

The neural routes
underlying the
formation of memories
about primitive
emotional experiences,
such as fear,
have been traced

Emotion, Memory and the Brain

by Joseph E. LeDoux

Despite millennia of preoccupation with every facet of human emotion, we are still

far from explaining in a rigorous physiological sense this part of our mental experience. Neuroscientists have, in modern times, been especially concerned with the neural basis of such cognitive processes as perception and memory. They have for the most part ignored the brain's role in emotion. Yet in recent years, interest in this mysterious mental terrain has surged. Catalyzed by breakthroughs in understanding the neural basis of cognition and by an increasingly sophisticated knowl-

edge of the anatomical organization and physiology of the brain, investigators have begun to tackle the problem of emotion.

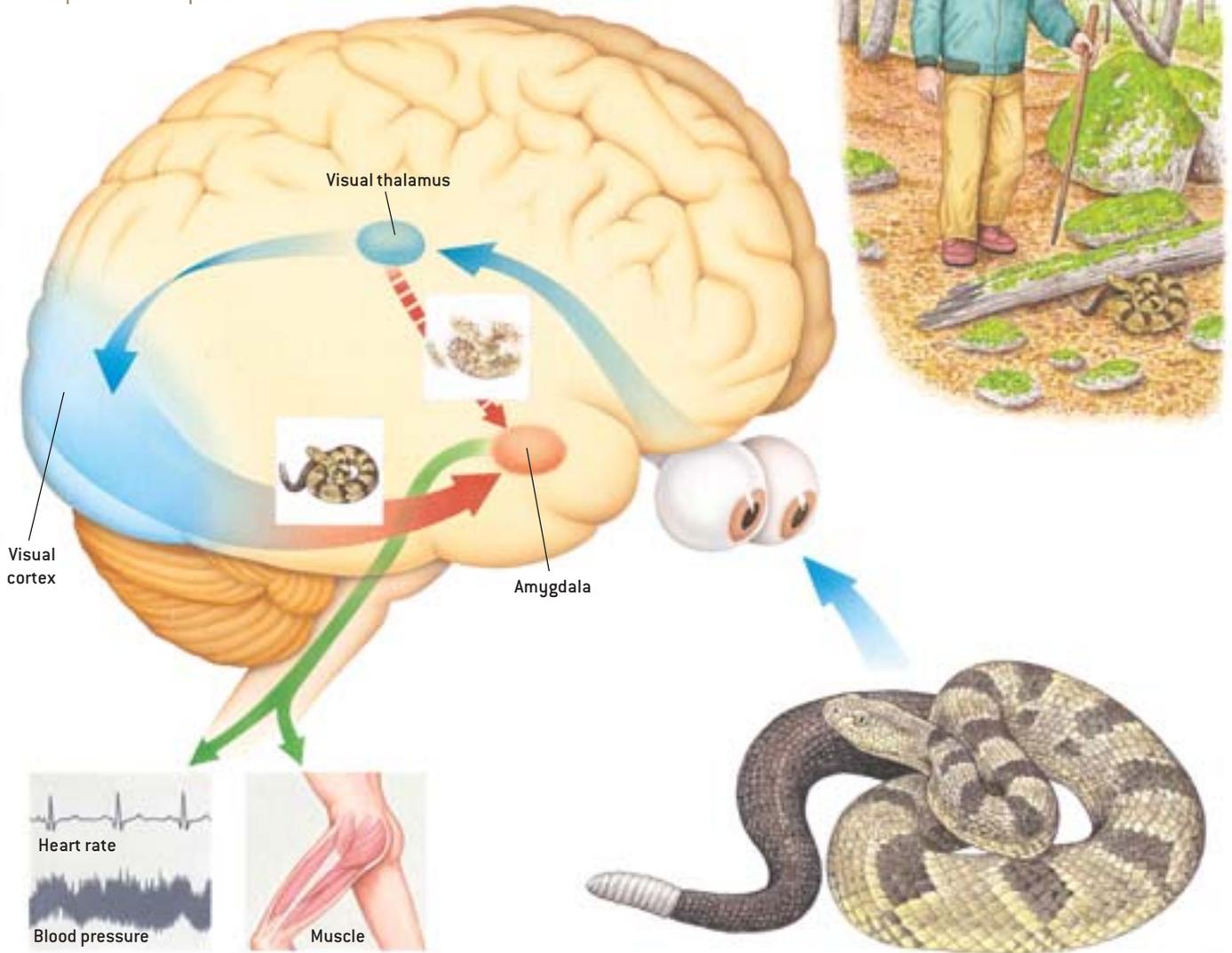
One quite rewarding area of research has been the inquiry into the relation between memory and emotion. Much of this examination has involved studies of one particular emotion—fear—and the manner in which specific events or stimuli come, through individual learning experiences, to evoke this state. Scientists, myself included, have been able to deter-

mine the way in which the brain shapes how we form memories about this basic, but significant, emotional event. We call this process “emotional memory.”

By uncovering the neural pathways through which a situation causes a creature to learn about fear, we hope to elucidate the general mechanisms of this form of memory. Because many human mental disorders—including anxiety, phobia, post-traumatic stress syndrome and panic attack—involve malfunctions

THE FEAR RESPONSE

CORTICAL AND SUBCORTICAL PATHWAYS in the brain—generalized from our knowledge of the auditory system—may bring about a fearful response to a snake on a hiker's path. Visual stimuli are first processed by the thalamus, which passes rough, almost archetypal information directly to the amygdala [red]. This quick transmission allows the brain to respond to the possible danger [green]. Meanwhile the visual cortex also receives information from the thalamus and, with more perceptual sophistication and more time, determines that there is a snake on the path [blue]. This information is relayed to the amygdala, causing heart rate and blood pressure to increase and muscles to contract. If, however, the cortex had determined that the object was not a snake, the message to the amygdala would quell the fear response.



in the brain's ability to control fear, studies of the neural basis of this emotion may help us further understand and treat these disturbances.

