were washed with 0.02*M* phosphate-buffered saline containing 0.05 percent Tween 20 (*p*H 8.0) between subsequent incubations at 25°C with hybridoma supernatant (2 hours) and rabbit antiserum to mouse IgG, IgM, and IgA (Calbiochem, La Jolla, Calif.), followed by peroxidase-conjugated goat gamma globulin directed against rabbit IgG (Fc fragment, heavy chain–specific) (Cappel Laboratories, Cochranville, Pa.). Incubations were for 2 hours each. The final color reaction was developed by adding *o*-phenylenediamine in dilute hydrogen peroxide; the enzymatic reaction was stopped with 8*N* H_2SO_4; and the plates were read within the hour by means of a titer plate reader (Flow Laboratories, Rockville, Md.) at 492 nm.

8. S. Hruby, E. C. Alvord, Jr., C.-M. Shaw, *Int. Arch. Allergy Appl. Immunol.* **36**, 599 (1969).
9. Rabbit antiserums to mouse IgG1, IgG2a, IgG2b, IgG3, IgA, and IgM were obtained from Litton Bionetics Laboratory, Kensington, Md. Quantitation was by radial immunodiffusion.
10. R. E. Martenson, G. E. Deibler, M. W. Kies, *J. Neurochem.* **18**, 2417 (1971); G. E. Deibler, personal communication.
11. Various concentrations of selected proteins or peptides were added to hybridoma supernatant (diluted 1:100), incubated for 6 hours at room temperature, and then portions were tested in triplicate with the ELISA technique for residual ability to bind 200 ng of monkey BP adsorbed to each well.
12. P. R. Carnegie, *Nature (London)* **229**, 25 (1971).
13. Human BP and twice crystallized thermolysin (100:1) were incubated in 50 m*M* tris-HCl, 5 m*M* CaCl, *p*H 7.5, for 30 minutes at 37°C. The reaction was stopped with 1*N* HCl (0.05 ml per milliliter of digest), centrifuged 20 minutes at 1000*g*, and the supernatant was lyophilized.
14. A liquid chromatograph (Varian model 5000, Palo Alto, Calif.) was used with an octadecylsilane, 10-μm silica, monomeric coverage, reverse-phase column and UV-50 detector. The mobile phase was 0.48 percent phosphoric acid, *p*H 3.0, and a gradient from 0 to 30 percent acetonitrile was established over 60 minutes.
15. Purified IgG1 from ascites fluid monoclonal antibody was covalently bound at 10 mg/g to cyanogen bromide–activated Sepharose 4B (Pharmacia, Piscataway, N.J.); 5 mg of thermolysin-digested human BP was added in 10 ml of 0.02*M* phosphate-buffered saline (*p*H 8.0) containing 0.05 percent Tween 20 to minimize nonspecific binding. After incubation for 30 minutes at 25°C, the unbound peptides were washed off with 20 ml of phosphate-buffered saline with Tween, and the Tween was washed off with 20 ml of phosphate-buffered saline without Tween in order not to interfere with the subsequent HPLC analysis. The specifically bound peptides were then eluted with 0.2*M* glycine HCl and 4*M* NaCl, *p*H 2.9.
16. W. C. Mahoney and M. A. Hermondson, *J. Biol. Chem.* **255**, 11199 (1980).
17. E. C. Alvord, Jr., S. Hruby, R. Petersen, M. W. Kies, in *The Aetiology and Pathogenesis of the Demyelinating Diseases*, H. Shiraki, T. Yonezawa, Y. Kuroiwa, Eds. (Japan Science Press, Tokyo, 1976), pp. 217–226.
18. We thank B. Jones, L. Katzenberger, and I. Laszlo for important technical assistance, J. D. Meyers for loaning us the Flow reader, C. J. Gibbs for a fresh-frozen chimpanzee brain, and E. H. Fischer for biochemical advice and assistance as well as the thermolysin. This research was supported in part by National Multiple Sclerosis Society research grant RG-805-D19, American Cancer Society grant RD-69, and National Institutes of Health grants CA-19148, CA-25558, and CA-26584.

