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Role of the Amygdala in Decision-Making

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ABSTRACT: The somatic marker hypothesis proposes that both the amygdala and the orbitofrontal cortex are parts of a neural circuit critical for judgment and decision-making. Although both structures couple exteroceptive sensory information with interoceptive information concerning somatic/emotional states, they do so at different levels, thus making different contributions to the process. We define “*primary inducers*” as stimuli that unconditionally, or through learning (e.g., conditioning and semantic knowledge), can (perceptually or subliminally) produce states that are pleasurable or aversive. Encountering a fear object (e.g., a snake), a stimulus predictive of a snake, or semantic information such as winning or losing a large sum of money are all examples of primary inducers. “*Secondary inducers*” are entities generated by the recall of a personal or hypothetical emotional event or perceiving a primary inducer that generates “thoughts” and “memories” about the inducer, all of which, when they are brought to memory, elicit a somatic state. The episodic memory of encountering a snake, losing a large sum of money, imagining the gain of a large sum of money, or hearing or looking at primary inducers that bring to memory “thoughts” pertaining to an emotional event are all examples of secondary inducers. We present evidence in support of the hypothesis that the amygdala is a critical substrate in the neural system necessary for triggering somatic states from primary inducers. The ventromedial cortex is a critical substrate in the neural system necessary for the triggering of somatic states from secondary inducers. The amygdala system is *a priori* a necessary step for the normal development of the orbitofrontal system for triggering somatic states from secondary inducers. However, once this orbitofrontal system is developed, the induction of somatic states by secondary inducers via the orbitofrontal system is less dependent on the amygdala system. Perhaps the amygdala is equivalent to the hippocampus with regard to emotions, that is, necessary for acquiring new emotional attributes (anterograde emotions), but not for retrieving old emotional attributes (retrograde emotions). Given the numerous lesion and functional neuroimaging studies illustrating the involvement of the amygdala in complex cognitive and behavioral functions, including “social cognition,” we suggest that this involvement is a manifestation of a more fundamental function mediated by the amygdala, which is to couple stimuli/entities with their emotional attributes, that is, the processing of somatic states from primary inducers.

KEYWORDS: amygdala; decision-making; orbitofrontal cortex; emotion; somatic marker; gambling task

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INTRODUCTION

The somatic marker hypothesis proposes that decision-making is a process that depends on emotion and that both the amygdala and the orbitofrontal cortex are parts of a neural circuit critical for judgment and decision-making.¹ Although both structures couple exteroceptive sensory information with interoceptive information concerning somatic/emotional states, they do so at different levels, thus making different contributions to the process.²

Clinical observations have revealed that patients with bilateral damage of the orbitofrontal cortex or the amygdala exercise poor judgment and decision-making in the social realm.¹ We have shown that this decision-making impairment can be demonstrated in the laboratory using neuropsychological tests of decision-making. To measure decision-making, we have used the gambling task, a paradigm designed to simulate real-life decisions in terms of uncertainty, reward, and punishment.³ The task has been described in detail elsewhere.⁴ Briefly, in the gambling task, subjects have to choose between decks of cards that yield high immediate gain but larger future loss, that is, long-term loss, and decks that yield lower immediate gain but smaller future loss, that is, long-term gain. The task consists of four decks of cards named A, B, C, and D. The goal in the task is to maximize profit on a loan of play

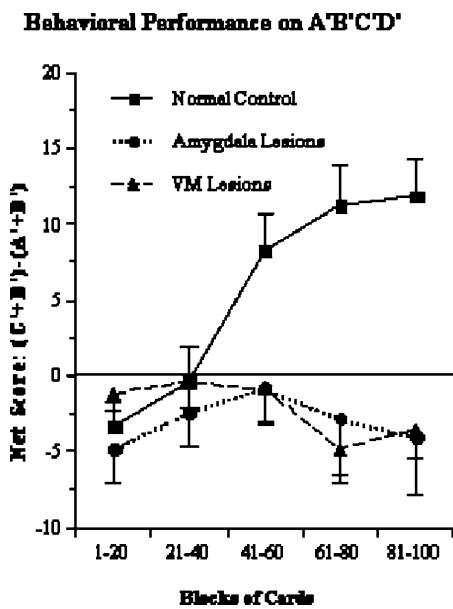


FIGURE 1. Relative to normal control subjects, patients with bilateral ventromedial prefrontal cortex lesions (VM lesions) or bilateral amygdala lesions (amygdala lesions) were impaired in their performance on the gambling task (GT). The figure shows net scores $((C'+D')-(A'+B'))$ of cards selected by each group across different blocks expressed as mean \pm SEM. Positive net scores reflect advantageous performance, whereas negative net scores reflect disadvantageous performance.

