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Loss Aversion in Major Depressive Disorder

By

Boadie W. Dunlop

Master of Science in Clinical Research

In Medicine

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By

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BA, Washington University, 1990

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An abstract of a thesis submitted to the Faculty of the James T. Laney School of Graduate Studies of Emory University in partial fulfillment of the requirements for the degree of

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Abstract

Loss Aversion in Major Depressive Disorder

By Boadie W. Dunlop

Major depressive disorder (MDD) is a common, disabling condition. Poor decision-making contributes to the physical morbidity, role dysfunction and suicide risk in patients with MDD, but very little research has attempted to objectively measure decision-making in MDD. "Loss aversion" is a behavioral economic measure of the degree to which individuals demonstrate greater sensitivity to the possibility of losing objects or money than to the possibility of gaining the same objects or amounts of money. This study aimed to identify whether loss aversion differed between patients with MDD and healthy control (HC) participants. Subjects completed a three-hour process of evaluation and testing in order to "earn" $100. One week later, they completed a decision-making task while undergoing a functional magnetic resonance imaging scan. The decision-making task involved presenting 120 trials of risky decisions which participants chose to accept or reject. Each risky decision represented an equal chance (50:50) of adding to or losing some of their $100 endowment. The amount to be won or lost varied from trial to trial to allow for models to be built from which loss aversion level was derived. Twenty-four HC and 19 MDD participants completed the study. Two methods for calculation of loss aversion were employed. In the subject-level analysis, mean loss aversion for the two groups differed significantly (HC: 1.64 ± 0.78, MDD: 1.19 ± 0.49, $p=.032$). However, after removal of 2 outliers, the difference was no longer significant (HC: 1.53 ± 0.55, MDD: 1.25 ± 0.41, $p=.085$). In the representative agent analysis, mean loss aversion was nearly identical (HC: 1.37; MDD = 1.34, p = n.s.). Multiple regression analyses suggested impulsivity was associated with greater loss aversion, and that there was an interaction between self-reported risk-taking and mood state, such that high-risk taking subjects had lower aversion to losses. These results suggest that at a group level, there are no meaningful differences in loss aversion between MDD and HC subjects. However, MDD occurring in a person with low impulsivity but high risk-taking may reduce sensitivity to loss, and thus contribute to poor decision-making in real-life situations.

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INTRODUCTION

Major depressive disorder (MDD) is a psychiatric diagnosis defined by a psychological and behavioral syndrome of increased sadness or reduced pleasure and motivation, along with associated symptoms such as changes in appetite and sleep, reduction in energy and thoughts of death or suicide. Difficulty making decisions is another diagnostic criterion of MDD.[1] This criterion is generally assumed to mean increased deliberation and lack of clarity in choosing under situations of uncertainty, and is typically thought to arise from the slowed mentation often present in depressed patients. However, this decision-making difficulty could also arise from changes in subjective value of potential outcomes, impulsivity, risk tolerance, or other factors that may change in depressed states. To date, little research has explored the specific ways in which patients with MDD differ from non-depressed people in controlled decision-making situations.

Decision-making may be defined as the ability to select an advantageous response from a range of available options. In choosing whether or not to undertake a risky decision, a person weighs the potential reward, or "gain", against the potential "loss" that may occur. Distorted choices about life situations among MDD patients compared to non-depressed individuals is observed frequently in clinical practice and has been established by prior research.[6] Controlled experiments demonstrate that individuals with MDD show altered decision-making in situations of uncertainty compared to healthy controls.[2-4] Traditionally these findings have been interpreted to arise from the depressed person's reduced desire for, and experience of, reward (i.e., "anhedonia"), the neural correlates of which have been identified. However, in life people often must make decisions where no particular reward is apparent, but in which they are at risk of losing something valuable. Depressed subjects typically demonstrate an attitude of "what does it matter anyway," or "at this point, I don't

really care," conveying an indifference to incurring further losses. Such distorted choices can have a profound impact on the life of the depressed patient and their loved ones. Examples of harm resulting from altered decision-making include:

- Repeated refusal to participate in pro-social or other activities that provide an opportunity for reward and lifting of mood, such as turning down an offer to go see a theater performance with friends.
- Reacting passively when faced with a potential financial loss, such as not correcting an error in a transaction that is not in their favor, or not acting to sell an investment that is clearly declining in value.
- Reducing efforts to maintain or strengthen important long-term relationships, such as choosing not to address an ongoing conflict with a spouse or not seeking to find ways to meet the spouse's needs.
- In the most extreme form of distorted decision-making, contemplating and attempting suicide.

