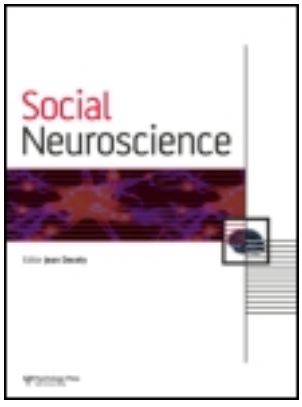


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# Risky decision-making in older adults without cognitive deficits: An fMRI study of VMPFC using the Iowa Gambling Task

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# Risky decision-making in older adults without cognitive deficits: An fMRI study of VMPFC using the Iowa Gambling Task

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Some older adults without neurological disease exhibit impaired decision-making in risky, nontransparent situations, like the Iowa Gambling Task (IGT). The prefrontal cortices are particularly vulnerable to age-related decline, and numerous studies implicate the ventromedial prefrontal cortex (VMPFC) in successful IGT performance. However, the relationship between IGT performance and VMPFC function in older adults has not yet been tested by fMRI. In the present study, older adults with seemingly no cognitive impairments performed the IGT and a non-gambling control task during fMRI. Group analyses indicate that in these older adults, regardless of IGT performance level, a right VMPFC subregion is activated during the IGT, while successful IGT performance is correlated with left VMPFC activation, suggesting that bilateral VMPFC during risky, nontransparent situations may contribute to successful decision-making in older adults. Individual subject analyses reveal substantial variation regarding the extent and location of VMPFC activation during the IGT, a finding not captured in the group analysis: There is no correlation between IGT performance and extent of activation in the right VMPFC, although there is such a correlation between left VMPFC activation and IGT performance.

***Keywords:*** Decision-making; Ventromedial prefrontal cortex; fMRI; Aging.

It is now well documented that the "normal" elderly population is the main target of telemarketing scams and various other fraudulent endeavors, and that 85% of fraud victims are over the age of 65 (Federal Trade Commission, 2005). In laboratory settings, some elderly individuals without noticeably compromised cognitive abilities also exhibit decision-making deficits when immediate gains need to be sacrificed for long-term profit, particularly in nontransparent situations such as the Iowa Gambling Task (IGT), a complex task that mimics some of the complexities of everyday life, in a laboratory setting (Bechara, Damasio, Damasio, & Anderson, 1994; Denburg et al., 2007; Fein, McGillivray, & Finn, 2007; Zamarian, Sinz, Bonatti, Gamboz, & Delazer, 2008). It has been hypothesized that this decision-making deficit, seen in some older adults, may be connected to age-related prefrontal cortex decline (Denburg et al., 2007) and/or age-related declines in executive functioning (Brand & Markowitsch, 2010a). On the other hand, lesion evidence and functional imaging findings in young adults implicate the ventromedial prefrontal cortex (VMPFC) in decision-making during risky, nontransparent situations (Bechara et al., 1994; Bechara, Tranel, & Damasio 2000; Fukui, Murai, Fukuyama, Hayashi, & Hanakawa, 2005; Lawrence, Jollant, O'Daly, Zelaya, & Phillips, 2009; Li, Lu, D'Argembeau, Ng, & Bechara, 2010). Here, for the first time, we turn to

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fMRI, to investigate the relationship between VMPFC activation and IGT performance in older adults.

## VMPFC AND DECISION-MAKING

VMPFC damage has been correlated with impaired decision-making in laboratory settings, as well as with real-life abnormal risk assessment and decision-making impairments (Bechara et al., 1994, 2000). Patients with VMPFC lesions typically perform at normal levels on standard neuropsychological assessments of working memory, verbal and spatial-perceptual abilities, and decision-making abilities in explicit, transparent scenarios (Bechara et al., 2000). However, these patients are impaired on decision-making tasks that involve risk, and in which all necessary information is *not* explicitly presented (such as the IGT, described below) (Bechara et al., 1994, 2000). VMPFC patients gravitate toward choices that have immediate benefits (but unknown long-term losses) in the IGT and other similar tasks involving decision-making under conditions of uncertainty and do not learn to avoid such risks (Bechara et al., 1994, 2000). Conversely, young, healthy, adult subjects will chose immediate benefits to start with, but rapidly learn to make more advantageous (i.e., "safer") choices in these nonexplicit, probabilistic situations, even though they are unable to calculate and/or verbalize the nature of the differences between the options from which they can choose (Bechara et al., 1994, 2000).

Functional imaging studies of young adults indicate that decision-making in nontransparent (i.e., risky) situations engages a neural system that includes VMPFC, as well as additional orbitofrontal cortex, amygdala, anterior cingulate cortex, insula, ventral striatum, and dorsolateral prefrontal cortex (DLPFC) (Bechara et al., 1994; Lawrence et al., 2009; Li, Lu, D'Argembeau, Ng, & Bechara, 2010). Functional imaging studies of IGT performance in young adults indicate that VMPFC is preferentially activated during "risky" choices compared to "safe" choices (Ernst et al., 2002; Fukui et al., 2005; Lawrence et al., 2009). However, functional imaging studies report conflicting findings regarding the correlation between VMPFC activity and IGT performance: Some work suggests that the blood oxygenation level dependent (BOLD) response of VMPFC in young adults is positively correlated with IGT performance (Fukui et al., 2005), while other studies have found no correlation between signal strength in VMPFC and IGT performance (Windmann et al., 2006).

## VMPFC AND OLDER ADULTS

As mentioned above, some seemingly cognitively intact older adults do exhibit decision-making deficits in risky, nontransparent situations such as in the IGT. These "impaired" older adults in fact produce a larger proportion of "bad" (i.e., risky) decisions than VMPFC patients (Denburg et al., 2007). Although the decision-making deficit seen in some older individuals does not completely mirror the deficits of patients with VMPFC lesions, (Bechara et al., 1994; Denburg et al., 2007), the VMPFC seems to be a good candidate for functional differences related to decision-making impairments in the older adult population.