Most of our knowledge about how the brain links memory and emotion has been gleaned through the study of so-called classical fear conditioning. In this process the subject, usually a rat, hears a noise or sees a flashing light that is paired with a brief, mild electric shock to its feet. After a few such experiences, the rat re-

sponds automatically to the sound or light, even in the absence of the shock. Its reactions are typical to any threatening situation: the animal freezes, its blood pressure and heart rate increase, and it startles easily. In the language of such experiments, the noise or flash is a conditioned stimulus, the foot shock is an unconditioned stimulus, and the rat's reaction is a conditioned response, which consists of readily measured behavioral and physiological changes.

Conditioning of this kind happens quickly in rats—indeed, it takes place as rapidly as it does in humans. A single pairing of the shock to the sound or sight can bring on the conditioned effect. Once established, the fearful reaction is relatively permanent. If the noise or light is administered many times without an accompanying electric shock, the rat's response diminishes. This change is called extinction. But considerable evidence suggests that this behavioral alteration is the

result of the brain's controlling the fear response rather than the elimination of the emotional memory. For example, an apparently extinguished fear response can recover spontaneously or can be reinstated by an irrelevant stressful experience. Similarly, stress can cause the reappearance of phobias in people who have been successfully treated. This resurrection demonstrates that the emotional memory underlying the phobia was rendered dormant rather than erased by treatment.

Fear and Emotional Memory

FEAR CONDITIONING has proved an ideal starting point for studies of emotional memory for several reasons. First, it occurs in nearly every animal group in which it has been examined: fruit flies,

dations of fear elicited by such stimuli.

My work has focused on the cerebral roots of learning fear, specifically fear that has been induced in the rat by associating sounds with foot shock. As do most other investigators in the field, I assume that fear conditioning occurs because the shock modifies the way in which neurons in certain important regions of the brain interpret the sound stimulus. These critical neurons are thought to be located in the neural pathway through which the sound elicits the conditioned response.

A decade ago, researchers in my laboratory and others identified major components of this system. Our study began at Cornell University Medical College, where I worked some years ago, when my colleagues and I asked a simple question:

ability to conditioning. This discovery suggested that a sound stimulus is transmitted through the auditory system to the level of the auditory thalamus but that it does not have to reach the cortex for fear conditioning to occur.

This possibility was somewhat puzzling. We knew that the primary nerve fibers that carry signals from the auditory thalamus extend to the auditory cortex. So David A. Ruggiero, Donald J. Reis and I looked again and found that cells in some regions of the auditory thalamus also give rise to fibers that reach several subcortical locations. Could these neural projections be the connections through which the stimulus elicits the response we identify with fear? We tested this hypothesis by making lesions in each one of the

These findings seemed to place us on the threshold of **BEING ABLE TO MAP** the entire stimulus response pathway.

snails, birds, lizards, fish, rabbits, rats, monkeys and people. Although no one claims that the mechanisms are precisely the same in all these creatures, it seems clear from studies to date that the pathways are very similar in mammals and possibly in all vertebrates. We therefore are confident in believing that many of the findings in animals apply to humans. In addition, the kinds of stimuli most commonly used in this type of conditioning are not signals that rats—or humans, for that matter—encounter in their daily lives. The novelty and irrelevance of these lights and sounds help to ensure that the animals have not already developed strong emotional reactions to them. So researchers are clearly observing learning and memory at work.

At the same time, such cues do not require complicated cognitive processing from the brain. Consequently, the stimuli permit us to study emotional mechanisms relatively directly. Finally, our extensive knowledge of the neural pathways involved in processing acoustic and visual information serves as an excellent starting point for examining the neurological foun-

Is the auditory cortex required for auditory fear conditioning?

In the auditory pathway, as in other sensory systems, the cortex is the highest level of processing; it is the culmination of a sequence of neural steps that starts with the peripheral sensory receptors, located, in this case, in the ear. If lesions in (or surgical removal of) parts of the auditory cortex interfered with fear conditioning, we could conclude that the region is indeed necessary for this activity. We could also deduce that the next step in the conditioning pathway would be an output from the auditory cortex. But our lesion experiments in rats confirmed what a series of other studies had already suggested: the auditory cortex is not needed in order to learn many things about simple acoustic stimuli.

