Emotion, Decision Making and the Orbitofrontal Cortex

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The somatic marker hypothesis provides a systems-level neuroanatomical and cognitive framework for decision making and the influence on it by emotion. The key idea of this hypothesis is that decision making is a process that is influenced by marker signals that arise in bioregulatory processes, including those that express themselves in emotions and feelings. This influence can occur at multiple levels of operation, some of which occur consciously and some of which occur non-consciously. Here we review studies that confirm various predictions from the hypothesis. The orbitofrontal cortex represents one critical structure in a neural system subserving decision making. Decision making is not mediated by the orbitofrontal cortex alone, but arises from large-scale systems that include other cortical and subcortical components. Such structures include the amygdala, the somatosensory/insular cortices and the peripheral nervous system. Here we focus only on the role of the orbitofrontal cortex in decision making and emotional processing, and the relationship between emotion, decision making and other cognitive functions of the frontal lobe, namely working memory.

It has long been known that different sectors of the human prefrontal cortex are involved in distinctive cognitive and behavioral operations. The insight regarding this functional specialization came from the clinical observation of neurological patients in whom damage to different sectors of the frontal lobe caused remarkably different neuropsychological defects, and this insight was the springboard for systematic attempts to characterize the defects in relation to cognitive processes defined in terms of their components. The ensuing results, based on experimental work in both humans with brain lesions as well as non-human primates, has generally supported the notion of functional specialization within the prefrontal cortices and has yielded a large body of work. The examples, in relation to dorsolateral cortex, encompass the work of Goldman-Rakic and her group (Goldman-Rakic, 1992), of Milner and Petrides (Milner *et al.*, 1985; Petrides, 1996) and of Fuster (Fuster, 1990). In this article we survey recent progress in relation to another prefrontal sector, the ventromedial, as studied in humans with brain lesions.

The ventromedial sector includes both the gyrus rectus and mesial half of the orbital gyri, as well as the inferior half of the medial prefrontal surface, from its most caudal aspect to its most rostral in the frontal pole. Areas 11, 12, 13, 25, 32 and 10 of Brodmann are included in this sector, as is the white matter subjacent to all of these areas [see Fig. 1, areas marked in red; see also pp. 24–25 of (Damasio, 1995)]. Damage to the ventromedial sector disrupts social behavior profoundly. Previously well-adapted individuals become unable to observe social conventions and unable to decide advantageously on matters pertaining to their own lives. Remarkably, the patient's intellectual abilities are generally well preserved, in the sense that they have normal learning and memory, language and attention, and they even perform normally on many so-called executive function tests, such as the Wisconsin Card Sorting Test. Equally remarkably, these patients have an abnormality in their processes of emotion and feeling. The abnormality is such that they do not engage emotions in relation to complex situations and events, e.g. the emotion and ensuing feeling of embarrassment which are induced by specific social contexts (Damasio *et al.*, 1991; Damasio and Anderson, 1993). The intriguing nature of these defects and the fact that they could not be accounted for by a primary problem with the availability of the pertinent social knowledge, with the ability to apply logic to such knowledge or with general defects of attention or language led to the development of an account known as the somatic marker hypothesis (Damasio, 1994, 1996).

The somatic marker hypothesis proposes that a defect in emotion and feeling plays an important role in impaired decision making. The hypothesis also specifies a number of structures and operations required for the normal operation of decision making. Because emotion is most importantly expressed through changes in the representation of body state, though not solely, and because the results of emotion are primarily repres- ented in the brain in the form of transient changes in the activity pattern of somatosensory structures, the emotional changes are designated under the umbrella term 'somatic state'. The term 'somatic' thus refers to internal milieu, visceral and musculoskeletal, of the soma rather than just to the musculoskeletal aspects. It should also be noted that although somatic signals are based on structures which represent the body and its states, from the brainstem and hypothalamus to the cerebral cortex, the 'somatic' signals do not need to originate in the body in every instance and can be generated intracerebrally (Damasio, 1994, 1995b). The summary of the proposal is presented below.

Background Assumptions

The somatic marker hypothesis is based on the following main assumptions: (i) that human reasoning and decision making depend on many levels of neural operation, some of which are conscious and overtly cognitive, some of which are not; conscious, overtly cognitive operations depend on sensory images based on the activity of early sensory cortices; (ii) that cognitive operations, regardless of their content, depend on support processes such as attention, working memory and emotion; (iii) that reasoning and decision making depend on the availability of knowledge about situations, actors, options for action and outcomes; such knowledge is stored in 'dispositional' form throughout higher-order cortices and some subcortical nuclei (the term dispositional is synonymous with implicit and non-topographically organized) [details on dispositional knowledge and the convergence zone framework are presented elsewhere (Damasio, 1989a,b, 1994; Damasio and Damasio, 1994)]; dispositional knowledge can be made explicit in the form of (a) motor responses of varied types and complexity

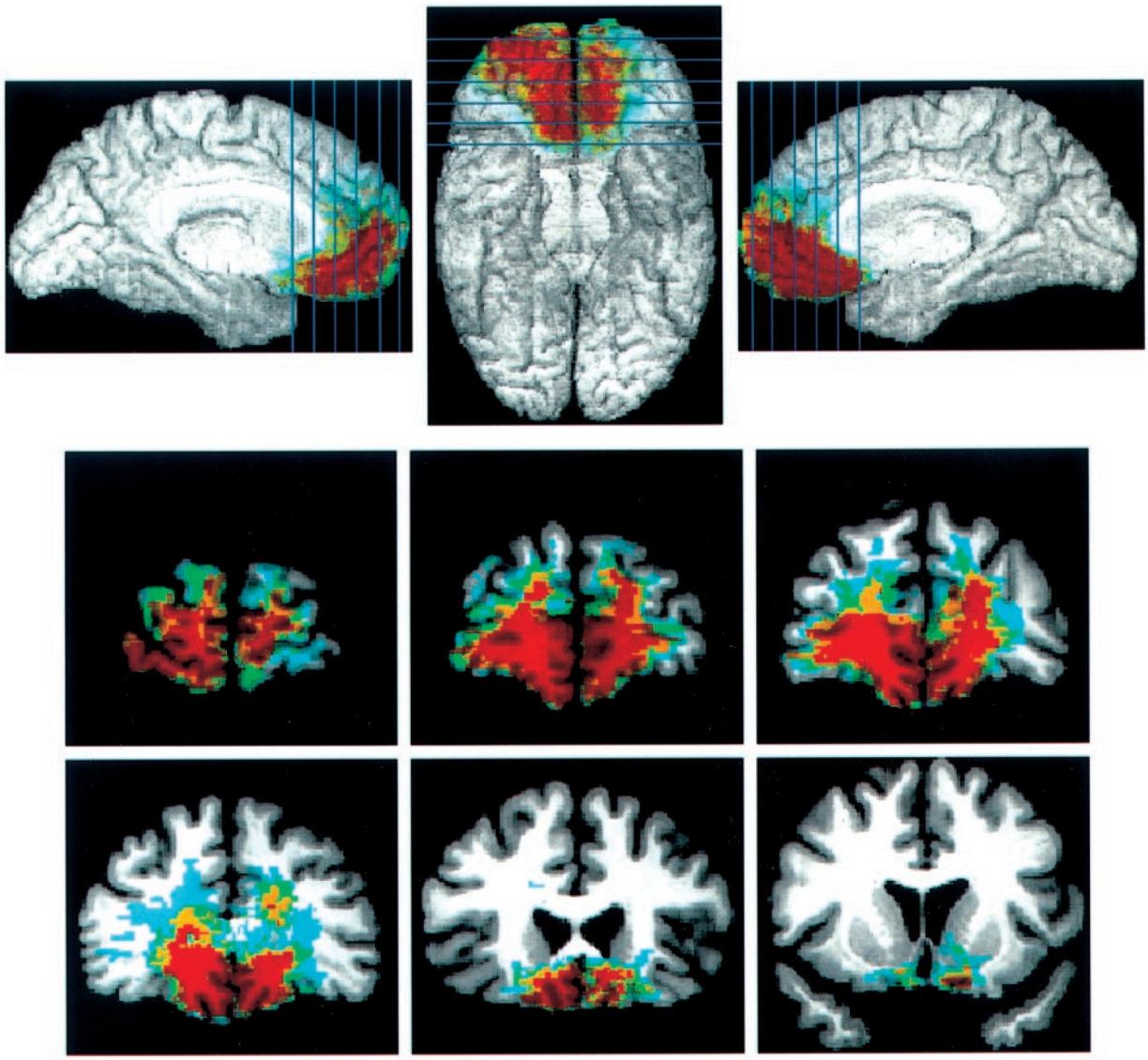

Figure 1. Overlap of lesions in the VM patients ($n = 13$). Red indicates an overlap of four or more patients.

