pothesis that facial asymmetry in emotional expression reflects hemispheric asymmetry of function.

HAROLD A. SACKEIM
Department of Psychology, New York University, New York 10003
RUBEN C. GUR
Department of Psychology, University of Pennsylvania, Philadelphia 19104

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3. P. H. Burke, *Hum. Biol.* **43**, 536 (1971).
4. The differences in facial width between left-side and right-side composites on the two measures were correlated substantially [$r(68) = .72$, $P < .001$].
5. The degree to which the tip of the nose deviates to the left or right is associated with handedness [P. R. Sutton, *Nature (London)* **198**, 909 (1967)]. Choice of the tip of the nose as a landmark could artifactually inflate asymmetry in facial size. In our laboratories, to establish facial midline we determine the best fitting line to a set of four points in the face, none of which are known to have consistent lateral deviation.
6. Composites were presented for 2 minutes in pairs on a solid white background with no external illumination. Slides were projected from a distance of 2 m with 300-W lamps to three raters who sat 1 m from the wall. For each pair, raters made difference judgments on a −5 to +5 scale. The correlations between pairs of raters were $r_{1,2} = .73$, $r_{1,3} = .76$, and $r_{2,3} = .80$.
7. R. Crumley, the facial surgeon cited by Ekman, knows of no data indicating *consistent* lateral asymmetry in these morphological characteristics (personal communication, 21 November 1979).
8. The only mention in Burke's report of a possible consistent difference was "The measurements on asymmetry suggest that in the maxillary area of the face, there is a tendency for the larger side to be on the left" (*3*, p. 546).
9. This literature is reviewed by H. A. Sackeim, M. S. Greenberg, A. L. Weiman, R. C. Gur, J. P. Hungerbuhler, and N. Geschwind (in preparation); findings are presented relating side of brain damage to uncontrollable outbursts of emotion.
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11. ———, *ibid.* **38**, 250 (1943).
12. In both studies Lynn and Lynn (*10, 11*) found associations between personality functioning and concordance between direction of smile asymmetry and handedness. In 1943 (*11*), they reported an association between direction of smile asymmetry and lateral eye dominance. These findings also support the hypothesis that hemispheric specialization is associated with asymmetry of facial expression.
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18. R. Campbell, *Cortex* **14**, 327 327 (1978). [Campbell has informed us (personal communication, 1 February 1980) that she has not questioned her data concerning asymmetries of posed smiles. "It seems to me . . . that the asymmetry of a posed smile is a real effect, but it is small compared with the asymmetry of a relaxed face."] W. Heller, unpublished manuscript; J. Rosen, D. K. Zeidler, in preparation; Borod and Caron and Rubin and Rubin (*19*). In related areas of research, Moscovitch and Olds (*20*) found more spontaneous unilateral facial gestures on the left than on the right side of the face during speech. Schwartz *et al.* (*21*) found asymmetry in facial electromyographic activity as a function of emotional conditions.
19. J. C. Borod and H. S. Caron, paper presented to the International Neuropsychological Society, New York, 31 January to 3 February 1979; R. Rubin and N. Rubin, *Neuropsychologia*, in press.
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12 December 1979

Neurobiology of Amnesia

Gold and Sternberg have recently suggested that a common neurobiological mechanism may underlie many examples of retrograde amnesia in experimental animals (*1*). This conclusion was based on their report that phenoxybenzamine (PBZ), an α-adrenergic antagonist, attenuated the amnesia produced by several different treatments: electrical stimulation of frontal cortex or amygdala, injection of pentylenetetrazol, diethyldithiocarbamate, or an inhibitor of brain protein synthesis cycloheximide (CXM). They suggested that formation of memory may depend in part on brain catecholamine concentrations and that amnesia in many if not all cases is related to effects on catecholamines.

This conclusion seems difficult to reconcile with previous research on amnesia and the biology of memory. In particular, a large body of evidence has suggested that brain protein synthesis during or shortly after training is required for the formation of long-term memory (*2*). If protein synthesis is required for the development of long-term memory, it is difficult to understand why an adrenergic blocking agent should reverse the amnesic effects of protein synthesis inhibition. Accordingly, we have reevaluated the report that PBZ can attenuate the amnesia produced by CXM.

In the original study (*1*), memory was assessed with the passive avoidance task—that is, retention was measured by the time taken to enter an area where footshock had previously been delivered. In this task, drugs can change response latencies for many reasons (*3*). Thus, if combined treatment of PBZ and CXM made animals ill, then response latencies at retest might be high for animals given both drugs. This result would give the appearance of improved retention but could more appropriately be explained as sickness. We have replicated the original findings of Gold and Sternberg, who tested mice 1 day after training (Table 1). We also tested mice 7 days after training, after the general health of the mice had had time to recover. In this case, however, the impairment in retention produced by CXM was not "attenuated" by PBZ (Table 1). Finally, we trained mice for 20 trials in the Deutsch carousel, an automated discrimination training apparatus in which the response measure (a choice between two objects) need not be confounded by changes in locomotor activity or by illness (*4*). When 20 retention trials were given the next day, we found that PBZ did not attenuate the amnesic effect of CXM (Table 1).