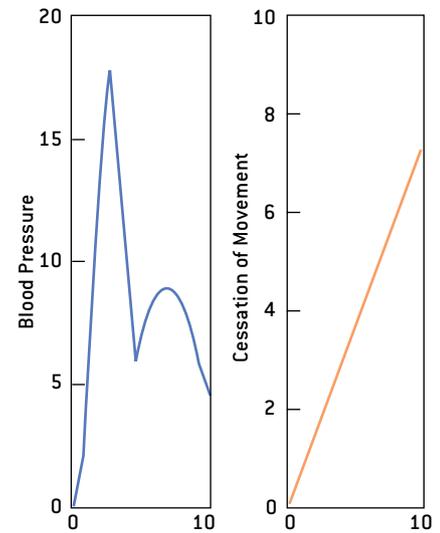
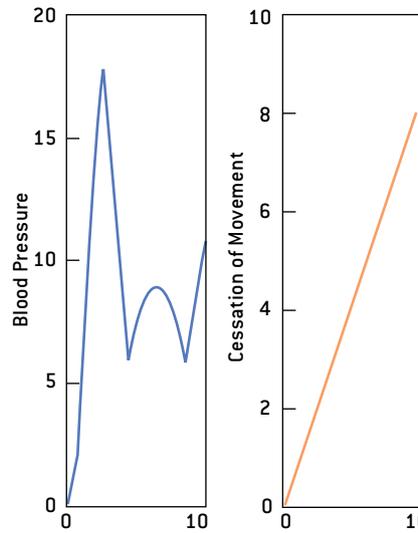
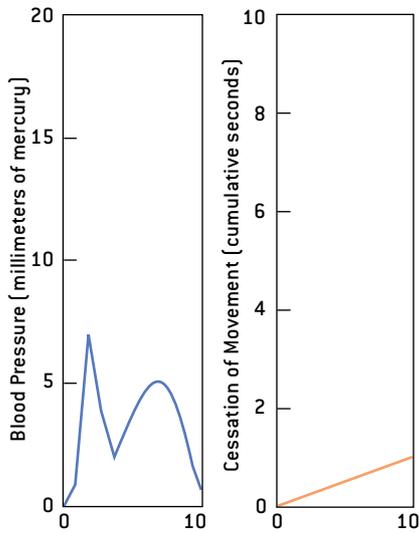
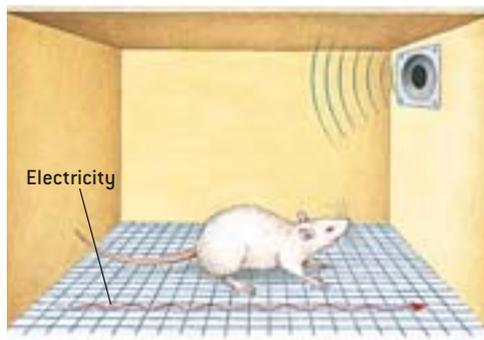
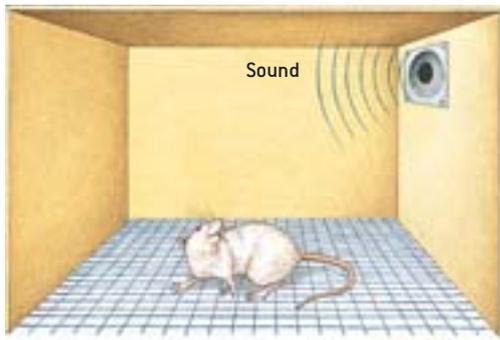
We then went on to make lesions in the auditory thalamus and auditory midbrain, sites lying below the auditory cortex. Both these areas process auditory signals: the midbrain provides the major input to the thalamus; the thalamus supplies the major input to the cortex. Lesions in both regions eliminated the rat's suscep-

subcortical regions with which these fibers connect. The damage had an effect in only one area: the amygdala.

Filling in the Picture

THAT OBSERVATION suddenly created a place for our findings in an already accepted picture of emotional processing. For a long time, the amygdala has been considered an important brain region in various forms of emotional behavior. In 1979 Bruce S. Kapp and his colleagues at the University of Vermont reported that lesions in the amygdala's central nucleus interfered with a rabbit's conditioned heart rate response once the animal had been given a shock paired with a sound. The central nucleus connects with areas in the brain stem involved in the control of heart rate, respiration and vasodilation. Kapp's work suggested that the central nucleus was a crucial part of the system through which autonomic conditioned responses are expressed.

In a similar vein, we found that lesions of this nucleus prevented a rat's blood pressure from rising and limited its ability to freeze in the presence of a fear-caus-



Time (seconds)

CLASSICAL FEAR CONDITIONING can be induced by pairing a sound and a mild electric shock to the foot of a rat. In one set of experiments, the rat hears a sound (left), which has little effect on the animal's blood pressure or patterns of movement. Next, the rat hears the same sound, coupled with a

foot shock (center). After several such pairings, the rat's blood pressure rises at the same time that the animal freezes for an extended period when it hears the sound. The rat has been fear-conditioned (right): sound alone achieves the same physiological changes as did sound and shock together.

ing stimulus. We also demonstrated, in turn, that lesions in areas connected to the central nucleus eliminated one of the two responses. Michael Davis and his associates at Yale University determined that lesions of the central nucleus, as well as lesions of another brain stem area to which the central nucleus projects, diminished yet another conditioned response: the increased startle reaction that occurs when an animal is afraid.

The findings from various laboratories studying different species and measuring fear in different ways all implicated the central nucleus as a pivotal component of fear-conditioning circuitry. It provides connections to the various brain stem areas involved in the control of a spectrum of responses.

Despite our deeper understanding of this site in the amygdala, many details of

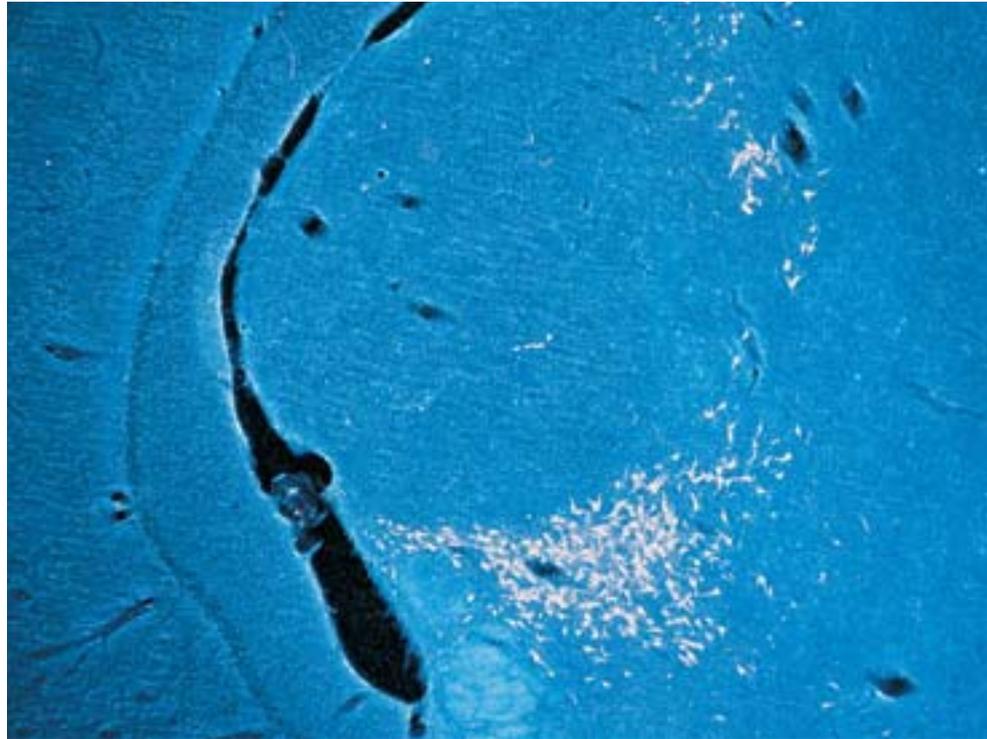
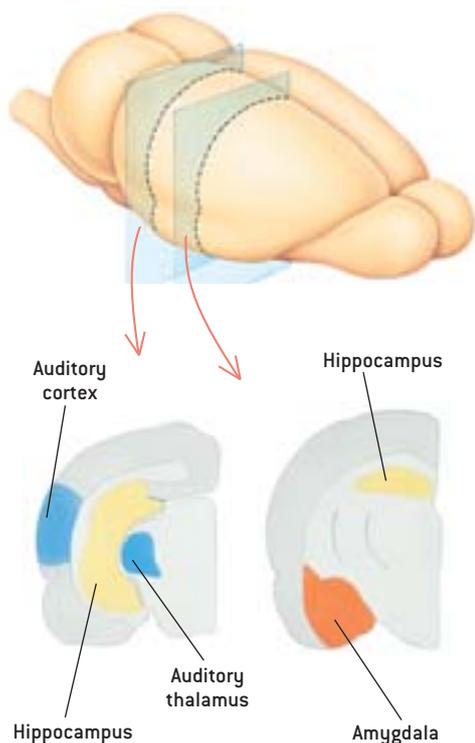
the pathway remained hidden. Does sound, for example, reach the central nucleus directly from the auditory thalamus? We found that it does not. The central nucleus receives projections from thalamic areas next to, but not in, the auditory part of the thalamus; an entirely different area of the amygdala, the lateral nucleus, receives inputs from the auditory thalamus. Lesions of the lateral nucleus prevented fear conditioning.