These situations commonly occur in major depressive disorder, and all share a theme of reduced sensitivity to loss, whether it is relationships with friends or spouse, financial position, or life itself. Non-depressed people, when faced with these situations, choose to act to protect against these potential losses, whereas depressed individuals often do not make that choice. Reduced motivation for pleasure is commonly cited as the reason depressed patients do not pursue potential reward in life situations. However, it is commonly the case in life that the motivation to act is based on the fear of losing what one already possesses. Thus, a decision not to pursue a social gathering may be interpreted as either a reduced sense of pleasure in companionship, or a reduced sense pain that the loss of a friendship may produce from sustained interpersonal detachment. Similarly, failure to pursue better

employment opportunities in the face of unstable current employment may reflect a reduced sensitivity to the potential loss of income and career advancement. Thus, reduced aversion to potential losses likely contributes to the altered decision-making of patients with major depression.

Sensitivity to loss, also known as "**loss aversion**" has heretofore received little attention in depression. The neurobiology of depression is associated with altered neural processing in the ventral striatum (nucleus accumbens), orbitofrontal cortex, anterior cingulate cortex, and dorsolateral prefrontal cortex, among other regions.[5] In healthy controls, these same brain regions are the primary sites of altered neural activity during decision-making in situations of potential loss, suggesting shared neurobiological processes between the experience of loss aversion and major depressive disorder.[6]

Neuroeconomics and Major Depressive Disorder

The concept of loss aversion is a core construct in the assessment of decision-making. In *Prospect Theory*, the most successful behavioral model for how people make decisions when the outcome of a choice is uncertain, loss aversion refers to the phenomenon that people are much more sensitive to the possibility of losing objects or money than they are to the possibility of gaining the same objects or amounts of money.[7,8] A common scenario to demonstrate loss aversion is that when choosing whether or not to accept a bet, non-depressed people typically need to be offered a reward at least twice as large as the amount they risk losing. Thus, people usually require a potential gain of at least $100 to make up for the exposure to a potential loss of $50, because the subjective impact of losses is roughly twice that of gains. Losses "hurt" more than gains "please;" consequently, potential losses are more powerful drivers of choice than potential gains. The difference in the "value," or

subjective impact to an individual, of gains and losses can be represented as a value function curve (**Figure 1**). On this curve, the slope of the line for in the area of losses is steeper than it is the area of gains, representing that an incremental amount of loss causes a greater reduction in subjective value than an equivalent amount of gain causes an increase in subjective value.

There is growing recognition that studying decision-making may provide a new way of understanding psychiatric disorders, including MDD.[9] Understanding how depressed patients make decisions in the face of uncertain gains or losses may meaningfully contribute to the clinical assessment and treatment of MDD in two primary ways. First, in terms of treatment, loss aversion differences in depression may inform psychotherapy approaches to MDD. Reduced loss aversion in a depressed patient, indicating a reduced valuation and possible detachment for his/her life situation and material standing, would warrant efforts to focus therapy on enhancing the patient's appreciation of their current resources. Alternatively, if a depressed patient demonstrates heightened loss aversion, such that they are unwilling to take reasonable risks in order to improve their mood and life situation, the therapy may focus on more realistic appraisals of probabilities for potential gains and losses. In terms of pharmacotherapy, the neural underpinnings of altered loss aversion may be associated with differential response to specific medication classes. For example, if heightened loss aversion is associated with enhanced fear processing circuitry, SSRIs may provide the best initial treatment option. Alternatively, diminished loss aversion stemming from reduced dopaminergic signaling in motivational pathways may indicate the need for a catecholaminergic strategy.