On average, typically aging older adults have disproportionally less prefrontal cortex in relation to the rest of the cortex than younger adults (Fjell et al., 2009; Peters, Sethares, & Moss, 1998; Raz, Gunning-Dixon, Head, Dupuis, & Acker, 1998; Tisserand et al., 2002). Differences in VMPFC volume have also been related to risky decision-making deficits in older adults with a variety of neurological conditions (Bechara et al., 1994; Rahman, Sahakian, Hodges, Rogers, & Robbins, 1999). For example, patients with mild frontotemporal dementia (affecting VMPFC) show impaired IGT performance, while working memory and planning abilities are normal (Rahman et al., 1999). In addition, early Parkinson's disease patients have impaired IGT performance and significantly less orbitofrontal/VMPFC proportional volume relative to healthy control subjects (Ibarretxe-Bilbao et al., 2009). However, it is not known if the IGT impairments found in the early stages of neurological disease are caused by the same structural or functional differences as IGT impairment in older adults with no known neurological disease.

## THE IGT

The IGT has been used for the past 15 years as a sensitive laboratory measurement of real-life decision-making impairments in numerous populations (e.g., Bechara et al., 1994; Denburg et al., 2007). Briefly, in the IGT, subjects are presented with four sets of playing cards, and told that they begin the game with a loan of $2000. The goal of the IGT is to win as much money as possible. To do so, subjects are instructed to select cards, one at a time, from any of the four sets. When a card is selected (i.e., turned over), subjects are told the monetary consequences associated with that card. All card choices result in subjects winning some money, but some card choices also result in subjects

losing money. Two of the four sets contain cards associated with the immediate gain of larger sums than the other two sets. However, these "win big" sets also contain cards associated with larger losses than the other two sets. In the end, "win big" choices total larger losses than the sums won. The reverse is the case for the low-paying sets. Over the course of the IGT (i.e., 100 card selections—a fact not known to the subjects)—it is most advantageous to choose cards from the two sets that have smaller immediate monetary gains. The underlying task in the IGT is to learn which sets are most advantageous over several card choices, and which ones are not. The overall net gain or loss associated with each set cannot be calculated by adults with intact memory and cognitive abilities (Bechara et al., 1994). Subjects' decisions appear to be based on estimates of the "goodness/badness" of each set formed over the course of the task, stemming from somatic markers associated with choices from the "good" and "bad" sets formed over time (Bechara, Damasio, Tranel, & Damasio, 1997).

In the present study, older adults completed an fMRI-adapted version of the IGT, which included blocks of IGT trials interleaved between blocks of non-gambling control task. Previous work indicates that interrupting the IGT with a second task, or rest periods, does not change IGT performance in younger, healthy subjects or in VMPFC lesion patients (Bechara et al., 1994; Li et al., 2010).



# METHODS

## Participants

Fifteen older adults (9 female, mean age = 77 years old, range: 58–95) participated in this study. Participants were recruited in collaboration with, and under a pilot grant from the University of Southern California's Alzheimer Disease Research Center (ADRC). Adults 55 years of age and older were recruited. None exhibited any cognitive or memory impairments as determined by the ADRC's standard assessment process, including neuropsychological, cognitive, and medical data. Inclusion criteria also included receiving at least a "normal for age" appraisal based on the ADRC's administration of the Mini-Mental State Examination and Neuropsychological battery as part of the National Alzheimer's Coordinating Center's Uniform Data Set (NACC UDS) (for a summary, see Table 1). All participants gave informed consent under a protocol approved by the Institutional Review Board of the University of Southern California.

## Experiment design and stimuli

The experiment consisted of the subject performing interleaved blocks of IGT trials and a non-gambling control task (described in detail below). Subjects were

**TABLE 1**
Summary of neuropsychological data for each subject, sorted by IGT performance group

| *Subject* | *IGT performance* | *Gender* | *MMSE* | *Digit span* | *Log. memory* | *BNT* | *TM-A/TM-B* |
|---|---|---|---|---|---|---|---|
| 1 | Unimpared | F | 29 | 6 | 11 | 23 | 40 / 84 |
| 2 | Unimpared | F | 30 | 8 | 18 | 30 | 16 / 48 |
| 3 | Unimpared | M | 30 | 7 | 14 | 30 | 31 / 47 |
| 4 | Unimpared | F | 30 | 8 | 17 | 29 | 40 / 123 |
| 5 | Unimpared | M | 27 | 6 | 13 | 29 | 30 / 70 |
| 6 | Chance | F | 30 | 7 | 11 | 30 | 24 / 78 |
| 7 | Chance | M | 30 | 8 | 9 | 25 | 27 / 78 |
| 8 | Chance | F | 30 | 7 | 16 | 22 | 43 / 74 |
| 9 | Impaired | F | 30 | 7 | 9 | 19 | 32 / 103 |
| 10 | Impaired | F | 28 | 6 | 15 | 15 | 62 / 300 |
| 11 | Impaired | M | 30 | 5 | 15 | 29 | 27 / 80 |
| 12 | Impaired | F | *nd* | *nd* | *nd* | *nd* | *nd* |
| 13 | Impaired | M | 29 | 6 | 12 | 30 | 31 / 114 |
| 14 | Impaired | F | 30 | 7 | 11 | 30 | 27 / 70 |

*Notes:* nd = no data available, MMSE = Mini-Mental State Exam, digit span = digit span forward length in NACC UDS, log. memory = logical memory in NACC UDS, BNT = Boston Naming Task, TM-A/TM-B = Trail Making Test, parts A and B in NACC UDS.

trained on both the IGT and control task immediately prior to scanning (outside the scanner), using practice trials (20 trials of each task type) similar, but not equal, to those presented during fMRI acquisition. None of the training sequences were used during the fMRI session.