Because this site gets information directly from the sensory system, we now consider it the sensory interface of the amygdala in fear conditioning. In contrast, the central nucleus appears to interface with the systems that control responses.

These findings seemed to place us on the threshold of being able to map the entire stimulus response pathway. But we still did not know how information re-

ceived by the lateral nucleus arrived at the central nucleus. Earlier studies had suggested that the lateral nucleus projects directly to the central nucleus, but the connections were fairly sparse. Working with monkeys, David Amaral and Asla Pitkanen of the Salk Institute for Biological Studies in San Diego demonstrated that the lateral nucleus extends directly to an adjacent site, called the basal or basolateral nucleus, which, in turn, projects to the central nucleus.

Collaborating with Lisa Stefanacci and other members of the Salk team, Claudia R. Farb and C. Genevieve Go in my laboratory at New York University found the same connections in the rat. We then showed that these connections form synaptic contacts—communicating directly, neuron to neuron. Such contacts indicate that information reaching the lat-



ANATOMY OF EMOTION includes several brain regions. Shown here in the rat, parts of the amygdala, the thalamus and the cortex interact to create

memories about fearful experiences, associated here with sound. Work in the past decade has located where fear is learned and remembered: certain parts

eral nucleus can influence the central nucleus via the basolateral nucleus. The lateral nucleus can also influence the central nucleus by way of the accessory basal or basomedial nucleus. Clearly, ample opportunities exist for the lateral nucleus to communicate with the central nucleus once a stimulus has been received.

The emotional significance of such a stimulus is determined by the sound itself and by the environment in which it occurs. Rats must therefore learn not only that a sound or visual cue is dangerous but under what conditions it is so. Russell G. Phillips and I examined the response of rats to the chamber, or context, in which they had been conditioned. We found that lesions of the amygdala interfered with the animals' response to both the tone and the chamber. But lesions of the

hippocampus—a brain region involved in declarative memor—interfered only with response to the chamber, not the tone. Declarative memory involves explicit, consciously accessible information, as well as spatial memory. At about the same time, Michael S. Fanselow and Jean-sok J. Kim of the University of California at Los Angeles discovered that hippocampal lesions made after fear conditioning had taken place also prevented the expression of responses to the surroundings.

Emotional Significance

THESE FINDINGS were consistent with the generally accepted view that the hippocampus plays an important role in processing complex information, such as details about the spatial environment where activity is taking place. Phillips and I also

demonstrated that the subiculum, a region of the hippocampus that projects to other areas of the brain, communicated with the lateral nucleus of the amygdala. This connection suggests that contextual information may acquire emotional significance in the same way that other events do—via transmission to the lateral nucleus.