money. Subjects are required to make a series of 100 card selections. However, they are not told ahead of time how many card selections they are going to make. Subjects can select one card at a time from any deck they choose, and they are free to switch from any deck to another at any time and as often as they wish. However, the subject's decision to select from one deck versus another is largely influenced by various schedules of immediate reward and future punishment. These schedules are pre-programmed and known to the examiner, but not to the subject. The reward/punishment schedules are set in such a way so that two of the decks of cards (A and B) yield high immediate gain but larger future loss, that is, long-term loss (disadvantageous decks), and two of the decks (C and D) yield lower immediate gain but smaller future loss, that is, long-term gain (advantageous decks).

We investigated the performance of normal control subjects with demographic characteristics matched to a group of patients with bilateral damage to the ventro-medial (VM) prefrontal cortex and a separate group of patients with bilateral damage to the amygdala. Normal subjects avoided the bad/disadvantageous decks (A and B) and preferred the good decks (C and D). By contrast, VM patients as well as amygdala patients did not avoid (i.e., they preferred) the bad decks (A and B) (FIG. 1). From these results we suggested that the VM and amygdala patients' performance profile is comparable to their real-life inability to decide advantageously.²

The more pertinent evidence in support of the somatic marker hypothesis and the reactivation of somatic signals related to prior experience is the failure to generate somatic signals when pondering decisions. This evidence comes from a study in which we added a physiological measure to the gambling task. The goal was to assess somatic state activation while subjects were making decisions during the

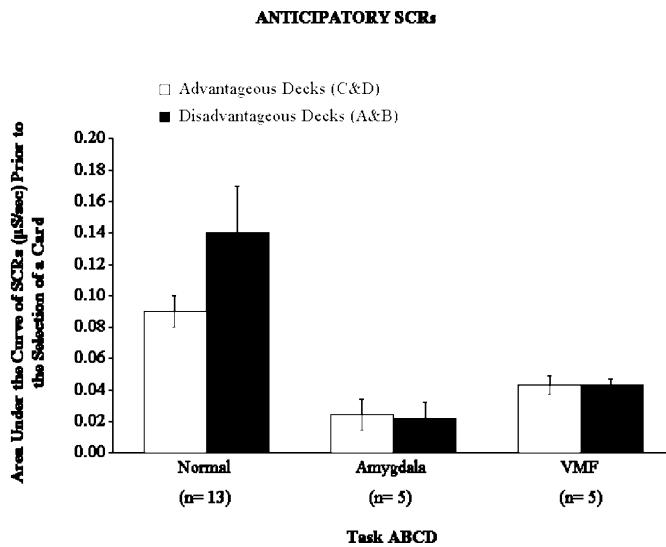


FIGURE 2. Means \pm SEM of anticipatory skin conductance responses (SCRs) (μ S/s) generated by controls, amygdala, or VMF patients in association with the advantageous decks (C and D) versus the disadvantageous decks (A and B).

gambling task. We studied normal subjects, VM patients, and amygdala patients. We had them perform the gambling task while we recorded their skin conductance responses (SCRs).² Normal subjects, as they became experienced with the task, began to generate SCRs prior to the selection of any cards, that is, during the time when they were pondering from which deck to choose. These anticipatory SCRs were more pronounced before picking a card from risky decks A and B when compared to safe decks C and D. The VM patients as well as the amygdala patients entirely failed to generate SCRs before picking a card (FIG. 2). These results provide strong support for the somatic marker hypothesis notion regarding the reactivation of signals related to previous individual contingencies. They suggest that decision-making is guided by emotional signaling (or somatic states) that are generated in anticipation of future events.