(some combinations of which are part of emotions) and (b) images. The results of motor responses, including those that are not generated consciously, can be represented in images; and (iv) that knowledge can be classified as follows: (a) innate and acquired knowledge concerning bioregulatory processes and body states and actions, including those which are made explicit as emotions; (b) knowledge about entities, facts (e.g. relations, rules), actions and action-complexes (stories), which are usually made explicit as images; (c) knowledge about the linkages between (b) and (a) items, as reflected in individual experience; and (d) knowledge resulting from the categorizations of items in (a), (b) and (c).

Specifics of the Hypothesis

The ventromedial prefrontal cortex is a repository of dispositionally recorded linkages between factual knowledge and bioregulatory states. Structures in ventromedial prefrontal cortex provide the substrate for learning an association between certain classes of complex situation, on the one hand, and the type of bioregulatory state (including emotional state) usually associated with that class of situation in past individual experience. The ventromedial sector holds linkages between the facts that compose a given situation, and the emotion previously paired with it in an individual's contingent experience. The linkages are 'dispositional' in the sense that they do not hold the representation of the facts or of the emotional state explicitly, but hold rather the potential to reactivate an emotion by acting on the appropriate cortical or subcortical structures (Damasio, 1989a,b, 1994; Damasio and Damasio, 1994). The experience we acquire regarding a complex situation and its components—a certain configuration of actors and actions requiring a response; a set of response options; a set of immediate and long-term outcomes for each response option—is processed in sensory imagetic and motor terms and is then recorded in dispositional and categorized form. But because the experience of some of those components has been associated with emotional responses, which were triggered from cortical and subcortical sites that are dispositionally prepared to respond, it is proposed that the ventromedial prefrontal cortex establishes a linkage between the disposition for a certain aspect of a situation (for

instance, the long-term outcome for a type of response option), and the disposition for the type of emotion that in past experience has been associated with the situation.

When subjects face a situation for which some factual aspects have been previously categorized, the pertinent dispositions are activated in higher-order association cortices. This leads to the recall of pertinently associated facts which are experienced in imagetic form. At the same time, the related ventromedial prefrontal linkages are also activated, and the emotional disposition apparatus is competently activated as well. The result of those combined actions is the reconstruction of a previously learned factual–emotional set.

The re-activation described above can be carried out via a 'body loop', in which the soma actually changes in response to the activation and the ensuing changes are relayed to somatosensory cortices; or via an 'as-if body loop', in which the body is bypassed and re-activation signals are conveyed to the somatosensory structures which then adopt the appropriate pattern. From both evolutionary and ontogenetic perspectives, the 'body loop' is the original mechanism but has been superseded by the 'as-if body loop' and is possibly used less frequently than it. The results of either the 'body loop' or the 'as-if body loop' may become overt (conscious) or remain covert (non-conscious).

The establishment of a somatosensory pattern appropriate to the situation, via the 'body loop' or via the 'as-if body loop', either overtly or covertly, is co-displayed with factual evocations pertinent to the situation and qualifies those factual evocations. This constrains the process of reasoning over multiple options and multiple future outcomes. For instance, when the somatosensory image which defines a certain emotional response is juxtaposed to the images which describe a related scenario of future outcome, and which triggered the emotional response via the ventromedial linkage, the somatosensory pattern marks the scenario as good or bad.

When this process is overt, the somatic state operates as an alarm or incentive signal. The somatic state is alerting you to the goodness or badness of a certain option–outcome pair. The device produces its result at the openly cognitive level. When the process is covert the somatic state constitutes a biasing signal. Using a non-conscious influence, e.g. through a non-specific neurotransmitter system, the device influences cognitive processing.

Certain option–outcome pairs can be rapidly rejected or endorsed, and pertinent facts can be more effectively processed. The hypothesis thus suggests that somatic markers normally help constrain the decision-making space by making that space manageable for logic-based, cost–benefit analyses. In situations in which there is remarkable uncertainty about the future and in which the decision should be influenced by previous individual experience, such constraints permit the organism to decide efficiently within short time intervals.

In this article we review a number of findings related to the investigation of the somatic marker hypothesis in human subjects with ventromedial prefrontal cortex (VM) damage. The lesions of some of the subjects who participated in the experiments described below are presented in Figure 1.

The Role of the VM in Decision Making

The Gambling Task

The study of the decision-making impairment of patients with VM lesions required an instrument for the detection and measurement of such impairments in the laboratory. The development of a card task known as 'the gambling task' (Bechara *et al.*, 1994) provided this tool. The essential feature of this task is that it mimics real-life situations in the way it factors uncertainty, reward and punishment. The task involves four decks of cards, named A, B, C and D. The goal is to maximize profit on a loan of play money. Subjects are required to make a series of 100 card selections, but are not told ahead of time how many card selections they are going to be allowed to make. Cards can be selected one at a time, from any deck, and subjects are free to switch from any deck to another, at any time and as often as they wish. The decision to select from one deck or another is largely influenced by schedules of reward and punishment. These schedules are pre-programmed and known to the examiner, but not to the subject (Bechara *et al.*, 1994, 1999a). They are arranged in such a way that every time the subject selects a card from deck A or B, s/he gets $100, and every time deck C or D is selected, the subject gets $50. However, in each of the four decks, subjects encounter unpredictable money loss (punishment). The punishment is set to be higher in the high-paying decks A and B, and lower in the low-paying decks C and D. In decks A and B the subject encounters a total loss of $1250 in every 10 cards. In decks C and D the subject encounters a total loss of $250 in every 10 cards. In the long term, decks A and B are disadvantageous because they cost more, a loss of $250 in every 10 cards. Decks C and D are advantageous because they result in an overall gain in the end, a gain of $250 in every 10 cards.

Insensitivity to Future Consequences following Bilateral Damage of the Prefrontal Cortex

A large sample of normal control subjects (n = 82, balanced in terms of gender, with 8–20 years of education, and between the ages of 20 and 64) has been tested with the original card version of the gambling task described above. Patients with lesions in different sectors of the frontal lobe (n = 45), or with lesions in areas of the lateral temporal cortex or occipital cortex (n = 35) have also been tested. Since the original manual version of the gambling task was described, a new computer version has been devised, and similar numbers of control subjects and patients have been tested with the new computer version. The results from either version of the gambling task are interchangeable. As the task progresses from the first to the 100th trial, normal controls gradually make more selections of cards from the good decks (C and D) and less selections from the bad decks (A and B) (Fig. 2 left). Patients with lesions in the dorsolateral sector of the prefrontal cortex (Bechara *et al.*, 1998), or in areas outside the prefrontal cortex (Bechara *et al.*, 1994), perform in a manner similar to that of normal subjects. In sharp contrast, patients with bilateral lesions of the VM do not increase the number of their selection of cards from the good decks (C and D); they persist in selecting more cards from the bad decks (A and B) (Fig. 2 left). The card selection profiles from normal controls show that a typical normal subject initially samples all decks and repeats selections from the bad decks A and B, probably because they pay more. However, eventually the normal subject switches to more and more selections from the good decks C and D, with only occasional returns to decks A and B. On the other hand, a typical VM patient behaves like a normal subject only in the first few selections. The patient begins by sampling all decks and selecting from decks A and B, and then makes several selections from decks C and D, but then soon returns more and more to decks A and B (Fig. 2 right).

