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Declarative memory is critical for sustained advantageous complex decision-making

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Abstract

Previous studies have reported conflicting evidence concerning the contribution of declarative memory to advantageous decision-making on the Iowa Gambling Task (IGT). One study, in which the measurement of psychophysiology during the task necessitated a 10-sec delay between card selections, found that six participants with amnesia due to hippocampal damage failed to develop a preference for advantageous decks over disadvantageous decks (Gutbrod et al., *Neuropsychologia*, Vol. 44, pp. 1315–1324, 2006). However, a single case study (where psychophysiology was not measured and no delay between card selections occurred) showed that an amnesic patient developed normal preference for advantageous decks (Turnbull & Evans, *Neuropsychologia*, Vol. 44, pp. 300–306, 2006). We sought to resolve these discrepant findings by examining IGT performances in five patients with profound amnesia (WMS-III General Memory Index $M=63$) and bilateral hippocampal damage caused by anoxia ($n=4$) or herpes simplex encephalitis ($n=1$). In one administration of the IGT, psychophysiology measurements were utilized and a 6-sec delay was interposed between card selections. In a second administration, no delay between card selections was interposed. While age-, sex-, and education-matched healthy comparison participants showed significant learning with a gradual preference for advantageous decks in both conditions, amnesic patients, irrespective of IGT administration condition and extent of medial temporal lobe damage, failed to develop this preference. These findings strongly discount the possibility that the delay between card selections explains why amnesic participants fail to learn in the IGT, and suggest instead a significant role for medial temporal lobe declarative memory systems in the type of complex decision-making tapped by the IGT.

Keywords

amnesia; Iowa Gambling Task; declarative memory; hippocampus; decision-making

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1. Introduction

The ability to make advantageous decisions relies on rational processes for weighing outcomes, but it is also highly influenced by emotions. This influence can operate in both positive and negative directions: emotions can cloud our judgment, but they can also play an important role in creating a bias (even at non-conscious level) for a certain course of action that is in our best long-range interests. Evidence for the importance of emotional processes in decision-making comes from patients with ventromedial prefrontal cortex (vmPFC) or amygdala damage, who have impaired emotion processing and defective real-world decision-making (Anderson, Barrash, Bechara, & Tranel, 2006; Eslinger & Damasio, 1985; Stuss & Levine, 2002; Tranel & Bechara, in press; Tranel & Hyman, 1990). Decision-making impairments can be seen even after damage to brain areas primarily involved in basic emotion processing, suggesting that decision-making relies on a complex network of neural structures, many of which are involved in a variety of complex emotional and cognitive processes.

A laboratory task sensitive to the decision-making impairments seen in vmPFC and amygdala patients is the Iowa Gambling Task (IGT) (Bechara, Damasio, Damasio, & Anderson, 1994; Bechara, Damasio, & Damasio, 2003; Bechara, Damasio, Damasio, & Lee, 1999; Fellows & Farah, 2005). In this task, participants select from four decks of cards, which are associated with differing amounts of reward and punishment. In order to succeed on the task, participants must learn that certain decks can be rewarding overall as they are associated with small rewards but also have small punishments. By contrast, other decks are disadvantageous overall because despite having larger immediate rewards, they also have larger long-term punishments. While healthy comparison subjects show a gradual preference for advantageous decks over trials, participants with vmPFC or amygdala damage show a preference for disadvantageous decks throughout trials (Bechara et al., 2003; Bechara et al., 1999; Fellows & Farah, 2005). These findings have been cited in support of the “somatic marker hypothesis,” which suggests that areas involved in emotion processing (such as the vmPFC and amygdala) are important for the development and integration of emotion-based cues which can bias decision-making (Bechara et al., 1994; Bechara, Damasio, & Damasio, 2000a; Damasio, 1994).