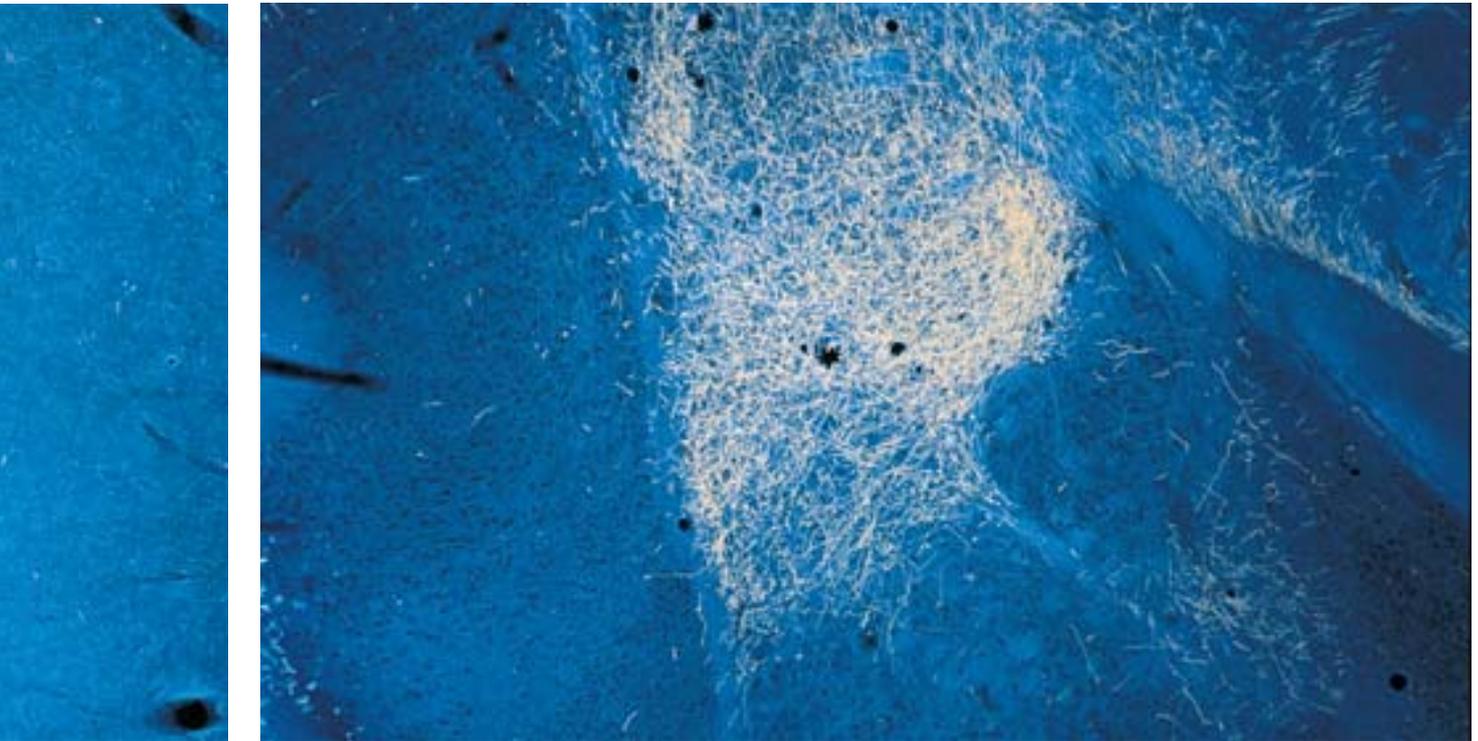
Although our experiments had identified a subcortical sensory pathway that gave rise to fear conditioning, we did not dismiss the importance of the cortex. The interaction of subcortical and cortical mechanisms in emotion remains a hotly debated topic. Some researchers believe cognition is a vital precursor to emotional experience; others think that cognition—which is presumably a cortical function—is necessary to initiate emotion or that emotional processing is a type of cognitive processing. Still others question whether cognition is necessary for emotional processing.

It became apparent to us that the auditory cortex is involved in, though not crucial to, establishing the fear response, at least when simple auditory stimuli are applied. Norman M. Weinberger and his col-

THE AUTHOR

JOSEPH E. LeDOUX is the Henry and Lucy Moses Professor of Science at New York University. His research is focused on brain mechanisms of emotion and memory. He is the recipient of two National Institute of Mental Health distinctions: a Merit Award and a Research Scientist Development Award. LeDoux's 1996 book, *The Emotional Brain* (Simon & Schuster), was an elaboration of the basic ideas in this *Scientific American* article. His new book, *Synaptic Self* (Viking Penguin), presents a theory of how broad networks in the brain, especially those involved in emotion and memory, are key to understanding the neural basis of personality.

ROBERTO OSTI (illustrations); ANDREW LEONARD/APL Microscopic (photographs)



of the thalamus (pink, left) communicate with areas in the amygdala (yellow, right) that process the fear-causing sound stimuli. These neural mechanisms

are thought to be similar in humans, so the study of emotional memory in rodents may illuminate aspects of human fear disorders.

leagues at the University of California at Irvine performed elegant studies showing that neurons in the auditory cortex undergo specific physiological changes in their reaction to sounds as a result of conditioning. This finding indicates that the cortex is establishing its own record of the event.

Experiments by Lizabeth M. Romanski in my laboratory determined that in the absence of the auditory cortex, rats can learn to respond fearfully to a single tone. If, however, projections from the thalamus to the amygdala are removed, projections from the thalamus to the cortex and then to the amygdala are sufficient. Romanski went on to establish that the lateral nucleus can receive input from both the thalamus and the cortex. Her work with rats complements earlier research in primates.

Molecular Mechanisms

ONCE WE HAD a clear understanding of the mechanism through which fear conditioning is learned, we tried to find out how emotional memories are established and stored on a molecular level. Farb and I showed that the excitatory

amino acid transmitter glutamate is present in the thalamic cells that reach the lateral nucleus. Chiye J. Aoki and I showed that it is also present at synapses in the lateral nucleus. Because glutamate transmission is implicated in memory formation, we seemed to be on the right track.

Glutamate has been observed in a process called long-term potentiation, or LTP, that has emerged as a model for the creation of memories. This process, which is most frequently studied in the hippocampus, involves a change in the efficiency of synaptic transmission along a neural pathway—in other words, signals travel more readily along this pathway once LTP has taken place. The mechanism seems to involve glutamate transmission and a class of postsynaptic excitatory amino acid receptors known as NMDA (for *N*-methyl-D-aspartate) receptors.

Various studies have found LTP in the fear-conditioning pathway. Marie-Christine Clugnet and I noted that LTP could be induced in the thalamo-amygdala pathway. Thomas H. Brown and Paul Chapman and their colleagues at

Yale discovered LTP in a cortical projection to the amygdala. Other researchers, including Davis and Fanselow, were able to block fear conditioning by blocking NMDA receptors in the amygdala. And Michael T. Rogan in my laboratory found that the processing of sounds by the thalamo-amygdala pathway is amplified after LTP has been induced. The fact that LTP can be demonstrated in a conditioning pathway offers new hope for understanding how LTP might relate to emotional memory.

Studies by Fabio Bordi, also in my laboratory, have suggested hypotheses about what is going on in the neurons of the lateral nucleus during learning. Bordi monitored the electrical state of individual neurons in this area when a rat was listening to the sound and receiving the shock. He and Romanski found that essentially every cell responding to the auditory stimuli also responded to the shock. The basic ingredient of conditioning is thus present in the lateral nucleus.

