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The role of emotion in decision-making: Evidence from neurological patients with orbitofrontal damage

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Abstract

Most theories of choice assume that decisions derive from an assessment of the future outcomes of various options and alternatives through some type of cost-benefit analyses. The influence of emotions on decision-making is largely ignored. The studies of decision-making in neurological patients who can no longer process emotional information normally suggest that people make judgments not only by evaluating the consequences and their probability of occurring, but also and even sometimes primarily at a gut or emotional level. Lesions of the ventromedial (which includes the orbitofrontal) sector of the prefrontal cortex interfere with the normal processing of "somatic" or emotional signals, while sparing most basic cognitive functions. Such damage leads to impairments in the decision-making process, which seriously compromise the quality of decisions in daily life. The aim of this paper is to review evidence in support of "The Somatic Marker Hypothesis," which provides a systems-level neuroanatomical and cognitive framework for decision-making and suggests that the process of decision-making depends in many important ways on neural substrates that regulate homeostasis, emotion, and feeling. The implications of this theoretical framework for the normal and abnormal development of the orbitofrontal cortex are also discussed.

1. Introduction

The orbitofrontal region of the prefrontal cortex includes the rectus gyrus and orbital gyri, which constitute the inferior surface of the frontal lobes lying immediately above the orbital plates. Lesions of this region are not usually restricted to the orbitofrontal cortex, but they extend into neighboring cortex and involve different size sectors of the ventromedial prefrontal (VM) region. The VM region includes the medial and varying sectors of the lateral orbitofrontal cortex, thus encompassing Brodmann's areas (BA) 25, lower 24, 32, and medial aspect of 11, 12, and 10, and the white matter subjacent to all of these areas. Patients with bilateral lesions of the VM cortex (Fig. 1) develop severe impairments in personal and social decision-making, in spite of otherwise largely preserved intellectual abilities. Before their brain damage, they have normal intelligence and creativity. After the damage, they develop difficulties in planning their workday and future; difficulties in choosing friends, partners, and activities (Bechara, Damasio et al., 2000; Bechara, Tranel, & Damasio, 2002).

The "Somatic Marker Hypothesis" was proposed in order to provide a neural explanation of the real-life decision-making defect of these patients. The main point of this hypothesis is that decision-making is a process guided by emotions. There is a link between the abnormalities in emotion and feeling of these patients and their severe impairment in judgment and decision-making in real-life (Bechara, Damasio et al., 2000, 2002).

We tested the somatic marker hypothesis using the gambling task (GT) paradigm for measuring decision-making (Bechara, Tranel, & Damasio, 2000). However, there are other paradigms, namely the "betting task" (also referred to as the Cambridge Gamble Task) developed by Rogers and colleagues (Rogers, Everitt et al., 1999), and tasks of delayed discounting (Bickel, Degrandpre, & Higgins, 1995). It has been shown that there is a significant correlation between performance on the GT, the "betting task," and tasks of delayed discounting (Monterosso, Ehrman, Napier, O'Brien, & Childress,

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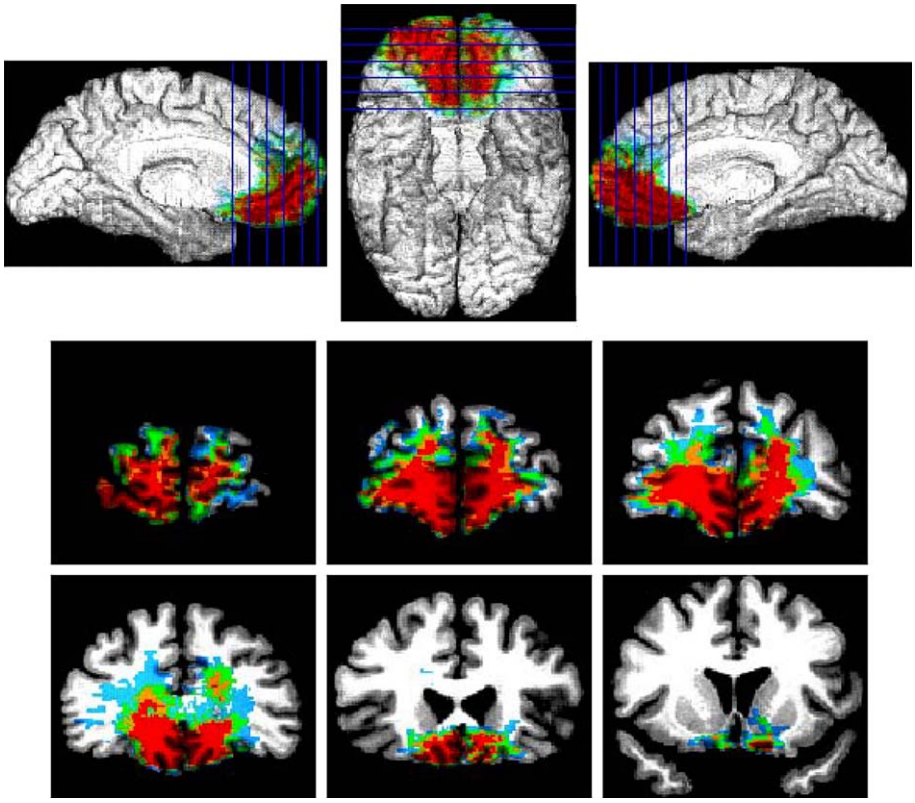

Fig. 1. Overlap of lesions in a group of VM patients. The red color indicates an overlap of four or more patients. From (Bechara, Damasio, & Damasio, 2000) (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this paper.).

2001), thus supporting the notion that these three sets of tasks may engage a common mechanism of decision-making, tied to the VM region.

2. The gambling task

The task has been described in detail elsewhere (Bechara, Tranel et al., 2000). Briefly, in the gambling task (also referred to as the Iowa gambling task), subjects have to choose between decks of cards which yield high immediate gain but larger future loss, i.e., long term loss, and decks which yield lower immediate gain but a smaller future loss, i.e., a 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 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, i.e., long term loss (disadvantageous decks), and two of the decks (C and D) yield lower immediate gain but a smaller future loss, i.e., a long term gain (advantageous decks).