16 March 1981; revised 23 June 1981

Affective Behavior in Patients with Localized Cortical Excisions: Role of Lesion Site and Side

Abstract. *The perception of emotion in verbal and facial expression, and the spontaneous production of conversational speech were studied in patients with unilateral focal excisions of frontal, temporal, or parieto-occipital cortex. Lesions of the left hemisphere impaired the matching of verbal descriptions to appropriate verbal categories of emotional states, whereas with lesions of the right hemisphere, the matching of different faces displaying similar emotional states was impaired. The effects of lesions of both left and right hemisphere occurred regardless of the locus of the lesion. On the other hand, frontal-lobe lesions had differential effects upon unsolicited talking; lesions of the left frontal lobe virtually abolished this behavior, whereas lesions of the right frontal lobe produced excessive talking. These data suggest that the nature of the behavioral stimulus as well as the locus and side of damage must be considered in the study of the neural basis of affective behavior.*

Although there has been extensive study of the role of the left and right hemispheres in the production of cognitive processes (*1*), there have been relatively few studies specifically designed to consider the complementary roles of the two hemispheres in the production of affective behavior. An understanding of the neural control of human affective behavior might be improved by studying those stimuli that seem most important in human social interaction, namely facial expression and language. We thus examined the effects of cortical excision upon the perception of emotion in facial expression, the perception of emotion in verbal expression, and the spontaneous production of conversational speech, by making use of experimental designs modeled on previous studies of affective behavior of nonhuman species (*2*). In addition, we compared these data to our previous investigation of the effects of cortical lesions on spontaneous facial expression (*3*).

The subjects were 20 right-handed normal control subjects and 58 patients at the Montreal Neurological Hospital who had undergone a unilateral excision of cortical tissue of the frontal (7 left, 14 right), temporal (13 left, 17 right), or parieto-occipital (4 left, 4 right) regions for the relief of epilepsy (*4*). When the temporal lobe was removed, the amygdala was partially or completely removed, and the hippocampus was partially removed.

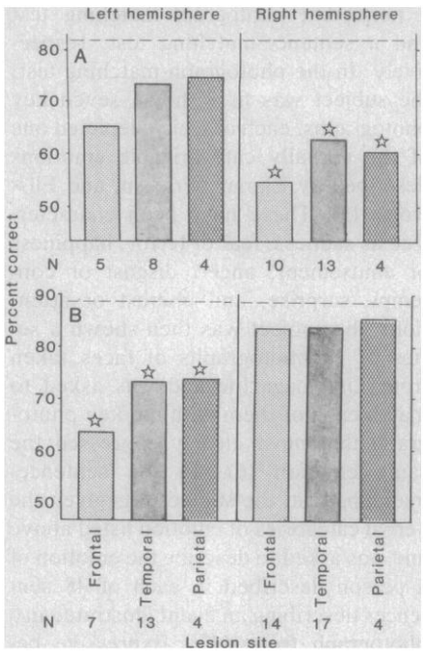
The perception of emotion in facial and verbal expression was measured by a nonverbal photograph-matching test and a sentence-matching test, respectively. In the photograph-matching test, the subject was first shown seven key photographs, each of which depicted one of the verbally categorizable emotions described by Ekman, Friesen, and Ellsworth (*5*). These have been characterized as sadness, fear or terror, happiness or amusement, anger, disgust or contempt, surprise, and interest or attention. The subject was then shown a series of 24 photographs of faces taken from *Life* magazine and was asked to match each of them with the key photograph that most closely expressed the same emotion (*6*). In the sentence-matching test, the subject was given the verbal categories of emotion listed above and was asked to describe the emotion of a person described in each of 48 sentences describing an event illustrated in a photograph from *Life*. Expressive behavior in the form of unsolicited talking was measured by noting each time a patient interrupted testing with comments about the test or with extraneous remarks.

Patients with lesions of the right hemisphere, irrespective of the lesion site, were significantly impaired on the photograph-matching test (Fig. 1A) whereas patients with lesions of the left hemisphere were significantly impaired on the verbal test (Fig. 1B) (*7*). Patients with left frontal-lobe lesions seldom interrupted testing by spontaneously talking, whereas those with right frontal-lobe lesions frequently did so (Fig. 2) [$F(5, 44) = 5.1$, $P < .05$].

