MEMORY RESEARCH
An Era of 'Good Feeling'

Researchers believe a chemically controlled 'good feeling machine' in the brain may hold the key to emotions, memory and learning

BY JOEL GREENBERG

e-mo-tion, *n. 1. an affective state of consciousness in which joy, sorrow, fear, hate, or the like, is experienced (distinguished from cognitive and volitional states of consciousness).*
—The American College Dictionary

Why do human beings—supposedly the masterpieces of evolution on this planet—have feelings? The very definition of emotion implies that it is a rather difficult to control, involuntary state of mind that seems to muddle and confuse as often as it aids our thinking and decision-making processes. Perhaps it won't be too long, some speculate, before we climb the next few evolutionary steps and shed these annoying, illogical processes that still link us to lower life forms.

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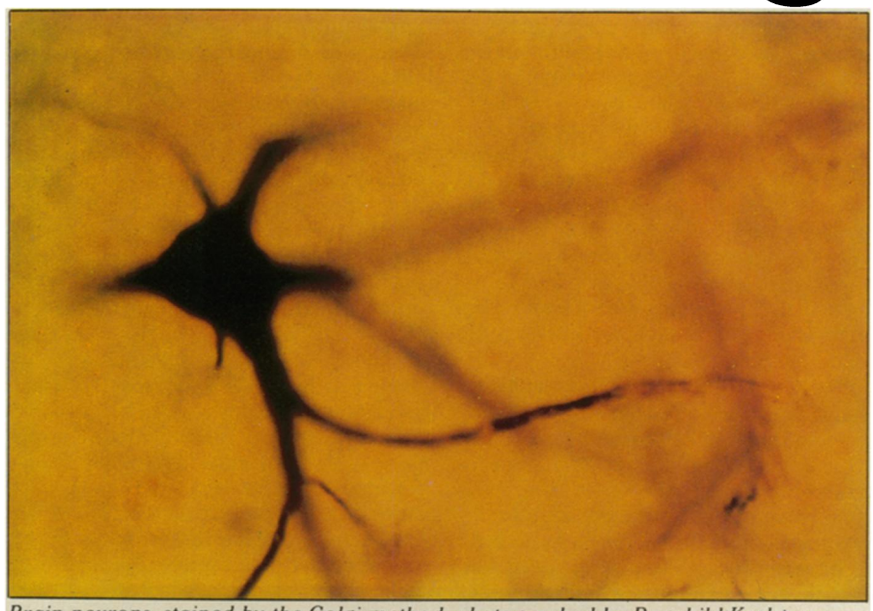
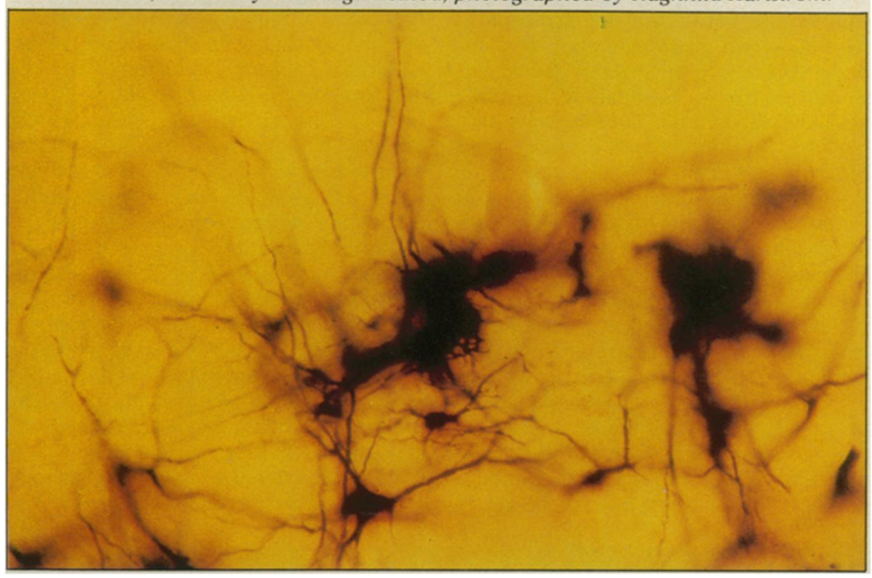
A small white rat with a tiny needle implanted in its brain huddles on the chrome ledge of its cage at Wyeth Laboratories in Radnor, Pa. The rat will not descend from the ledge onto the wire mesh floor for quite some time. It remembers that it got shocked by stepping on the wire several days before. In the next cage, a second rat sits perched on its ledge recalling its own electric shock. But this rat will step down much sooner than its nearby companion. The second rat has no active brain implant.