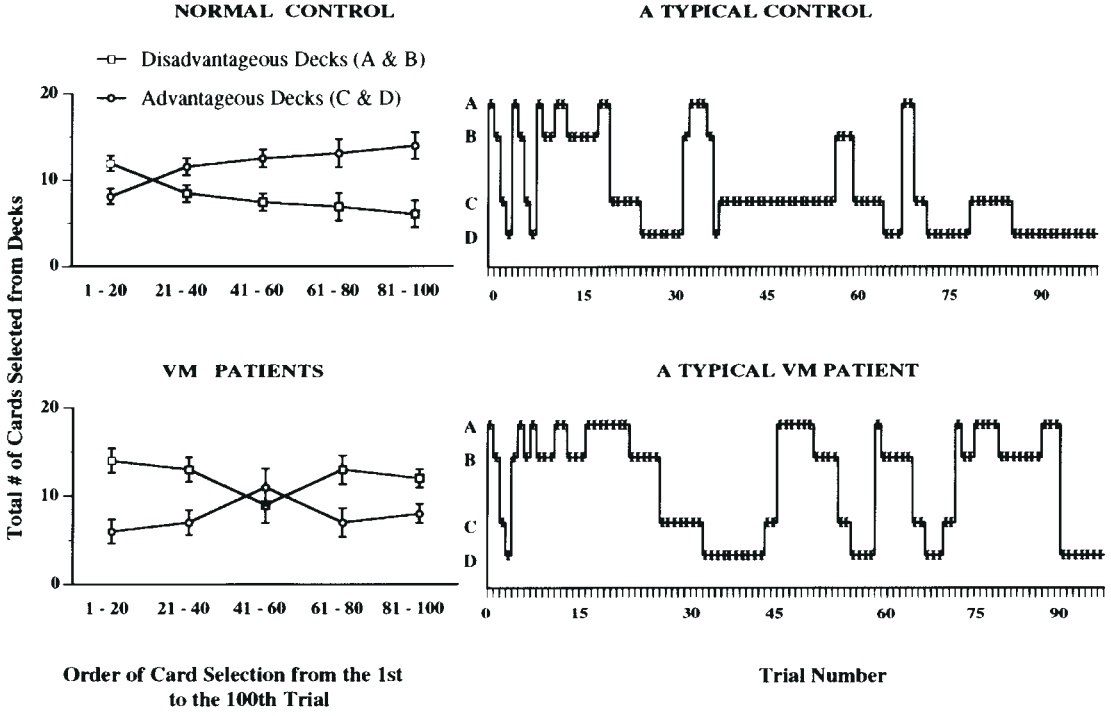

Figure 2. (Left panels) Card selection on the gambling task as a function of group (normal control, VM patients), deck type (disadvantageous versus advantageous), and trial block. Normal control subjects (n = 82) shifted their selection of cards towards the advantageous decks. The VM frontal patients (n = 15) opted for the disadvantageous decks. (Right panels) Profiles of card selections (from the first to the 100th selection) obtained from a typical control and a typical VM patient. Although the VM patient made numerous switches, he returned more often to the disadvantageous decks.

In the normal population, performance on the gambling task does not seem to depend on education or gender, although a few preliminary reports suggest that males perform slightly better than females (LeLand *et al.*, 1998; Reavis *et al.*, 1998). Most intriguing is that, as a group, older adults (above 64 years of age) perform poorly on this task relative to younger adults (i.e. age 26–56) (Denburg *et al.*, 1999). It should be noted, however, that performance on the gambling task in older adults is dichotomous, i.e. some perform very well and some perform very poorly. This finding raises an important question as to why this happens in some older adults and not others, the answer to which may help explain why some older adults are especially vulnerable to advertising fraud in real life.

In the VM patient population, the decision-making impairment, as measured by the gambling task, is stable over time. When a sample of six VM frontal patients and five normal controls were re-tested after various time intervals (1 month after the first test, 24 h later and for the fourth time, 6 months later), the performance of VM patients did not improve. On the other hand, the performance of normal controls improved significantly over time (Fig. 3).

These results demonstrate that the VM patients' performance profile is comparable to their real-life inability to learn from their previous mistakes. This is especially true in personal and social matters, a domain for which in life, as in the gambling task, an exact calculation of the future outcome is not possible and choices must be based on approximations.

Biases Guide Decisions

The results described above prompted the following question: what is the basis for the 'myopia for the future' that plagues VM frontal patients? For many years, many theorists of decision making assumed that the feelings triggered when making a decision or a risky choice were not integral to the decision-making process. In this sense, the decision-making theorists assumed that risky decision making was essentially a cognitive activity devoid of an emotional component. These theories suggest that people assess the possible outcomes of their actions through some type of cost–benefit analysis. However, several authors have proposed an alternative theoretical account which highlights the role of the affect experienced during the time of deliberation prior to making decisions (Schwartz and Clore, 1983; Zajonc, 1984; Damasio *et al.*, 1990).

Evidence in support of this idea comes from studies of normal control subjects and patients with bilateral VM frontal damage during their performance on the gambling task, and the analysis of their psychophysiological activity during task performance (Bechara *et al.*, 1996). Skin conductance response (SCR) activity has been recorded so far in a large sample of normal subjects (n = 55) and VM patients (n = 15) during the performance of the gambling task. Despite some variations in the methods for collecting the SCR data (Bechara *et al.*, 1996, 1999a), the general principles remain the same. Every time the subject picks a card, the deck from which that card was picked is recorded, and the magnitude of the SCR in the time window (~5 s) right before the subject picked the card is measured. In addition, the magnitude of the SCR in the time window (~5 s) after the card was picked is also measured. Thus, three types of responses are identified. (i) The reward SCRs, those occurring after turning cards with reward only. (ii) The punishment SCRs, those occurring after turning cards with reward and punishment. (iii) The anticipatory SCRs, those occurring before turning a card from a deck, during the time the subject ponders from which deck to choose (Bechara *et al.*, 1996).

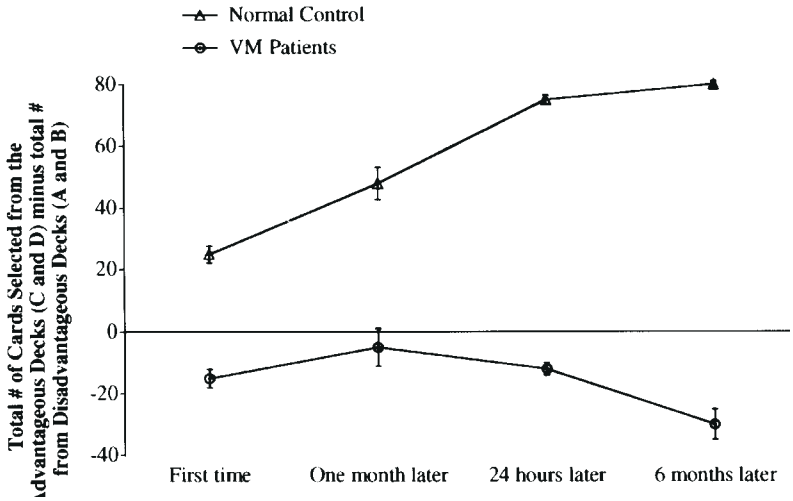

Figure 3. A learning curve revealing the level of performance of normal control ($n = 5$) and VM patients ($n = 6$) on the gambling task, as a function of repetition over time. The VM patients failed to show a significant improvement as a function of repeated testing.