## The IGT

The basic principles of the IGT were briefly mentioned above; for a detailed description of the IGT, see Bechara et al. (1994). To adjust the IGT for use in the scanner, we modified an already fMRI-adapted version of the IGT developed by Li et al. (2010), which included blocks of IGT trials interleaved between blocks of non-gambling control task.

Subjects participated in four scanning runs. Each run contained 100 IGT trials (i.e., card choices) divided equally into five blocks (i.e., 20 trials each). These IGT blocks were interleaved with five blocks of the non-gambling control task (also containing 20 trials each, described in the next section). For both tasks, the inter-trial interval was 4 s.

Four variants of the IGT were used: "ABCD," "KLMN," "EFGH," and "IJOP." The "ABCD" variant of the IGT is the original IGT paradigm (Bechara et al., 1994), which was described in the introduction. The "KLMN" variant is structured similarly to "ABCD," but has been slightly modified to reduce possible carry-over effects from performing the "ABCD" variant. These modifications include a decrease in the difference between the overall gains associated with the "good" sets of cards compared to the "bad" sets, as well as a decrease in the immediate gains of the "bad" sets (Preston, Buchanan, Stansfield, & Bechara, 2007). The "EFGH" and "IJOP" variants are constructed to be a mirror image of the "ABCD" and "KLMN" variants: There are immediate losses (i.e., money is lost on most trials), and only occasional card choices result in winning money. This is the opposite of the "ABCD" and "KLMN" variants, in which there are immediate gains and long-term losses.

For the first 10 subjects, each of the four IGT variants was presented in one of the four scanning runs. However, preliminary analyses of performance indicated that all of the 10 subjects were performing at chance (i.e., not significantly different than chance/random performance as determined by the binomial test) for the "EFGH" and "IJOP" IGT variants (the variants in which money is lost on every trial, and winning occurs occasionally). Thus, for the remaining five subjects, these variants were excluded. Instead, two runs each of the "ABCD" and "KLMN" IGT variants were presented.

## Non-gambling control task

The visual and auditory stimuli in this control task were as similar to the IGT presentation as possible: Four sets of cards were presented, just as in the IGT. However, instead of each set being labeled with a letter on the back of its top card, a number was presented. These numbers changed on each trial. Subjects were instructed to press the button corresponding to the set with the largest number displayed. A correct response resulted in the subject "winning" the amount on the card; corresponding auditory and visual feedback were then presented as in the IGT.

## fMRI procedures

Data were collected at the Dana and David Dornsife Cognitive Neuroscience Imaging Center's Siemens MAGNETOM Trio with Tim 3T scanner. A high-resolution anatomical image was acquired in the coronal plane, with a T1-weighted MP-RAGE pulse sequence for each subject ($1 \times 1 \times 1$ mm isotropic voxels, TI = 900 ms, TR = 2070 ms, TE = 4.13 ms, flip angle = 7°). Functional MRI data were collected across four scanning runs, using a T2*-weighted, single-shot, echo-planar imaging (EPI) pulse sequence: TR = 2000 ms, TE = 25 ms, flip angle = 90, interleaved acquisition of 35 coronal slices, slice thickness = 3.5 mm (no gap), in-plane resolution = $3 \times 3$ mm, field of view = $192 \times 192$ mm, 408 volumes collected.

Stimuli were presented and synchronized to the MR image acquisition via Matlab (MathWorks, Inc., Natick, MA, USA), using the Psychophysics Toolbox for Matlab (Brainard, 1997; Pelli, 1997). Visual stimuli contained within the two tasks were presented to subjects through a mirror attached to the head coil, which allowed subjects to view images back-projected onto a screen behind them in the scanner bore. Auditory feedback was delivered via electrostatic headphones. Subjects indicated their judgments using two four-button, MR-compatible response boxes, one held in each hand. Subjects' responses were recorded in Matlab.

## Data analysis

Fourteen of the 15 scanned subjects were analyzed as described below (one subject was excluded because of self-report of prior knowledge of the IGT). EPI data preprocessing and analysis were conducted with FSL software (Oxford Centre for Functional Magnetic Resonance Imaging of the Brain, Oxford, UK). Preprocessing of the data was conducted with FSL's

fMRI Expert Analysis Tool (FEAT). Preprocessing included motion correction (Jenkinson, Bannister, Brady, & Smith, 2002), brain extraction (Smith, 2002), spatial smoothing with a Gaussian full-width, half-maximum 5.0-mm filter, high-pass temporal filtering by Gaussian-weighted least-squares straight line fitting with sigma = 120 s, and pre-whitening (Woolrich, Ripley, Brady, & Smith, 2001). In addition, deionizing of the data was performed by probabilistic independent components analysis (ICA) (via FSL's MELODIC 3.0) to identify global trends in signal change not associated with the frequency of task blocks or individual trials. These components were then filtered out of the BOLD signal prior to the multiple-regression analyses in order to reduce noise in the BOLD signal changes identified as correlating with the performance of the IGT and/or control task. The criteria for a component to be filtered out were twofold: (1) identified by the ICA to be contributing to greater than 1% of the variance in a subject's BOLD data set; (2) having a principal frequency component not corresponding to the frequency of the task blocks (0.006 25 Hz) or the frequency of single trials (0.25 Hz).

As reviewed in the introduction, previous studies of younger adults using group analysis have found that (1) VMPFC regions are preferentially activated during the IGT, and (2) VMPFC activation is positively correlated with IGT performance. Therefore, we restricted our analyses to the VMPFC. For the purposes of these analyses, VMPFC was defined as the mesial half of the orbital surface continuing into the medial surface of the frontal lobe up to a line, parallel to the AC–PC line, from the beak of the callosum to the frontal pole. The anterior and posterior limits are the very anterior end of the frontal lobe and posteriorly to the most posterior coronal cut in which orbital cortex is still clearly seen. Masks of VMPFC voxels were generated manually in FSLView on each subject's structural MRI (Figure 1).