In a previous study (*3*) we recorded the frequency of spontaneous facial expressions in a similar patient population, finding a large reduction in spontaneous facial expression in patients with left or right frontal-lobe lesions, compared with patients with temporal- or parietal-lobe lesions. Thus the increased spontaneous talking of the right frontal-lobe lesion patients in the present study stands in marked contrast to their relatively infrequent changes in facial expression.

The extremely limited spontaneous talking of our patients with left frontal-lobe lesions supports a number of previous reports describing a striking impoverishment of the spontaneous narrative speech produced by patients with left frontal lesions (*8*), an observation that has been quantified with the Thurstone Word Fluency Test (*9, 10*) in either written or oral form. The frequent spontaneous talking of the right frontal-lobe patients can probably be ascribed to the tendency of right frontal lesions to pro-

0036-8075/81/1002-0089$01.00/0



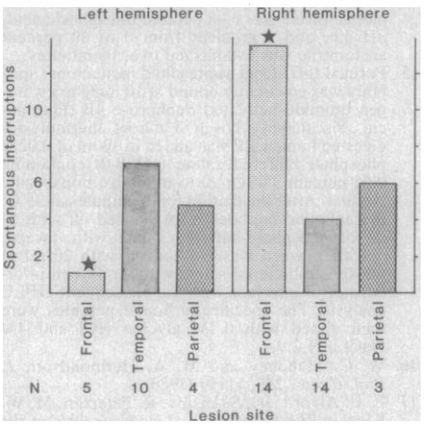


Fig. 1 (left). Summary of the tests of receptive function. (A) Lesions anywhere in the right hemisphere significantly impaired matching the emotional expression in photographs of faces. (B) Lesions anywhere in the left hemisphere significantly impaired matching a verbal descriptor such as sad or happy to a verbal description of an emotional situation. The dotted line indicates the control level, and stars indicate the group differed significantly from the analogous group in the opposite hemisphere. Fig. 2 (right). Summary of the spontaneous interruptions during the tests of receptive function. Patients with left frontal lesions made virtually no comments, whereas patients with right frontal lesions were excessively talkative. The frontal-lobe groups each differed significantly from all other groups (Tukey's multiple comparisons, P's $< .05$) with the exception of the left temporal-lobe group, which differed only from the left frontal-lobe group. No other differences were significant.

duce impulsiveness and rule-breaking behavior (*11*) of which irrelevant talking during testing would seem to be an example.

Waxman and Geschwind (*12*) have described excessive writing behavior in patients with temporal lobe epilepsy, and patients with the so-called "temporal-lobe personality" have been described as excessively talkative (*13*). This tendency to be talkative is, in our experience, more frequently associated with right temporal-lobe lesions. The failure to observe an increase in spontaneous talking by the right temporal-lobe patients in the current study is probably the result of two factors. (i) Since talking was a form of rule-breaking behavior in the current study, the temporal patients may have been more inhibited in their talking than they would have been in normal conversation. (ii) As only the initiation of spontaneous talking was recorded and not the duration or content, the possibility that the right temporal-lobe patients talk longer than other patient groups was not assessed. On the basis of studies of neurological and psychiatric patients it has been proposed that the right hemisphere plays a special role in the production of affective behavior and the perception of socially relevant stimuli such as facial expression and affective tone in voices (*14*).

This proposal has received support from studies that have used split-visual-field techniques (*15*), dichotic listening procedures (*16*), or measurements of lateral eye gaze (*17*) in normal subjects.

Our studies of the perception of emotion in facial and verbal expression, as well as the production of spontaneous talking and facial expression, suggest that previous emphasis upon the right hemispheric control of affective behavior has neglected a complementary role of the left hemisphere. This conclusion is further supported by our observation (*3, 9, 18*) that neither facial expression nor mood are differentially affected by intracarotid Amytal Sodium injection into the left or right hemispheres. It seems that the nature of the stimulus as well as the locus and side of damage must also be considered when studying the effects of cortical lesions on affective behavior. We suggest that techniques involving the naturalistic observation of behavior, which have long been used in the analysis of affective behavior in nonhuman species (*2*), be advanced in the study of cortical function in humans as well.