What has actually "stimulated memory storage," in the first rat, Wyeth researchers believe, is the administration of enkephalin — a recently discovered "natural opiate" of the brain that has triggered the latest round of excitement in behavioral neuroscience (see p. 374). Even after the last chemical traces of the injected enkephalin have left the rat's nervous system — and more than three days since its shock experience — the memory of that experience remains much more intense in the first rat than it does in the second.



Photos: Courtesy of J. Allan Hobson, *Dreamstage* and Hoffman-LaRoche, Inc.

Brain neurons, stained by the Golgi method, photographed by Ragnhild Karlstrom.



Wyeth researchers Larry Stein and James D. Belluzzi believe these results may be an accurate reflection of part of the machinery of human memory and learning systems. And they further suggest that rather than detracting from the process, feelings and emotions are actually *essential* to our ability to remember and learn.

Stein, a psychopharmacologist, muses over that prospect as he stares at his bulletin board array — a semi-circle of brain drawings surrounding newspaper clippings of Richard Nixon's Watergate demise. "Strong feelings help us to select out from a very confusing input those [inputs] which are pertinent and relevant," he says. "I concur with [biochemist] Adrian Dunn [of the University of Florida] that feelings are serving some evolutionary purpose" by performing such a function, and that "people reduced to pure logic machines couldn't compete." And key fuels for emotions and memory, he suggests, are enkephalins and endorphins.

The discovery of those two "natural opiate peptides" raised at least as many questions as it answered. "They seem to function in the interface between pain and feeling," says Frederick K. Goodwin, chief

of the clinical psychobiology branch of the National Institute of Mental Health. "How we are feeling emotionally has a lot to do with how much we can tolerate physical pain."

It has long been known that morphine and heroin, the drug equivalents of endorphins and enkephalins, trigger a euphoric response that either eliminates pain or causes the person not to care about it. (Endorphins and enkephalins have similar properties, but the endorphin molecule is the larger of the two.) The discovery that such substances occur naturally lent credence to the idea of "natural highs," such as those reported by long-distance runners and persons undergoing religious experiences. In connection with this, endorphins are already being tested, on a very preliminary basis, on persons suffering from depression and schizophrenia (SN: 11/11/78, p. 326).

But perhaps even more important in the long run, their discovery has begun to fill in some gaps about the role of emotions in brain functioning. In extensive work with animals, Stein and Belluzzi have found "reward systems" in the brain based on the catecholamine neurotransmitters noradrenaline (the equivalent of norepinephrine) and dopamine. Rats would repeatedly perform tasks that would enable them to self-administer these transmitters (or their chemical precursors).

But then came the discovery of the natural opiates, which the brain also obviously craves and seeks out, "and we wondered for a while why the brain would have duplicated itself" in having two sets of reward systems, Stein says. As a result of their own work and that of others, Stein and Belluzzi theorize that the brain contains a two-pronged "good feeling machine" fueled on one level by catecholamines and on the other by opiate peptides.

One half of the machine seeks *incentives* — it wants to be excited, stimulated and interested at a time "when things are dull," according to Stein. The natural "turn-on" for such emotions is dopamine, and the drug equivalent that can also turn on the system is cocaine (and amphetamines, to a lesser extent). The machine's other half seeks *quiescence* when the system has been overstimulated or subjected to pain, extreme hunger or to other strong "needs." "Then, you want your drive reduced, you want gratification," Stein says. In this case, the natural "turn-off" is enkephalin (or endorphin), and the drug-induced switch comes from heroin or morphine. Such chemicals "produce a state of indifference to drives."