Bordi was able to divide the acoustically stimulated cells into two classes: habituating and consistently responsive.

Habituating cells eventually stopped responding to the repeated sound, suggesting that they might serve to detect any sound that was unusual or different. They could permit the amygdala to ignore a stimulus once it became familiar. Sound and shock pairing at these cells might reduce habituation, thereby allowing the cells to respond to, rather

er their threshold, increasing the cells' sensitivity to the same stimulus. Consistently responsive cells were also broadly tuned. The joining of a sound and a shock could make the cells responsive to a narrower frequency range or could shift the tuning toward the frequency of the stimulus. Weinberger has shown that cells in the auditory system do alter their tuning

we can hope only to keep them under wraps. Studies by Maria A. Morgan in my laboratory have illuminated how the brain regulates emotional expressions. Morgan showed that when part of the prefrontal cortex is damaged, emotional memory is very hard to extinguish. This discovery indicates that the prefrontal areas—possibly by way of the amygdala—

The apparent permanence of these memories raises an important **CLINICAL QUESTION**: Can emotional memory be eliminated?

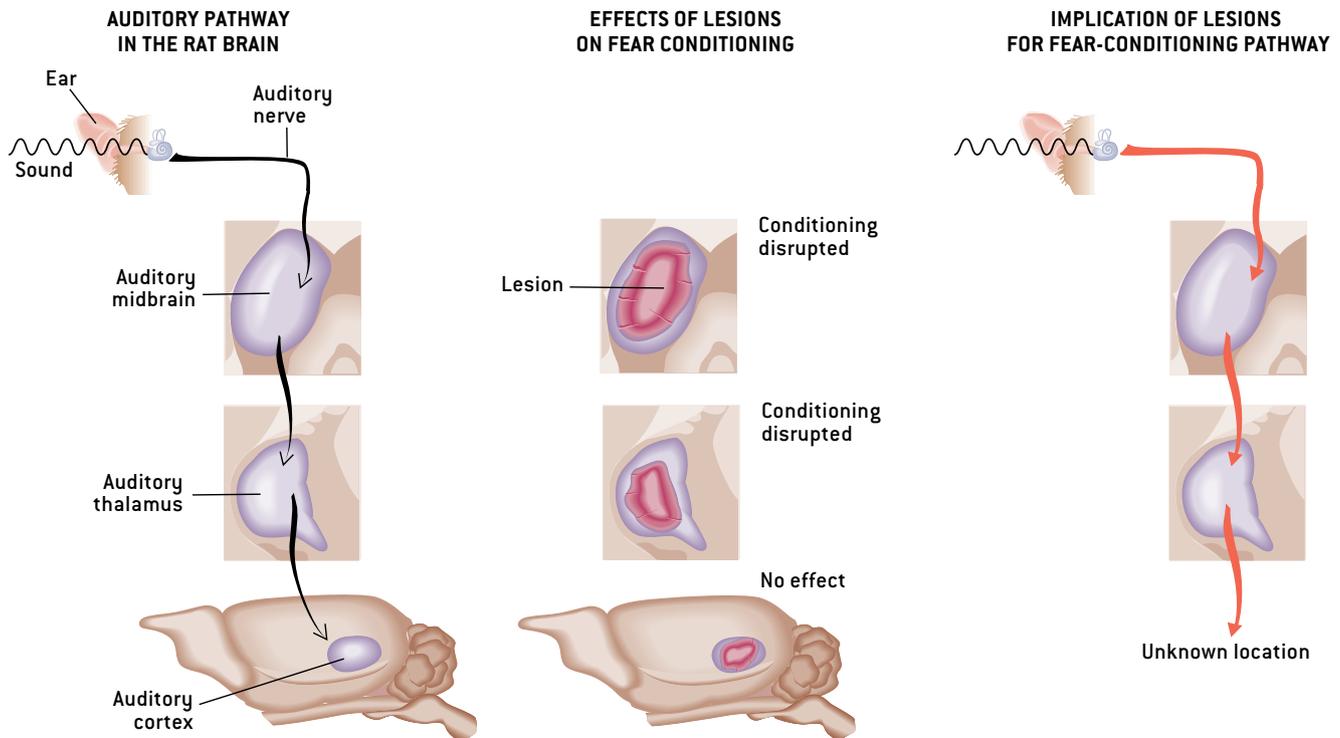
than ignore, significant stimuli.

The consistently responsive cells had high-intensity thresholds: only loud sounds could activate them. That finding is interesting because of the role volume plays in judging distance. Nearby sounds are presumably more dangerous than those that are far away. Sound coupled with shock might act on these cells to low-

to approximate the conditioned stimulus. Bordi and I detected this effect in lateral nucleus cells as well.

The apparent permanence of these memories raises an important clinical question: Can emotional learning be eliminated, and, if not, how can it be toned down? It appears to be quite difficult to get rid of emotional memories, and at best

normally control expression of emotional memory and prevent emotional responses once they are no longer useful. A similar conclusion was proposed by Edmund T. Rolls and his colleagues at the University of Oxford during primate studies. The researchers studied the electrical activity of neurons in the frontal cortex of the animals.



BRAIN LESIONS have been crucial to pinpointing the sites involved in experiencing and learning about fear. When a sound is processed by the rat brain, it follows a pathway from ear to midbrain to thalamus to cortex (left). Lesions can be made in various sites in the auditory pathway to determine

which areas are necessary for fear conditioning (center). Only damage to the cortex does not disrupt the fear response, which suggests that some other areas of the brain receive the output of the thalamus and are involved in establishing memories about experiences that stimulate fear (right).

CREATION OF MEMORY has been linked to a process called long-term potentiation, or LTP, in which the neurotransmitter glutamate and its NMDA (for *N*-methyl-D-aspartate) receptors bring about strengthened neural transmission. Once LTP is established, the same neural signals produce larger responses (*right*). Emotional memories may also involve LTP in the amygdala. Glutamate (*red circle in top micrograph*) and NMDA receptors (*red circle in bottom micrograph*) have been found in the region of the amygdala where fear conditioning takes place.