Given the complexity of the IGT, where participants must maintain and update a representation of the contingencies associated with multiple decks of cards over time in order to make advantageous decisions, it seems intuitive that memory systems would play a critical role in successful performance of the IGT (e.g., Maia & McClelland, 2004). Studies have implicated memory, especially working memory, as being important for successful performance on the IGT (Bechara, Tranel, & Damasio, 2000b; Fellows & Farah, 2005). However, the necessity of other memory systems besides working memory in complex decision-making has not been clarified. Since advantageous decision-making may often require intact emotion processing, researchers have suggested that emotional memory systems might also be utilized for decision-making (Turnbull & Evans, 2006). Previous research has shown that certain types of simple learning and decision-making can be performed using emotion-based systems rather than the declarative memory system. For example, the severely amnesic patient Boswell was able to learn associations between individuals and affective valences based on previous interactions despite having no declarative memory for these interactions (Tranel & Damasio, 1993). However, this was a rather simple interaction where strong and consistent valences and rewards were associated with each of the people. It is likely that more complex forms of learning require the involvement of multiple memory systems. For example, in the IGT, not only are emotional representations formed (helping to bias behavior towards good outcomes), but choice-outcome associations must be continually formed and updated. A deck that was associated with high rewards may suddenly yield a severe punishment. The IGT in fact models many real-world situations in this regard: we are often confronted with decision-making challenges where the contingencies and magnitudes of reward and punishment are not completely reliable, and may

change substantially over time. Also, research on emotional memory has shown that while the amygdala can work independently of hippocampus as in classical fear conditioning, the amygdala can also work in concert with the hippocampus serving to enhance the emotional content of declarative memory (Cahill, Babinsky, Markowitsch, & McGaugh, 1995; Eichenbaum & Cohen, 2001; Richardson, Strange, & Dolan, 2004). Moreover, the amygdala is important for remembering the gist of complex emotional events, while the hippocampus is required for memory for details (Adolphs, Tranel, & Buchanan, 2005). Therefore, both systems play an important role in creating a cohesive representation of a complex situation.

Non-declarative memory systems have been implicated in certain aspects of complex learning as well (Knowlton, Mangels, & Squire, 1996). Amnesic participants with hippocampal damage and declarative memory impairments have been shown to have intact performance on complex tasks such as the Weather Prediction Task and the Wisconsin Card Sorting Task (Janowsky, Shimamura, Kritchevsky, & Squire, 1989; Knowlton, Squire, & Gluck, 1994; Leng & Parkin, 1988; Shoaieirat, Mayes, MacDonald, Meudell, & Pickering, 1990). Just as with the IGT, successful performance on these tasks requires learning and integration of task contingencies across time. However the extent to which decision-making on the IGT requires declarative memory systems mediated by the hippocampus, and/or hippocampal-independent memory systems, has not been well defined. Off the face of it, due to the arbitrary associations that must be created of multiple experiences between individual decks and punishment schedules over time, it would seem likely that the IGT would require declarative memory. The declarative memory system is critical for relational memory and supports relational representations of successive events and the information about the arbitrary or accidental co-occurrences of people, places, and things along with the spatial, temporal and interactional relations among them (Cohen & Banich, 2003; Cohen & Eichenbaum, 1993; Eichenbaum & Cohen, 2001). However, previous research using the IGT has provided conflicting evidence for the role of declarative memory in complex decision-making.

Turnbull and Evans (2006) reported a case study of an 85-year-old man with amnesia due to a left posterior cerebral artery stroke who performed the Iowa Gambling Task and showed the normal gradual preference for advantageous decks over time. In fact, the amnesic participant even improved his performance on subsequent administrations of the IGT. However, Gutbrod et al. (2006) reported a group study, in which 6 participants with amnesia and bilateral hippocampal damage due to anoxia, encephalitis, or stroke, and 6 participants with amnesia and basal forebrain damage due to encephalitis or stroke, did not show the normal preference for advantageous decks. Instead they chose equally from the advantageous and disadvantageous decks and did not gravitate towards the advantageous decks over time. These two studies differed in their presentation of the IGT: the second study measured psychophysiology during the task which interposed a 10 second delay between card selections while the first study did not interpose a delay between card selections. Gutbrod et al. (2006) suggest that this difference may be critical as previous studies have found that even short delays (e.g., 1000 ms) can affect amnesics' performance on tasks such as classical conditioning (e.g., Clark & Squire, 1998).

