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Insensitivity to future consequences following damage to human prefrontal cortex

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Abstract

Following damage to the ventromedial prefrontal cortex, humans develop a defect in real-life decision-making, which contrasts with otherwise normal intellectual functions. Currently, there is no neuropsychological probe to detect in the laboratory, and the cognitive and neural mechanisms responsible for this defect have resisted explanation. Here, using a novel task which simulates real-life decision-making in the way it factors uncertainty of premises and outcomes, as well as reward and punishment, we find that prefrontal patients, unlike controls, are oblivious to the future consequences of their actions, and seem to be guided by immediate prospects only. This finding offers, for the first time, the possibility of detecting these patients' elusive impairment in the laboratory, measuring it, and investigating its possible causes.

Introduction

Patients with damage to the ventromedial sector of prefrontal cortices develop a severe impairment in real-life decision-making, in spite of otherwise preserved intellect. The impairments are especially marked in the personal and social realms (Damasio, Tranel, & Damasio, 1991). Patient E.V.R. is a prototypical example of this condition. He often decides against his best interest, and is unable to learn

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from his mistakes. His decisions repeatedly lead to negative consequences. In striking contrast to this real-life decision-making impairment, E.V.R.'s general intellect and problem-solving abilities in a laboratory setting remain intact. For instance, he produces perfect scores on the Wisconsin Card Sorting Test (Milner, 1963), his performances in paradigms requiring self-ordering (Petrides & Milner, 1982), cognitive estimations (Shallice & Evans, 1978), and judgements of recency and frequency (Milner, Petrides, & Smith, 1985) are flawless; he is not preseverative, nor is he impulsive; his knowledge base is intact and so is his short-term and working memory as tested to date; his solution of verbally posed social problems and ethical dilemmas is comparable to that of controls (Saver & Damasio, 1991). The condition has posed a double challenge, since there has been neither a satisfactory account of its physiopathology, nor a laboratory probe to detect and measure an impairment that is so obvious in its ecological niche. Here we describe an experimental neuropsychological task which simulates, in real time, personal real-life decision-making relative to the way it factors uncertainty of premises and outcomes, as well as reward and punishment. We show that, unlike controls, patients with prefrontal damage perform defectively and are seemingly insensitive to the future.

Materials and methods

The subjects sit in front of four decks of cards equal in appearance and size, and are given a $2000 loan of play money (a set of facsimile US bills). The subjects are told that the game requires a long series of card selections, one card at a time, from any of the four decks, until they are told to stop. After turning *each* card, the subjects receive some money (the amount is only announced after the turning, and varies with the deck). After turning *some* cards, the subjects are *both* given money *and* asked to pay a penalty (again the amount is only announced after the card is turned and varies with the deck and the position in the deck according to a schedule unknown to the subjects). The subjects are told that (1) the goal of the task is to maximize profit on the loan of play money, (2) they are free to switch from any deck to another, at any time, and as often as wished, but (3) they are not told ahead of time how many card selections must be made (the task is stopped after a series of 100 card selections). The pre-programmed schedules of reward and punishment are shown on the score cards (Fig. 1). Turning any card from deck A or deck B yields $100; turning any card from deck C or deck D yields $50. However, the ultimate future yield of each deck varies because the penalty amounts are higher in the high-paying decks (A and B), and lower in the low-paying decks (C and D). For example, after turning 10 cards from deck A, the subjects have earned $1000, but they have also encountered 5 unpredicted punishments bringing their total cost to $1250, thus

