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Reward-Related Decision Making in Older Adults: Relationship to Clinical Presentation of Depression

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Abstract

Objective—Impairment in reward processes has been found in individuals with depression and in the aging population. The purpose of this study was twofold: 1. To use an affective neuroscience probe to identify abnormalities in reward-related decision making in late-life depression. 2. To examine the relationship of reward-related decision making abnormalities in depressed, older adults to the clinical expression of apathy in depression. We hypothesized that relative to elderly, healthy subjects, depressed, elderly patients would exhibit impaired decision making and that apathetic, depressed patients would show greater impairment in decision making than non-apathetic, depressed patients.

Methods—We used the Iowa Gambling Task to examine reward-related decision making in 60 non-demented, elderly patients with non-psychotic major depression and 36 elderly, psychiatrically healthy participants. Apathy was quantified using the Apathy Evaluation Scale. Of those with major depression, 18 individuals reported clinically significant apathy whereas 42 participants did not have apathy.

Results—Older adults with depression and healthy comparison participants did not differ in their performance on the IGT. However, apathetic, depressed older adults adopted an advantageous strategy and selected cards from the conservative decks compared to non-apathetic, depressed older adults. Non-apathetic, depressed patients showed a failure to adopt a conservative strategy and persisted in making risky decisions throughout the task.

Conclusions—This study indicates that apathy in older, depressed adults is associated with a conservative response style on a behavioral probe of the systems involved in reward-related decision making. This conservative response style may be the result of reduced sensitivity to rewards in apathetic individuals.

Keywords

reward; decision making; late-life depression; apathy

INTRODUCTION

Apathy, defined as a state of primary motivational impairment not attributable to diminished level of consciousness, cognitive impairment, or emotional distress, is a common, debilitating symptom of depression (Marin, 1990; Marin *et al.*, 1991; Starkstein and Leentjens, 2008). This deficit in motivation results in diminished goal-directed behavior, lack of intellectual interest and initiative, and indifference or flattening of affect. Apathy affects 1/3 of non-demented, depressed adults and is particularly common in late-life depression (Forsell *et al.*, 1993; Krishnan *et al.*, 1995; Lampe and Heeren, 2004; Mehta *et al.*, 2008). As a barrier to recovery from depression, apathy predicts poor response to antidepressants and chronicity (Chaturvedi and Sarmukaddam, 1986; Lavretsky *et al.*, 1999; Levkovitz *et al.*, 2011; Marin *et al.*, 2003).

Apathy of late-life depression occurs in the context of neurobiological abnormalities related to the positive valence network (Alexopoulos *et al.*, 2013), one of the main domains in the Research Domain Criteria (RDoC) matrix. Impairment in the positive valence system leads to the abandonment of rewarding activities, strengthening the conviction that little meaning or value is left in life and promoting depressive symptoms. Apathy may be related to the approach motivation construct of the positive valence system, specifically the component process of action selection/preference-based decision making. Action selection/preference-based decision making is defined as processes involved in the evaluation of costs and benefits and selection of an action or course of actions from among a set of alternatives. For clarity and brevity, these processes will be referred to as reward-related decision making throughout this manuscript.

Reward-related decision making depends on motivation, evaluation of the rewards and punishments associated with different options, and responsiveness to available rewards. Depressed individuals exhibit impairment in reward-related decision making on both behavioral measures and self-report scales (Elliott *et al.*, 1998; Eshel and Roiser, 2010; Henriques *et al.*, 1994; Vrieze *et al.*, 2013). Further, impairment in reward-related decision making in late-life depression is associated with critical clinical outcomes including functional impairment and suicidality (Dombrovski *et al.*, 2012; Jollant *et al.*, 2005, 2010).