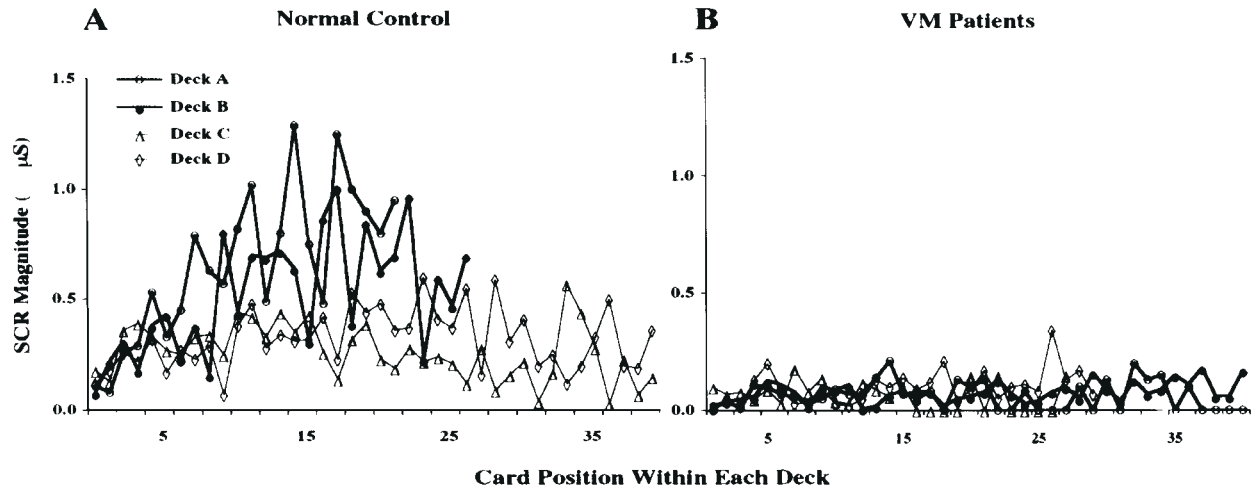

Figure 4. Magnitudes of anticipatory SCRs as a function of group [normal control (*A*) ($n = 12$) versus VM patients (*B*) ($n = 7$)], deck and card position within each deck. Note that control subjects gradually began to generate high-amplitude SCRs to the disadvantageous decks. The VM patients failed to do so.

The results from the psychophysiological experiments conducted so far reveal that normal controls and VM patients generate SCRs as a reaction to reward or punishment. Normal controls, however, as they become experienced with the task, also begin to generate SCRs before the selection of any card. The anticipatory SCRs generated by normal controls: (i) develop over time (i.e. after selecting several cards from each deck, and thus encountering several instances of reward and punishment); and (ii) actually become more pronounced before selecting cards from the disadvantageous decks (A and B). These anticipatory SCRs are absent in the VM patients (Fig. 4). This suggests that VM patients have a specific impairment in their ability to generate anticipatory SCRs in response to a possible outcome of their action. Since SCRs are physiological indices of an autonomically controlled change in somatic state, it seems reasonable to conclude that the absence of anticipatory SCRs is an indication that these patients' ability to change somatic states in response to an imagined scenario is severely compromised. In this perspective, the failure to enact a somatic state appropriate to the consequences of a response would be a correlate of their inability to choose advantageously.

Risk Taking versus Impaired Decision Making

None of the bilateral VM patients tested so far have performed advantageously on the gambling task. However, not every normal control subject performs advantageously. Approximately 20% of normal adults who describe themselves as high-risk takers in real life end up selecting more cards from the bad decks relative to the good ones (Bechara *et al.*, 1999a). When looking at the anticipatory SCRs in these normal individuals, it is often found that the magnitudes of the anticipatory SCRs in relation to the bad decks are slightly lower than those in relation to the good decks (Bechara *et al.*, 1999a). The opposite is true (i.e. higher anticipatory SCRs with the bad decks relative to the good decks) in normal individuals who play advantageously. The most critical distinction between these normal individuals and the VM patients, however, is that these normal individuals do generate anticipatory SCRs. The VM patients, on the other hand, do not

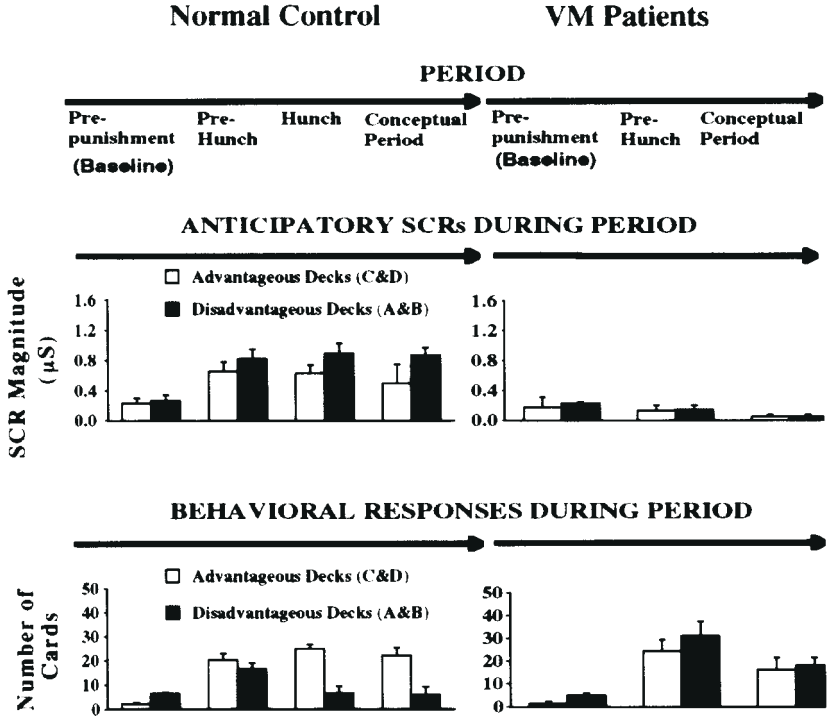

Figure 5. Anticipatory SCRs and behavioral responses (card selection) as a function of four periods (pre-punishment, pre-hunch, hunch and conceptual) from normal control subjects ($n = 10$) and VM patients ($n = 6$).

generate anticipatory SCRs at all. These physiological results are very important because they separate individuals with high-risk-taking behavior from individuals with VM frontal lobe dysfunction. When taking a risk, the somatic states signaling the possible negative consequences of the outcome are enacted. However, the individual can override these biases by higher cognitive processes. In the case of VM damage, these biases are never enacted and never enter the decision-making process. This suggests that taking a risk is not the same as having poor judgement and impaired decision making. The issue of risk taking versus decision making was addressed in a previous study that showed that orbitofrontal patients risked significantly less of their accumulated reward than controls, thus suggesting a pattern of conservative behavior (Rogers *et al.*, 1999). Yet, these same patients made suboptimal choices and spent more time deliberating their choices (Rogers *et al.*, 1999). Another study suggested that while frontal patients were impulsive and made poor decisions, they did not express a high-risk-taking behavior (Miller, 1992). This evidence suggests that risk-taking behavior and impaired decision making are not synonymous.

Biases Do Not Need To Be Conscious

Given the important role that biases play in decision making, it is important to determine if these anticipatory responses (biases) develop after the subject knows which decks are good or bad, or if they precede such explicit knowledge. This question was addressed in an experiment in which ten normal subjects and six VM frontal patients were tested on the gambling task, while their SCRs were being recorded as before. However, in this experiment, every time a subject had picked ten cards the game was stopped briefly and the subject was asked to describe whatever s/he knew was going on in the game (Bechara *et al.*, 1997). The analysis of the subjects' answers suggested that they went through four distinct periods across the task. The first was a pre-punishment period, when subjects sampled the decks, before they encountered any punishment. The second was a pre-hunch period, when subjects began to encounter punishment, but had no clue about what was going on in the game. The third was a hunch period, when subjects began to express a hunch about the decks that were riskier, even if they were not sure about their guess. The fourth was a conceptual period, when subjects knew very well the contingencies in the task, which decks were the good ones, which decks were the bad ones and why this was so (Fig. 5). It is interesting that 30% of the control subjects did not reach the fourth, or conceptual, period in this experiment, yet they performed normally on the gambling task.