BRYAN KOLB
Department of Psychology,
University of Lethbridge,
Lethbridge, Alberta, Canada T1K 3M4
LAUGHLIN TAYLOR
Montreal Neurological Institute,
3801 University Street,
Montreal, Quebec, Canada H3A 2B4

References and Notes

1. See, for example. H. Hécaen and M. L. Albert, *Human Neuropsychology* (Wiley, New York, 1978); B. Kolb and I. Q. Whishaw, *Fundamentals of Human Neuropsychology* (Freeman, San Francisco, 1980).
2. R. E. Myers, *Acta Neurobiol. Exp.* **32**, 567 (1972); C. M. Butter and D. R. Snyder, *ibid.*, p. 525; B. Kolb and A. J. Nonneman, *Physiol. Behav.* **13**, 637 (1974); A. J. Nonneman and B. Kolb, *Behav. Biol.* **12**, 41 (1974).
3. B. Kolb and B. Milner, "Observations on spontaneous facial expression after focal cerebral excisions and after intracarotid injection of Amytal Sodium," *Neuropsychologia*, in press.
4. The patients were examined from 3 weeks to 10 years after their operations; they had a mean age of 26 years (range 15 to 48), and a mean Wechsler Adult Intelligence Scale score of 104 (range 79 to 146). All subjects had speech represented in the left hemisphere as indicated by carotid Amytal Sodium testing or by cortical stimulation at the time of surgery. None of the patients was dysphasic nor exhibited contralateral neglect at the time of testing. See B. Kolb and B. Milner ("Performance of complex arm and facial movements after focal brain lesions," *Neuropsychologia*, in press) for representative brain maps. There were approximately equal numbers of males and females in each group.
5. P. Ekman, W. V. Friesen, P. Ellsworth, *Emotion in the Human Face* (Pergamon, Toronto, 1973).
6. In a preliminary study we ascertained that 20 control subjects agreed upon the verbal description of the emotion displayed for all the 7 key photographs, and that for the 24 stimulus photographs 70 percent or more of the control subjects agreed upon the matching key photograph that expressed the same emotional expression. Similarly, more than 70 percent of the control subjects agreed as to the emotion described in the sentences. Thus, an answer was considered correct if it agreed with the majority response (70 percent or more) in the preliminary study.
7. Analyses of variance on the photograph and verbal matching tests yielded a significant main effects of hemisphere [$F(5, 38) = 5.9$, $P < .01$; $F(5, 53) = 7.0$, $P < .01$] but not for the main effects of lesion locus or the hemisphere by locus interactions ($F < 2$, $P > .05$). Significant follow-up tests (Tukey's multiple comparisons) are shown in Fig. 1. There were no obvious trends or patterns to the errors on either test. Subjects in all groups were unlikely to confuse widely disparate expressions such as "happiness" and "anger" but they were likely to confuse such similar expressions as "surprise" and "fear."
8. O. L. Zangwill, *Int. J. Neurol.* **5**, 395 (1966); R. Bonner, S. Cobb, W. H. Sweet, J. C. White, *Res. Publ. Assoc. Res. Nerv. Ment. Dis.* **31**, 392 (1953); A. R. Luria, *Higher Cortical Functions in Man* (Basic Books, New York, 1966).
9. B. Milner, in *Brain Mechanisms Underlying Speech and Language*, C. H. Millikan and F. L. Darley, Eds. (Grune & Stratton, New York, 1967).
10. ——, in *The Frontal Granular Cortex and Behavior*, J. M. Warren and K. Akert, Eds. (McGraw-Hill, New York, 1964); A. L. Benton, *Neuropsychologia* **6**, 63 (1968); J. G. Borkowski, A. L. Benton, O. Spreen, *ibid.* **5**, 135 (1967); E. Perret, *ibid.* **12**, 323 (1974); A.-M. Ramier and H. Hécaen, *Rev. Neurol.* **123**, 17 (1970).
11. B. Milner, *Neuropsychologia* **3**, 317 (1965).
12. S. G. Waxman and N. Geschwind, *Neurology* **24**, 629 (1974).
13. D. Blumer and D. F. Benson, in *Psychiatric Aspects of Neurological Disease*, D. F. Benson and D. Blumer, Eds. (Grune & Stratton, New York, 1975); J. H. Pincus and G. J. Tucker, *Behavioral Neurology* (Oxford Univ. Press, New York, 1974).
14. G. Gainotti, *Cortex* **8**, 41 (1972); K. M. Heilman, R. Scholes, R. T. Watson, *J. Neurol. Neurosurg. Psychiatry* **38**, 69 (1975); D. M. Tucker, R. T. Watson, K. M. Heilman, *Neurology* **27**, 947 (1977); E. D. Ross and M.-M. Musulam, *Arch. Neurol.* **36**, 144 (1979); H. Buchtel, F. Campari, C. DeRisio, R. Rota, *Ital. J. Psychol.* **5**, 159 (1978).
15. R. G. Ley and M. P. Bryden, *Brain Lang.* **7**, 127 (1979); S. J. Dimond and L. Farrington, *Acta Psychol.* **41**, 255 (1977); S. J. Dimond, L. Farrington, P. Johnson, *Nature (London)* **261**, 690 (1976).
16. F. L. King and D. Kimura, *Can. J. Psychol.* **26**, 111 (1972); M. Haggard and A. Parkinson, *Q. J. Exp. Psychol.* **23**, 168 (1971); A. Carmon and I.