The Iowa Gambling Task has been designated as a well-validated paradigm to study reward-related decision making (Bechara *et al.*, 1994, 1996, 1997). In the classic version of the task, participants are instructed to choose cards from one of four decks in order to win as much money as possible. The four decks have different schedules of reward and loss. Two decks are associated with higher immediate reward and higher long-term punishment, yielding an overall net loss, whereas the other two decks have lower immediate gain and lower long-term punishment, yielding an overall net gain. The task is structured that in order to win the most money, participants need to identify which decks are the advantageous or conservative decks and then select cards only from those decks. Therefore, performance on the IGT provides a measure of reward-related decision making. In this manuscript, we use performance on the IGT to examine how behavioral abnormalities of the positive valence system are expressed clinically in older adults suffering from depression.

Performance on the IGT is influenced by both depression and advancing age. The few studies that have used the IGT to examine reward-related decision making in mid-life depression have yielded conflicting findings, with some finding a disadvantageous or riskier approach to the task in depressed patients and others observing a conservative response bias in depressed patients that results in larger net gains (Cella *et al.*, 2009; Dalgleish *et al.*, 2004; Must *et al.*, 2006; Smoski *et al.*, 2008). In the aging population, approximately 40% of healthy older adults fail to learn to shift their selections from the risky decks to the conservative decks (Bauer *et al.*, 2012; Denburg *et al.*, 2007; Fein *et al.*, 2007; Rogalsky *et al.*, 2012).

The primary objectives of this present study were twofold: 1. to investigate IGT performance in older, depressed adults relative to elderly non-psychiatric comparison subjects and 2. to examine the relationship of IGT performance to the presence of apathy in elderly depressed patients. We hypothesized that relative to elderly, non-psychiatric comparison subjects, depressed, elderly patients would exhibit impaired reward-related decision making on the IGT and that apathetic, depressed patients would show greater impairment in decision making on the IGT than non-apathetic depressed patients.

METHODS

Participants

The study included 60 non-demented, elderly (>60 years) patients with non-psychotic major depression and 36 elderly, psychiatrically healthy participants. Subjects were recruited for an escitalopram trial through radio and print advertisements. Data was collected after the 2-week single-blind, placebo lead in and drug wash out period. The Weill Cornell Medical College Institutional Review Board approved all procedures. After a complete description of the study to the participants, written informed consent was obtained.

The depressed group met the DSM-IV-TR criteria and Research Diagnostic Criteria for unipolar major depression and had a >18 on the 24-item Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960). Exclusion criteria for the depressed group were: (1) major depression with psychotic features (according to the DSM-IV-TR); (2) history of other Axis I psychiatric disorders prior to the onset of depression; (3) severe medical illness (i.e., metastatic cancer, brain tumors, unstable cardiac, hepatic or renal disease, myocardial infarction) within the 3 months preceding the study; (4) neurological disorders (i.e., dementia or delirium according to the DSM-IV criteria, history of stroke, head trauma, multiple sclerosis, and brain degenerative diseases, including Parkinson's disease); (5) drugs causing depression (i.e., steroids, α -methyl-dopa, clonidine, reserpine, tamoxifen, and cimetidine); (6) conditions often associated with depression (i.e., endocrinopathies other than diabetes, lymphoma, and pancreatic cancer); (7) Mini-Mental State Examination (Folstein *et al.*, 1975) score <25; and (8) current psychotherapy. Exclusion criteria for non-depressed participants were the same as above as well as no history of any psychiatric illness.

Assessment

DSM-IV diagnosis was based on the SCID-R (First *et al.*, 2002), administered at entry to the study. Depressive symptoms were assessed using the 24-item Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960). Overall cognitive impairment was rated with the Mini-Mental State Examination (MMSE) (Folstein *et al.*, 1975) and the Dementia Rating Scale (Mattis, 1988). Apathy was quantified using the self-rated Apathy Evaluation Scale (AES), a psychometrically validated instrument in older normal individuals and psychiatric patients (Clarke *et al.*, 2007; Marin *et al.*, 1991). An AES score greater than 38 was considered to be clinically significant apathy (Clarke *et al.*, 2007).