In an effort to resolve these discrepant findings, the current study was designed to determine whether the delay between card selections contributes to amnesic participants' performance on the IGT, and in a broader sense, to further understand the role of the hippocampus and medial temporal lobe in complex decision-making. In order to do so we evaluated the performance of five amnesic subjects with bilateral hippocampal damage on the Iowa Gambling Task, both with and without a delay interposed between card selections.

2. Methods

2.1 Participants and procedures

Participants were five individuals (1 woman) with amnesia and 10 healthy comparison participants (2 women) drawn from the Patient Registry of the Division of Behavioral Neurology and Cognitive Neuroscience at the University of Iowa and the Iowa City community. All participants gave informed written consent approved by the Institutional Review Board of the University of Iowa.

Of the five participants with amnesia, four sustained bilateral hippocampal damage, with no apparent damage elsewhere, from an anoxic/hypoxic event (e.g., cardiac arrest, one-time seizure event (non-epileptic)) and one sustained more extensive bilateral damage (including to amygdala) from herpes simplex encephalitis. Structural magnetic resonance imaging (MRI) examinations were completed on four of the five patients confirming bilateral hippocampal damage. For participant 2563 (who wears a pacemaker and was unable to undergo the MRI examination) anatomical analysis was based on computerized tomography, and only damage in the hippocampal region was visible. For three patients, high-resolution volumetric MRI analyses were conducted revealing significantly reduced hippocampal volumes (studentized residual differences in hippocampal volume relative to a matched comparison group were decreased by 2 to 4 z-scores) (Allen, Tranel, Bruss, & Damasio, 2006). For participant 2308, who sustained more extensive damage (and for whom high-resolution volumetric MRI analyses are not available), a coronal section from an MRI is shown in Figure 1. This participant has bilateral damage to hippocampus, amygdala, and insula with more extensive medial and lateral temporal lobe damage on the left than the right; however, there is no visible damage to the prefrontal cortex.

All patients had memory impairments that were sufficiently severe to interfere with activities of daily living, including preventing them from independent living or employment since the onset of their amnesia. Neuropsychological testing confirmed a selective and severe memory impairment disproportionate to any deficits in general cognitive (e.g., language, attention, executive function) or intellectual functioning. Performance on the Wechsler Memory Scale-III (General Memory Index) was at least 25 points lower than performance on the Wechsler Adult Intelligence Scale-III (Full Scale IQ) (mean FSIQ-GMI difference =29.2), with an average delay score on the memory scale (63.2) that was more than 3 standard deviations below the population mean. Participants were severely impaired in delayed recall on the Rey Auditory Verbal Learning Test; only 1 of the participants could report more than a single item (out of 15) despite multiple study opportunities. Four of the five amnesic participants were administered the Wisconsin Card Sorting Task, a measure of executive function, and all performed within normal limits. Comparison participants were free of neurological or psychiatric conditions and were matched to the amnesia participants on sex, age, and education (separately by subgroup; see below). There were no significant differences between groups on age ($p > .1$) or education ($p > .7$). Table 1 presents the demographic and neuropsychological characteristics of the participants.

The computerized version of the IGT was administered according to the standard protocol described by Bechara, Damasio & Damasio (2000a). Participants made 100 card selections from four decks of cards in an order of their choosing and they were free to choose from any deck at any time. Each time a card was selected, the participant received a monetary reward, but at unpredictable times, some selections also resulted in a monetary punishment. Decks A and B are considered disadvantageous, as they have large gains but also large punishments resulting in a net loss of money, while decks C and D are advantageous as they have small gains but also small punishments resulting in a net gain of money. Participants were not

informed about the specific differences between decks or that the task would be terminated after 100 card selections.