Nachson, *Acta Psychol.* **37**, 351 (1973); M. Safer and H. Leventhal, *J. Exp. Psychol. Hum. Percept. Perform.* **3**, 75 (1977).
17. G. E. Schwartz, R. J. Davidson, F. Maer, *Science* **190**, 286 (1975); R. E. Gur, R. C. Gur, L. J. Harris, *Neuropsychologia* **13**, 35 (1975); M. Kinsbourne, *Science* **176**, 539 (1972); P. Bakan, *Percept. Mot. Skills* **28**, 927 (1969).
18. But see also H. Terzian, *Acta Neurochir.* **12**, 230 (1964); G. F. Rossi and G. Rosandini, in *Brain Mechanisms Underlying Speech and Language*, C. H. Millikan and F. L Darley, Eds. (Grune & Stratton, New York, 1967).
19. Supported by a grant to B.K. from the Natural Sciences and Engineering Research Council of Canada and a grant from the Medical Research Council of Canada to B. Milner. We thank B. Milner, I. Q. Whishaw, R. H. Barnsley, and T. Schallert for comments on an earlier version and A. Allen for typing.

2 December 1980; revised 13 April 1981

Role of Mediodorsal Thalamic Nucleus in Olfactory Discrimination Learning in Rats

Abstract. *Severe deficits in the acquisition of an olfactory learning-set task resulted from lesions of the central (olfactory) component of the mediodorsal thalamic nucleus but not from large lesions that destroyed olfactory projections to the amygdala. Complex olfactory learning may be mediated by the olfactory thalamocortical system and not by olfactory projections to the limbic system.*

A prominent projection for olfactory impulses to the central segment of the mediodorsal thalamic nucleus has now been firmly established by experimental anatomical and neurophysiological studies (*1*). This segment of the mediodorsal nucleus projects to several frontal cortical areas including the lateral orbital cortex (*2*). The existence of a thalamic-neocortical projection for olfactory information challenges the traditional view of the olfactory system as a primitive sensory modality having only basal forebrain projections and involved primarily in species-specific or affective behaviors. However, the functional significance of this olfactory cortical projection has not been established (*3*). In behavioral studies we have shown that, when provided with odor cues, rats can acquire learning sets as efficiently as primates trained with visual stimuli do (*4*). We now report that this form of learning in the rat is severely disrupted by lesions of the olfactory thalamic cortical system, but not by lesions of olfactory projections to the limbic system.

Twenty-seven adult male rats were trained on a discrete-trials, "go, no-go" discrimination procedure in a wind-tunnel olfactometer (*4*). On each trial either the positive (S^+) or negative (S^-) stimulus was presented for 3 seconds. Key responses by the subject in the presence of the S^+ stimulus resulted in termination of the trial and delivery of a 0.05-ml water reward; key responses in the presence of the S^- stimulus were not reinforced (*5*). Prior to surgery, animals were trained to discriminate a flashing light (S^+) from a steady light (S^-).