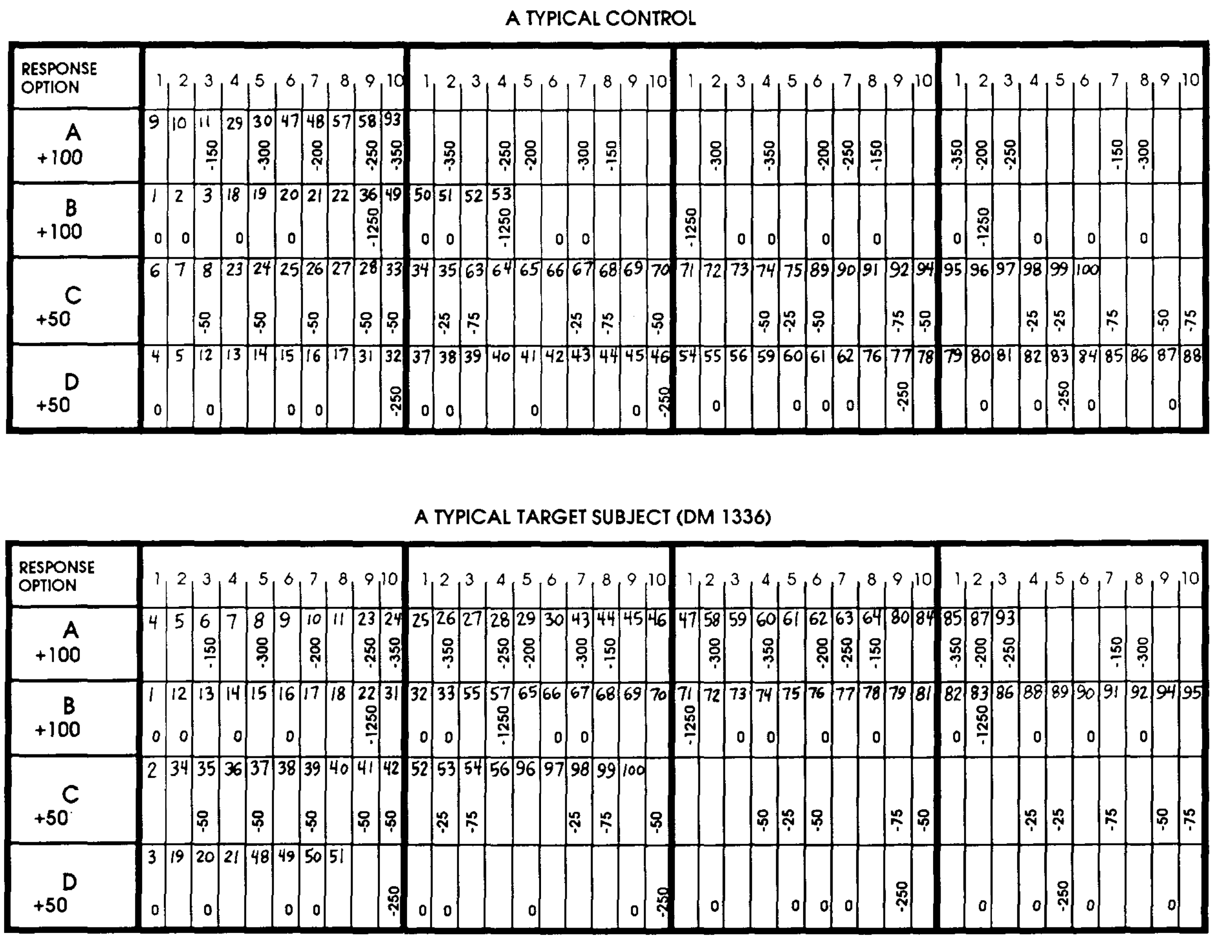

Fig. 1. *The top score card represents that of a typical control subject, and the bottom one that of a typical target subject. The hand-written numbers represent the profiles of card selections from the first to the 100th card. Control subjects select more from decks C and D, whereas target subjects select more from decks A and B.*

incurring a net loss of $250. The same happens on deck B. On the other hand, after turning 10 cards from decks C or D, the subjects earn $500, but the total of their unpredicted punishments is only $250 (i.e. subject nets $250). In summary, decks A and B are equivalent in terms of overall net loss over the trials. The difference is that in deck A, the punishment is more frequent, but of smaller magnitude, whereas in deck B, the punishment is less frequent, but of higher magnitude. Decks C and D are also equivalent in terms of overall net loss. In deck C, the punishment is more frequent and of smaller magnitude, while in deck D the punishment is less frequent but of higher magnitude. Decks A and B are thus "disadvantageous" because they cost the most in the long run, while decks C and D are "advantageous" because they result in an overall gain in the long run.