3. Behavioral findings in VM patients

We investigated the performance of normal control subjects with demographic characteristics matched to a group of patients with bilateral damage to the VM region of the prefrontal cortex (Fig. 1) and a separate group of patients with damage to the lateral occipital or lateral temporal cortex (brain-damaged controls). Normal and brain-damaged control subjects avoided the bad/disadvantageous decks (A and B) and preferred the good decks (C and D). By contrast, VM patients did not avoid (i.e., they preferred) the bad decks (A and B) (Fig. 2). From these results we suggested that the VM patients' performance profile is comparable to their real-life inability to decide advantageously in situations involving choosing between immediate vs. delayed reward or punishment. This is especially true in personal and social matters, a domain for which in life, as in the

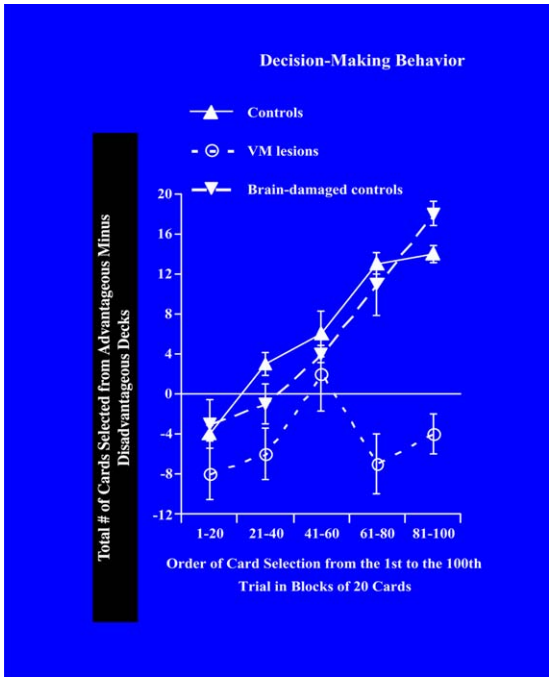

Fig. 2. Relative to normal controls and brain-damaged controls, VM patients were impaired in their performance on the gambling task. The figure shows net scores ((C + D) − (A + B)) of cards selected by each group across different blocks expressed as means ± SEM. Positive net scores reflect advantageous performance while negative net scores reflect disadvantageous performance.

task, an exact calculation of the future outcomes is not possible and choices must often be based on approximations, hunches, and guesses (Bechara, Damasio et al., 2000).

3.1. Biases guide decisions

Based on these behavioral results, we asked the following questions: Why do these patients have this "myopia" for the future? Why can they not "foresee the future"?

To answer these questions, we added a psychophysiological measure while playing the gambling task. The goal was to assess somatic state activation when making decisions during the gambling task. We studied two groups: normal subjects and VM patients. We had them perform the gambling task while we recorded their skin conductance response (SCR) activity (Bechara, Tranel, Damasio, & Damasio, 1996). Both normal controls and VM patients generated SCRs after they had picked the card and were told that they won or lost money. The most important difference, however, was that normal controls, as they became experienced with the task, they began to generate SCRs prior to the selection of any cards, i.e., during the time when they were pondering from which deck to choose. These anticipatory SCRs were more pronounced before picking a card from the risky decks A and B, when compared to the safe decks C and D. VM patients entirely failed to generate any SCRs before picking a card (Fig. 3). These results provide strong support for the notion that decision-making is guided by emotional signals (or somatic states), which are generated in anticipation of future events.

4. Right versus left VM damage

Given the functional asymmetry of the cerebral hemispheres, it is important to determine whether the

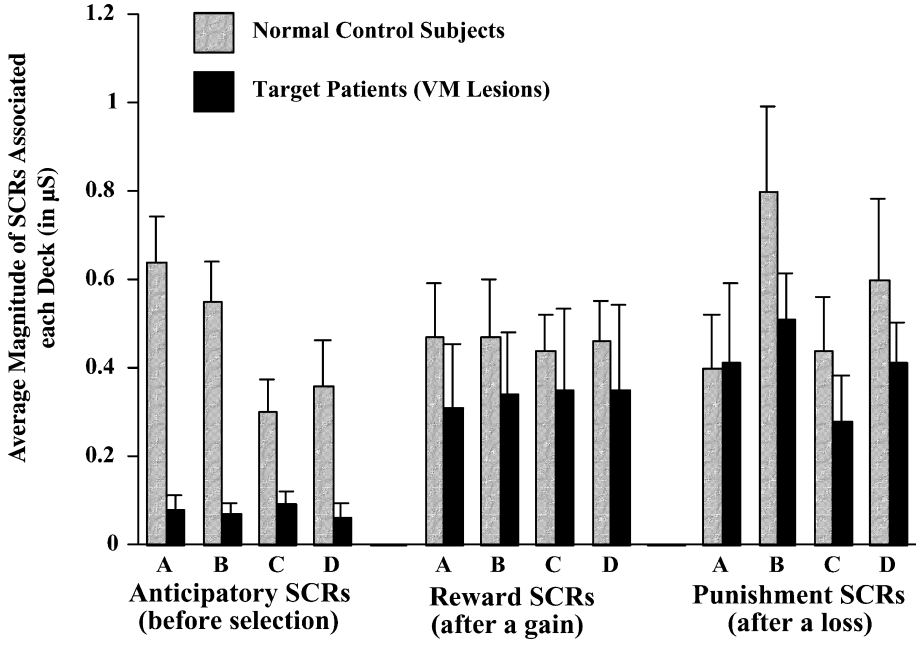

Fig. 3. Means ± SEM of the magnitudes of anticipatory, reward, and punishment SCRs generated by normal controls and target patients (VM lesions) averaged across all cards selected from a given deck.

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 a unilateral damage on the medial and orbital side of the prefrontal cortex. We have collected data from such rare patients with right or left VM lesions (Tranel, Bechara, & Denburg, 2002). 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 VM patients with bilateral lesions (Fig. 4). 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.

One pertinent question in relation to this finding is why did the deficit follow right-sided, as opposed to left-sided lesions? One possible explanation relates to the lesion, electrophysiological and functional neuroimaging work linking the processing of approach behaviors and positive emotions to the left prefrontal cortex, and the processing of avoidance behaviors and negative emotions to the right prefrontal cortex (Davidson & Irwin, 1999; Davidson, Jackson, & Kalin, 2000). It is predicted from this work that hypo functioning left prefrontal cortices should be associated with insensitivity to "positive," and perhaps increased sensitivity to "negative," consequences. In contrast, hypo functioning right prefrontal cortices should be associated with insensitivity to "negative," and perhaps increased sensitivity to "positive," consequences. In the gambling task used in this study, an increased sensitivity to reward, combined with decreased sensitivity to punishment, associated with right side lesions can explain the preference of right prefrontal patients to the disadvantageous decks, and thus support this notion of processing positive versus negative emotions in left versus right prefrontal cortices, respectively.