IGT administration with patients with amnesia occurred under two different conditions, one with a delay (Delay) and one without a delay (No Delay). The Delay condition was administered first. This occurred when the protocol in our laboratory was to administer the IGT with psychophysiological measurements, which out of necessity interpose a 6-second delay after feedback is given before the next card selection can occur (due in particular to the manner in which electrodermal activity is recorded). Then, capitalizing on the fact that all of the amnesic patients have sufficiently severe memory impairments that they could be tested with the same version of the IGT (but with No Delay) and have no explicit memory of having previously performed the task, we tested the patients again using the No Delay condition of the IGT. To ensure even further that the patients did not explicitly remember previously performing the task, the second administration (No Delay condition) was done 1–7 years after the Delay condition (average = 4 years). The severity of the memory impairment in the amnesic participants, both on standardized tests and in the real world (e.g., the patients do not remember the examiners or their names, despite multiple testing sessions), and the stability of their neuropsychological profiles over regular neuropsychological evaluations (e.g., no significant improvement of memory function due to recovery and no decline of other cognitive functions due to aging or dementia), lend support to the validity of using the same version of the IGT in the Delay and No Delay conditions without concern that declarative memory for the task will play a factor in the second (No Delay) administration. This is not the case for normal, non-memory-impaired individuals, as noted below, which necessitated the following approach to utilizing healthy comparison participants.

In healthy participants who are not memory impaired, the first administration of the IGT would contaminate the results of the second administration, due to learning effects that have been previously reported with repeated administrations of the IGT (e.g., Bechara et al., 2000a). To work around this, we employed two different comparison groups, one for each of the different delay conditions (Delay v. No Delay). Specifically, five comparison participants completed the IGT in Delay condition, while another five comparison participants completed the IGT in the No Delay condition. Each of the comparison groups was matched to the amnesic group on critical demographic factors, including age, education, and gender ratio (see Table 1).

2.2. Data Analysis

Following convention, the Iowa Gambling Task performance was calculated by dividing the 100 trials into 5 blocks of 20 card selections each and calculating the number of card selections from “advantageous” decks (decks C and D) and subtracting the number of card selections from “disadvantageous” decks (decks A and B). Scores above zero indicate that more advantageous cards were selected than disadvantageous cards, resulting in a net gain of money, while scores below zero indicate that more disadvantageous cards were selected resulting in a net loss of money. Data were analyzed using a mixed 2×5 ANOVA with one between-subjects factor (Group: amnesic v. comparison) and one within-subjects factor (Block: trial blocks in the IGT, in sets of 20 trials/block). This analysis was applied to each condition (Delay and No Delay) to assess group differences and learning across the blocks.

3. Results

3.1. Performance on the Iowa Gambling Task

Figure 2 shows the performance of amnesic and comparison participants on the Delay version of the IGT (i.e., with the 6-sec delay interposed between card selections). In the ANOVA applied to these data, the interaction between Group and Block had a tendency towards

significance ($F(4, 32) = 2.3, p = .07$). In fact, the Figure suggests an interaction, and we believe the lack of statistical significance is due to lack of statistical power, perhaps because of our relatively small sample size. Moreover, the Figure shows that there was early learning in the comparison participants in the task, as they essentially reached maximum performance in the second trial block and maintained their performance throughout the rest of the task. The Group ($F(1, 8) = 25.8, p < .001$) and Block ($F(4, 32) = 3.5, p < .02$) main effects were significant. The comparison participants, however, drove the block effect, as seen using a one-way repeated measures ANOVA for each group separately. In these follow-up analyses, we found that the comparison participants showed a main effect of Block ($F(1.3, 5.5) = 12.2, p < .001$, adjusted Greenhouse-Geisser values), suggesting a strong preference for advantageous decks. In contrast, the patients with hippocampal amnesia did not show a main effect of Block ($F(1.5, 6.3) < 1, p = .68$) and the patients had scores that remained close to zero throughout the task, indicating that they did not develop a preference for advantageous or disadvantageous decks.

Figure 3 shows the performance of amnesic and comparison participants on the No Delay version of the IGT (i.e., *without* the delay interposed between card selections). The interaction between Group and Block was not significant ($F(4, 32) = 1.3, p = .27$), and again, the comparison participants reached their peak performance in the first phase of the task and then stayed fairly level across the rest of the game. The Group ($F(1, 8) = 15.9, p < .004$) and Block ($F(4, 32) = 3.2, p < .02$) main effects were significant. Using a one-way repeated measures ANOVA for each group separately, we found that the block main effect is driven by the comparison participants, as they have a significant main effect of Block ($F(4, 16) = 3.5, p < .03$) showing a preference for advantageous decks. However, the amnesic participants did not exhibit a significant main effect of Block ($F(4, 16) < 1, p = .56$) and had scores that remained close to zero throughout the task, again indicating no preference for either type of deck throughout the task.