The performances of a group of normal control subjects (21 women and 23 men) in this task were compared to those of E.V.R. and other frontal lobe subjects (4 men and 2 women). The age range of normal controls was from 20 to 79 years; for E.V.R.-like subjects it was from 43 to 84 years. About half the number of subjects in each group had a high school education, and the other half had a college education. E.V.R.-like subjects were retrieved from the Patient Registry of the Division of Behavioral Neurology and Cognitive Neuroscience. Selection criteria were the documented presence of abnormal decision-making and the existence of lesions in the ventromedial prefrontal region.

To determine whether the defective performance of E.V.R.-like subjects on the task is specific to ventromedial frontal lobe damage, and not merely caused by brain damage in general, we compared the performances of E.V.R.-like subjects and normal controls, to an education matched group of brain-damaged controls. There were 3 women and 6 men, ranging in age from 20 to 71 years. These controls were retrieved from the same Patient Registry and were chosen so as to have lesions in occipital, temporal and dorsolateral frontal regions. Several of the brain-damaged controls had memory defects, as revealed by conventional neuropsychological tests.

Finally, to determine what would happen to the performance if it were repeated over time, we retested the target subjects and a smaller sample of normal controls (4 women and 1 man between the ages of 20 and 55, matched to E.V.R. in level of education) after various time intervals (one month after the first test, 24 h later, and for the fourth time, six months later).

Results

Fig. 2 (left) shows that normal controls make more selections from the good decks (C and D), and avoid the bad decks (A and B). In sharp contrast, E.V.R.-like subjects select fewer from the good decks (C and D), and choose more from the bad decks (A and B). The difference is significant. An analysis of