The results of the first neuroeconomics investigation of adults with MDD were recently published.[10] The authors found normal reward prediction and consumption

patterns in depressed subjects, which were unexpected and run counter to clinical experience where significantly depressed patients clearly report less anticipation of potential gains. It is possible that these findings may be explained by a relatively low level of severity in the recruited outpatient depressed subjects in this trial. Depression severity was assessed only via the self-report Beck Depression Inventory II. Remarkably, the depressed patients had a higher success rate and earned more money during the trial than the control subjects. As these outcomes depended on reaction time, this sample of depressed patients could not have been psychomotor retarded, suggesting a relatively mildly ill sample.

Other studies have evaluated decision-making among depressed children. Boys with depression at age 10 or 11 demonstrated reduced ability to distinguish between options involving a small or large possible reward, whereas this deficit was not present in boys with an anxiety or externalizing disorder.[11] In another study comparing children aged 9-17 with depression versus healthy controls, reduced activation of the OFC, ACC and dorsal striatum was found in the MDD patients, especially during the anticipation and experience of small rewards.[12]

Although there is great complexity in the neurochemical regulation of these brain regions, the emotion-processing regions are significantly affected by serotonin signaling, whereas the reward and cognition systems are influenced much more by dopamine transmission.[13] A great deal of evidence supports the role of dopamine signaling from the midbrain to the ventral striatum in reward prediction. This signal may prepare the organism for action, either to pursue reward or to act to avoid loss, engaging the hypothesized "limbic-motor interface" function of the ventral striatum.[14] In healthy controls, tryptophan depletion does not affect reward prediction, but does enhance punishment prediction.[15] Thus, reduction in serotonin function in MDD may be specific for

experiences of negative affect, but may not contribute significantly to reward prediction, which may be mediated by other mechanisms. However, an earlier study found that tryptophan-depleted healthy controls showed reduced ability to discriminate between large and small rewards, but did not have disturbed processing of losses.[16] How these findings in healthy controls relate to the neurobiology of decision-making in depressed patients is uncertain.

This study had the goal of assessing loss aversion in MDD, with the primary hypothesis that loss aversion would be lower in MDD than in controls. An alternative hypothesis could be that loss aversion is *increased* in major depression as a result of heightened emotion (fear) processing via the amygdala-insula-ventral ACC system. Either result would be important to understanding how decision-making in depressed subjects differs from that of healthy subjects, though the implications for treatment would differ.

METHODS

Hypotheses:

The primary hypothesis of this study, stated in terms of the null hypotheses, was:

> The level of behavioral loss aversion, determined from choices made by subjects about a series of gambles, will be statistically equal between subjects experiencing a major depressive episode versus subjects who have no history of mental illness, controlling for age, gender and past-year household income.

Study Design:

A case-control design was used to address the hypotheses about behavioral and neural loss aversion.

The study consisted of three visits:

A) *Screening Visit*

At this visit, informed consent for participation was obtained, and the psychiatric evaluation and depression rating scales were administered. Subjects were assessed for inclusion and exclusion criteria.

B) *Neuropsychological Testing and Endowment Visit*

This visit was scheduled as soon as possible after the first visit. This visit served three purposes: (1) *Endowment*: to have the subject perform "work" to "earn" money that was at risk during the Neuroimaging session; (2) *Data Collection*: to perform personality

assessments evaluating decision-making styles and neuropsychological tasks assessing cognitive functions that may contribute to performance on the gambling task; (3) *Practice*: to complete a brief version of the loss aversion task that was performed in the fMRI scanner, to reduce learning effect confounds. For completing the "work" (i.e. the tasks) of this visit, the subject will be shown $100 (drawn from a petty cash account), and allowed to hold the money for 30 seconds. It will then be placed in an envelope with the participant's initials written on it while the participant watches. The participant will be told that this is "their money" that they will be using during the fMRI scanning session.