A multiple-regression analysis (using FSL's FMRIB Improved Linear Model) was then applied to each voxel within each subject's VMPFC mask. The IGT blocks were modeled with a regressor derived from a convolution of the block design and a gamma function to represent the hemodynamic response function. Regressors representing the motion correction parameters were also included.

Analysis of VMPFC response to the IGT proceeded along two paths. First, we explored the VMPFC response during the IGT in each individual subject. The response properties of the anatomically defined VMPFC region of interest (ROI) for each subject were each analyzed separately in a multiple-regression analysis, in the native space of each subject's structural MRI. To further describe individual subject variability, the total number of voxels with a significant BOLD response to the IGT and the mean BOLD response during the IGT were also calculated for each subject's VMPFC ROI.

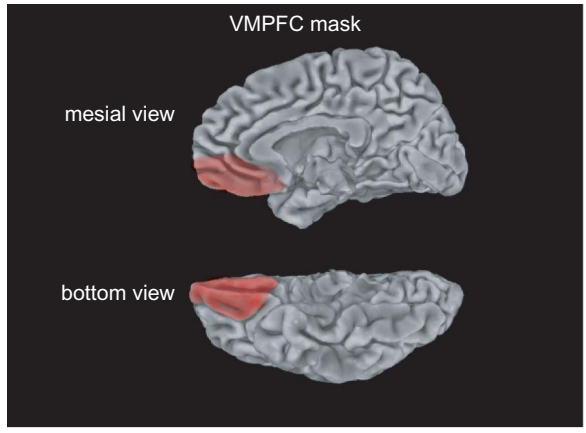


**Figure 1.** VMPFC mask used for subsequent fMRI analyses (right hemisphere is shown, but both hemispheres were included in the VMPFC mask).

Secondly, a group analysis (typically used in fMRI during studies of the IGT in younger adults, as described in the introduction) was conducted. To do so, each subject's functional data were transformed into MNI space and resampled into $1 \times 1 \times 1$ mm voxels, using FSL's FMRIB's Linear Image Registration Tool (Jenkinson et al., 2002; Jenkinson & Smith, 2001). The multiple scanning runs for each subject were combined into a higher-level, mixed-effects analysis, in which, across subjects, a pairwise comparison was computed to identify VMPFC voxels with greater BOLD signal during the IGT blocks than during the control task blocks. A further analysis was then performed to identify VMPFC voxels whose activations during IGT trials were significantly accounted for by IGT performance level across subjects (defined as overall ratio of "good" to "bad" set choices). Thresholding and multiple comparisons were controlled for by FSL's standard cluster thresholding option (a threshold of $z = 2.3$, masked by a cluster probability threshold of $p < .05$).

# RESULTS

## Behavioral results

In the control task, response accuracy approached ceiling performance ($M = 95.6\%$, $SD = 3.5$) and did not significantly vary across blocks or scanning runs. Thus, control task performance will not be discussed further. IGT performance (of the "ABCD" and "KLMN" IGT

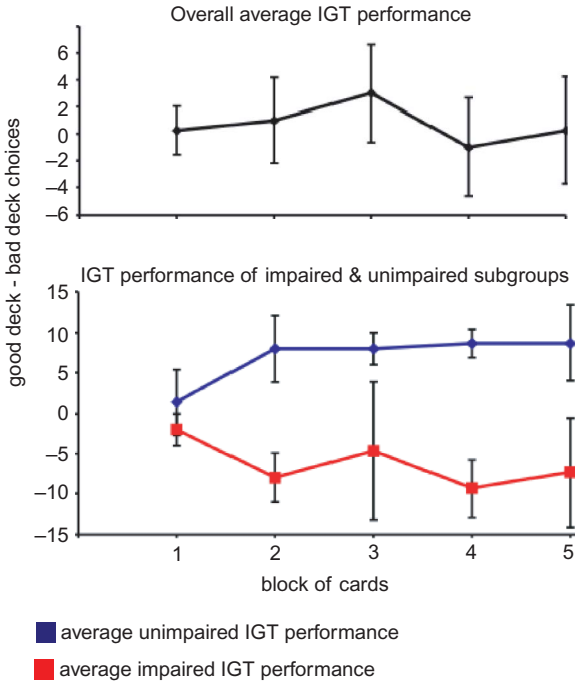


**Figure 2.** Top. Overall IGT performance, averaged across all subjects. Bottom. Average IGT performance for subjects performing significantly below (impaired, red) and above (unimpaired, blue). Error bars represent standard error of the mean.

variants) during fMRI acquisition was congruent with previous findings in older adults outside the scanner (Denburg et al., 2007). A binomial test indicates that average overall performance across subjects (collapsed across scanning runs) did not significantly differ from chance ($z = 0.6$, $p = .27$) (Figure 2). Binomial tests on each subject's IGT performance identified 5 subjects as performing significantly above chance, 3 subjects with performance not significantly different than chance, and 6 subjects with performance significantly below chance. Each of these levels of performance is plotted in Figure 2. IGT performance was not correlated with any of the neuropsychological battery data collected (Table 1). IGT performance was also not correlated with age, $r = –.18$, $p = .27$ (Table 1).

## fMRI individual subject results

Each subject's mean percent signal change and number of voxels passing threshold (IGT, control task, $p < .05$, family-wise error corrected, no cluster-size threshold) in the left and right VMPFC ROIs are listed in Table 2. (There was no significant correlation between total number of functional voxels in the VMPFC ROIs and IGT performance; therefore, the total number of significant functional voxels is reported.)