In normal controls, when the anticipatory SCRs from each of these four periods were examined, it was found that there was no significant anticipatory activity during the pre-punishment period. There was a substantial rise in anticipatory responses during the pre-hunch period, i.e. before any conscious knowledge developed. This anticipatory SCR activity was sustained for the rest of the task. When the type of choice from the different decks was examined for each period, the results revealed that there was a preference for the high-paying decks (A and B) during the pre-punishment period. There was a hint of a shift in the pattern of card selection, away from the bad decks, as early as in the pre-hunch period. This preference for the good decks became more pronounced during the hunch and conceptual periods. Even those 30% of controls who did not reach a full conceptual knowledge of the relative goodness or badness of the decks ended up playing advantageously. The VM frontal patients, on the other hand, never reported a hunch. They also never developed anticipatory SCRs, and continued to choose more cards from decks A and B relative to C and D. However, 50% of VM frontal patients did reach the conceptual period, in which

they were able to recognize and identify the bad decks. Even so, they still performed disadvantageously (Bechara *et al.*, 1997).

These results show that VM frontal patients continue to choose disadvantageously in the gambling task, even after realizing the consequences of their action. This suggests that the anticipatory SCRs represent unconscious biases, probably derived from prior experiences with reward and punishment. These biases help deter the normal subject from pursuing a course of action that is disadvantageous in the future. This biasing effect occurs even before the subject becomes aware of the goodness or badness of the choice s/he is about to make. Even without these biases, the knowledge of what is right and what is wrong may become available, as happened in 50% of the VM patients. However, by itself, such knowledge is not sufficient to ensure an advantageous behavior. Although the frontal patient may be fully aware of what is right and what is wrong, s/he still fails to act accordingly. These patients may 'say' the right thing, but 'do' the wrong thing.

Relationship between Emotion, Memory and Decision Making

It has been established that the memory of facts is improved when the facts are learned in connection with an emotion (Cahill *et al.*, 1995; Roozendaal *et al.*, 1996), although under extreme conditions (e.g. intense arousal) emotions can actually impair memory (Easterbrook, 1959). The prefrontal cortex, especially its dorsolateral (DL) sector, has been linked to the ability to remember facts for a short period of time, i.e. working memory (Goldman-Rakic, 1987; Fuster, 1991; D'Esposito *et al.*, 1995; Smith *et al.*, 1995; Courtney *et al.*, 1997). Thus, it became pertinent to ask whether cognitive functions related to working memory were distinct from those related to decision making. In other words, do working memory and decision making depend at least in part on separate anatomical substrates? Furthermore, it seemed pertinent to investigate whether the mechanism by which emotion boosts working memory (or improve the short term memory for certain facts) is the same as, or different from, the mechanism through which emotion biases decision making.

Decision Making and Working Memory are Distinct Operations of the Prefrontal Cortex

The rationale for the notion that working memory and decision making are distinct functions comes from the observations that VM frontal patients suffer from impairments in decision making, while preserving a normal level of memory and intellect. On the other hand, although some DL frontal patients complain of memory impairments, they do not appear to suffer from impairments in decision making, as judged from their behavior in real life. Using modified delay-task procedures (delayed response and delayed non-matching to sample) to measure working memory (Goldman-Rakic, 1987; Fuster, 1991), and the gambling task to measure decision making, the following experiment was performed. A group of 21 normal control subjects, nine patients with bilateral VM frontal lesions and ten patients with right or left lesions of the DL sector of the prefrontal cortex were tested on the delay and gambling tasks (Bechara *et al.*, 1998). The gambling task was the same task mentioned previously, and the delay task procedures were modifications of classical delay tasks.

Delay tasks that are used in non-human primates are too simple for use with humans. Therefore, a distracter was introduced during the delay between the cue and the response. The purpose of the distracter was to interfere with the ability of the subject to rehearse the position or the color of the cues during the delay, and thus to increase the demands of the tasks on working memory. In the *delayed response* experiment, four cards appeared for 2 s on a computer screen, with two of the cards face down and the other two face up, showing red or black colors. The cards disappeared for one, 10, 30 or 60 s and then reappeared, but this time all the cards were face down. The correct response was to select the two cards that were initially face up. During the delay, the subject had to read aloud a series of semantically meaningless sentences. Scores were calculated as the percent of correct choices made by the subject at the 10, 30 and 60 s delays. Impaired performance on the delayed response task was defined as achieving a percent correct score of 80 or less at the 60 s delay, a cutoff score below which no normal control ever performed (Bechara *et al.*, 1998). In the *delayed non-matching to sample* experiment, the task was similar to the delayed response task except that only one card appeared initially on the computer screen for 2 s. The card was face up and was either red or black. After the card disappeared for 1, 10, 30 or 60 s, four cards appeared on the screen, all face up, two of which were red and two black. The correct response was to select the two cards that were opposite in color (non-matching) to the initial sample card.

In this experiment we used two types of delay tasks because studies in non-human primates show that different areas of the DL frontal cortex are associated with different domains of working memory. The inferior areas of the dorsolateral sector have been associated with object memory, whereas the superior areas have been associated with spatial memory (Goldman-Rakic, 1987, 1992; Wilson *et al.*, 1993). Similar dissociations were found in humans (Courtney *et al.*, 1996). The delayed response tasks have been designed to tax the spatial (*where*) domain of working memory, whereas the delayed non-matching to sample tasks are supposed to tax the object (*what*) domain of working memory (Fuster, 1990; Wilson *et al.*, 1993). Since the lesions in the patients we studied were not restricted to the inferior or superior regions, and the lesions spanned a wide area of DL frontal cortices, we used both types of delayed tasks because we anticipated that both domains of working memory (spatial and object) may be affected. In other words, our attempt was not to sort out differences between different types of working memory, but rather to cover a range of working memory with one task. Therefore, the results we report here are an average of the results obtained from both delay tasks. In the next section, we use the term 'delay tasks' to refer to both procedures (delayed response and delayed non-matching to sample) [results obtained with each individual delay task are given elsewhere (Bechara *et al.*, 1998)].

This experiment revealed two intriguing findings. First, working memory is not dependent on the intactness of decision making, i.e. subjects can have normal working memory in the presence or absence of deficits in decision making. Some VM frontal patients who were severely impaired in decision making (i.e. abnormal in the gambling task) had superior working memory (i.e. normal in the delay tasks). On the other hand, decision making seems to be influenced by the intactness or impairment of working memory, i.e. decision making is worse in the presence of abnormal working memory. Patients with right DL frontal lesions and severe working memory impairments showed low normal results in the gambling task (Fig. 6). In summary, working memory and decision making were asymmetrically dependent. Second, although all VM patients tested in this experiment were impaired on the gambling task, they were split in their performance in the delay tasks. Five patients were

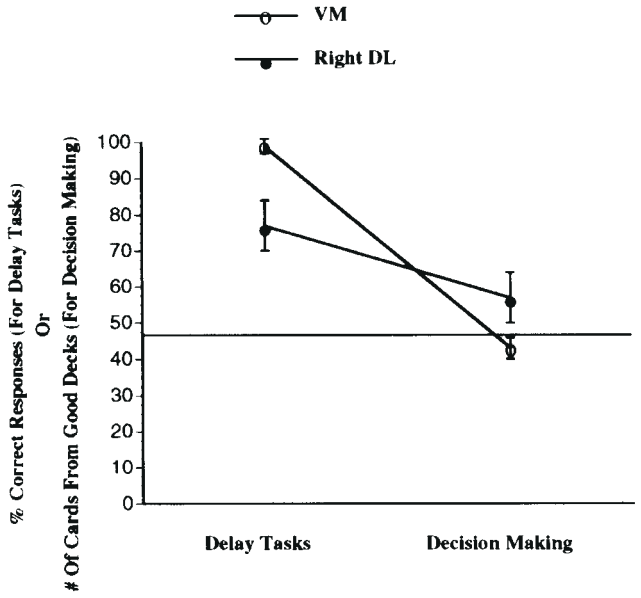

Figure 6. Means ± SEM of the average of percent correct responses from the two delay tasks, or the total number of cards selected from the good decks, that were made by VM patients ($n = 4$) with more anterior lesions and by patients with right DL lesions ($n = 4$). Note that the VM patients were severely impaired on the gambling task (low number of choices from the good decks), but normal on the delay tasks (high % correct response). On the other hand, the right DL patients were impaired on the delay tasks and, although their gambling task performance is considered advantageous, it falls in the low normal range.

abnormal in the delay tasks (Abnormal Gambling/Abnormal Delay) and four were normal in the delay tasks (Abnormal Gambling/Normal Delay) (Fig. 7, graphs). The most important finding is that all patients in the Abnormal Gambling/Abnormal Delay group had lesions that extended posteriorly, possibly involving the basal forebrain region. However, the other group (Abnormal Gambling/Normal Delay) had lesions that were more anterior and did not involve the basal forebrain (Fig. 7, anatomy).