Accordingly, the effects of PBZ on CXM-produced amnesia seem best interpreted as illness or some other temporary effect caused by the injection of both PBZ and CXM. A variety of known side effects of inhibitors of brain protein synthesis have been evaluated and have been dissociated from their amnesic effects (*2*). In particular, the possibility that CXM impairs memory by disrupting catecholamine metabolism has been re-

Table 1. Retention performance of mice as affected by saline, phenoxybenzamine (PBZ) (2 mg per kilogram of body weight), cycloheximide (CXM) (160 mg/kg), or a combination of PBZ and CXM. For passive avoidance training, the first drug was given 30 minutes before training and the second immediately after training. Discrimination training was the same except that the second drug was given 10 minutes before training. The number of mice per group is indicated in the headings. Mann-Whitney *U* tests were used to evaluate passive avoidance differences; *t*-tests were used for discrimination data ($\alpha = .05$).

Group	Passive avoidance latency (median sec)		Correct discriminations ($\bar{X} \pm$ S.E.M.) ($N = 18$)
	Retention on day 1 ($N = 45$)	Retention on day 7 ($N = 48$)	
1. Saline-saline	283*	215*	11.2 ± 0.8*
2. Saline-CXM	104†	56.5†	9.1 ± 0.6†
3. PBZ-saline	364*	156*	11.8 ± 0.7*
4. PBZ-CXM	245*	78.5†	8.9 ± 0.6†

*Significantly different from group 2. †Significantly different from group 1.

0036-8075/80/0815-0836$00.50/0

peatedly evaluated and can be discounted (*5*). Accordingly, the available evidence remains consistent with a requirement for protein synthesis in long-term memory storage. This view does not, of course, exclude an important role for catecholamines in some aspects of learning and memory.

LARRY R. SQUIRE
Veterans Medical Center, San Diego,
and *Department of Psychiatry,*
University of California, San Diego,
La Jolla 92037
HASKER P. DAVIS
Department of Psychology,
University of California, Berkeley 94720
CURT W. SPANIS
Department of Biology,
University of San Diego,
San Diego, California 92110

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3 November 1978; revised 29 June 1979

We were pleased that Squire *et al.* were able to replicate our findings. We also noted that CXM-treated mice appear ill for several days after an injection, although mice pretreated with PBZ were not noticeably more ill. We believe the fact that CXM produces illness lends support to the hypothesis that CXM, like other amnestic treatments, elicits physiological stress responses that impair memory storage. The PBZ also attenuates amnesias produced by many other treatments in the absence of obvious illness.

With regard to the specific data Squire *et al.* provide, all groups show decreased retention performance at the day 7 test

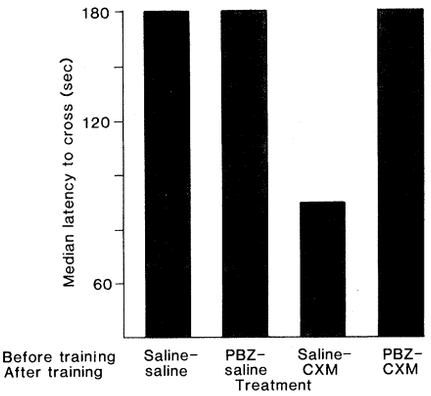

Fig. 1. Retention latencies of rats trained in a one-trial inhibitory avoidance task (3-mA, 2-second footshock) and tested 1 week later. Rats received an injection of saline or PBZ (2 mg per kilogram of body weight) 30 minutes before training and an injection of saline or CXM (2.8 mg/kg) immediately after training. The injection of CXM after the trial produced significant amnesia ($P < .05$, two-tailed Mann-Whitney U test), and PBZ treatment before training attenuated the amnesia.

interval. Just as amnesia is seldom, if ever, complete (that is, retention latencies of amnesia groups are above those of nonshocked controls: approximately 20 seconds), attenuation of amnesia may also be incomplete. The day 7 results may simply reflect different rates of forgetting, a finding that would be interesting but that would not alter our general conclusion. In direct response to their findings, we examined retention performance after 1 week in an analogous experiment with rats. Under these conditions, PBZ still attenuated CXM-produced amnesia (Fig. 1).

In addition, we now have more evidence about the generality of our findings. Several other peripherally administered adrenergic antagonists block the amnesias produced by electrical stimulation of frontal cortex and the amygdala for both inhibitory (passive) avoidance training and for Y-maze discriminated-avoidance training (a task similar to that used by Squire *et al.*) (*1*). Thus, the findings seem general to both rats and mice, to several adrenergic antagonists, to at least two behavioral situations and, under some conditions, at test intervals as long as 1 week after training. It seems unlikely that the attenuation of amnesia seen under these various combinations of conditions can be attributed to illness.

Finally, we wish to emphasize that our data do not directly bear on the issue of whether protein synthesis is involved in memory storage processing; protein synthesis must at least provide the constituents necessary for memory processing. Our results do, however, cause us to question the attribution of antibiotic effects on memory to inhibition of protein synthesis. Whether CXM acts on memory because of inhibition of protein synthesis that is specifically involved in memory processing or whether inhibition of protein synthesis is a stressor that elicits physiological responses that impair memory is still open to question (*2*). An examination of physiological stress responses [such as a transient decrease in brain norepinephrine content that is highly correlated with other amnesias (*3*)] after CXM injections may help to resolve this issue.

PAUL E. GOLD
DEBRA B. STERNBERG
Department of Psychology,
University of Virginia,
Charlottesville 22901

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25 January 1980