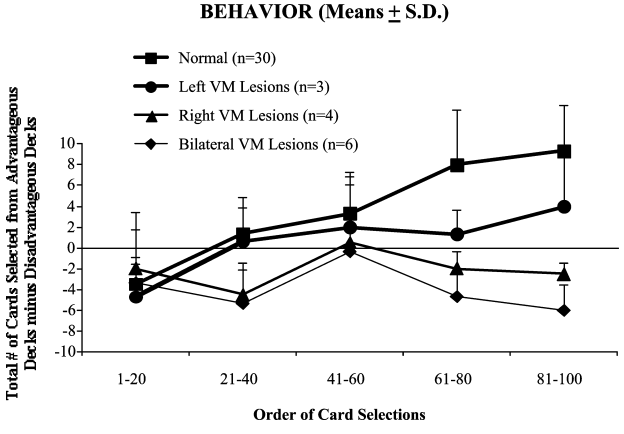

Fig. 4. Net scores ((C + D) − (A + B)) of cards selected by each group (normal control subjects, right VM, left VM, and bilateral VM subjects) across different blocks expressed as means ± SD. Positive net scores reflect advantageous performance while negative net scores reflect disadvantageous performance. From Tranel et al. (2002).

5. Developmental versus adult onset of VM damage

Patients who acquired VM prefrontal lobe damage during childhood are relatively rare. However, evidence from two young adults who acquired focal damage to the prefrontal cortex in early childhood, prior to 16 months of age, revealed very important facts (Anderson, Bechara, Damasio, Tranel, & Damasio, 1999). The patients with early-onset VM lesions superficially resemble adult-onset patients in terms of disrupted social behavior, which contrasts with normal basic cognitive abilities. These patients show insensitivity to future consequences, and their behavior is guided by immediate consequences, both in the social world and on the gambling task. The ability to generate somatic signals in anticipation of future outcomes (anticipatory SCRs) was also defective. However, a closer analysis revealed several distinctive features. First, the inadequate social behaviors are present throughout development and into adulthood, i.e., there was no recovery of function such as happens with language when the left hemisphere is damaged at an early age. Second, these behavioral defects are more severe in early-onset patients relative to adult-onset. Third, the inadequate emotional responses are also more severe. Finally, the early-onset patients cannot retrieve socially relevant knowledge at factual level as adult-onset patients do (Anderson et al., 1999).

6. Peripheral mechanisms of decision-making

The key idea of the somatic marker 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. What is the evidence that supports the notion that physiological changes related to emotion (somatic states), which arise in the body outside the brain, do play a role in influencing decisions?

There are three possible neural routes by which somatic signals expressed in the body can feedback to the brain and influence cognition. One is through the spinal cord, another is through the vagus nerve, and a third is an endocrine route. Several lines of evidence prompted

the testing of the hypothesis that the vagus nerves might be the critical peripheral conduit for somatic signals to influence decision-making. Subjects with cervical spinal cord injury did not show impairment in decision-making as measured by the gambling task (North & O'Carroll, 2001). On the other hand, in a preliminary study, we have collected data from subjects with primary polyneuropathies affecting primarily small diameter and/or autonomic fibers, and observed mild impairments in the gambling task (Bechara, Tranel et al., 1998). In this preliminary study, we have collected data from 20 subjects with peripheral neuropathies, mainly of the sensory type. We compared their performance in the gambling task to that of 15 demographically matched controls. We found that the subjects with peripheral neuropathy performed deficiently on the gambling task relative to the controls. However, since peripheral neuropathy does not represent a complete "disconnection" between the body and the brain, it is not surprising that the impairment is relatively mild in relation to some of the performances seen in subjects with brain lesions. There is also evidence that stimulation of the vagus nerve improves memory (Clark, Naritoku, Smith, Browning, & Jensen, 1999), thus providing an indirect support for the hypothesis that the vagus nerve may be the more important peripheral substrate for the process of decision-making.

We tested the hypothesis with epileptic patients with implanted left vagus nerve stimulators. To assess decision-making we used the gambling task. Patients performed two repeat versions of this task. Using a counterbalanced design, low level vagal nerve stimulation (VNS) was covertly delivered during one of the two sessions of performing the gambling task. The cognitive status of the subjects was assessed in the un-stimulated state with a standard battery of neuropsychological tests measuring intellect, memory, language, perception, attention, executive function, and mood. Despite normal IQ scores, overall, these subjects performed disadvantageously on the gambling task. This may not be surprising given that the majority of these subjects are unable to function independently in the real-world. Most intriguing, subjects showed an incremental improvement in performance (selecting more advantageous cards) in the stimulated relative to the un-stimulated condition. Although preliminary, these results suggest that VNS influences decision-making (Martin, Bechara, Denburg, Granner, & Tranel, 2001). These results also add to the evidence supporting of the role of the vagus nerve in cognition and emotion.

7. Decision-making versus other frontal lobe functions

In a series of studies with non-human primates and human subjects, Petrides (1985, 1990) has established a link between frontal lobe damage and learning *conditional associations*, i.e., the ability to associate responses with specific stimuli on the basis of repeated feedback. However, closer investigations revealed that the posterior DL sector may be the critical region for this function. Shallice and colleagues have attempted to investigate deficits in *planning* ability associated with frontal lobe damage using tasks that require the planning and execution of sequences of responses. They used the Tower of Hanoi (and a variant, the Tower of London) (Shallice, 1982), and other tasks that resemble more closely real-world activities (Shallice & Burgess, 1991). Patients with frontal lobe lesions were found to have deficits in planning as measured by these laboratory tasks. However, the VM sector does not seem critical for mediating this type of planning function since many VM patients perform well on the Tower of Hanoi, and are only mildly impaired on other complex planning tasks. Thus, it seems that this type of planning deficit is more severe when the basal forebrain is damaged, or when the DL sector is damaged. Finally, a link between frontal lobe damage and the ability to make *cognitive estimations* has been established in a few studies (Shallice & Burgess, 1991; Smith & Milner, 1984). However, this function also does not seem to depend on the VM sector of the prefrontal cortex, since many VM patients perform normally on this type of task (Saver & Damasio, 1991).