HEMISPHERIC ASYMMETRY ASSOCIATED WITH THE DECISION-MAKING IMPAIRMENT

Given the functional asymmetry of the cerebral hemispheres, it is important to determine whether the decision-making deficit associated with damage to the VM prefrontal cortex is caused mostly by unilateral right or left lesions. Unfortunately, this question has been difficult to address with lesion studies, because of the rarity of patients who have unilateral damage on the medial and orbital side of the prefrontal cortex. We collected data from such rare patients with right or left VM lesions.⁵ Performance on neuropsychological tests was normal in all VM patients and without difference between VM patients with left or right lesions. We tested these VM patients on the gambling task, which has been shown to be sensitive to bilateral VM damage. Clinical interviews indicated that left VM patients were not severely impaired in real-life decisions, as reflected, for instance, by their ability to hold gainful employment, and their performance on the gambling task fell in the low normal range. By contrast, the right VM patients were severely impaired in real-life decisions, and their performance on the gambling task was as poor as that of VM patients with bilateral lesions. These results suggest that the type of decision-making behavior measured by the gambling task may depend primarily on VM cortices in the right hemisphere.

We conducted similar experiments in patients with right versus left amygdala damage. It is important to note that in all these unilateral amygdala damage cases, the damage was not restricted to the amygdala, but it included surrounding cortices in the medial temporal lobe. The results were similar to those from VM patients. The performance of left amygdala patients on the gambling task was similar to that of normal controls. By contrast, the right amygdala patients were severely impaired in their performance on the gambling task, similar to patients with bilateral amygdala lesions (FIG. 3).

These results suggest that the type of decision-making behavior measured by the gambling task may depend primarily on the right amygdala. However, we caution that the results in relation to the right versus left amygdala lesions are preliminary. The number of subjects in each group is small. Furthermore, the ecological validity of a decision-making deficit associated with right as opposed to left amygdala damage has not been tested yet, that is, we are not clear whether right amygdala patients

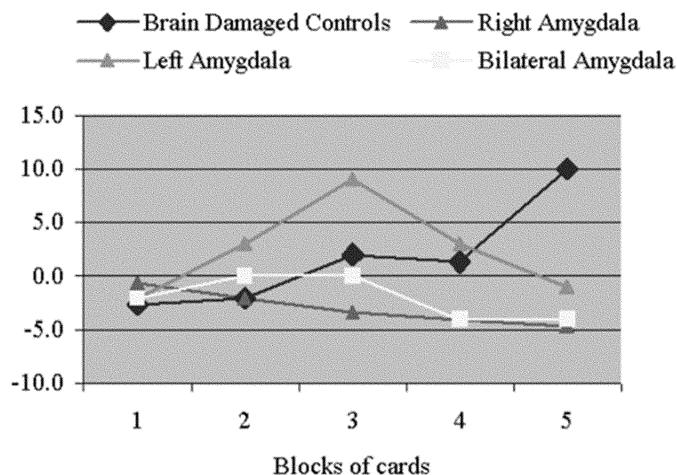


FIGURE 3. Net scores $((C'+D')-(A'+B'))$ of cards selected by each group across different blocks expressed as mean \pm SEM. Positive net scores reflect advantageous performance, whereas negative net scores reflect disadvantageous performance.

have poorer decision-making and social behavior functioning than do left amygdala patients.

THE ORBITOFRONTAL CORTEX AND AMYGDALA PLAY DIFFERENT ROLES IN EMOTIONAL PROCESSING

Given the importance of both the VM cortex and the amygdala in decision-making and somatic state activation, the important question is: what are the different roles, if any, that the VM cortex and the amygdala play in emotional processing, somatic state activation, and decision-making? Several authors have addressed precisely this question in animal studies (e.g., see Refs. 6–10). We will shed light on this issue based on human studies.

Somatic states can be induced from (1) primary inducers and (2) secondary inducers.¹¹ *Primary inducers* are stimuli/entities that are innate or learned to be pleasurable or aversive. Once they are present in the immediate environment, they automatically and obligatorily elicit a somatic response. Examples of primary inducers include the encounter of a fear object (e.g., a snake) or a stimulus predictive of a snake. Semantic information such as winning or losing a large sum of money, which instantly, automatically, and obligatorily elicits a somatic response, is also an example of primary inducer. *Secondary inducers* are entities generated by the recall of a personal or hypothetical emotional event, that is, “thoughts” and “memories” about the primary inducer that, when they are brought to working memory, elicit a somatic state. Examples of secondary inducers include the emotional response elicited by the memory of encountering a snake, the memory of losing a large sum of money, or, for example, the imagination of gaining or losing a large sum of money.

