability to recognize odours, he cannot identify different odours as different or identical odours as the same. His pattern of abilities and deficits clearly and consistently indicates that the perceptual phenomena of detection and discrimination are dissociable by cerebral damage.

H.M.'s odour discrimination impairment is not attributable to his well-documented memory deficit. Although the 15 s interstimulus interval in the method of signal detection might have increased the difficulty of the task for H.M., he was also impaired on two other tests of odour quality, the triangle match-to-sample test and common odour matching, in which the memory component was minimal. Moreover, during numerous experiments, H.M. has consistently demonstrated a normal ability to hold and use information in immediate or short-term memory (Corkin *et al.*, 1981). None of the tests used in this study, with the exception of odour and object naming, required the use of information outside his intact, immediate memory. For example, in the common odour matching task, H.M. often sniffed the sample odour only once prior to sequentially sniffing each of the 10 potential match stimuli. Then, with confidence, he would select a match, for example, from the middle of the array. When asked to check his choice by again sniffing the sample and chosen match stimulus, he invariably confirmed his choice, which was correct only by chance; it appeared that H.M. could remember which

match had been positive while testing others, regardless of its location in the array. Not even his poor performance at odour naming is explained by the global anterograde amnesia. All the odours used were items of common experience to people in childhood, and H.M.'s memory for details from that period of his life is normal. His performance was not improved when odour names were given. It is also unlikely that his inability to name common odours is due to retrograde amnesia because the deficit is specific to the olfactory mode. He easily names by sight or touch the same objects he cannot identify by smell. Once, having correctly identified a lemon by sight, he sniffed it and remarked, 'Funny, it doesn't smell like a lemon!'

Impairment of olfactory abilities is also seen after left or right unilateral temporal lobectomies that include the same olfactory and subcortical structures removed in H.M. Rausch *et al.* (1977) found deficits on a delayed matching-to-sample task; Eskenazi *et al.* (1981) described poor performance on various tests of odour discrimination, including matching, differentiation, identification and delayed recognition memory. Comparing the magnitude of these deficits to H.M. suggests that he is more severely impaired in odour quality discrimination, perhaps because olfactory structures were removed bilaterally in his case. H.M.'s deficit in odour recognition is also greater than that of patients with unilateral or bilateral amygdalotomy, who demonstrate mild and transient deficits in odour naming (Hughes and Andy, 1979). Unlike some patients with unilateral temporal lobe lesions (Rausch and Serafetinides, 1975), frontal lobe lesions (Potter and Butters, 1980), or Korsakoff's disease (Jones *et al.*, 1978), H.M. is not impaired in the ability to detect the presence of an odour.

Considering that H.M. had undergone a supraorbital craniotomy and bilateral retraction of the frontal lobes, the residual olfactory capacity was impressive. Yet his normal capacity for detection indicates that the olfactory bulbs and tracts must be at least partially intact. Furthermore, the limits of the estimated damage allow for a partially intact secondary olfactory route from the olfactory tubercle and adjacent cortex to the orbitofrontal olfactory neocortex, both by way of the mediodorsal thalamus and by intracortical connections. The medial temporal lobe resection probably did eliminate a substantial portion of the afferents to the olfactory frontal cortex and thalamus. Apparently the remaining inputs from the olfactory tubercle and cortex are insufficient to support odour discrimination, but are adequate to allow odour detection. The strength and selectivity of the olfactory deficits revealed in H.M. suggest a critical role for medial temporal lobe structures in the perception of odour quality. Taking these results together with previous findings of deficits in odour discrimination after damage to connections between the mediodorsal thalamus and the frontal cortex in man and animals, it may be concluded that an intact temporal olfactory pathway is not sufficient to support olfactory perceptual functions. Apparently both divisions of the higher olfactory pathways are necessary for the discrimination and identification of odours. The most striking aspect of H.M.'s performance, a complete dissociation between detection and discrimination, may be uniquely related to involvement of medial temporal lobe structures bilaterally.

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