3.2. Follow-up Analyses

3.2.1. Delay v. No Delay condition in amnesic participants—In order to directly assess differences between administration conditions in the amnesic participants, we used a one-way repeated measures ANOVA, with Condition and Block as within-subject factors. The interaction between Condition and Block was not significant ($F(4, 16) < 1, p = .69$), and neither were the main effects of Condition ($F(1, 4) = 2.1, p = .21$) and Block ($F(1.8, 7.3) < 1, p = .73$, adjusted Greenhouse-Geisser values). These outcomes indicate that the performance of amnesic participants did not differ between conditions.

3.2.2. Contributions of the amygdala—Previous research has found that bilateral amygdala damage impairs performance on the IGT (Bechara et al., 1999). In the current study, participant 2308 has bilateral damage to the amygdala as well as bilateral hippocampal damage. We wanted to ensure that his performance did not differ from the other four patients whose damage was restricted to the hippocampus. Despite the additional medial temporal lobe damage, we found no significant difference between participant 2308's performance and the other patients' performance in either the Delay ($F(1, 3) < 1, p = .76$) or No Delay ($F(1, 3) < 1, p = .63$) conditions. We also checked whether this participant contributed disproportionately to the group results. He did not. Specifically, when we removed 2308 from the group data, the remaining ($n = 4$) amnesic participants still differed significantly from the comparison participants in both the Delay ($F(1, 7) = 21.21, p < .002$) and No Delay ($F(1, 7) = 11.92, p < .01$) conditions.

3.2.3 Escape-from-punishment behavior—In order to characterize further the observed impairment in decision-making in the amnesic participants, we analyzed their Gambling Task performance by examining their performance on individual trials. Specifically, we were interested in the extent to which they displayed and if they followed a “win/stay, lose/shift”

strategy, which has been shown to be intact in rats with hippocampal lesions (McDonald & White, 1993). Across the entire data set (all 100 card selections) we found that when the amnesic participants made a card selection that resulted in a punishment, no matter the magnitude, they chose from a different deck on their next card selection 82% of the time across both conditions (no significant difference between conditions $t=1.019$, $p=.338$). The healthy comparison participants, however, only switched decks when punished 57% of the time across both conditions (no significant difference between conditions $t=1.651$, $p=.137$). Since we found no differences between conditions in either the amnesic or comparison group in overall escape-from-punishment behavior or in standard IGT performance scores, we collapsed the individual groups across conditions by averaging across all 10 data points for each group (i.e., we compared the average of the comparison participants, 5 with Delay, 5 with No Delay with the average of the amnesic participants, 5 with Delay, 5 with No Delay) for the following analyses.

As comparison participants learned which decks were advantageous, they were less likely to move to another deck immediately after being punished from one of these advantageous decks. Thus, across blocks we observed a significant decline ($F(4, 36) = 6.9$, $p < .001$) in the number of times comparison participants switched decks after being punished. This suggests that they did not learn to avoid all punishment but rather to avoid just those decks that disproportionately punished, and that particular decks can be advantageous despite having small punishments. In contrast, the amnesic participants, whose declarative memory impairments prevent them from integrating and forming the kind of relational information needed to track and remember their experiences with each deck, and the pattern and magnitudes of reward and punishment associated with each of the four decks across time, did not show a significant decline ($F(1.9, 17.2) < 1$, $p = .78$, adjusted Greenhouse-Geisser values) in the number of times they switched decks after being punished. Rather they tend to respond to all punishments, no matter the magnitude, in the same way: avoidance. Using a two-way repeated measures ANOVA we verified that there is a significant difference between the performance of the amnesic and comparison participants ($F(1, 18) = 15.8$, $p < .001$). Figure 4 shows how escape-from-punishment behavior changed across block and groups.