Role of the Amygdala

Our evidence suggests that the amygdala is a critical substrate in the neural system necessary for the processing of primary inducers. It couples the features of primary inducers, which can be processed subliminally (e.g., via the thalamus) or explicitly (e.g., via early sensory and high-order association cortices), with the somatic state associated with the inducer. This somatic state is evoked via effector structures such as the hypothalamus, basal forebrain, ventral striatum, periacqueductal gray (PAG), and other brain-stem nuclei. Thus, the induction of somatic states from primary inducers requires the integrity of primary and high-order association cortices and/or thalamus, of effector structures and of the amygdala, which serves as a convergence-divergence zone that couples inducer and effector.

Several lines of studies support this notion. Monkeys with mesial temporal lesions that include the amygdala have an increased tendency to approach "emotionally competent" stimuli, such as, snakes,^{12–14} suggesting that the object of fear can no longer evoke a state of fear. Animal studies also showed that conditioning is highly dependent on the integrity of the amygdala system.^{15–22} In humans, studies have shown that amygdala lesions reduce, but do not block, autonomic reactivity to an aversive loud sound² and block the conditioned autonomic response to the same aversive loud sound.^{23,24} Amygdala lesions in humans have also been shown to reduce autonomic reactivity to a variety of stressful stimuli.^{25,26} The results of functional neuroimaging studies are also consistent with lesion studies. Activation of the amygdala has been shown in classical conditioning experiments.²⁷

Amygdala lesions block the emotional response not only to unconditioned or conditioned emotional stimuli, but also to complex cognitive information that through learning has acquired properties that automatically and obligatorily elicit emotional responses. Examples of this cognitive information are learned concepts such as "winning" or "losing." For instance, the announcement that you have won "a Nobel Prize," "an Oscar Award," or "a lottery ticket" can instantly, automatically, involuntarily, and obligatorily elicit an emotional response. We have evidence from the gambling task experiments to support this notion. Amygdala lesions block the somatic (emotional) response to the winning or losing of various amounts of money.² This is also consistent with functional neuroimaging studies revealing amygdala activation in reaction to winning and losing money.²⁸ Also interesting is that humans tend to automatically, involuntarily, and obligatorily elicit a "pleasure" response when they solve a puzzle or uncover a solution to a logical problem. In functional neuroimaging experiments involving the asking of human subjects to find solutions to series of logical problems, there were amygdala activations associated with the "aha" in reaction to finding the solution to a given logical problem.²⁹

Role of the Ventromedial Cortex

Our evidence suggests that the VM cortex is a trigger structure for somatic states from secondary inducers. Once somatic states from primary inducers are induced, signals from these somatic states are relayed to the brain. Representations of these signals can remain covert at the level of the brain stem, or they can reach the insular/SII, SI cortices, and posterior cingulate cortices and be perceived as a feeling. Evidence from functional neuroimaging studies suggests that the posterior cingulate

and retrosplenial cortex are consistently activated in feeling states.³⁰ The idea that the insula/ SII, SI cortices are necessary for feeling to occur is also supported by clinical observations in subjects with focal brain lesions.^{1,31,32} We also have preliminary evidence that when a primary inducer (an aversive loud sound) induces a somatic response in normal subjects, measured as changes in SCR activity and heart rate, the subjects provide a subjective rating of the noise as "too loud." Interestingly, right hemisphere subjects do trigger a somatic response to the loud sound similar to that of normal controls, but do not report feeling the sound as too loud (unpublished observations).

The VM cortex is a trigger structure for somatic states from secondary inducers. It serves as a convergence-divergence zone, which links (a) a certain category of event based on memory records in high-order association cortices to (b) the effector structures that induce the somatic responses and to (c) the substrates of feeling in, for example, the insula/ SII, SI cortices. In some instances, the VM cortex couples knowledge of secondary inducer events to covert response effectors at the level of the basal forebrain or brain stem. The anticipatory SCRs acquired during the pre-hunch period of the gambling task are an example of this instance.³³ In this case, a conscious pondering from which deck to choose (a secondary inducer) elicits a covert somatic response.