Functional variation in the pathway between this region of the cortex and the amygdala may make it more difficult for some people to change their emotional behavior. Davis and his colleagues found that blocking NMDA receptors in the amygdala interferes with extinction, which hints that it is an active learning process. Such learning could be situated in connections between the prefrontal cortex and the amygdala. More experiments should disclose the answer.

Placing a basic emotional memory process in the amygdalic pathway yields obvious benefits. The amygdala is a critical site of learning because of its central location between input and output stations. Each route that leads to the amygdala—sensory thalamus, sensory cortex and hippocampus—delivers unique information. Pathways originating in the sensory thalamus provide only a crude perception of the external world, but because they involve only one neural link, they are quite fast. In contrast, pathways from the cortex offer detailed and accurate representations, allowing us to recognize an object by sight or sound. But these pathways, which run from the thalamus to the sensory cortex to the amygdala, involve several neural links. And each link in the chain adds time.

Conserving time may be the reason there are two routes—one cortical and one subcortical—for emotional learning. Animals, and humans, need a quick-and-dirty reaction mechanism. The thalamus activates the amygdala at about the same time as it activates the cortex. The arrangement may enable emotional responses to begin in the amygdala before we completely recognize what it is we are reacting to or what we are feeling.

The thalamic pathway may be particularly useful in situations requiring a rapid response. Failing to respond to danger is more costly than responding inappropriately to a benign stimulus. For instance, the sound of rustling leaves is

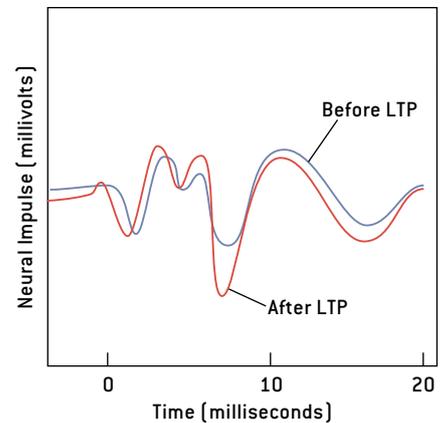
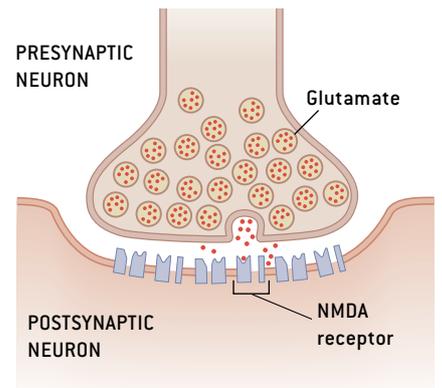
enough to alert us when we are walking in the woods without our first having to identify what is causing the sound. Similarly, the sight of a slender curved shape lying flat on the path ahead of us is sufficient to elicit defensive fear responses [see *illustration on page 63*]. We do not need to go through a detailed analysis of whether or not what we are seeing is a snake. Nor do we need to identify the snake as a reptile or note that its skin can be used to make belts and boots. All these details are irrelevant and, in fact, detrimental to an efficient, speedy and potentially lifesaving reaction. The brain simply needs to be able to store primitive cues and detect them. Later, coordination of this basic information with the cortex permits verification (yes, this is a snake) or brings the response (screaming, sprinting) to a stop.

Storing Emotional Memory

ALTHOUGH THE AMYGDALA stores primitive information, we should not consider it the only learning center. The establishment of memories is a function of the entire network, not just of one component. The amygdala is certainly crucial, but we must not lose sight of the fact that its functions exist only by virtue of the system to which it belongs.

Memory is generally thought to be the process by which we bring back to mind some earlier conscious experience. The original learning and the remembering, in this case, are both conscious events. Researchers have determined that declarative memory is mediated by the hippocampus and the cortex. But removal of the hippocampus has little effect on fear conditioning—except conditioning to context.

In contrast, emotional learning that comes through fear conditioning is not declarative learning. Rather it is mediated by a different system, which may operate independently of conscious awareness. Emotional information may be



stored within declarative memory, but it is kept there as a cold declarative fact. For example, if a person is injured in an auto accident in which the horn gets stuck, he or she may later react when hearing the blare of car horns. The person may remember the details of the accident, such as where and when it occurred and who was involved. These are declarative memories that are dependent on the hippocampus. The individual may also become tense, anxious and depressed as the emotional memory is reactivated through the

their activities are joined seamlessly in our conscious experience. That does not mean that we have direct conscious access to our emotional memory; it means instead that we have access to the consequences—such as the way we behave or the way our bodies feel. These consequences combine with current declarative memory to form a new declarative memory. Emotion is not just unconscious memory: it exerts a powerful influence on declarative memory and other thought processes. As James L. McGaugh and

The distinction between declarative memory and emotional memory is an important one. W. J. Jacobs of the University of British Columbia and Lynn Nadel of the University of Arizona have argued that we are unable to remember traumatic early-life events because the hippocampus has not yet matured enough to consciously form accessible memories. The emotional memory system, which may develop earlier, clearly forms and stores its unconscious memories of these events. For this reason, the trauma may affect

Emotion is not just unconscious memory: it exerts a **POWERFUL INFLUENCE** on declarative memory and other **THOUGHT PROCESSES**.

amygdalic system. The declarative system has stored the emotional content of the experience, but it has done so as a fact.

Emotional and declarative memories are stored and retrieved in parallel, and

his colleagues at the University of California at Irvine have convincingly shown, the amygdala plays an essential part in modulating the storage and strength of memories.