Which of the two types of rewards is sought by the brain at a particular time depends on the balance of the person's inputs and needs at that time, Stein and Belluzzi say. And while taking cocaine or heroin is a direct gratification of those needs, the *natural* operation of the machine works in the reverse fashion: Whatever makes an individual feel good stimulates the natural release of the appropriate brain neurotransmitter, according to the theory. "Some guys ... dive out of planes," Stein says. "That's one thing I could never figure, but I've got a feeling it's doing a lot for their catecholamines."

On the other hand, the failure to produce those sought-after rewards constitutes a "bad feeling" or a "punishment." Sometimes the external environment can't supply what the person wants to trigger the reward system — as might occur when a person loses a loved one or fails in his or her job. In other cases, Stein says, "the good feeling system doesn't work — no matter what's happening out there in the world, it's not engendering good feelings." The second case constitutes a breakdown of the machinery and, Stein believes, triggers what is known as serious depression (suggesting that some tricyclic antidepressants work specifically to stimulate brain norepinephrine).

Assuming this machine exists, the next question is "why?" Belluzzi and Stein think such a mechanism is not only valuable but "necessary for survival." And the key, they say, lies in the link between feelings and memory. "Good and bad feelings [take the] place of a lot of information," Stein says. They are "an alternative to remembering everything you need" for survival.

"For the organism to survive, it's got to figure out the important things to attend to — where is food, and so on," says Belluzzi, a biopsychologist. The brain's reward and punishment system, say the researchers, provides two critical functions: It "tells you in the face of a lot of competing inputs which are important and which are unimportant," says Stein; and it also tells you "you'd better *remember* what just happened because you may need that information at some later time — rewards and punishments ... connect to the learning machinery," says Stein.

At a very basic level, then, memory might involve "remembering what it was that occurred just before the good feeling, because that becomes a signal and potential cause of the good feeling," Stein suggests. However, he notes, there are usually a number of neuronal inputs competing within the memory system. He uses the example of a starving man confronted with an unknown food, which looks like his favorite food, lobster. "If it also smells like lobster, he may be more inclined to eat it, because his memory tells him that lobster was good. Then a friend provides some social input by telling him the stuff is great to eat. And the man is just ready to dig in, when he notices several dead bodies lying there with this food right in front of them. This finally puts in the big negative and you don't eat at all."

The serious emotional problems, such as depression, result more from the breakdown of the good feeling system than from lack of environmental inputs, Stein reiterates. "The normal brain ... finds ways to produce good feelings one way or another," he says. "Even if you're in prison, you can see a little flower in a crack and say, 'Ahh, look at that beautiful flower,' and generate a positive feeling. So when you come to think of it, that abnormal brain of a depressive must be quite abnormal indeed when a successful businessman who has a nice family and everything going for him walks out the window one day — that's bad chemistry."

While Stein, Belluzzi and NIMH's Goodwin agree that there may be some exceptions to this view, they and others have essentially adopted a biological model of depression and other serious emotional illnesses. From his neurochemical studies with "normal" people, however, Goodwin says depression may not be the debilitating factor in itself. After all, Stein and others note that everyone undergoes periodic emotional lows when things are not going well.

Instead, Goodwin suggests that "certain personality types tend to sort out more with certain psychiatric illnesses." Persons with abnormally low levels of certain catecholamines or other neurotransmitters, for example, might be more aggressive than depressive — but when a depressive period comes, they attempt suicide rather than look for ways to counteract the bad feelings.

"There appears to be a chemical basis to variation in people, which may directly produce illness, but may also *interact* with illness," Goodwin says. "Depression may have a totally different chemical base that we haven't thought about yet." The object, he says, "is to try to re-establish equilibrium in the system." Or, "to put it another way," says Stein, "depression is an inability of the brain to produce a good feeling." □