Two lines of studies support the notion that the VM cortex is a trigger structure for somatic states from secondary inducers. First, lesions of the VM cortex interfered with the generation of somatic responses (SCRs and heart rate) from internally generated images of emotional situations, for example, recalling a happy wedding or the death of a loved one. In this procedure, the subject is asked to think about a situation in his/ her life in which he/she felt each of the following emotions: happiness, sadness, fear, and anger. After a brief description of each memory is obtained, the subject is then put to a physiological test. The subject is asked to image and re-experience each emotional experience, while the skin conductance response (SCR) and heart rate are monitored. As a control condition, the subject is asked to recall and image a nonemotional set of events. At the conclusion of the task, emotional as well as neutral, each subject is asked to rate how much emotion he/she felt (on a scale of 0–4). Using this emotional imagery procedure, we tested patients with bilateral VM lesions. It is clear that the patients were able to retrieve previous happy, sad, angry, and fearful experiences, that is, they were able to recall emotion-laden events (such as weddings, funerals, car accidents, and family disputes) that occurred before their brain lesion. However, they had difficulties reexperiencing the emotion of these situations as reflected by low physiological activity and low subjective rating of feeling the emotion, relative to normal control subjects (FIG. 4). This was also true in relation to emotional events that occurred after the onset of their VM damage. This suggests that damage to the VM cortex weakens the ability to reexperience an emotion from the recall of an appropriate emotional event. The second line of support comes from studies showing that lesions of the VM cortex blocked autonomic reactivity during the pondering of a decision with possible negative outcome, that is, anticipatory SCRs during the gambling task.³⁴

Functional neuroimaging studies are also consistent with the lesions results. Functional neuroimaging studies have shown activations or deactivations in the VM region during the recall and imagery of personal emotional events.^{35–37} Activations in the VM region were also revealed during "guessing," "betting," "gambling," and

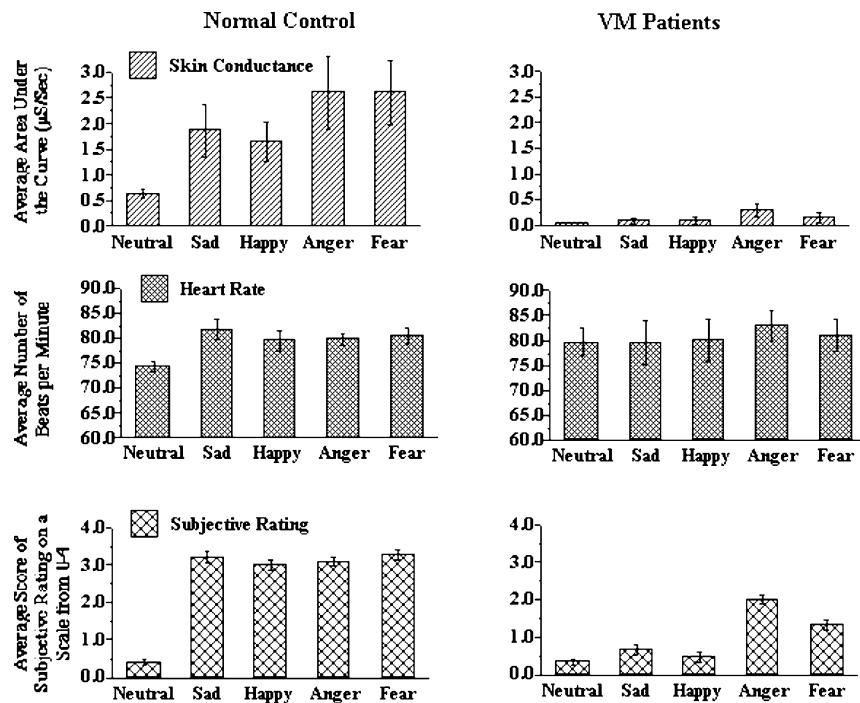


FIGURE 4. Skin conductance response (SCR), heart rate, and subjective rating of the feeling associated with the imagery of a personal emotional event experienced by individual normal control subjects versus ventromedial (VM) prefrontal patients. In the VM group, the SCRs generated during the imagery procedure were abnormally low, the changes in heart rate were not significant, and the subjective ratings of feeling the target emotion were low, despite having a vivid memory and recall of the imagined personal emotional event.