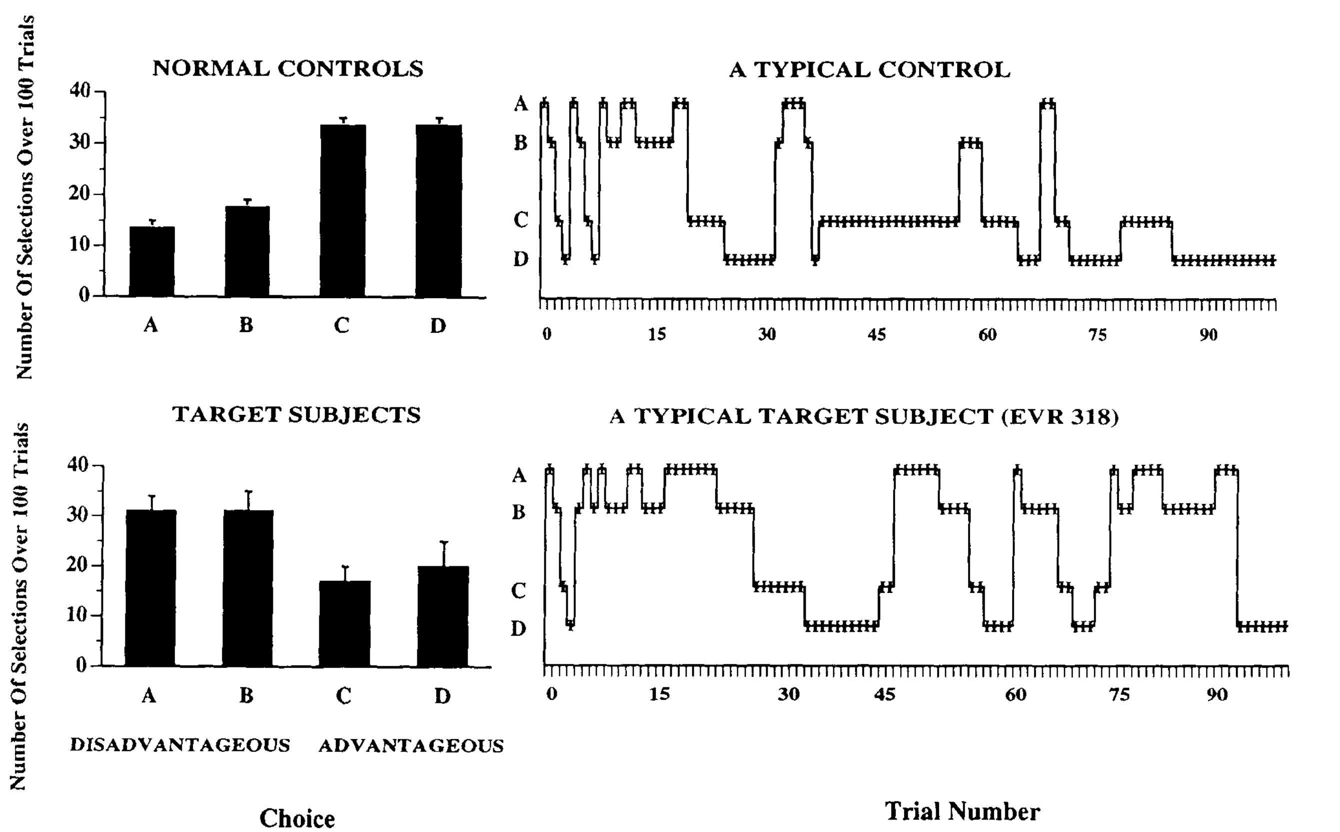

Fig. 2. *(Left panels) Total number of cards selected from each deck (A, B, C or D) by normal controls (n = 44) and E.V.R.-like subjects (n = 7). Bars represent means ± s.e.m. (Right panels) Profiles of card selections (from the first to the 100th selection) obtained from a typical control and patient E.V.R.*

variance comparing the number of cards from each deck chosen by normal controls and by target subjects revealed a significant interaction of group (controls vs. targets) with choice (A, B, C, D) ($F(3,147) = 42.9$, $p < .001$). Subsequent Newman–Keuls t-tests revealed that the number of cards selected by normal controls from deck A or B were significantly *less* than the number of cards selected by target subjects from the same decks ($ps < .001$). On the contrary, the number of cards selected by controls from decks C or D were significantly *higher* than the numbers selected by target subjects ($ps < .001$). Within each group, comparison of the performances among subjects from different age groups, gender and education yielded no statistically significant differences.

Fig. 2 (right) shows that a comparison of card selection profiles revealed that controls initially sampled all decks and repeated selections from the bad decks A and B, probably because they pay more, but eventually switched 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, E.V.R. behaves like normal controls only in the first few selections. He does begin by sampling all decks and selecting from decks A and B, and he does make several selections from decks C and D, but then he returns more frequently and more systematically to decks A and B. The other target subjects behave similarly.

Fig. 3 reveals that the performance of brain-damaged controls was no different

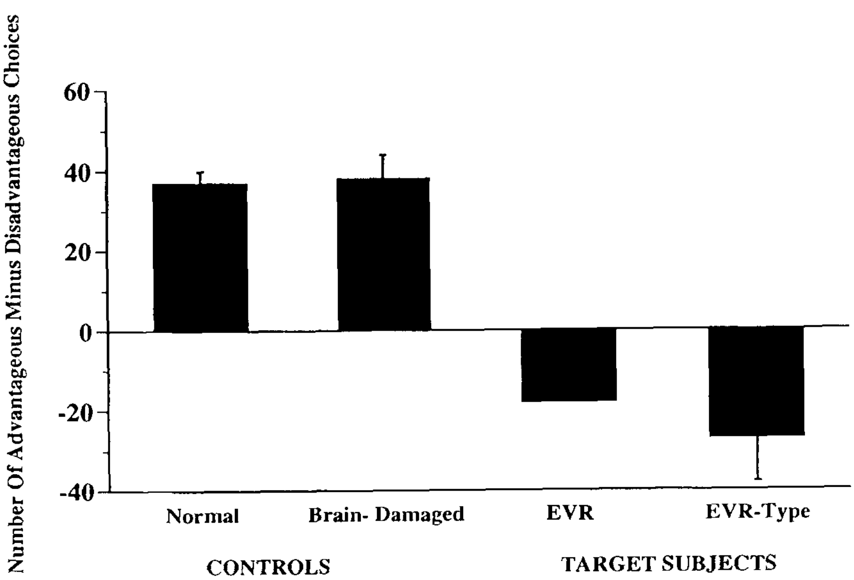

Fig. 3. *Total number of selections from the advantageous decks (C + D) minus the total numbers of selections from the disadvantageous decks (A + B) from a group of normal controls (n = 44), brain-damaged controls (n = 9), E.V.R., and E.V.R.-like subjects (n = 6). Bars represent means ± s.e.m. Positive scores reflect advantageous courses of action, and negative scores reflect disadvantageous courses of action.*

from that of normal controls, and quite the opposite of the performance of the prefrontal subjects. One-way ANOVA on the difference in the total numbers of card selections from the advantageous decks minus the total numbers of selections from the disadvantageous decks obtained from normal and brain-damaged controls did not reveal a significant difference between the two groups ($F(1,52) = 0.1$, $p > .1$), but the difference between the normal and E.V.R.-like groups was highly significant ($F(1,50) = 74.8$, $p < .001$).