There was a significant correlation between the number of left VMPFC voxels activated and IGT performance ($r = .82$, $p = .0002$), as well as a significant correlation between the mean percent signal change in the left VMPFC and IGT performance ($r = .74$, $p = .001$) (Figure 3). There was no such significant correlation for the right VMPFC for number of voxels passing threshold ($r = –.12$, $p = .33$) or mean percent signal change ($r = –.19$, $p = .26$). The correlation

**TABLE 2**
Gender, IGT score, left and right VMPFC mean percent signal change, and number of VMPFC voxels passing threshold for the IGT versus baseline task ($p < .05$, family-wise error corrected), for each subject.

| | | | | *Left VMPFC* | | *Right VMPFC* | |
|---|---|---|---|---|---|---|---|
| *Subject* | *IGT performance* | *Gender* | *Average IGT score* | *% signal change* | *No. of voxels* | *% signal change* | *No. of voxels* |
| 1 | Unimpared | F | 2.97 | 0.452 | 45 | 0.402 | 16 |
| 2 | Unimpared | F | 2.37 | 0.39 | 40 | 0.337 | 22 |
| 3 | Unimpared | *M* | 2.12 | 0.439 | 41 | 0.385 | 35 |
| 4 | Unimpared | F | 1.97 | 0.331 | 39 | 0.264 | 45 |
| 5 | Unimpared | M | 1.93 | 0.492 | 66 | 0.4 | 68 |
| 6 | Chance | F | 1.125 | 0.299 | 30 | 0.195 | 4 |
| 7 | Chance | M | 0.671 | 0.295 | 18 | 0.384 | 8 |
| 8 | Chance | F | 0.353 | 0.277 | 22 | 0.301 | 10 |
| 9 | Impaired | F | −1.979 | 0.191 | 0 | 0.204 | 20 |
| 10 | Impaired | F | −1.98 | 0.306 | 11 | 0.378 | 20 |
| 11 | Impaired | M | −2.07 | 0.342 | 33 | 0.997 | 55 |
| 12 | Impaired | F | −2.1525 | 0.305 | 4 | 0.41 | 47 |
| 13 | Impaired | M | −2.27 | 0.254 | 0 | 0.295 | 22 |
| 14 | Impaired | F | −2.54 | 0.232 | 10 | 0.286 | 45 |

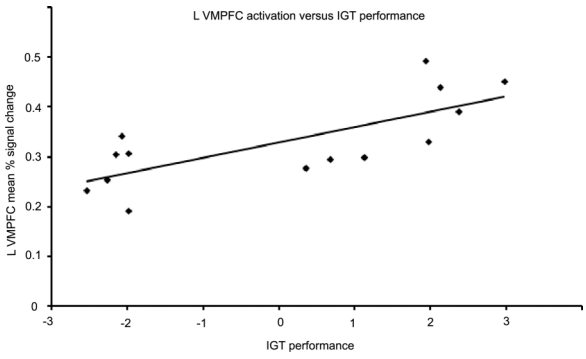


**Figure 3.** Left VMPFC mean percent signal change (IGT > control task) versus IGT performance.

between number of voxels passing threshold in the left and right VMPFC activation for each subject was not significant ($r = .35$, $p = .12$). In addition, the correlation between mean percent signal change for the left and the right VMPFC was significant ($r = .27$, $p = .16$).

## fMRI group results

The voxel-wise, repeated-measures *t*-test identified a right VMPFC subregion (MNI coordinates: 8, 38, 14) significantly more activated during the IGT than during the control task ($p < .05$, family-wise error corrected) (Figure 4, panel A). The analysis of IGT performance and BOLD response demonstrated that increased activation in a subregion of the left VMPFC (MNI coordinates: –26, 38, –12), a region contralateral to the IGT-activated area found in the right hemisphere, was significantly explained by greater IGT performance ($p < .05$, family-wise error corrected) (Figure 4, panel B).

# DISCUSSION

We report (for the first time) on the neural correlates of IGT decision-making in older adults, using fMRI. We also replicated, during scanning, older adults' IGT performance seen in behavioral studies (Denburg, Tranel, & Bechara, 2005; Denburg et al., 2007; Fein et al., 2007).[1] Our study has two major findings: (1) right VMPFC was activated during the IGT, regardless of performance level; and (2) left VMPFC activation was positively correlated with IGT performance. These findings, and our interpretations, are discussed in detail below. The present study does not include a younger adult control group, and thus we compare our results to those found in previous studies of younger adults.

## Older adults' IGT performance

Behavioral studies of younger adults (performed outside the scanner) typically do *not* report any subgroup of subjects performing significantly worse than chance on the IGT (Bechara et al., 1996, 1997), unlike comparable studies performed in older adults—i.e., Denburg et al. (2005, 2007) and Fein et al. (2007). However, fMRI studies of younger adults have in fact detected subgroups of young adults with impaired IGT performance during fMRI acquisition (Fukui et al., 2005; Li et al., 2009). This discrepancy suggests that the added noise and attentional demands associated with performing a complex task in an MR scanner may actually affect IGT performance, at least, in younger adults. However, the impairments seen in our older adult subjects, while in the scanner, mirror those found in a similar population outside the scanner (Denburg et al., 2005, 2007), suggesting that in our cohort the scanner environment did not affect performance. Therefore, we conclude that our fMRI findings are likely to reflect activation differences related to IGT performance and not differences in attentional abilities. This age-related dissociation in IGT performance inside versus outside the MR scanner suggest that the factors contributing to successful IGT performance in younger adults may not be the same that contribute to successful IGT performance in older adults. This behavioral dissociation also highlights the importance of studying the neural processes underlying specific decision-making impairments directly in older adults, and not assuming that findings in younger adults can be extrapolated to an older population. The present study is an initial step in this direction. In addition, our results suggest that an fMRI-adapted IGT paradigm is a viable approach to study the neural correlates of decision-making in the older adult populations.