“learning reversal” tasks, which all involve elements of pondering responses with possible reward or punishment outcomes.^{38–43}

PRIMARY AND SECONDARY INDUCER PROCESSING MAY BE EVOKED BY THE SAME STIMULUS

Although different structures might be critical for primary versus secondary inducer processing, in a normal brain primary and secondary inducer processing can be elicited by the same stimulus and at the same time. For example, perceiving a primary inducer (e.g., looking at an emotional stimulus) may generate “thoughts” and “memories” about the inducer, which now serve as secondary inducers. Thus, operations of the two systems (primary and secondary inducers) are very difficult to disentangle in a normal brain, and they can be brought to light only in patients with lesions in structures critical for the processing of primary or secondary inducers.

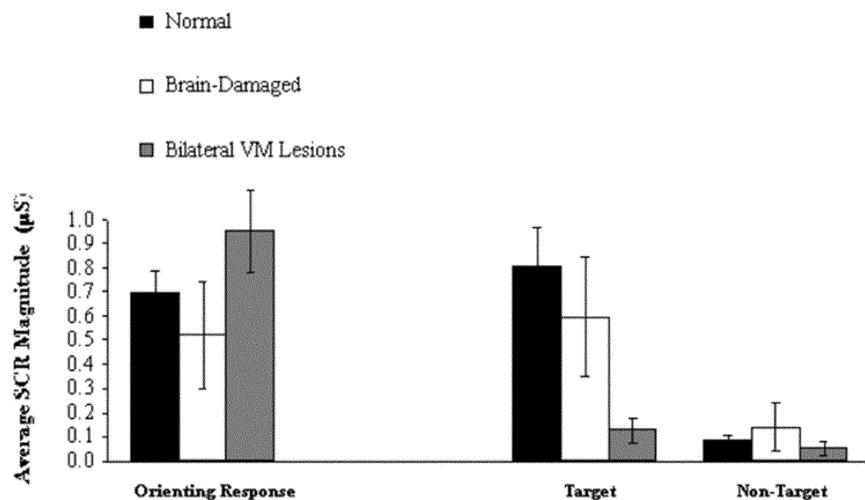


FIGURE 5. Skin conductance response (SCR) magnitudes (means \pm SEM) to orienting stimuli, neutral pictures, and emotionally charged pictures in normal controls, brain-damaged controls, and amygdala patients.

Support for this notion comes from experiments in which normal control subjects, VM patients, and amygdala patients were shown two types of visual stimuli: (1) target stimuli, including pictures of emotionally charged stimuli such as mutilations; and (2) nontarget stimuli, including pictures of emotionally neutral stimuli such as farm scenes and abstract patterns. During the viewing of these pictures, the skin conductance response (SCR), a highly sensitive index of autonomic responding, was recorded. When viewing the target and nontarget stimuli, normal control subjects displayed large-amplitude SCRs to the target pictures and little or no response to the nontargets (FIG. 5). By contrast, the amygdala patients generated some responses to the target pictures, but these responses were significantly attenuated relative to those of normal subjects.

Moreover, VM patients generated almost no response to the target pictures and completely failed to show the standard target and nontarget SCR difference (FIG. 6). This was all, despite the fact that the ability of amygdala and VM patients to generate SCRs to basic physical stimuli was intact.

These results suggest that these emotional pictures have some “primary inducer” properties that automatically and obligatorily trigger somatic responses. However, the emotional pictures also bring to working memory thoughts, memories, or empathy to the person depicted in the picture (i.e., secondary inducers), which in turn trigger somatic responses. The partial block of somatic responses to the target pictures in amygdala patients is most likely due to the block of the automatic and obligatory somatic responses to these pictures by amygdala damage and the sparing of the somatic responses triggered by thoughts, memories, or empathy, which are mediated by the VM cortex. On the other hand, the block of somatic responses to the target pictures in VM patients is most likely due to the block of the somatic responses trig-