8. Decision-making and working memory are mediated by separate anatomical sectors

The frontal lobe function that we addressed in detail in relation to decision-making is working memory. The rationale for the notion that working memory and decision-making are distinct functions comes from the observations that VM patients suffer from impairments in decision-making, while preserving a normal level of memory and intellect. On the other hand, although some patients with lesions in the dorsolateral sector of the prefrontal cortex (DLPC) 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, and the gambling task to measure decision-making, the following experiment was performed. A group of normal control subjects, patients with bilateral VM lesions and patients with right or left lesions of the DL sector of the prefrontal cortex were tested on the delay and gambling tasks (Bechara, Damasio, Tranel, & Anderson, 1998).

Delay tasks that are used in non-human primates are too simple for use with humans. Therefore, a distractor was introduced during the delay between the cue and the response. The purpose of the distractor was to

interfere with the ability of the subject to rehearse 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 faces down. The correct response was to select the two cards that were first face up. During the delay, the subject had to read aloud a series of semantically meaningless sentences. The scores were calculated as the percent of correct choices that were 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 cut-off score below which no normal control ever performed. 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 one, 10, 30, or 60 s, four cards appeared on the screen, all were face up, two of them were red, and two were black. The correct response was to select the two cards of opposite 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 DLPC are associated with different domains of working memory. The inferior areas of the DLPC have been associated with object memory, whereas the superior areas have been associated with spatial memory (Wilson, Scalaidhe, & Goldman-Rakic, 1993). A similar dissociation was found in humans, using functional neuroimaging techniques (Courtney, Ungerleider, Keil, & Haxby, 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. 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 the DLPC, we used both types of delayed tasks because we anticipated that both domains of working memory (spatial and object) might 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 set of tasks. 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.

The 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 DLPC lesions and severe working memory impairments showed low normal results in the gambling task.

Although all VM patients tested in this experiment were impaired on the gambling task, they were split in their performance in the delay tasks. Some patients were abnormal in the delay tasks (abnormal gambling/abnormal delay), and some were normal in the delay tasks (abnormal gambling/normal delay). 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. 5).

These findings reveal a double dissociation (cognitive and anatomic) between deficits in decision-making (anterior VM) and working memory (right DLPC). However, the dissociation is asymmetrical: deficits in decision-making occur independent of deficits in working memory; deficits in working memory compromise decision-making (Bechara, Damasio et al., 1998).

9. Decision-making versus impulse control or response inhibition

Working memory includes several components, e.g., short-term storage, rehearsal, and executive processes operating on the contents of storage (Smith, 2000; Smith & Jonides, 1999). The DLPC appears involved specifically in the executive process of working memory, i.e., the monitoring of mnemonic operations rather than the short-term storage of information (Petrides, 2000; Petrides, Alivisatos, & Frey, 2002). Neurons in DLPC project to the hippocampal region and the overlaying temporal cortices, and neurophysiological studies in monkeys support the concept of prefrontal "top down" control of temporal lobe memory functions (Tomita, Ohbayashi, Nakahara, Hasegawa, & Miyashita, 1999). Studies in non-human primates have shown that impaired delay task performance can also result from impairments in selective attention (Heilman, Watson, Valenstein, & Goldberg, 1987; Rizzolatti & Camarda, 1987) and response inhibition (Fuster, 1996; Mishkin, 1964). Since in the GT paradigm the subjects are rewarded repeatedly before encountering a loss when choosing cards from a bad deck, it might be argued that impaired performance on the GT is caused by defective

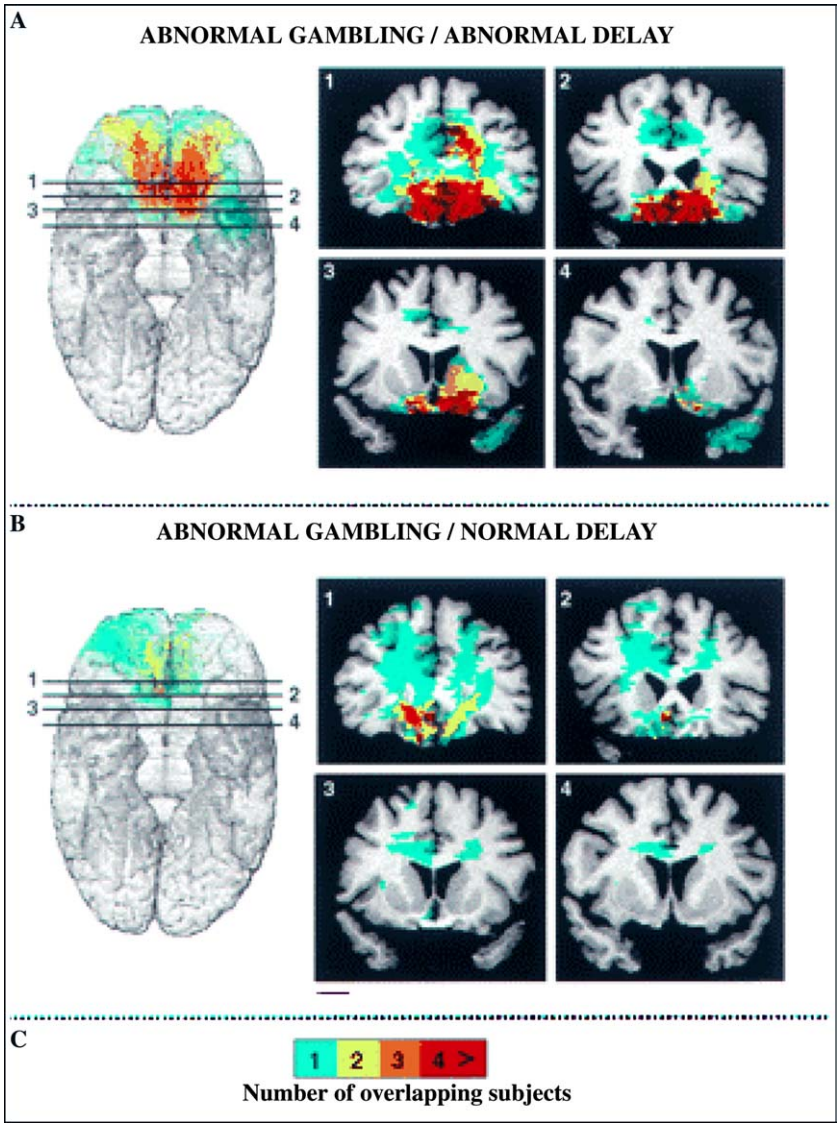

Fig. 5. Separate mapping of VM lesions for Group 1 (A) and Group 2 (B) subjects. The maximal overlap of subjects in (A) is seen spanning the whole extent of the mesial orbital surface of the frontal lobe. It reaches the most posterior sector (coronal slice 3 and 4) where basal forebrain structures are found. However, in (B) the maximal overlap is mostly anterior extending only to slice 1 and 2. Slices 3 and 4 do not show any lesion. From Bechara, Damasio et al. (1998).

response inhibition, i.e., inability to suppress previously rewarded responses, and shifting attention to the good decks.