As a result of repeated testing, E.V.R.'s performance did not change, one way or the other, when tested one month after the first test, 24 h later, and for the fourth time, six months later. This pattern of impaired performance was also seen in other target subjects. On the contrary, the performance of normal controls improved over time.

Discussion

These results demonstrate that E.V.R. and comparable subjects perform defectively in this task, and that the defect is stable over time. Although the task involves a long series of gains and losses, it is not possible for subjects to perform an exact calculation of the net gains or losses generated from each deck as they play. Indeed, a group of normal control subjects with superior memory and IQ, whom we asked to think aloud while performing the task, and keep track of the magnitudes and frequencies of the various punishments, could not provide calculated figures of the net gains or losses from each deck. The subjects must rely on their ability to develop an estimate of which decks are risky and which are profitable in the long run. Thus, the patients' performance profile is comparable to their real-life inability to decide advantageously, especially in personal and social matters, a domain for which in life, as in the task, an exact calculation of the future outcomes is not possible and choices must be based on approximations. We believe this task offers, for the first time, the possibility of detecting these patients' elusive impairment in the laboratory, measuring it, and investigating its possible causes.

Why do E.V.R.-like subjects make choices that have high immediate reward, but severe delayed punishment? We considered three possibilities: (1) E.V.R.-like subjects are so *sensitive to reward* that the prospect of future (delayed) punishment is outweighed by that of immediate gain; (2) these subjects are *insensitive to punishment*, and thus the prospect of reward always prevails, even if they are not abnormally sensitive to reward; (3) these subjects are generally *insensitive to future consequences*, positive or negative, and thus their behavior is always guided by immediate prospects, whatever they may be. To decide on the merit of these possibilities, we developed a variant of the basic task, in which the schedules of reward and punishment were reversed, so that the punishment is immediate and the reward is delayed. The profiles of target subjects in that task suggest that they were influenced more by *immediate* punishment than by delayed reward (unpublished results). This indicates that neither insensitivity to punishment nor hypersensitivity to reward are appropriate accounts for the defect. A qualitative aspect of the patients' performance also supports the idea that immediate consequences influence the performance significantly. When they are faced with a significant money loss in a given deck, they refrain from picking cards out of that same deck, for a while, just like normals do, though unlike normals they then return to select from that deck after a few additional selections. When we combine the profiles of both basic task and variant tasks, we are left with one reasonable possibility: that these subjects are unresponsive to future consequences, whatever they are, and are thus more controlled by immediate prospects.

How can this "myopia" for the future be explained? Evidence from other studies suggests that these patients possess and can access the requisite knowledge to conjure up options of actions and scenarios of future outcomes just as normal controls do (Saver & Damasio, 1991). Their defect seems to be at the level of acting on such knowledge. There are several plausible accounts to explain such a defect. For instance, it is possible that the representations of future outcomes that these patients evoke are unstable, that is, that they are not held in working memory long enough for attention to enhance them and reasoning strategies to be applied to them. This account invokes a defect along the lines proposed for behavioral domains dependent on dorsolateral prefrontal cortex networks, and which is possibly just as valid in the personal/social domain of decision-making (Goldman-Rakic, 1987). Defects in temporal integration and attention would fall under this account (Fuster, 1989; Posner, 1986). Alternatively, the representations of future outcomes might be stable, but they would not be *marked* with a negative or positive value, and thus could not be easily rejected or accepted. This account invokes the somatic marker hypothesis which posits that the overt or covert processing of somatic states provides the *value mark* for a cognitive scenario (Damasio, 1994; Damasio et al., 1991). We have been attempting to distinguish between these two accounts in a series of subsequent experiments using this task along with psychophysiological measurements. Preliminary results favor the latter account, or a combination of the two accounts. Those results also suggest that the biasing effect of the value mark operates covertly, at least in the early stages of the task.

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