## Right VMPFC activation during the IGT, regardless of performance

In our sample, we found only one *right* VMPFC region significantly activated during IGT performance compared to the control task across all subjects. This right

[1] Our results for the "ABCD" IGT variant and the similar "KLMN" IGT coincide with Denburg et al.'s "ABCD" IGT variant data (no other variant was used by Denburg et al.). To our knowledge, no study has tested older adults on the loss-oriented IGT variants that yielded chance performance in the current study, and thus these IGF variants were excluded from further analyses.

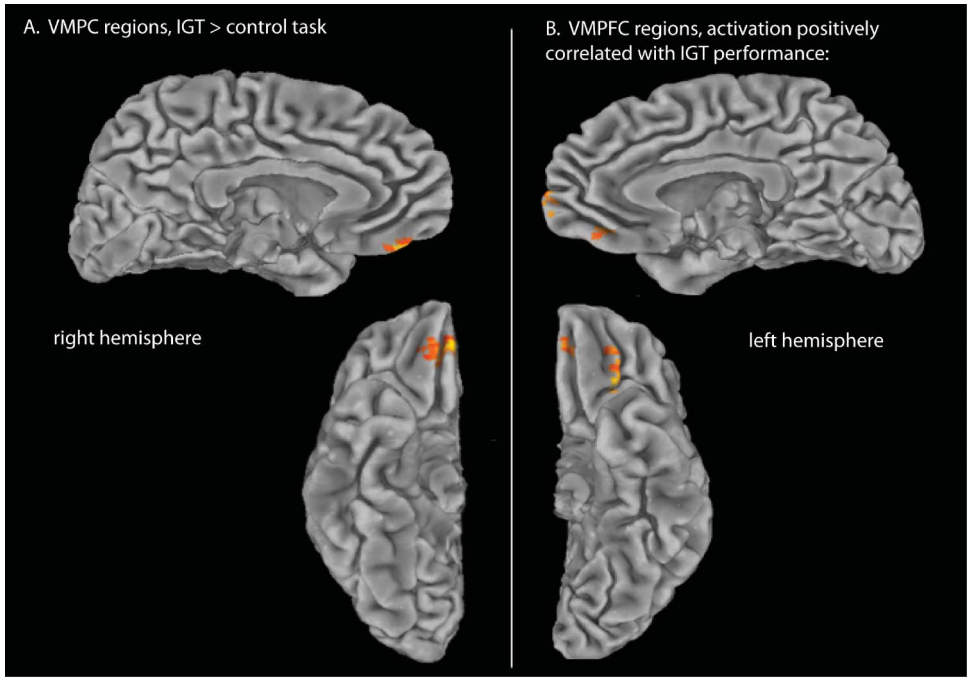


**Figure 4.** (A) VMPFC regions with greater BOLD response during the IGT than during the baseline task, $p < .05$, family-wise corrected. (B) VMPFC regions with a BOLD response positively correlated with IGT performance, $p < .05$, family-wise corrected.



VMPFC region's BOLD response and extent of activation (i.e., number of voxels) were not significantly correlated with level of IGT performance. This finding is concordant with previous studies in younger adults (Lawrence et al., 2009; Li et al., 2010), in that our group-averaged results indicate that the BOLD response in VMPFC was significantly greater during performance of the IGT than during performance of the control task (Figure 4, panel A).

However, there is a difference between the present older adults' VMPFC activation during the IGT and those previously found in younger adults; namely, laterality. Several studies of younger healthy adults have described bilateral VMPFC/OFC (orbitofrontal cortex) activation during the IGT (Fukui et al., 2005; Lawrence et al., 2009; Li et al., 2010). Some studies (e.g., Lawrence et al.) have also described regions within VMPFC whose activation is positively correlated with IGT performance. In contrast, we found no correlation between right VMPFC activation (peak BOLD response or number of voxels) and IGT performance. More specifically, subjects with unimpaired and impaired IGT performance both had similar peak and extent of activation in right VMPFC. Subjects performing at chance also had similar peak activations in right VMPFC, although the extent of this activation ($M = 7$ voxels) was noticeably less than the extent seen in unimpaired ($M = 37$ voxels) or impaired performers ($M = 35$) (Table 2). In conclusion, our findings in the right VMPFC differ from those previously found in younger adults. However, left VMPFC findings, discussed next, more closely follow the pattern seen in younger adults.

## Left VMPFC activation positively correlated with IGT performance

In our sample, we found only a *left* VMPFC region whose activation was positively correlated with IGT performance. Due to the block design of our experiment, we are not able to dissect various aspects of the IGT (anticipation, choice, feedback, etc.) and thus cannot determine to what element of the IGT the left VMPFC activation is responding. However, combining this left VMPFC- performance correlation with the fact that a right VMPFC region was activated during the IGT across all performance levels, our results show that the older adult subjects who performed the IGT successfully had, on average, bilateral VMPFC activation, even with a left hemisphere bias, whereas the subjects with impaired IGT performance had lower activation levels with a right-lateralized bias. We suggest as a possible explanation that the recruitment of additional neural regions in older adults reflects compensation for age-related prefrontal functional decline

(e.g., West, 1996). Similarly, additional activation associated with higher performance in older adults has been reported for a variety of cognitive tasks that engage prefrontal cortex, such as cognitive control, selective attention, and memory tasks (Cabeza, Anderson, Locantore, & McIntosh 2002; Cabeza et al., 2004; de Sanctis, Gomez-Ramirez, Sehatpour, Wylie, & Foxe, 2009; Gutchess, Kensinger, & Schacte, 2007). However, this possibility is confounded by the finding that, in older adults, proportional volumes of VMPFC and of orbitofrontal cortex are positively correlated with IGT performance, while dorsolateral prefrontal cortex and amygdala volumes are not correlated with IGT performance (Mohlman et al., 2009). Thus, future studies combining fMRI and volumetric measurements of VMPFC may help explain how this activation spread in VMPFC associated with successful decision-making (in uncertain, risky situations) may be related to anatomical changes occurring with aging.