It is important to note that in this experiment only the patients with right DL lesions were impaired on these working memory tasks. All patients with left DL frontal lesions had normal working memory. The absence of a working memory impairment in left DL patients is not surprising because, during the delay, the verbal memorization of cues was probably avoided by the interference procedure, thus rendering the task primarily non-verbal. This is consistent with several functional neuroimaging studies in humans that showed higher activation in the right DL frontal cortex, relative to the left, during the performance of similar delay tasks (Jonides *et al.*, 1993; Petrides *et al.*, 1993; McCarthy *et al.*, 1994; D'Esposito *et al.*, 1995a,b; Smith *et al.*, 1995; Swartz *et al.*, 1995).

These findings reveal a double dissociation (cognitive and anatomic) between deficits in decision making (anterior VM) and working memory (right DL). They reinforce the special importance of the VM region in decision making, independently of a direct role in working memory.

The Emotional Mechanism that Biases Decision Making is Distinct from the Emotional Mechanism that Improves Memory

The previous discussion leads to the question of whether the mechanism by which emotion improves memory is the same as,

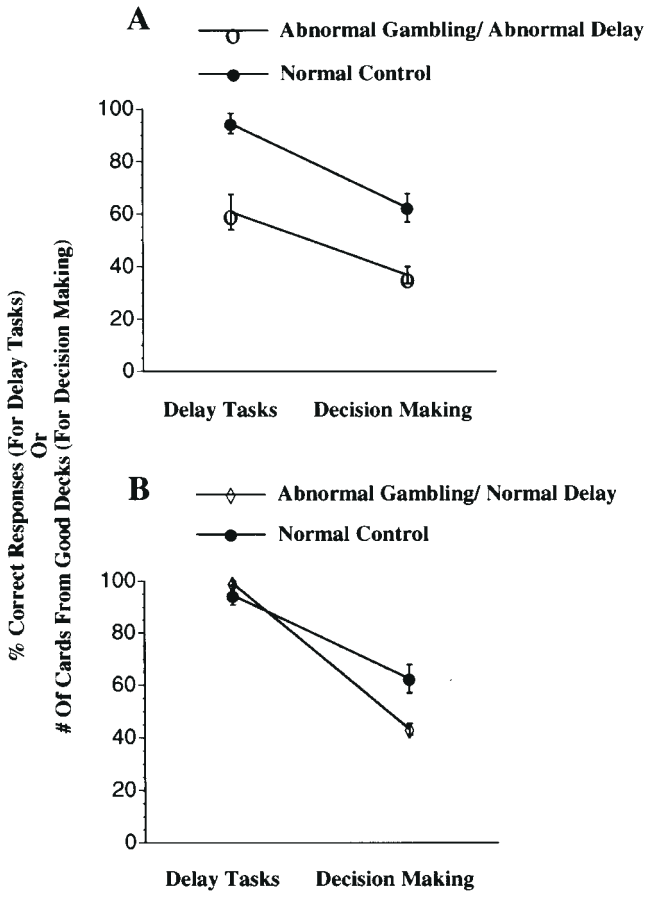

Figure 7 (Graphs) The behavioral results on the gambling task and the delay tasks from the groups of patients shown in Figure 7 (Anatomy).

or different from, the mechanism through which emotion biases decisions. The amygdala has been found to be necessary for emotions to improve memory (Cahill *et al.*, 1995). Our own work has also shown that the amygdala is important in the creation of biases and in decision making (Bechara *et al.*, 1999a). This suggests that in the amygdala, the mechanisms through which emotion modulates memory and decision making may be inseparable. The remaining question is whether these mechanisms might be separable in the VM cortex. In order to answer this last question, we tested 12 normal control subjects and six VM patients with anterior lesions that spared the basal forebrain for their memory of a series of neutral and emotionally charged pictures. The series of pictures involved four sets, with four pictures in each set. Each set of four pictures contained two neutral (e.g. farm scenes) and two emotional (e.g. raped and mutilated bodies') pictures. The pictures in set 1 were presented once each; those in set 2 were presented twice each; in set 3, four times each; and in set 4, eight times each. Five minutes after viewing all the pictures, subjects were tested for their recall of each picture they saw, and for the overall content of the picture. The recall of picture content was calculated for each subject as a function of repetition times and emotional content.

As might be expected, both normal controls and VM patients showed improved memory as a result of repetition. The most important finding, however, was that both groups showed a response to the emotion manipulation, producing a better memory curve for pictures with emotional content than for neutral pictures (Fig. 8). Thus, this experiment actually