Although the mechanisms of shifting attention and response inhibition (included in the executive process of working memory) and decision-making are asymmetrically dependent as discussed earlier, we argue that impulsiveness, which usually means the lack of response inhibition, is fundamentally different from decision-making, both cognitively and anatomically. Decision-making as exemplified in the GT paradigm involves (1) a dilemma that requires evaluation of pros and cons of various response options, i.e., there is no easy answer. (2) Most important, the outcome of a given action is uncertain and unpredictable. Deficits in decision-making may be described as a type of *cognitive impulsiveness*, a term that has been used previously in human studies (Barratt, 1994), and it may be analogous to the term "impulsive outcome" referring to a failure to delay gratification and evaluate the outcome of a planned action (Evenden, 1999). A real-life example would be a person who finds a briefcase with $100,000 in it in a dark alley. The person may deliberate on whether to keep or return the money. Thus in this scenario, there is (1) a moral dilemma, and (2) most important, the outcome of keeping or returning the money is uncertain and unpredictable. On the other hand, mechanisms of impulsiveness or response inhibition involve (1) a learned inhibition that does not require evaluation of pros and cons of various response options. (2) Most important,

the outcome of a given action is certain and predictable. A real-life example would be the same person finding a pile of money spread out on a table inside a bank. In this scenario, a normal person (1) would not stand up and evaluate the pros and cons of leaving or grabbing the money, unless the person is a robber and considering robbing the bank, in which case the whole evaluation process of whether to rob the bank or not, and the consequences of each course of action, will invoke the process of decision-making. (2) Most important, in the normal case, the outcomes of leaving or steeling the money are certain and predictable. Any impulse to have access to the pile of money is simply inhibited; perhaps in the same way as any impulse to get up and run away from an approaching dentist with a tooth driller is also inhibited. If the person acted without thinking and reached for the money, then this can be a sign of poor impulse control; perhaps analogous to some disinhibited frontal lobe patients who quickly grab items that do not belong to them, such as the pen or glasses of the examiner on the table in front of them. However, evidence suggests that there may be several mechanisms of impulse control or response inhibition that can be measured by different tasks and attributed to different neural regions. These different mechanisms of impulse control include *motor impulsiveness*, which has been proposed in humans to have several forms (Evenden, 1999). This includes: (1) impulsive preparation, which involves making a response before all the necessary information has been obtained; and (2) impulsive execution, which involves quick action without thinking (Evenden, 1999). However, functional neuroimaging and lesion studies suggest that although the anterior cingulate is critical for motor impulsiveness, there may be a distinction between two sub-types of motor impulsiveness.

(i) Motor impulsiveness of non-affective nature, which reflects an inability to inhibit a pre-potent response that is non-affective. The Stroop test, in which the subject must name the print color of a word and inhibit the stronger tendency to read the name of a color itself, provides a laboratory measure of this type of impulse control. The supracallosal sector of the anterior cingulate appears critical for this mechanism based on functional neuroimaging studies (Carter et al., 1998; Frith, Friston, Liddle, & Frackowiak, 1991; Garavan, Ross, & Stein, 1999; Pardo, Pardo, Janer, & Raichle, 1990). Stuss and colleagues have presented data of performance on the Stroop from a large number of patients with lesion of the prefrontal cortex (Stuss, Floden, Alexander, Levine, & Katz, 2001) that support the notion that this general area (cingulate and mesial aspect of the superior frontal gyrus) may be critical for the type of response inhibition required by the Stroop.

(ii) Motor impulsiveness of affective nature reflects an inability to inhibit a pre-potent response that is affective, i.e., a pre-potent rewarded response. Go/no Go tasks, delayed alternation, and reversal learning are prime examples of paradigms that measure this type of behavioral control. The subgenual sector of the anterior cingulate appears critical for this type of impulsiveness, as reflected by impairments in reversal learning of previously rewarded responses (Owen, Roberts, Polkey, Sahakian, & Robbins, 1991; Rolls, Hornak, Wade, & McGrath, 1994).

(iii) In addition to motor impulsiveness, evidence suggests that there may be a similar mechanism at the "thought" or "short-term memory" level that we call: *perceptual impulsiveness*. This simply reflects an inability to inhibit a recurrent thought held in working memory. Perseveration on the Wisconsin Card Sorting Task (WCST) and inability to shift attentional sets (ID-ED shift) are laboratory measures of this type of deficit in impulse control (Dias, Robbins, & Roberts, 1996; Dias, Robbins, & Roberts, 1997; Milner, 1963). The lateral frontal and anterior insular cortices appear critical for this type of impulsiveness, based on functional neuroimaging (Konishi et al., 1999; Lombardi et al., 1999) as well as lesion (Anderson, Damasio, Jones, & Tranel, 1991; Milner, 1963) studies using the WCST, and based on lesion studies using the attention set shifting (shift attention from one perceptual dimension of a complex visual stimulus to another) task (Owen et al., 1991, 1993).

10. Conclusions

The somatic marker hypothesis provides a systems-level neuroanatomical and cognitive framework for decision-making and its influence 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. The orbitofrontal cortex represents one critical structure in a neural system subserving decision-making. However, the orbitofrontal cortex alone does not mediate decision-making. Decision-making arises from large-scale systems that include other cortical and subcortical components that include the amygdala, the somatosensory/insular cortices, and the peripheral nervous system.