This "spreading" of activation into the left VMPFC correlated with better IGT performance would not have been predicted from previous studies of patients with VMPFC lesions (Clark, Manes, Antoun, Sahakian, & Robbins, 2003; Tranel, Bechara, & Denburg, 2002). The lesion evidence indicates that the right VMPFC is critical for successful IGT performance: patients with right VMPFC damage made more risky choices in the IGT than patients with left VMPFC damage as well as control subjects (Clark et al., 2003; Tranel et al., 2002). At first glance, these lesion findings may appear to contradict our fMRI findings in older adults. However, this is not the case, once we consider the effects of possible age-related declines in prefrontal function (discussed above). Our results indicate that the right VMPFC is similarly activated in both impaired and unimpaired IGT performers. Perhaps this right VMPFC involvement in itself is not adequate, in older subjects, for successful IGT performance as it would have been in younger subjects. In fact, successful IGT performance in the older subjects may also require additional activation of the left VMPFC. This explanation has partial support in the finding of Lee, Leung, Fox, Gao, and Chan (2007) that left orbitofrontal cortex/VMPFC is deactivated during risky decisions (in an explicit, risky-gains task) in younger adults, but is activated during the same risky-gains task in older adults. Also, in young adults, the right VMPFC (and not the left VMPFC) was found to be activated during unexpected affective judgment making (Northoff et al., 2006). Furthermore, the level of right VMPFC activation during the affective judgments was significantly and positively correlated with IGT performance tested outside the scanner (Northoff et al., 2006). The combination of this right-lateralized activation trend in VMPFC in younger subjects with successful IGT performance, and our finding that right-lateralized activation alone was not sufficient for successful IGT performance in older adults, suggests that older adults who perform well on the IGT may recruit additional VMPFC resources whose involvement may not be necessary for younger adults to achieve unimpaired performance.

## Gender differences and the IGT

One additional explanation for our findings may be related to gender differences in activation laterality (Bolla, Eldreth, Matochik, & Cadet, 2004). VMPFC lesion studies suggest that an intact left VMPFC may be critical for IGT performance in *females* in the presence of damage to right VMPFC, whereas the right VMPFC seems to be necessary for successful IGT performance in *males* (Tranel et al., 2005). The results of Clark et al. (2003) may have been skewed because of gender differences: only one-third of their patients with right VMPFC damage were male. Due to the small sample size of each gender in the current study, we cannot fully evaluate the contribution of gender. However, as an exploratory analysis, we calculated a voxel-wise, two-sample *t*-test to identify VMPFC voxels that are more activated by the IGT in males than females, and vice versa. We found a trend that coincides with the gender differences predicted by the lesion work: The IGT elicited greater BOLD response in the left VMPFC of our female subjects, and greater BOLD response in the right VMPFC of our male subjects (Figure 5). Given the fact that we had more female than male subjects (females outnumbered males 3:2), it is possible that the female subjects' left VMPFC activation might have been driving our results. However, our two male subjects with unimpaired IGT performance showed greater *left* VMPFC activation than right (as did the female subjects with unimpaired IGT performance). On the other hand, the two male subjects with impaired IGT performance showed a greater extent of VMPFC activation on the right (55 and 22 voxels, respectively) than the left (33 and 0 voxels, respectively), suggesting that gender differences might not be the entire explanation. Additionally, we found no significant difference between the performance of our male and female subjects ($t = 0.8$, $p = .96$), suggesting that the left VMPFC activation, positively correlated with IGT performance, is not due to having female subjects outperforming the males, and thus driving this left VMPFC result.

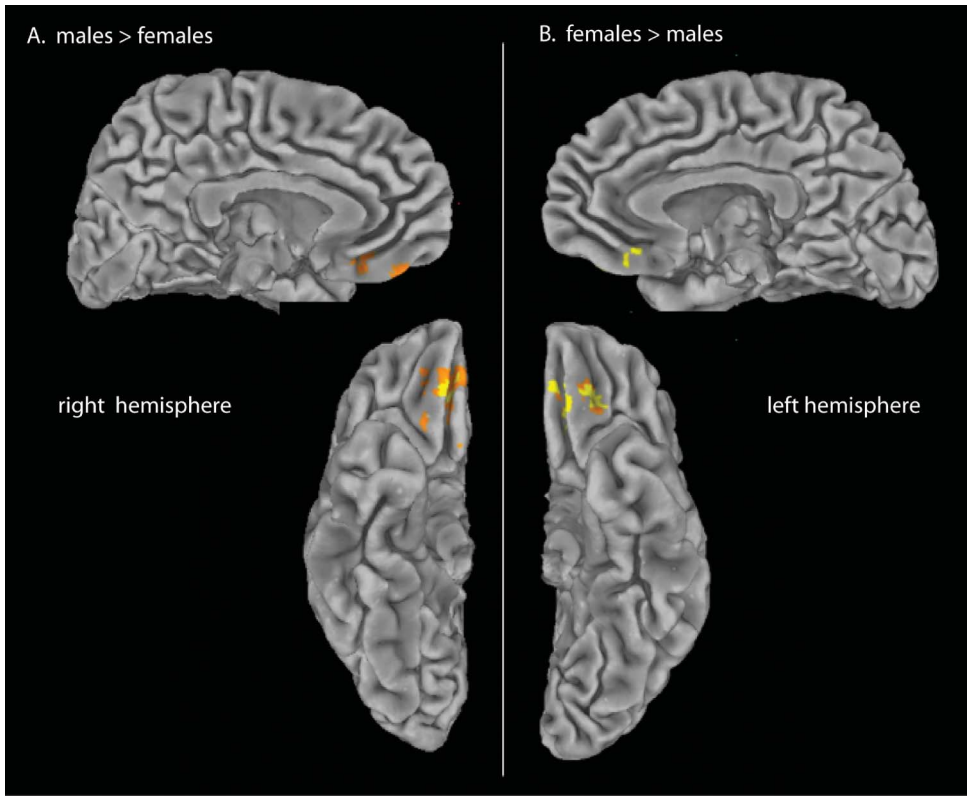


**Figure 5.** Preliminary gender analysis. VMPFC regions with greater BOLD response during the IGT for males than females (A), and for females greater than males (B), $p < .05$, family-wise error corrected.