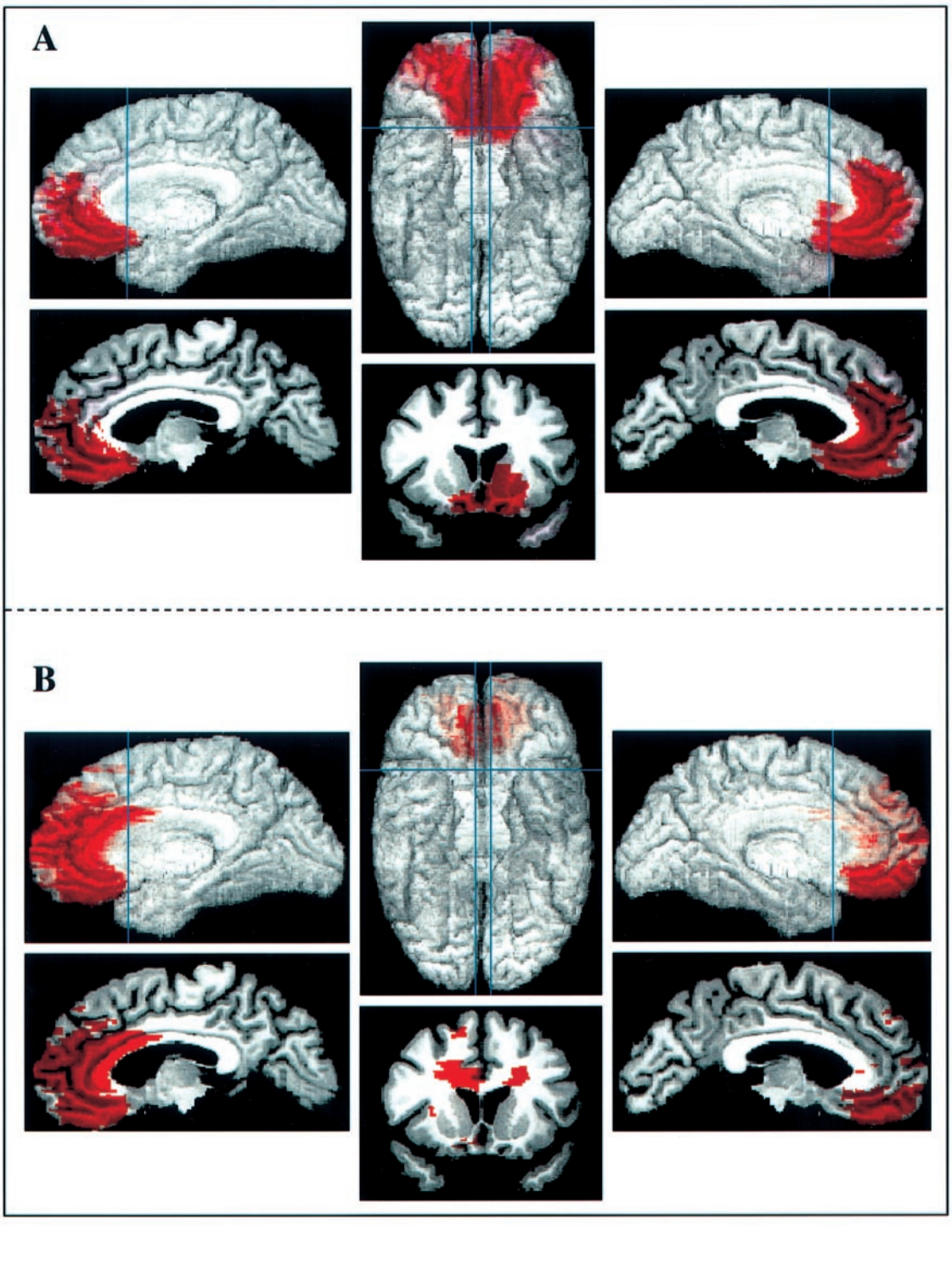

Figure 7. (Anatomy) Separate mapping of VM lesions for the group with Abnormal Gambling/Abnormal delay (*A*) ($n = 5$) and the group with Abnormal Gambling/Normal Delay (*B*) ($n = 4$). Red indicates an overlap of two subjects or more. The maximal overlap of lesions in (*A*) is seen spanning the whole extent of the mesial orbital surface of the frontal lobe. It reaches the posterior sector (coronal slice 4), where basal forebrain structures are found. However, in (*B*) the maximal overlap is mostly anterior extending only to slice 1 and 2. Slices 4 does not show any lesion. Coronal sections are arranged according to radiological convention, i.e. right is left, and vice versa.

separated the memory curve that is a function of repetition from the curve that is a function of emotional content. The results indicate that the VM patients are able to use emotional content in order to enhance their memory, suggesting that the mechanism through which emotion modulates decision making is different from that through which emotion modulates memory. These

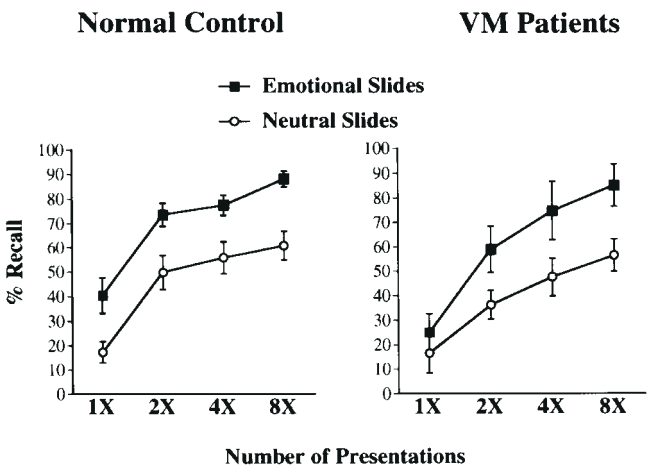

Figure 8. Recall scores in normal control ($n = 12$) and VM patients with anterior lesions that spare the basal forebrain ($n = 4$) as a function of repetition and emotional content. The VM patients showed a strong improvement in recall as a function of the emotional manipulation. We note that although in VM patients with basal forebrain lesions the overall recall is somewhat lower than in normal controls (not shown in the figure), these patients still show a strong improvement in recall as a function of the emotional manipulation.

results also support the conclusion that the decision-making impairment of VM patients cannot be explained by a deficit in the recall of emotional events.

Why Do VM Frontal Patients Fail to Trigger Somatic States when They Contemplate Decisions?

The series of studies outlined earlier helped establish that decision making is critically dependent on the generation of somatic states or biases. Why do VM patients fail to generate these biases or emotional signals? Is it because they no longer can re-experience emotions? Is it because they need a much higher threshold for triggering an emotion? Is it because they no longer can attach emotional significance to a neutral event, as, for instance, in conditioning? Our research addressing these questions is still in its preliminary phase. The nature of the mechanism responsible for the failure of VM patients to trigger somatic states when pondering decisions remains unspecified. The following is a preliminary search for the answer.

Emotional Conditioning

We have tested whether one reason for VM frontal patients to fail to trigger anticipatory biases (anticipatory SCRs) when contemplating a decision in the gambling task is due to a failure to couple an exteroceptive stimulus (or event) with the somatic state of a punishment. These patients may have a defect in acquiring fear conditioning. To test this possibility directly, we used a fear-conditioning procedure, which consisted of using four different colors of monochrome slides as conditioned stimuli (CS) and a startlingly aversive loud sound (100 db) as the unconditioned stimulus (US) (Bechara *et al.*, 1995). Electrodermal activity (SCR) served as the dependent measure of autonomic conditioning. The emotional conditioning of each subject included three phases: (i) a habituation phase; (ii) a conditioning phase. In this phase, only one of the colors was paired with the US. These CS slides were presented at random among the other colors; and (iii) an extinction phase.

A group of ten VM patients and ten matched control subjects were tested in the experiment just mentioned. The VM patients did condition to the loud noise (Tranel *et al.*, 1996; Bechara *et al.*, 1999a). This suggests that the VM cortex is not essential for emotional conditioning. Consequently, it is reasonable to assume that the failure of VM patients to acquire anticipatory SCRs in the gambling task, and their decision-making impairment, cannot be explained by a failure to acquire conditioned emotional responses.

The Experience of Emotions

Recently, we have started to address the question of whether one reason that VM frontal patients fail to trigger anticipatory biases (anticipatory SCRs) is the inability to re-experience the emotional state associated with punishment when recalling previous instances of punishment. A variety of procedures can be used to induce emotions in human subjects, such as watching emotional film clips, looking at pictures charged with emotions or recalling highly emotional personal events. In this preliminary study, emotional imagery was used as a method to induce emotional states. The subjects are asked to think about and describe a situation in their lives in which they felt each of the following emotions: happiness, sadness, fear and anger. After a brief description of each story is obtained, the subject is asked to imagine and re-experience each emotional situation while their physiological activity (SCR, heart rate, respiratory frequency, skin temperature and facial EMG) is monitored. As a control condition, the subject is also asked to recall and imagine a non-emotional situation, e.g. getting up that morning, showering, dressing up, having breakfast and then going to work.

We tested eight VM patients with this procedure. They were all able to retrieve previous emotional experiences. Most importantly, they generated higher physiological activity (e.g. SCR and heart rate) during the imagery of the angry situations than during the neutral situations (Damasio *et al.*, 1997; Tranel *et al.*, 1998). Although all the VM patients reliably re-experienced anger, the re-experience of fear was less reliable, i.e. some could not experience it at all, and those who could did so with a less intense response. Whereas the VM patients were able to re-experience anger and in some cases fear, most of them had difficulties conjuring up a happy or sad emotion. This suggests that damage to the VM cortex weakens the ability to re-experience an emotion from the recall of an appropriate emotional event. Consequently, it is reasonable to assume that the failure of VM patients to acquire anticipatory SCRs, coupled to their decision-making impairment, is in part due to their inability to re-experience the emotion of a previously fearful situation. Obviously, this is a preliminary finding that requires further investigation.

The same is also true for the induction of an emotion by external stimuli such as the viewing of emotionally charged pictures. Indeed, earlier studies showed that VM patients failed to generate SCRs to emotionally charged pictures when they viewed these pictures passively (Damasio *et al.*, 1990). However, the same patients generated normal magnitude SCRs to the same target pictures when they were asked to view and describe the content of the pictures (Damasio *et al.*, 1990). During the gambling task, VM patients would generate SCRs when they lost a large sum of money, but the magnitude of these SCRs was never as high as that of normal controls (Bechara *et al.*, 1999a). Together, these results suggest that these patients may have a weakened ability to process the affective attribute of an emotional stimulus or to actually experience the emotion associated with that stimulus. This weakness may contribute to the failure to trigger somatic states when deliberating about options for

a decision. However, the fact that these VM patients are not completely emotionless suggests that this weakness is not the sole factor responsible for the failure. Nonetheless, it is an intriguing thought that if the experience of punishment would be more intense, the VM patients might overcome the failure to re-experience the emotional state of punishment, and therefore improve the decision-making impairment. For instance, in the gambling task, if the punishment was made several times the amount that is effective in normal subjects, it may become effective and VM patients might begin to choose advantageously.