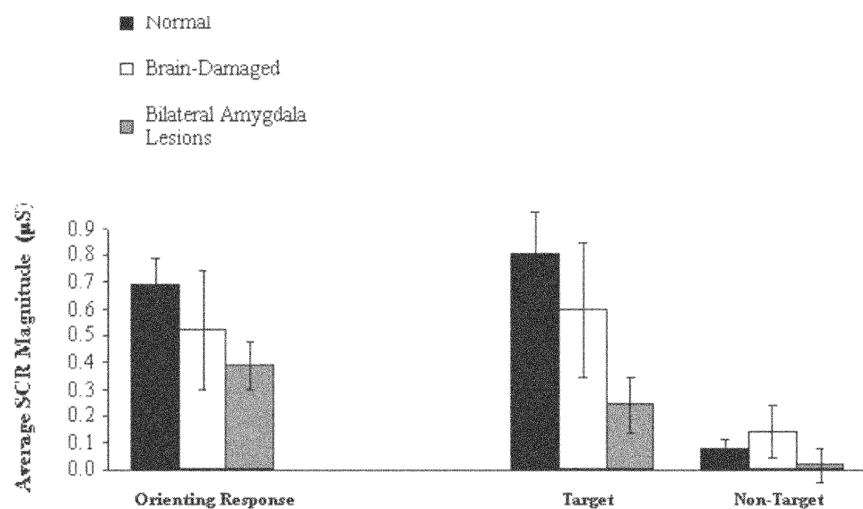


FIGURE 6. Skin conductance response (SCR) magnitudes (means \pm SEM) to orienting stimuli, neutral pictures, and emotionally charged pictures in normal controls, brain-damaged controls, and VM patients.

gered by thoughts, memories, or empathy, and the possible sparing of some automatic and obligatory somatic responses, which are mediated by the amygdala.

DEVELOPMENT OF THE ORBITOFRONTAL SYSTEM IS DEPENDENT ON THE AMYGDALA SYSTEM

Our evidence supports the notion that the amygdala system is *a priori* a necessary step for the normal development of the orbitofrontal system for triggering somatic states from secondary inducers. However, once this orbitofrontal system is developed, the induction of somatic states by secondary inducers via the orbitofrontal system becomes less dependent on the amygdala system. Using the same emotional imagery procedure described earlier, we tested one patient with selective bilateral amygdala damage due to Urbach Weitze disease.⁴⁴ Because most patients with bilateral amygdala damage have bilateral lesions that involve medial temporal lobe structures (i.e., amygdala plus hippocampal and entorhinal cortices), it is difficult to interpret results obtained from such patients. For this reason, the following experiments were conducted in this one patient with selective bilateral amygdala damage. The results were intriguing:

If the emotional event occurred after the onset of the amygdala damage (i.e., more recent events), then this amygdala patient showed weak somatic responses during the internally generated images of each emotional event. The patient had a vivid memory of the emotional event, but lacked the emotion of that memory (FIG. 7).

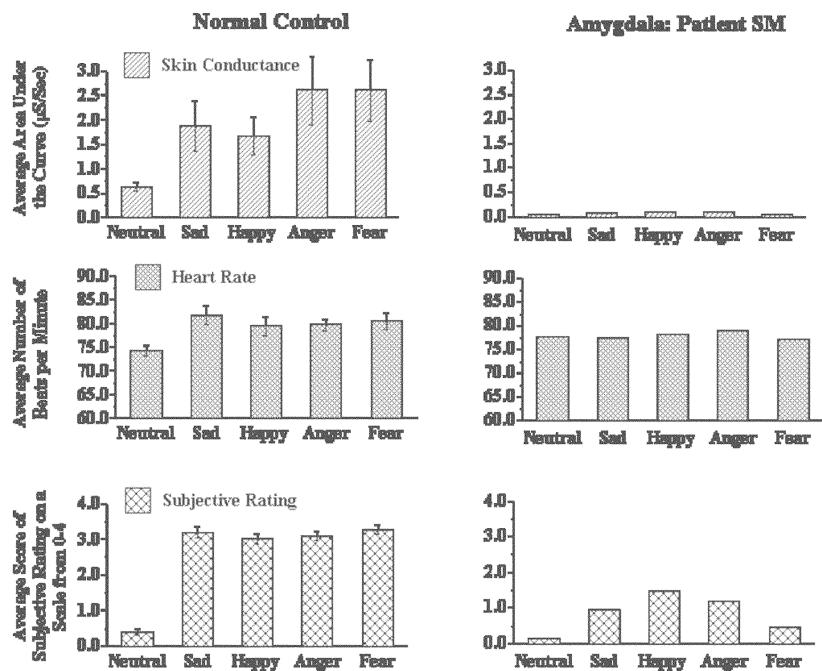


FIGURE 7. Skin conductance response (SCR), heart rate, and subjective rating of the feeling associated with the imagery of a personal emotional event experienced by individual normal control subjects versus a patient with selective bilateral amygdala lesions (patient S.M.). The emotional event in the amygdala patient was recent, that is, certainly after the onset of the amygdala damage. The emotional events in the control subjects were as recent as those of the amygdala patient.