Thus far, we have presented a case in which decision-making is influenced by signals arising in bioregulatory processes of the body proper. However, are decisions always associated with emotion and body states? The answer is "no" because somatic markers may influence decisions via a "body loop" or "as-if-loop." In the body loop mechanism, an appropriate emotional (somatic) state is actually re-enacted, and signals from its activation are then relayed back to subcortical and cortical somatosensory processing structures, especially in the

somatosensory (SI and SII) and insular cortices. This anatomical system is described as the "body loop." The enacted somatic state can then act consciously or non-consciously on the neural processes that enable the person to do, or to avoid doing a certain action. However, after emotions have been expressed and experienced at least once, one can form representations of these emotional experiences in the somatosensory/insular cortices. Therefore, after emotions are learnt, one possible chain of physiologic events is to by-pass the body altogether, activate the insular/somatosensory cortices directly, and create a fainter image of an emotional body state than if the emotion were actually expressed in the body. This anatomical system is described as the "as if body loop" (Fig. 6). However, the important question is: which decisions engage the "body loop," and which ones engage the "as-if-loop"? The answer to this question is still subject to ongoing investigations. But a preliminary answer is as follows:

Behavioral economists describe three classes of choice: (1) choice under certainty; (2) choice under risk; and (3) choice under ambiguity (uncertain) (Einhorn & Hogarth, 1985; Ellsberg, 1961). In choice under certainty the likelihood of outcome of the choice is fully specified and is equal to 100%, i.e., the choice is a sure thing. An example will be to choose between a 100% chance to win $100 or $50. In choice under risk the likelihood of outcome of the choice is fully specified by a probability distribution, i.e., the choice is risky. An example will be to choose between 50% chance to win $100 and 100% chance to win $50. In choice under ambiguity, the likelihood associated with the outcome of the choice is not specified at all, and it is completely unstated. An example is a choice between an unknown opportunity to win $100 and the certainty to win $50. Preliminary studies using the gambling and "betting" tasks described previously support the hypothesis that the "body loop" mode of operation becomes increasingly prominent as decisions move from certainty to risk, to ambiguity (full uncertainty). Rogers, Everitt et al. (1999) developed a decision-making task, the "betting" task, which was shown to be sensitive to orbitofrontal lobe damage. Functional neuroimaging studies using the same task revealed increased activation in the orbitofrontal region, right parietal cortices, and uncus (Rogers et al., 1999), all areas that include the target regions that we hypothesize as critical for decision-making. However, there is a fundamental difference between the "betting" task and our gambling task. In the gambling task, subjects are not explicitly told the pay-off structure of the task. Rogers argued that the lack of specified contingencies would make it difficult to characterize the underlying deficit. The argument was that at least in some cases, a person may make disadvantageous choices because she/he is failing to take long-range interests into account, or because s/he is unaware of the actual contingencies. This

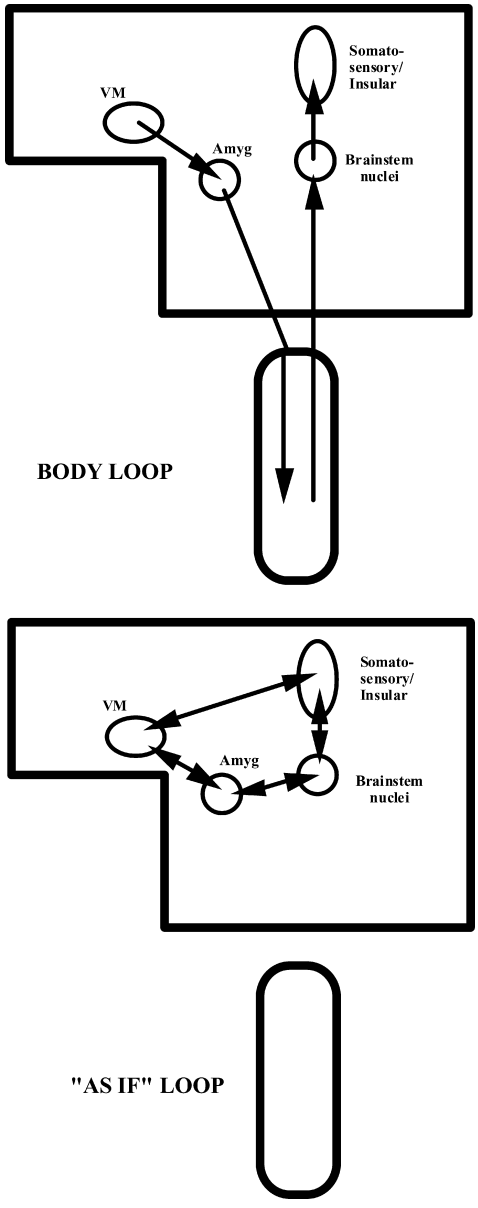

Fig. 6. Simple diagrams illustrating the "body loop" and "as if loop" chain of physiologic events. In both "body loop" and "as if loop" panels, the brain is represented by the top black perimeter and the body by the bottom one.

was one of the reasons why Rogers and colleagues designed the "betting" task to measure deficits in orbitofrontal functioning, in which the contingencies were made more explicit. In this task, subjects are asked to decide among choices in which odds explicitly favor one of the available options. In the "betting" task, while the outcomes of individual trials may not be 100% certain, and according to the labels mentioned earlier this would be called a task of risk, the level of certainty ranges from very high (i.e., 90%) to somewhat risky (i.e., 60%). By contrast, in the gambling task, which according to the labels mentioned earlier would be called a task of ambiguity, in which the level of uncertainty remains high

throughout. Subjects never acquire knowledge about the probabilities of reward and punishment, even when they reach conceptual knowledge about the overall goodness and badness of the various choices. Preliminary findings indicate that normal subjects generate minimal anticipatory SCRs during the "betting" task, especially in relation to the most certain choices compared to the most risky choices. Most important, the overall average of anticipatory SCRs generated during the "betting" task are lower than those from the gambling task, thus consistent with the hypothesis that decision-making under ambiguity where the outcome is unknown, unpredictable, and cannot be estimated will engage the "body loop." By contrast, decision-making under certainty, where the outcome is explicit and predictable, will engage the "as-if body loop."

11. Developmental implications

The functions of the prefrontal cortex may not develop fully until the age of 21 (Begley, 2000; Rubia et al., 2000). During this period, the development of neural connections that underlie more complex behaviors, including decision-making and the control over powerful temptations, is still taking place (Eslinger, 1999). There are several pre-existing factors that may promote abnormal development of the prefrontal cortex and its connectivity during this vulnerable period of development. Some of these factors are hereditary (e.g., positive family history of substance abuse), but others are environmental or the product of gene–environment interactions. In light of our evidence that impairments associated with early-onset damage of the orbitofrontal cortex do not recover over time, these factors may help create a sub-clinical deficit in mechanisms of decision-making and impulse control, which in turn increases the propensity of the affected individual to make poor and "risky" decisions that escalate during adulthood into antisocial behaviors and disorders such substance abuse and addiction (Chassin, Pitts, Delucia, & Todd, 1999; Paschall & Flewelling, 2002; Sher, Martin, & Wood, 1997). Thus understanding the critical developmental mechanisms of the orbitofrontal cortex should help us understand how one can avert developmental instances of poor and risky decisions.