The computerized Iowa Gambling Task (IGT) (Bechara *et al.*, 1997) was administered in the standard fashion, involving 100 card selections from four decks (A, B, C, and D).

Participants were instructed to choose cards from one of the four decks presented on the screen and that the aim of the task was to win as much money as possible. Some card selections were followed by reward only (monetary gain) whereas others were followed by a reward and a punishment (monetary loss). The task was manipulated such that decks with lower immediate gain have lower long-term punishment, yielding an overall net gain (decks C and D, referred to as conservative or advantageous decks); decks with higher immediate reward have higher long-term punishment, yielding an overall net loss (decks A and B, referred to as risky or disadvantageous decks). Reward amounts ranged from \$40 to \$80 for decks C and D and \$80 to \$170 in decks A and B. Losses ranged from \$25 to \$375 for decks C and D and \$150 to \$2500 for decks A and B. Participants were not informed about the number of trials or the reward/punishment schedules, and the schedules could not be deduced mathematically.

To quantify performance on the IGT, the 100 card selections were divided into five discrete blocks of 20 cards each, and for each Trial Block, a performance score was calculated by subtracting the number of risky deck choices (A and B) from the number of conservative deck choices (C and D), $([C+D]-[A+B])$. Average response patterns over the five blocks of the task were also calculated and provided an overall index of reward-related decision making performance. The number of cards selected from each deck was computed to determine deck preferences. Furthermore, the contingencies for the frequencies of losses differ between decks, allowing examination of the sensitivity to punishment frequency. The tendency to avoid decks with frequent losses (decks A and C) versus decks with infrequent losses (decks B and D) was examined by subtracting the total number of choices from decks B and D (infrequent larger losses) from decks A and C (frequent smaller losses), $([A+C]-[B+D])$ (Stocco *et al.*, 2009).

Statistical Analyses

Statistical analysis was performed with SPSS 19.0 (SPSS, Inc.). Univariate analysis of variance (ANOVA) assessed for differences in demographic and clinical characteristics (age, years of education, HDRS, AES) between depressed subjects and non-depressed, healthy controls and then among apathetic, non-apathetic, and healthy control groups. A repeated measures analysis of variance, with group (depressed vs. non-depressed and apathetic vs. non-apathetic vs. healthy controls) as the between-subjects factor and trial

block as the within-subjects factor, was performed to analyze IGT performance among groups over time. Post-hoc Tukey tests for honestly significant differences (HSD) were performed to determine significant group differences and to control for Type 1 errors. Post-hoc independent samples *t*-tests and follow-up univariate ANOVAs were then used to determine significant differences in trial block between groups. Independent samples *t*-tests were used to calculate deck preferences and sensitivity to punishment frequency among apathetic and non-apatetic groups.

RESULTS

Depressed and non-depressed comparison participants were similar in age, years of education, and overall cognitive function, as measured by the MMSE and DRS. As expected, depression severity, as measured by the HDRS, significantly differed between the groups ($t(94) = -33.21, p < 0.001$). Furthermore, to assess the differences in IGT performance over time between the two groups, a repeated measures analysis of variance, with group as the between-subjects factor and trial block as the within-subjects factor, was performed. The results showed no significant effect of trial block between groups ($F(3.57, 335.36) = 0.49, p = 0.73$), indicating that no differences in IGT performance over time exists between depressed subjects and non-depressed controls (Figure 1). Furthermore, depressed and non-depressed comparison participants did not differ significantly in deck preferences ($t(94) = 0.40, p = 0.69$) or in sensitivity to punishment frequency ($t(94) = -0.43, p = 0.67$).

Apathetic, non-apatetic, and control participants also were similar in age, years of education, and overall cognitive functioning (Table 1). However, baseline AES scores were significantly greater for apathetic participants than for non-apatetic and control participants ($F(2, 93) = 192.30, p < 0.001$). Depression severity also significantly differed among the groups ($F(2, 93) = 606.12, p < 0.001$).