C) *MRI Scanning Visit*

The MRI scanning session occurred 5-10 days following the screening visit, to minimize the potential risk-seeking that can occur in response to a windfall gain (i.e. playing with "house money"). Prior to the scan a urine pregnancy test (for women of child-bearing potential) was performed. Subjects were reminded they had earned $100 for the "work" they had performed at the previous visit, and that the amount of money that he/she would receive depended on their performance on the gambling task in the fMRI scanner. The subject was informed that they will have the potential to gain up to an additional $120 or lose $60, so that they would receive at least $40 after the scanning session in compensation for their time. They will then entered the MRI scanner to perform the loss aversion task, consisting of deciding whether or not to accept a series of gambles offering the potential to gain or lose money.[6] Examples of the gambles shown to patients and the time sequencing is shown in **Figure 2**.

The 1-hour MRI scanning session was conducted at the Biomedical Imaging and Technology Center, and included: (1) high resolution 3D T1-weighted anatomical imaging

for registration purposes, and (2) an fMRI sequence. The structural MRI acquisition time was approximately 7 minutes. For the fMRI task, subjects were imaged while performing the decision-making task. Subjects were presented with a total of 6 runs of 40 trials, each of which presented a mixed gamble entailing a 50/50 chance of gaining a certain amount of money or losing another amount. Each run required approximately 7 minutes to complete. Possible gains ranged from $0-40 (in $4 increments) and possible losses ranged from $0-20 (in $2 increments). There were 120 possible combinations of gains and losses (fully crossed 11x11, excluding the $0 gain vs $0 loss option) which were presented across the three runs. After the first 3 runs, the three runs were repeated, so that that subject responded twice to all possible options. Participants were asked to evaluate whether or not they would like to play each of the gambles presented to them. Using a button press, subjects indicated that they accepted or rejected each individual gamble. They were told that one trial from three of the six runs would be selected at random, and if they had accepted that gamble during the scanning, the outcome would be decided with the equivalent of a coin toss (computerized random number generator), and their $100 would be increased or reduced accordingly. If they had rejected the randomly selected gamble, then that gamble would not be played. Total scanning time was approximately 50 minutes.

Subjects

Recruitment of subjects occurred through two ongoing programs studying depression at Emory University. Healthy control subjects will also be recruited from another study of healthy controls. Additional healthy controls will be recruited through flyers and posters at Emory.

Inclusion and exclusion criteria.

Inclusion criteria for depressed subjects to participate in the study were:

1) Age 18-60 years.

2) Primary DSM-IV TR Diagnosis of Major Depressive Disorder, either single episode or recurrent, assessed by the Structured Clinical Interview for DSM-IV.[17]

3) Major Depressive Episode of at least 8 weeks duration.

4) Hamilton Depression 17-item Rating Scale (HAM-Depression) [18] score ≥18 at screening.

5) Ability to tolerate a one-hour MRI session (based on an MRI screening form).

Exclusion criteria were:

1) Lifetime DSM-IV TR Axis I diagnosis of bipolar disorder, psychotic disorder, obsessive compulsive disorder, eating disorder, or cognitive disorder.

2) DSM-IV TR substance abuse or dependence within six months of the screening visit.

3) Positive urine drug screen at the screening visit.

4) An active, uncontrolled medical condition that may contribute to depressive symptoms, in the opinion of the investigator.

5) Active medical condition thought to affect CNS dopamine signaling (e.g. Parkinson's disease, Tourette's disorder).

6) Current DSM-IV TR Axis II diagnosis (personality disorder or mental retardation).

7) Any metal in the body (including pins, clips, plates, IUD, dental braces or unremoveable piercing), or employed in a metal-working occupation.

8) Women who are pregnant, breastfeeding, or expect to become so during the study.

9) Significant risk for suicide (e.g. active plan or intent to die) in the opinion of the investigator.

For control subjects, inclusion criteria were: (1) age 18-60 years, (2) a HAM-Depression score <8, and (3) ability to tolerate a one-hour MRI session. Control subjects will be excluded if they: (1) meet DSM-IV TR criteria for any current Axis I or II diagnosis, with the exception of simple phobia or substance abuse, (2) meet DSM-IV TR criteria for substance abuse within 6 months of the screening visit, (3) have a positive urine drug screen, (4) have an uncontrolled medical condition, (5) Have an active medical condition thought to affect CNS dopamine signaling, (6) have any metal in their body, as described above, (7) are pregnant or breast-feeding.