After 10 to 14 days of postoperative recovery, the rats were tested for retention of the visual discrimination problem. On the next day they were trained to discriminate the odor of propyl acetate (S^+) from that of ethyl acetate (S^-). Stimulus concentration for both odorants was approximately 0.05 percent of vapor saturation. Training on this problem was terminated when 90 percent correct responding was achieved in a block of 20 trials. On the next day the positive and negative values of the stimuli were reversed and training was continued until the 90 percent correct responding criterion was achieved. This procedure was continued until six successive discrimination reversals had been completed. Finally, animals were trained to criterion on a simple detection problem in which the odor of amyl acetate (at approximately 0.005 percent of vapor saturation) served as S^+ and no odor served as S^-.

Stereotaxically directed lesions were aimed at the mediodorsal nucleus of 16 rats and at the lateral olfactory tract at the level of the anterior amygdala in four rats. Seven rats with sham lesions served as controls. Histological analysis (*6*) revealed that the amygdaloid lesions bilaterally transected the lateral olfactory tract, destroyed bordering pyriform cortex, and invaded the anterior amygdala (Fig. 1F). Discrete lesions of the central part of the mediodorsal nucleus or of the

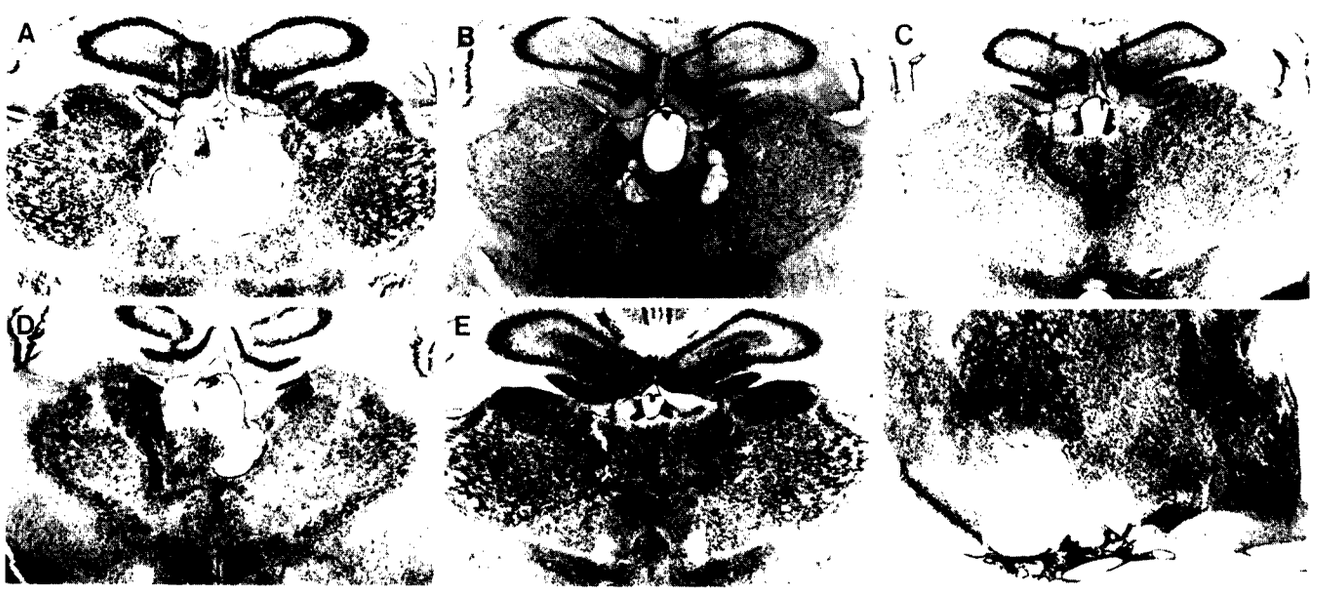


Fig. 1. (A to C) Representative lesions from animals in the large MD group. (D) Thalamic control group. The lesion is located just rostral to the mediodorsal nucleus. (E) Small MD group. Small bilateral lesions are located in the ventral aspect of the central component of the mediodorsal nucleus. (F) Representative lesion in the amygdaloid group. Lesions in this group were bilaterally symmetrical and transected the lateral olfactory tract at the level of the anterior amygdala.

0036-8075/81/1002-0091$01.00/0