In contrast, this amygdala patient showed almost normal somatic responses to internally generated images of emotional situations, if these events had occurred very early in life, presumably prior to the onset of the amygdala damage (FIG. 8).

These results suggest that perhaps at the process level, the amygdala is equivalent to the hippocampus with regard to emotions, that is, necessary for acquiring new emotional attributes (anterograde emotions), but not the retrieval of old emotional attributes (retrograde emotions).

CONCLUSION

The evidence presented so far supports the hypothesis that the amygdala is a trigger structure for somatic states from primary inducers. Primary inducers are entities that innately or through learning have acquired emotional significance. When they are presented in the immediate environment, they automatically and obligatorily elicit an emotional response. In contrast, the VM cortex is a trigger structure for

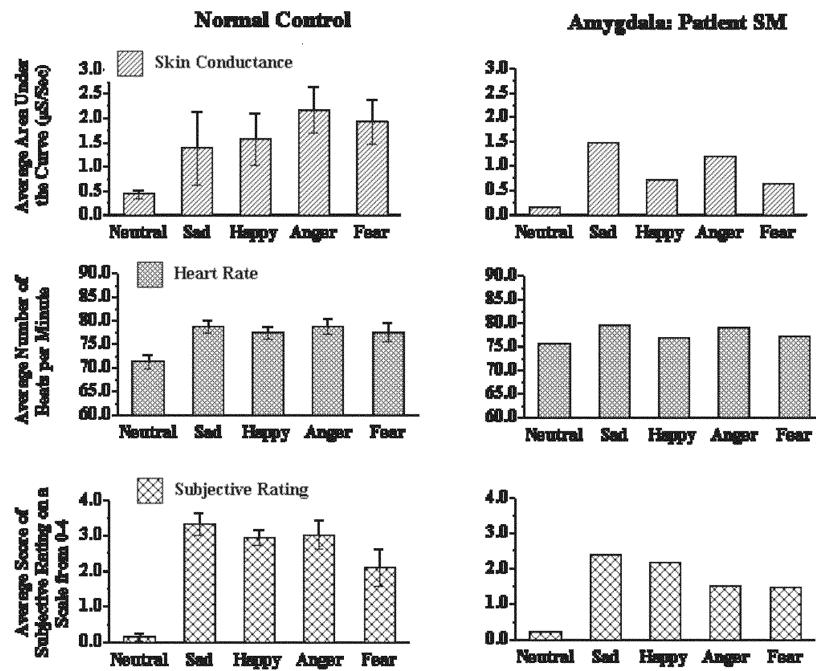


FIGURE 8. Skin conductance response (SCR), heart rate, and subjective rating of the feeling associated with the imagery of a personal emotional event experienced by individual normal control subjects versus a patient with selective bilateral amygdala lesions (patient S.M.). The emotional event in the amygdala patient was early in life (around the age of 16), that is, most likely before the onset of the amygdala dysfunction in this patient. The emotional events in the control subjects were as recent as those of the amygdala patient.

somatic states from secondary inducers. Secondary inducers are “thoughts” or “memories” or “imagination” of primary inducers. When they are brought into working memory, they elicit an emotional response.

Numerous lesion and functional neuroimaging studies have shown that the amygdala is involved in complex cognitive and behavioral functions, including the judgment of emotion in facial expressions,⁴⁵ the judgment of trustworthiness in faces,^{46,47} or the judgment of an advantageous strategy in the gambling task.^{42,43} However, these deficits expressed at a complex behavioral level are most likely the manifestations of a simpler defect in one fundamental function of the amygdala, which is to couple stimuli/entities with their emotional attributes, that is, the processing of somatic states from primary inducers.

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