To assess differences in IGT performance over time among the apathetic, non-apatetic, and control groups, a repeated measures analysis of variance with a Greenhouse-Geisser correction determined a significant effect of trial block ($F(3.55, 329.82) = 8.69, p < 0.001$) and group ($F(2, 93) = 4.43, p < 0.05$). The interaction between group and trial blocks ($F(7.09, 329.82) = 2.15, p < 0.05$) was also significant, indicating that non-apatetic and apathetic, depressed patients and healthy controls displayed different decision making patterns during the task (Figure 2). Follow-up univariate ANOVAs specifically showed a marginally significant difference among groups on Trial Block 2 ($F(2, 93) = 2.67, p < 0.1$) and a significant difference among groups on Trial Block 4 ($F(2, 93) = 5.08, p < 0.05$). Post-hoc Tukey tests of HSD revealed that the apathetic group selected significantly more cards from the conservative decks than the non-apatetic group in Trial Block 4, with no significant difference between the apathetic and healthy control groups.

To specifically investigate the deck preferences between the apathetic and non-apatetic participants, independent samples *t*-tests were conducted between the apathetic and non-apatetic groups. Apathetic participants selected significantly fewer cards ($t(58) = 3.0, p < 0.05$) from risky decks (A and B) than the non-apatetic participants. Furthermore, apathetic participants selected significantly more cards ($t(58) = -3.0, p < 0.05$) from the conservative

decks (C and D) compared to non-apathetic participants (Figure 3). As a measure of overall performance of the entire task, the apathetic group made significantly more advantageous decisions ($t(58) = -3.0, p < 0.05$) and earned significantly more money than the non-apathetic group.

Lastly, to assess participants' sensitivity to punishment frequency, the difference between the number of card selections from the low (B and D) and the high (A and C) loss-frequency decks was calculated. The apathetic and non-apathetic groups both preferred decks offering low-frequency penalties (B and D) over those with high-frequency penalties ($t(58) = 0.46, p = 0.65$). Therefore, there was no significant difference in sensitivity to punishment frequency between the apathetic and non-apathetic groups (Figure 4).

DISCUSSION

The principal finding of this study is that apathy in depressed, older adults is expressed as a conservative response style on a behavioral probe of the positive valence system. Apathetic, depressed older adults more effectively evaluated costs and benefits and shifted their selections to the conservative decks. In contrast, non-apathetic, depressed older adults did not adopt an advantageous strategy and continued to make risky decisions on the task. This is the first study, to our knowledge, to examine how apathy impacts reward-related decision making abilities in elderly, depressed adults.

The conservative response style of apathetic, depressed older adults on the IGT may reflect either a reduced motivation to seek rewarding experiences or a reduced sensitivity to rewards. Depression has been shown to be associated with deficits in reward-related decision making (Elliot *et al.*, 1996; Eshel and Roiser, 2010; Henriques *et al.*, 1994), high variability in action selection (Kunisato *et al.*, 2012), and impulsive and inconsistent reward valuation (Takahashi *et al.*, 2008). Neuroimaging studies indicate that apathy in late-life depression is associated with abnormal functional connectivity within reward systems. Apathy in late-life depression is accompanied by low resting functional connectivity (FC) of the nucleus accumbens with the amygdala, caudate, putamen, globus pallidus, and thalamus and increased FC with the dorsomedial prefrontal cortex, superior frontal cortex, and the insula (Alexopoulos *et al.*, 2013).

The RDoC framework proposes that apathy is also a clinical expression of dysfunction of the Arousal and Regulatory System (Alexopoulos and Arean, 2013). The arousal construct is defined as the sensitivity of the individual to both internal and external stimuli and apathy has been conceptualized as a lack of responsiveness to stimuli or self-initiated action (Stuss *et al.*, 2000). Even though arousal is conceptualized as distinct from, but interacting with, motivational value, apathy may represent as a behavioral manifestation of dysfunction in this system. Our findings suggest that networks necessary for arousal may interact with networks critical for approach motivation to produce abnormal decision making.