References

Anderson, S. W., Bechara, A., Damasio, H., Tranel, D., & Damasio, A. R. (1999). Impairment of social and moral behavior related to early damage in the human prefrontal cortex. *Nature Neuroscience, 2*, 1032–1037.

Anderson, S. W., Damasio, H., Jones, R. D., & Tranel, D. (1991). Wisconsin card sorting test performance as a measure of frontal lobe damage. *Journal of Clinical and Experimental Neuropsychology, 3*, 909–922.

Barratt, E. S. (1994). Impulsiveness and aggression. In J. Monahan & H. J. Steadman (Eds.), *Violence and mental disorder: Developments in risk assessment* (pp. 61–79). Chicago: University of Chicago.

Bechara, A., Damasio, H., & Damasio, A. R. (2000). Emotion, decision-making, and the orbitofrontal cortex. *Cerebral Cortex, 10*, 295–307.

Bechara, A., Damasio, H., Tranel, D., & Anderson, S. W. (1998). Dissociation of working memory from decision making within the human prefrontal cortex. *The Journal of Neuroscience, 18*, 428–437.

Bechara, A., Tranel, D., & Damasio, A. R. (2002). The somatic marker hypothesis and decision-making. In F. Boller & J. Grafman (Eds.), *Handbook of neuropsychology: Frontal lobes* (Vol. 7, (2nd ed., pp. 117–143). Amsterdam: Elsevier.

Bechara, A., Tranel, D., & Damasio, H. (2000). Characterization of the decision-making impairment of patients with bilateral lesions of the ventromedial prefrontal cortex. *Brain, 123*, 2189–2202.

Bechara, A., Tranel, D., Damasio, H., & Damasio, A. R. (1996). Failure to respond autonomically to anticipated future outcomes following damage to prefrontal cortex. *Cerebral Cortex, 6*, 215–225.

Bechara, A., Tranel, D., Wilson, J., Heberlein, A. S., Ross, M., & Damasio, A. R. (1998). Impaired decision-making in peripheral neuropathy. *Society for Neuroscience Abstracts, 24*, 1176.

Begley, S. (2000). Getting inside a teen brain: Hormones aren't the only reason adolescents act crazy: Their gray matter differs from children's and adults'. *Newsweek, February 28*, 58–59.

Bickel, W. K., Degrandpre, R. J., & Higgins, S. T. (1995). The behavioral economics of concurrent drug reinforcers—A review and reanalysis of drug self-administration research. *Psychopharmacology, 118*, 250–259.

Carter, C. S., Braver, T. S., Barch, D. M., Botvinick, M. M., Noll, D., & Cohen, J. D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science, 280*, 747–749.

Chassin, L., Pitts, S. C., Delucia, C., & Todd, M. (1999). A longitudinal study of children of alcoholics: Predicting young adult substance abuse disorders, anxiety, and depression. *Journal of Abnormal Psychology, 108*, 106–119.

Clark, K. B., Naritoku, D. K., Smith, D. C., Browning, R. A., & Jensen, R. A. (1999). Enhanced recognition memory following vagus nerve stimulation in human subjects. *Nature Neuroscience, 2*, 94–98.

Courtney, S. M., Ungerleider, L. G., Keil, K., & Haxby, J. V. (1996). Object and spatial visual working memory activate separate neural systems in human cortex. *Cerebral Cortex, 6*, 39–49.

Davidson, R. J., & Irwin, W. (1999). The functional neuroanatomy of emotion and affective style. *Trends in Cognitive Sciences, 3*, 11–21.

Davidson, R. J., Jackson, D. C., & Kalin, N. H. (2000). Emotion, plasticity, context, and regulation: Perspectives from affective neuroscience. *Psychological Bulletin, 126*, 890–909.

Dias, R., Robbins, T. W., & Roberts, A. C. (1996). Dissociation in prefrontal cortex of affective and attentional shifts. *Nature, 380*, 69–72.

Dias, R., Robbins, T. W., & Roberts, A. C. (1997). Dissociable forms of inhibitory control within prefrontal cortex with an analog of the Wisconsin card sort test: Restrictions to novel situations and independence from "on-line" processing. *Journal of Neuroscience, 17*, 9285–9297.

Einhorn, H. J., & Hogarth, R. M. (1985). Ambiguity and uncertainty in probabilistic inference. *Psychological Reviews, 92*, 433–461.

Ellsberg, D. (1961). Risk, ambiguity, and the savage axioms. *Quarterly Journal of Economics, 75*, 643–669.

Eslinger, P. J. (1999). Conceptualizing, describing, and measuring components of executive function. In G. R. Lyon & N. A. Krasnegor (Eds.), *Attention, memory and executive function* (pp. 420–441). Baltimore: Paul H. Brooks.

Evenden, J. (1999). Impulsivity: A discussion of clinical and experimental findings. *Journal of Psychopharmacology, 13*, 180–192.

Frith, C. D., Friston, K., Liddle, P. F., & Frackowiak, R. S. J. (1991). Willed action and the prefrontal cortex in man—a study with PET. *Proceedings of the Royal Society of London Series B. Biological Sciences, 244*(1311), 241–246.

Fuster, J. M. (1996). *The prefrontal cortex. Anatomy, physiology, and neuropsychology of the frontal lobe* (3rd ed.). New York: Raven Press.

Garavan, H., Ross, T. J., & Stein, E. A. (1999). Right hemispheric dominance of inhibitory control: An event-related functional MRI study. *Proceedings of the National Academy of Sciences of the United States of America, 96*(14), 8301–8306.

Heilman, K. M., Watson, R. T., Valenstein, E., & Goldberg, M. E. (1987). Attention: Behavior and neuronal mechanisms. In F. Plum, V. B. Mountcastle, & S. T. Beiger (Eds.), *The handbook of physiology, sect 1, the nervous system* (Vol. 5(2), pp. 461–481). Bethesda, MD: American Physiological Society.

Konishi, S., Kawazu, M., Uchida, I., Kikyo, H., Asakura, I., & Miyashita, Y. (1999). Contribution of working memory to transient activation in human inferior prefrontal cortex during performance of the Wisconsin card sorting test. *Cerebral Cortex, 9*, 745–753.

Lombardi, W. J., Andreason, P. J., Sirocco, K. Y., Rio, D. E., Gross, R. E., Umhau, J. C., et al. (1999). Wisconsin card sorting test performance following head injury: Dorsolateral fronto-striatal circuit activity predicts perseveration. *Journal of Clinical and Experimental Neuropsychology, 21*, 2–16.