4. Discussion

One purpose of this study was to resolve previous conflicting findings concerning the role of declarative memory in decision-making on the Iowa Gambling Task. We found that participants with amnesia due to bilateral hippocampal damage were unable to develop the normal preference for advantageous decks in the Iowa Gambling Task, and this occurred both when there was a 6 second delay between card selections and when no delay was interposed between card selections. Our results are consistent with the findings of Gutbrod et al. (2006), and suggest that the hippocampus (and perhaps other medial temporal lobe structures) are necessary for complex decision-making of the type tapped by the IGT. However, our results strongly discount the possibility that the delay interposed between card selections is the crucial factor that adversely affects the performance of amnesic participants on the IGT, an idea proposed by Gutbrod et al. (2006) to explain their findings. We argue that declarative memory is necessary for forming and updating the relational representation between the decks and their associated rewards and punishments, resulting in the amnesic participants' impaired ability to make sustained advantageous decisions over time.

While our findings are in line with the only other multi-patient investigation of IGT performance in amnesics (Gutbrod et al., 2006), they run counter to the single-patient report by Turnbull and Evans (2006). The patients both in the current study and in Gutbrod et al.'s study have well defined bilateral hippocampal damage. However there is uncertainty as to whether Turnbull and Evans' patient had bilateral or unilateral hippocampal damage. The authors' note that based on radiological evidence, damage is only visible in the left hemisphere,

including posterior regions of the hippocampus and parahippocampal gyrus. While the extent to which unilateral hippocampal preservation may have contributed to their patient's strikingly intact performance on the IGT remains unclear, it does raise interesting questions regarding the necessity of bilateral versus unilateral hippocampal damage to produce the kind of severe decision-making deficits observed in the current study. Another possibility left open by our data and the Gutbrod et al. study, which would also be compatible with the findings from Turnbull and Evans (2006), is that unilateral right-sided hippocampal damage is sufficient to impair IGT performance. Adding complexity to this issue is the likelihood that there are sex-related functional hemispheric asymmetries in medial temporal lobe structures (e.g., Tranel & Bechara, in press), and unilateral damage may impair or spare performance depending on the side and on the gender of the participant. In any event, it would seem that the preponderance of evidence at this point supports the conclusion that bilateral hippocampal damage and declarative amnesia impairs IGT performance. Future work is needed to help untangle the nuances of these relationships.

It is very important to differentiate the impaired performance of participants with hippocampal damage on the IGT from the abnormal performance of participants with ventromedial prefrontal cortex damage or amygdala damage. Both of the latter groups of patients show a preference for the disadvantageous decks in the IGT, while participants with hippocampal damage do not show a preference for the advantageous *or* disadvantageous decks. Rather, they pick comparably from both decks, resulting in Gambling Task performance scores that remain close to zero throughout the task (see Figures 2 and 3) (Bechara et al., 1999). One participant included in this study (2308) has more extensive bilateral medial temporal lobe damage that includes the amygdala and hippocampus; however, his performance did not differ from the other amnesics who have damage only to the hippocampus. This finding replicates earlier reports by Bechara et al. (1999) where patients with bilateral amygdala *and* hippocampal damage chose comparably from both deck types resulting in scores near zero in the IGT, while patients with only bilateral amygdala damage showed a preference for disadvantageous decks resulting in negative scores on the IGT.

Advantageous decision-making requires the contribution and orchestration of multiple cognitive systems. Based on our results, there seems to be two separate but related processes that play an important role in advantageous decision-making on the IGT. One process is the evocation of an emotional representation of the outcome value, which is referred to as a somatic marker. The triggering of these somatic markers relies on emotion processing structures such as the vmPFC and amygdala. Secondly, the formation and maintenance of a choice-outcome association must occur flexibly over time, a process that seems to require declarative memory. Our amnesic participants seem to be able to create an instantaneous emotional representation of an outcome (as seen in our follow-up 'lose-shift' analysis; Figure 4), but are unable to update this representation over time. Moreover, the finding that patients with bilateral amygdala damage have different patterns of performance when additional hippocampal damage is present suggests that the contribution of declarative memory may occur earlier and be more fundamental to advantageous decision-making. That is, it seems that patients with amygdala and vmPFC damage would need normal declarative memory to develop a preference for particular decks, even those that are disadvantageous.