These findings should be considered in the context of the limitations of this study. All groups demonstrated deteriorating performance in later time blocks of the IGT. Even though this pattern is common in the IGT literature, there is no unimpaired reference group in our

study. Furthermore, since the IGT is one of several well-studied decision making tasks, it is important to determine whether other complex decision making tasks reveal similar patterns. Specifically, paradigms that are used to study additional constructs in the positive valence system (e.g., the monetary incentive delay task evaluates reward prediction) should be used to examine other aspects of approach motivation. Identifying distinct, biologically driven behavioral targets will help inform the development of therapeutic interventions for late-life depression.

Despite these limitations, the presence of apathy in older adults with late-life depression may have critical implications for pharmacological treatment. For example, Yuen and colleagues (2014) demonstrated that in geriatric depression, apathy is separable from depression with regards to medication response and neural correlates. That is, apathy in elderly depressed patients persists despite improvement in depression. Further, structural abnormalities of the posterior subgenual cingulate and lower uncinate fasciculus appear to interfere with response of apathy to an SSRI.

Apathy of late-life depression is also resistant to traditional psychotherapy interventions. Apathy may present an obstacle for patients with late-life depression because they have difficulties initiating tasks and may not feel rewarded when even engaging in pleasurable activities. Therefore, treatments that entail increasing exposure to rewarding activities (Alexopoulos and Arean, 2013; Dirmaier *et al.*, 2012; Gawrysiak *et al.*, 2012; Hunnicutt-Ferguson *et al.*, 2012; Moss *et al.*, 2012; Riebe *et al.*, 2012) as well as concrete techniques that reduce apathetic states (e.g., the use of prompts, reminders, token economies) may be more suitable for targeting apathy in late-life depression.

In conclusion, this study indicates that apathy in older, depressed adults is associated with a conservative response style on a behavioral probe of systems involved in reward-related decision making. The clinical findings detailed in this study highlight the impact of apathy on the positive valence system in late-life depression. The implications of these findings are twofold: 1. To explore the role of the interaction of the positive valence system and the arousal regulatory system in the clinical expression of late-life depression; 2. To identify novel treatment targets for apathetic depression.

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Figure 1.

Average IGT performance over time for healthy controls and depressed older adults. The x-axis represents the five trial blocks of the task and the y-axis shows the average IGT performance score, which is calculated by subtracting the total number of cards chosen from the risky decks from the total number of cards chosen from the conservative decks.

Figure 2.

Average IGT performance over time for healthy controls, non-apathetic, and apathetic participants. The *x*-axis represents the five trial blocks of the task and the *y*-axis shows the average IGT performance score, which is calculated by subtracting the total number of cards chosen from the risky decks from the total number of cards chosen from the conservative decks.

Figure 3.

Average number of cards selected from risky and conservative decks by non-apathetic and apathetic patients.

Figure 4.
Average number of cards selected from high punishment frequency and low punishment frequency punishment decks by non-aphathetic and apathetic patients.

Table 1

Demographic and clinical characteristics of healthy controls, and non-apathetic and apathetic participants.

	Healthy Controls (N = 36)	Non-Apathetic (N = 42)	Apathetic (N = 18)	F	p
Age (years)	71.6 (6.8)	72.2 (7.7)	71.1 (7.3)	0.156	0.856
Education (years)	16.4 (2.2)	16.0 (3.4)	16.6 (1.8)	0.351	0.705
MMSE	28.5 (0.9)	28.2 (2.1)	28.2 (1.9)	0.289	0.750
DRS	137.2 (4.0)	136.1 (4.9)	135.9 (5.1)	0.727	0.486
HDRS	1.14 (2.1)	22.4 (3.3)	25.0 (3.7)	606.109	0.000
AES	22.9 (3.2)	31.4 (4.3)	46.1 (5.2)	192.297	0.000