Martin, C., Bechara, A., Denburg, N., Granner, M., & Tranel, D. (2001). The effect of vagus nerve stimulation on decision-making. *Society for Neuroscience Abstracts*, *27*.

Milner, B. (1963). Effects of different brain lesions on card sorting. *Archives of Neurology, 9*, 90–100.

Mishkin, M. (1964). Perseveration of central sets after frontal lesions in monkeys. In J. M. Warren & K. Akert (Eds.), *The frontal granular cortex and behavior* (pp. 219–241). New York: McGraw-Hill.

Monterosso, J., Ehrman, R., Napier, K., O'Brien, C. P., & Childress, A. R. (2001). Three decision-making tasks in cocaine-dependent patients: Do they measure the same construct? *Addiction, 96*, 1825–1837.

North, N. T., & O'Carroll, R. E. (2001). Decision making in patients with spinal cord damage: Afferent feedback and the somatic marker hypothesis. *Neuropsychologia, 39*, 521–524.

Owen, A. M., Roberts, A. C., Hodges, J. R., Summers, B. A., Polkey, C. E., & Robbins, T. W. (1993). Contrasting Mechanisms of Impaired Attentional Set-Shifting in Patients With frontal-lobe damage or Parkinsons-Disease. *Brain, 116*, 1159–1175.

Owen, A. M., Roberts, A. C., Polkey, C. E., Sahakian, B. J., & Robbins, T. W. (1991). Extra-dimensional versus intra-dimensional set shifting performance following frontal-lobe excisions, temporal-lobe excisions or amygdalo-hippocampectomy in man. *Neuropsychologia, 29*, 993–1006.

Pardo, J. V., Pardo, P. J., Janer, K. W., & Raichle, M. E. (1990). The anterior cingulate cortex mediates processing selection in the stroop attentional conflict paradigm. *Proceedings of the National Academy of Sciences of the United States of America, 87*, 256–259.

Paschall, M. J., & Flewelling, R. L. (2002). Post-secondary education and heavy drinking by young adults: The moderating effect of race. *Journal of Studies on Alcohol, 63*, 447–455.

Petrides, M. (1985). Deficits on conditional associative learning tasks after frontal and temporal lobe lesions in man. *Neuropsychologia, 23*, 601–614.

Petrides, M. (1990). Nonspatial conditional learning impaired in patients with unilateral frontal but not unilateral temporal lobe excisions. *Neuropsychologia, 28*, 137–149.

Petrides, M. (2000). Dissociable roles of mid-dorsolateral prefrontal and anterior inferotemporal cortex in visual working memory. *Journal of Neuroscience, 20*, 7496–7503.

Petrides, M., Alivisatos, B., & Frey, S. (2002). Differential activation of the human orbital, midventrolateral, and mid-dorsolateral prefrontal cortex during the processing of visual stimuli. *Proceedings of the National Academy of Sciences of the United States of America, 99*, 5649–5654.

Rizzolatti, G., & Camarda, R. (1987). *Neural circuits for spatial attention and unilateral neglect*. Amsterdam: North-Holland Elsevier.

Rogers, R. D., Everitt, B. J., Baldacchino, A., Blackshaw, A. J., Swainson, R., Wynne, K., et al. (1999). Dissociable deficits in the decision-making cognition of chronic amphetamine abusers, opiate abusers, patients with focal damage to prefrontal cortex, and tryptophan-depleted normal volunteers: Evidence for monoaminergic mechanisms. *Neuropsychopharmacology, 20*, 322–339.

Rogers, R. D., Owen, A. M., Middleton, H. C., Williams, E. J., Pickard, J. D., Sahakian, B. J., et al. (1999). Choosing between small, likely rewards and large, unlikely rewards activates inferior and orbital prefrontal cortex. *Journal of Neuroscience, 20*, 9029–9038.

Rolls, E. T., Hornak, J., Wade, D., & McGrath, J. (1994). Emotion-related learning in patients with social and emotional changes associated with frontal lobe damage. *Journal of Neurology, Neurosurgery, and Psychiatry, 57*, 1518–1524.

Rubia, K., Overmeyer, S., Taylor, E., Brammer, M., Williams, S. C., Simmons, A., et al. (2000). Functional frontalisation with age: Mapping neurodevelopmental trajectories with fMRI. *Neuroscience and Biobehavioral Reviews, 24*, 13–19.

Saver, J. L., & Damasio, A. R. (1991). Preserved access and processing of social knowledge in a patient with acquired sociopathy due to ventromedial frontal damage. *Neuropsychologia, 29*, 1241–1249.

Shallice, T. (1982). Specific impairments of planning. *Philosophical Transactions of the Royal Society of London*, *298*, 199–209.

Shallice, T., & Burgess, P. W. (1991). Deficits in strategy application following frontal lobe damage in man. *Brain, 114*, 727–741.

Sher, K. J., Martin, E. D., & Wood, P. K. (1997). Alcohol use disorders and neuropsychological functioning in first-year undergraduates. *Experimental and Clinical Psychopharmacology, 5*, 304–315.

Smith, E. E. (2000). Neural bases of human working memory. *Current Directions in Psychological Science, 9*, 45–49.

Smith, E. E., & Jonides, J. (1999). Storage and executive processes in the frontal lobes. *Science, 283*, 1657–1661.

Smith, M. L., & Milner, B. (1984). Differential effects of frontal lobe lesions on cognitive estimation and spatial memory. *Neuropsychologia, 22*, 697–705.

Stuss, D. T., Floden, D., Alexander, M. P., Levine, B., & Katz, D. (2001). Stroop performance in focal lesion patients: Dissociation of processes and frontal lobe lesion location. *Neuropsychologia, 39*, 771–786.

Tomita, H., Ohbayashi, M., Nakahara, K., Hasegawa, I., & Miyashita, Y. (1999). Top-down signal from prefrontal cortex in executive control of memory retrieval. *Nature, 401*, 699–703.

Tranel, D., Bechara, A., & Denburg, N. L. (2002). Asymmetric functional roles of right and left ventromedial prefrontal cortices in social conduct, decision-making, and emotional processing. *Cortex, 38*, 589–612.

Wilson, F. A. W., Scalaidhe, S. P. O., & Goldman-Rakic, P. S. (1993). Dissociation of object and spatial processing domains in primate prefrontal cortex. *Science, 260*, 1955–1958.