While the IGT is a complex task, there are other complex tasks on which amnesic patients perform successfully. For example, amnesic patients demonstrate significant learning on the Weather Prediction Task (WPT), a task in which participants must decide the outcome (rain or sun) based on probabilities associated with the collective pattern of four cards (Knowlton et al., 1994). Many amnesic patients, including those who participated in the current study (see Table 1), show intact performance on the Wisconsin Card Sorting Task (WCST) (Janowsky et al., 1989; Leng & Parkin, 1988; Shoaie et al., 1990). In this task participants must sort a

deck of cards based on a rule (e.g., by color, shape, number) that can only be determined from experimenter feedback and that changes intermittently without the participants' knowledge. Amnesic patients also perform normally on a collaborative referencing task (Duff, Hengst, Tranel, & Cohen, 2006), a task that requires patients to develop meaningful and appropriate references for a set of abstract stimuli and use those labels across a series of dynamic interactions with a partner. Thus, it seems unlikely that a general factor of "complexity" can provide a parsimonious account of the current findings of amnesic performance on the IGT.

The IGT, however, differs from tasks like the Weather Prediction Task and the Wisconsin Card Sorting Task in a number of ways, and in particular, very likely places greater demands on declarative memory. With regard to the WPT, it is a probabilistic task, while the IGT is a deterministic task with a set schedule for the frequency of punishments. Decks A and D have five small punishments for every ten times that deck is selected, while decks B and C have one larger punishment every tenth time the deck is selected (Bechara et al., 2000a). The IGT has variable values of punishment (e.g., \$25 to \$2000), and the punishments must sometimes be ignored because they can be received from a deck that is advantageous overall. In the WPT and WCST, there is only one form of "punishment," an incorrect answer, which always has the same value and meaning and is never meant to be ignored. In the WCST task contingencies frequently change and do not have to be maintained to form integrated representations over long periods of time (which differs from the 100 trials in the IGT). Finally, in the collaborative referencing task, participants are not required to learn arbitrarily related, experimenter-generated information, but rather draw on pre-existing mental representations to self-generate appropriate and meaningful card labels, such as "siesta man" for a figure that could be seen as a man resting or reclining. In contrast, the IGT requires the formation of novel and arbitrary relationships across successive experiences of the individual decks and their reward schedules. These other tasks all lack critical elements of declarative memory and patients with hippocampal amnesia are not impaired. In the IGT, which appears to have significant declarative memory demands, patients with hippocampal amnesia fail to show normal learning.

Even in situations where amnesic patients succeed at other forms of emotion-based learning, like the amnesic participant who developed preferences for people depending on the affective valence associated with their interactions (Tranel & Damasio, 1993), these tend to be simple and consistent associations with no variations in valence across experiences. Sensitivity to the rewards and punishments in the IGT is a critical component in successful performance. Amnesic patients are not insensitive to punishment: they have an immediate response both behaviorally (as seen in our follow-up analysis, see Figure 4) and physiologically to punishment in the IGT (Gutbrod et al., 2006). (Although it is possible that the valence of the punishments is not sufficiently aversive (participants do not win or lose real money) to create an association strong enough to learn normally in the absence of declarative memory). However, successful IGT performance requires more than basic emotional learning. Participants must also be able to form and update a long-term representation that integrates the variations in reward and punishments across decks and across experiences with each deck resulting in an overall "impression" of the deck. Healthy comparison participants were able to draw on these long-term relational representations and stay with advantageous decks even when receiving frequent (if small) punishments. Without this relational record, amnesic patients have no choice but to rely on the immediately available information (whether the card had a positive or negative outcome) and base their decision to stay with a deck or leave a deck on that individual outcome. This finding is consistent with other work from our laboratory demonstrating that patients with bilateral hippocampal damage and profound amnesia exhibit exaggerated "updating," or significantly larger change scores than healthy comparison participants, of their moral judgments of others after learning new complex social information about unfamiliar persons (Croft, Duff, Anderson, Adolphs, & Tranel, 2008). In both our moral judgment study and the current IGT study we observe amnesic patients over-valuing the affective information that is

immediately at hand as declarative memory impairments strip away the necessary contextual information required to make appropriate and advantageous decisions.