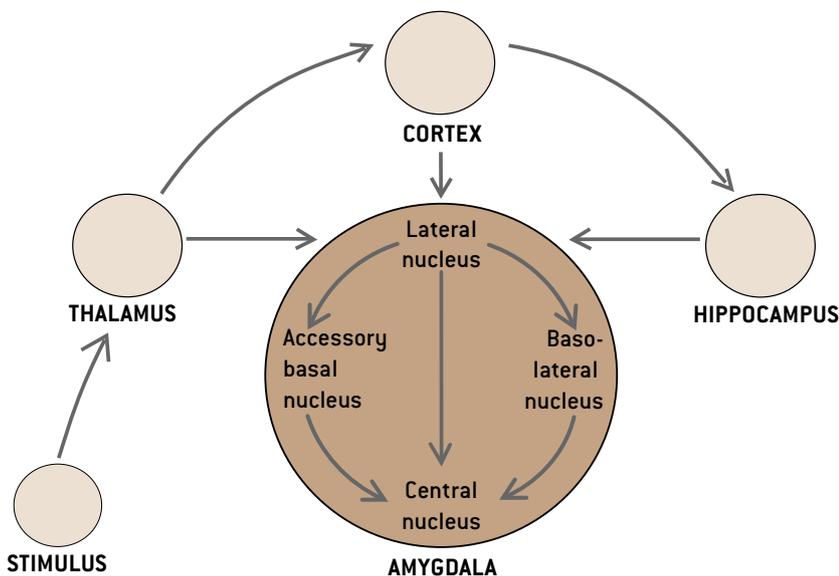
mental and behavioral functions in later life through processes that remain inaccessible to consciousness.

Because pairing a tone and a shock can bring about conditioned responses in animals throughout the phyla, it is clear that fear conditioning cannot be dependent on consciousness. Fruit flies and snails, for example, are not creatures known for their conscious mental processes. My way of interpreting this phenomenon is to consider fear a subjective state of awareness brought about when brain systems react to danger. Only if the organism possesses a sufficiently advanced neural mechanism does conscious fear accompany bodily response. This is not to say that only humans experience fear but, rather, that consciousness is a prerequisite to subjective emotional states.

Thus, emotions or feelings are conscious products of unconscious processes. It is crucial to remember that the subjective experiences we call feelings are not the primary business of the system that generates them. Emotional experiences are the result of triggering systems of behavioral adaptation that have been preserved by evolution. Subjective experience of any variety is challenging turf for scientists. We have, however, gained understanding about the neural system that underlies fear responses. This same system may give rise to subjective feelings of fear.

Structure of the Amygdala

THE AMYGDALA plays an important role in emotional behavior. Experiments in rodents have elucidated the structures of various regions of the amygdala and their role in learning about and remembering fear. The lateral nucleus receives inputs from sensory regions of the brain and transmits these signals to the basal, the accessory basal and the central nuclei. The central nucleus connects to the brain stem, bringing about physiological changes. —J.É.LéD.



If so, studies of the neural control of emotional responses may also hold the key to understanding subjective emotion.

Postscript

MUCH HAS HAPPENED in the study of emotion, memory and the brain since this article was written in 1994, some of which I will summarize.

Additional studies have extended our understanding of the anatomical organization of the amygdala. This work affirms the importance of the lateral nucleus as the gateway into the amygdala and further suggests that information processing occurs at the level of subregions with the lateral nucleus. The importance of the subregional organization of the lateral amygdala is also emphasized by studies in which the activity of neurons has been recorded in response to a tone conditioned stimulus (CS) before and after fear conditioning. The results showed that the CS-elicited activity in the dorsal subnucleus of the lateral amygdala increases dramatically through pairing of the CS with the foot-shock unconditioned stimulus and that different populations of cells in this area are involved in initial learning and in memory storage. Because the cellular activity is learned before fear is expressed, the cellular changes are a plausible part of the explanation of how fear behavior is learned and remembered.

The molecular mechanisms underlying fear learning and memory have been pursued through studies of LTP in brain slices of the lateral amygdala. This work suggests that the induction of LTP can take place by either of two mechanisms. Both of these mechanisms require the influx of calcium into lateral amygdala cells that are postsynaptic—that is, on the receiving end of the signal—to the sensory input pathways. One form of LTP involves calcium entry through voltage-gated calcium channels; the other involves NMDA receptors. Both of these are cellular pathways that, when opened, allow calcium ions to enter the cell. Other studies showed that in live animals, fear conditioning, like LTP, depends on NMDA receptors and the voltage-gated calcium channels. Also, fear conditioning

alters neural activity in the lateral amygdala in a manner that closely resembles what happens when LTP is induced in this region, suggesting that LTP is a plausible model of learning.

The elevation of calcium that occurs in postsynaptic neurons during LTP and fear learning triggers a cascade of other chemical processes that leads to a sustained state of enhanced synaptic efficacy between the pre- and postsynaptic neurons. This is a cellular definition of memory. For fear conditioning and many other forms of learning in various species, elevated calcium activates catalytic enzymes called protein kinases (MAP kinase and protein kinase A, among others). These kinases then travel to the cell nucleus, where they activate gene transcription factors (such as CREB), which initiate the synthesis of RNA and proteins. The proteins then travel back to the previously active synapses and stabilize the connection. Because similar molecular steps are involved in different forms of memory in different species, it seems that the uniqueness of different kinds of memory has less to do with the underlying molecules than with the circuits in which they act.

Protein synthesis is not only involved in the initial formation of the memory of an aversive experience but is also called into play when these memories are recalled, which suggests that each time such a memory is activated it has to be restored (reconsolidated) by new protein synthesis. This may be a process by which memories are updated in light of experiences that occurred after the initial memory.

Stimulated by progress in rodent studies, researchers have begun to examine fear processing in the human brain.



MEMORIES of disturbing experiences form deep within our brains.

Studies of patients with damage to the amygdala have shown that this region is required for fear conditioning and other aspects of emotional memory. And functional imaging has shown that the human amygdala is activated during fear conditioning, even under conditions where the CS is prevented from entering consciousness, showing that fear memories can be established unconsciously.

Emotions and memory contribute significantly to our personality, our self. With so much progress made in understanding the brain mechanisms of emotion and memory, we can hope that new research will turn more toward questions about how these factors interact in the shaping of personality, an important topic that neuroscientists have not considered in much detail so far. SA

MORE TO EXPLORE

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