Further studies with larger groups of each gender are needed to investigate the interaction between laterality of VMPFC involvement, gender, and IGT performance. The left VMPFC activation that we found to be positively correlated with successful IGT performance suggests that this interaction may be especially important in understanding the neural basis of specialized decision-making deficits in older adults.

## Age-related cognitive and attentional changes

The role of executive function in IGT performance continues to be debated (for a review, see Brand & Markowitsch, 2010a, 2010b; McCarrey, Henry, & Luszcz, 2010). The IGT is an ambiguous task, possibly taxing attention, speed of processing, working memory, feedback mechanisms, and choice selection resources—-all of which fall under the general description of executive function. Some studies have found a correlation between IGT performance and executive function abilities, while others have not (for a review, see Zamarian et al., 2008). However, no such significant correlations were found among the subjects in the present study. This lack of significant correlation of IGT performance with our neuropsychological measures (Table 1) suggests that IGT impairments can be present (without executive functioning deficits) in high-functioning older adults. In addition, patients with focal VMPFC lesions who have impaired IGT performance do not exhibit executive function deficits (e.g., Damasio, Tranel, & Damasio, 1990). Thus, we will now discuss another possibility, namely that age-related changes in emotional processes may account for some decision-making deficits in these older adults.

One possible explanation of the IGT performance deficits present in some older adults may be related to the positivity shifts seen in older adults' perspectives and self-perceptions. Older persons typically attend to and remember relatively better positive information than negative information when compared with younger adults (Charles, Mather, & Carstensen, 2003; Mather & Carstensen 2005). Older adults also display a shift toward internalizing positive external information but not negative information (Gutchess, Kensinger, & Schacter, 2007; Gutchess, Kensinger, Yoon, & Schacter, 2007). When judgments of emotional content are not explicitly required, older adults (in comparison to younger adults) typically exhibit a

greater increase in attention to and memory of positive stimuli, than to negative or neutral stimuli. Younger adults, on the other hand, attend to and remember better both positive *and* negative stimuli when compared to neutral stimuli. This age-related decrease in attention to negative information, however, does not hold when emotional judgments are explicitly required (Kensinger, Garoff-Eaton, & Schacter, 2007). The IGT does not require explicit emotional judgments, but it does elicit feelings associated with anticipating winning or losing, as well as with the revealing of the amount won or lost as a result of each card choice. VMPFC lesion patients have also been found to have decision-making deficiencies related to a lack of learning from negative feedback (Wheeler & Fellows, 2008). In addition, in younger adults, VMPFC activity during affective judgments was found to be positively correlated with IGT performance (Northoff et al., 2006).

## Age-related differences in neurophysiological responses

The above mentioned positivity shift associated with aging has also been demonstrated in neurophysiological studies during the IGT. Somatic responses to risk have traditionally been quantified via skin conductance responses (SCRs) of the autonomic nervous system. It is well documented that, as young adults (who have unimpaired IGT performance) make more and more card selections in the IGT, they develop an anticipatory skin conductance response (SCR) to the risky sets, but not to the safe sets (Bechara et al., 1997, 2000). Thus, although the subjects are not able to verbalize why they are avoiding some sets (and choosing others more often), their SCRs indicate that their nervous systems can distinguish between the two types of sets (i.e., risky versus safe sets). However, patients with bilateral VMPFC damage (who have impaired IGT performance) do not develop this anticipatory SCR to the risky sets. Damasio et al. (1991; Bechara et al., 2000) propose that VMPFC lesions impair real-life decision-making and impair IGT performance because of the VMPFC's critical role in generating a somatic marker of risky events.[2] Based on the lack of SCRs to risky choices in VMPFC patients impaired on the IGT, and the presence of SCRs to risky choices in young healthy adults, one might predict that older adults who have unimpaired IGT performance would also show SCRs in response to the risky choices as the younger subjects do. Conversely, one might predict that older adults impaired on the IGT would be more similar to VMPFC lesion patients and fail to have any elevated SCR to the risky sets. However, Denburg et al. (2006, 2007) found that older adults who have unimpaired IGT performance had a greater SCR during anticipation of the "safe" sets compared to the "risky" sets (the opposite of what has been found in the younger adults). Older adults with impaired IGT performance had equal SCRs to the "risky" and "safe" sets. These neurophysiological findings, when combined with the fMRI findings in the current study, suggest that successful IGT performance in older adults may not be due to a retention of VMPFC function similar to the one observed in younger adults, but rather to strong responses to positive (i.e., "safe") information, and this would include bilateral VMPFC involvement.

## Summary

The present study explored how older adults' performance in the IGT is related to VMPFC activation. We found that a right VMPFC region is activated in all subjects during the IGT, regardless of level of performance. However, successful (i.e., unimpaired) decision-making in the IGT was correlated with left VMPFC activation rather than with this right VMPFC activation. We interpret this finding as suggesting that bilateral VMFPC activation is necessary for successful IGT performance in older adults. This pattern appeared to be consistent for both males and females. More generally, as the first study of its kind with older adults, we have demonstrated that using an fMRI-adapted IGT paradigm is a feasible approach to investigate specific decision-making deficits in the seemingly healthy, nondemented older adult population.

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[2]For the purposes of this discussion, we have briefly summarized and perhaps simplified the relationship between VMPFC and somatic responses during the IGT. The important elements for the current discussion with implications regarding somatic responses and aging have been highlighted. See Damasio (1996) and Bechara et al. (2000) for a more complete discussion.

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