The IGT is considered an analogue of real world decision-making (Damasio, 1994; Denburg et al., 2007), and our results reflect some of the difficulties amnesics show in the real world. Not one of our amnesic participants can live independently, hold full-time employment, manage their finances, or navigate flexibly through the world, as a result of their memory impairment. One recent study found that patients with mild dementia of the Alzheimer's type show impairments on the IGT resembling those of our amnesic patients, as they too select comparably from the advantageous and disadvantageous decks resulting in Gambling Task performance scores (advantageous minus disadvantageous) near zero throughout the task (Sinz, Zamarian, Benke, Wenning, & Delazer, 2008). In Alzheimer's disease, though, the memory impairment is part of a broader array of cognitive deficits. Our study (along with that of Gutbrod et al., 2006) shows that the relational memory deficit seen in circumscribed amnesia is sufficient to cause impairment on the IGT. Taking this a bit further, our findings may begin to help explain the real-world challenges the patients face. In the real world, where the complexities of life often cannot be avoided, the necessity of declarative memory cannot be underestimated. However, a more systematic investigation to characterize the real-world decision-making difficulties in those with profound declarative memory impairments is necessary to fully understand the contributions of declarative memory in the real world. Our finding that amnesic patients are impaired at this task, which was developed to tap into real world decision-making impairments, is not surprising considering the complexity and unpredictability of the task.

In summary, these findings support the idea that complex decision-making relies on a neural network including emotional processing systems, working memory, and declarative memory. Our findings emphasize the critical role of declarative memory on complex decision-making on the Iowa Gambling Task.

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Figure 1.
Magnetic resonance image for participant 2308.
Note: Image is a T-1 weighed coronal section at the level of the hippocampus.

Figure 2.

Performance of amnesia (grey line) and comparison (black line) participants on the IGT with a 6-sec delay between card selections.

Figure 3.
Performance of amnesia (grey line) and comparison (black line) participants on the IGT without a delay between card selections.

Figure 4. Percentage of card selections where amnesia (grey line) and comparison (black line) participants switch decks on the subsequent card selection after receiving a punishment, averaged across both conditions.

Table 1

Demographic and neuropsychological characteristics of the participants

Participant	Sex	Education (Years)	Age tested with delay (Years)	Age tested without delay (Years)	WAIS-III FSIQ	WMS-III GMI	AVLT Trial 5/ Delay	WSCT		Etiology	Hippocampal Volume (z-scores)
								Categories	Pers. Errors		
1606	M	12	51	58	91	66	6 / 0	6(>16%)	26(14%)	Anoxia	-3.99
1846	F	14	38	42	84	57	7 / 2	6(>16%)	6(73%)	Anoxia	-4.23
2308	M	18	45	48	87	45	5 / 0	N/A	N/A	HSE	N/A
2363	M	16	44	50	98	73	9 / 0	6(>16%)	12(23%)	Anoxia	-2.64
2563	M	16	48	49	102	75	7 / 1	5(11-16%)	32(2%)	Anoxia	N/A
Mean ± SD		15.2±2.2	45.2 ±4.9	49.4±5.7							
Comparison Participants with Delay	4										
Mean ± SD	M	15±1.7	53±4.4								
	1 F										
Comparison Participants Without Delay	4										
Mean ± SD	M	15.2±2.2		49.8±6.4							
	1 F										

Note, M =male; F =female; SD =standard deviation; WAIS-III =Wechsler Adult Intelligence Scale-III; FSIQ =Full Scale Intelligence Quotient; WMS-III =Wechsler Memory Scale-III; GMI =General Memory Index' AVLT =Auditory Verbal Learning Test; WCST =Wisconsin Card Sorting Test. Pers. Errors =perseverative errors. WCST scores are presented as scaled score (percentile).