The Issue of Impulsiveness and Response Inhibition

The notion of impulsiveness is often linked to the function of the prefrontal cortex (Miller, 1992; Fuster, 1996), and is usually understood as a lack of response inhibition. In other words, the subject is unable to suppress or withhold a previously rewarding response, and the behavior appears impulsive. It is important to address this issue of impulsiveness in relation to the foregoing studies.

First, it is important to distinguish between *motor* and *cognitive* impulsiveness. *Motor impulsiveness* is usually studied in animals under the umbrella of 'response inhibition'. After establishing a habit to respond to a stimulus that predicts a reward, there is a sudden change in the contingencies of the task that requires the inhibition of the previously rewarded response. Go/no-go tasks, delayed alternation and response shifting are examples of experimental design that measure this type of impulsive behavior (Mishkin, 1964; Freedman, 1986; Diamond, 1990; Fuster, 1990; Stuss, 1992; Dias *et al.*, 1996; Freedman *et al.*, 1998). In humans, impulsive behavior is often uncovered in neuropsychological tasks that detect 'perseverative errors', such as the Wisconsin Card Sorting Task, or in experimental tasks such as delayed alternation (Freedman, 1986; Freedman *et al.*, 1998). *Cognitive impulsiveness*, on the other hand, which can be seen as related to an inability to delay gratification, is a more complex form of disinhibited behavior. Cognitive impulsiveness may be illustrated with the example in which a child sees a piece of a candy on the table and is told by the parent 'no, you must wait 30 min before you can have the candy; otherwise, you face punishment'. The child understands the information and holds for a short while but after 2 min can no longer delay the gratification, resist the temptation and inhibit the response to reach for the candy.

Previous studies have shown that VM patients with lesions that spare the basal forebrain do not show motor impulsiveness and do not perseverate in conventional neuropsychological tests, although those with lesions that involve the basal forebrain may (Bechara *et al.*, 1998). We can also state that VM patients during their performance of the gambling task switch decks whenever they receive punishment, just as normal controls do. Such a performance does not suggest a lack of inhibition to a previously rewarding response (Fig. 2). VM patients are also unimpaired in delay task procedures (i.e. delayed non-matching to sample) considered sensitive to deficits in response inhibition (Bechara *et al.*, 1998).

On the other hand, the behavior of VM patients in the gambling task, and in real life, can be viewed as similar to the cognitive impulsiveness of the child with the candy. That is to say, when the patients are presented with a deck of cards which yields a large immediate reward, even if it can cost a large loss in the future, the patients seem unable to delay the gratification of the reward for too long. Their tendency to return quickly and more often to the decks that yield high immediate reward seems to suggest such a mechanism. The question, however, is 'who' decides when to suppress, or not to suppress, such a response as the seeking of a large immediate reward? Somatic states may indeed serve as the decision maker in such a situation. The following is a proposal of how somatic states may interact with mechanisms of response inhibition.

Using the impulsive behavior of the child with the candy as an illustrative example, one can see the conflict created by the decision to reach or not to reach for the candy. There are positive somatic states generated by the immediate and available reward (the candy), or the large sum of money in the gambling task. On the other hand, there are negative somatic states generated by the delayed punishment threatened by the parent or the possible loss of a large sum of money in the gambling task. If the threat of punishment were severe enough, then the evoked negative somatic states generated by that threat would counteract the positive somatic states produced by the immediate reward. The choice to seek the reward would thus be marked with a negative value, and the response to reach for the immediate reward might be inhibited. However, if the situation were that of a mild punishment, which would let the immediate reward outweigh the future punishment, the negative somatic states triggered by the possible punishment might not be sufficiently strong to counteract the positive states triggered by the immediate reward. In this case, the choice would be marked with a positive value. In our example, the child reaches for the candy and the behavior may be considered normal, advantageous and not impulsive. This example illustrates two different readings of the same situation involving an immediate reward and a future punishment. The difference, however, is that in one situation the inhibition of the action to seek the reward should be inhibited because the delayed punishment outweighs the immediate reward. In the other situation, the action to seek the reward should not be inhibited because the immediate reward outweighs the delayed punishment. The construct of impulsiveness and response inhibition by itself does not explain when to inhibit a given response or not. The activation of somatic states provides the important signals leading to whether to inhibit the response under consideration or not.

Conclusion

With the exception of a few theories on decision making (Janis and Mann, 1977; Mann, 1992), most current theories of choice use a cognitive perspective. These theories assume that decisions derive from an assessment of the future outcomes of various options and alternatives through some type of cost–benefit analyses. Some of these theories have addressed emotion as a factor in decision making, but mostly as a consequence of a decision (e.g. the disappointment or regret experienced after some risky decision) rather than as the reactions arising directly from the decision itself at the time of deliberation. The somatic marker hypothesis proposes that individuals make judgements not only by assessing the severity of outcomes and their probability of occurrence, but also and primarily in terms of their emotional quality. Lesions of the VM prefrontal cortex interfere with the normal processing of somatic or emotional signals, but leave other cognitive functions minimally affected. This damage leads to pathological impairments in the decision-making process which seriously compromise the efficency of everyday-life decisions. The somatic marker proposal is consistent with the views of others who invoke a primary role for mood, affect and emotion in decision making (Schwartz and Clore, 1983; Zajonc, 1984; LeDoux, 1996). However, it differs

from the view that body signals only introduce noise into the decision-making system (Rolls, 1999). Shallice has proposed a model for decision making that invokes the idea of marking various options with a value (Shallice, 1993). However, the nature of these markers is not specified, and it is implied that they are cognitive in nature. Thus, the views of both Rolls and Shallice are more consistent with the 'as-if body loop' component of the somatic marker hypothesis. The fundamental notion of the somatic marker hypothesis is that bioregulatory signals, including those that constitute feeling and emotion, provide the principal guide for decisions and are the basis for the development of the 'as-if body loop' mode of operation.

The somatic marker hypothesis and the experimental strategies used to study decision making in neurological patients provide parallels and direct implications for understanding the nature of several psychiatric disorders. For instance, substance abusers are similar to VM patients in that when faced with a choice that brings some immediate reward (i.e. taking a drug), at the risk of incurring a loss of reputation, job, home and family, they choose the immediate reward and ignore the future consequences. Using the gambling task (Grant *et al.*, 1997; Petry *et al.*, 1998; Bechara *et al.*, 1999b) or related decision-making tasks (Rogers *et al.*, 1999), recent studies have indicated that impairment in decision making may stand at the core of the problem of substance abuse. Similarly, the personality profile of VM patients bears some striking similarities to psychopathic (or sociopathic) personality, so much so that we have used the term 'acquired sociopathy' to describe the condition of patients with VM damage (Damasio *et al.*, 1990). The qualifier 'acquired' signifies that the condition in VM patients follows the onset of brain injury, and occurs in persons whose personalities and social conduct were previously normal. The patients are usually not destructive or harmful to others, a feature that tends to distinguish the 'acquired' form of the disorder from the standard 'developmental' form. Indeed, recent evidence has indicated that the earlier the onset of VM damage, the more severe the antisocial behavior, suggesting that early dysfunction in the prefrontal cortex may, by itself, cause abnormal development of social and moral behavior (Anderson *et al.*, 1999). Recent studies have begun to look at the possibility that the psychopathic behavior seen in cases in which no neurological history has been identified may be linked to abnormal operation of the neural system involving the VM (Schmitt *et al.*, 1999). Finally, in addition to the disorders mentioned above, applications of the somatic marker hypothesis may extend to psychiatric disorders that include schizophrenia (Wilder *et al.*, 1998), pathological gambling, depression, and attention deficit and hyperactivity disorders (ADHD).

Notes

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