All study procedures were approved by the Emory University Institutional Review Board. The Department of Psychiatry Data Safety Monitoring Board received annual reports about the incidence of adverse events, study drop-out and preservation of confidentiality. All subjects signed written informed consent forms to participate before any study procedures were conducted. The study was conducted in accord with the Declaration of Helsinki and its amendments.[19]

Predictor Variables

The predictor variables for the study included the following:

Variable	**Description**
Beck Depression Inventory (BDI) [20]	21-item self-report measure of depression severity
Hamilton Anxiety Rating Scale (HAM-Anxiety) [21]	14-item clinician-administered questionnaire of anxiety severity.
Behavioral Inhibition/Behavioral Activation Scale (BIS/BAS) [22]	20-item questionnaire assessing sensitivity to pursuing or inhibiting movement toward goals with 4 Subscales
Barratt Impulsiveness Scale (BIMPS) [23]	30-item questionnaire providing global measure of impulsivity or rashness of actions.
Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ) [24]	48-item questionnaire measuring behavioral inhibition when under threat situations and approach behavior with respect to reward.
Domain Specific Risk Taking Scale (DOSPERT) [25]	30-item questionnaire assessing risk taking in 5 content domains

Outcome Variables

The outcome variable was the measure of behavioral loss aversion (lambda, λ).

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Other Variables to control for potential confounding: Age, household income and intelligence were used as control variables for the analysis, due to their established relationship with both risk for MDD and potential independent association with loss aversion. Age and income was captured for self-report forms. Intelligence was measured through using the Wechsler Abbreviated Scale of Intelligence (WASI) [26], requiring about 40 minutes to administer.

Sample Size

Based on previous studies using healthy control subjects, significant differences in neural activation patterns in decision-making during gambles involving gain and loss can be identified with as few as 16 subjects.[6, 27] Loss aversion measurements have not been previously conducted in a depressed sample, so a two sample comparison power analysis can only be estimated. Previous fMRI studies using other decision-making or cognitive tasks have demonstrated that a sample size of 20-25 subjects per group is sufficient to identify statistically significant differences in activation and deactivation maps between depressed and control groups. [12, 28] In their classic paper that defined loss aversion, Kahneman and Tversky found loss aversion (λ) in healthy volunteers to be 2.3.[7] Our hypothesis was that depressed participants will demonstrate lower loss aversion than healthy controls, and we estimated a $\lambda = 1.2$. Standard deviations for loss aversion have not been reported are reported in the economic or neuroeconomic literature, so we conservatively estimate a standard deviation of 1.5 for both groups. From these estimates, group sample sizes of 30 and 30 achieve 81% power to detect a difference of 1.1 with a significance level (alpha) of 0.05 using a two-sided two-sample t-test.

Statistical Analysis

The demographic and questionnaire data were evaluated for normality using visual inspection of boxplots, histograms, scatterplots, and Kolmogorov-Smirnov tests. Where normal, these data were summarized with means and standard deviations; non-normally distributed data were summarized with medians and ranges.

Several methods have been used in the economics literature for the calculation of loss aversion. In this analysis, we compared the relative levels of behavioral loss aversion in situations of uncertainty between Depressed and Healthy Control subjects using two methods. Both methods used logistic

regression on the behavioral data with the size of the potential gain and loss as independent variables and acceptance/rejection as the dependent variable.

In the first analysis, **"Subject Level Analysis,"** the logistic regressions were performed separately for each subject, and a group mean level of loss aversion was calculated from the individual lambdas.. The logistic regression for this analysis took the form of:

$$\text{Log}\,[P/(1-P)] = \beta_0 + \beta_1\,\text{Gain}^{\alpha} + \beta_2\,\text{Loss}^{\alpha}$$

Here the log probability of the acceptance of gambles was determined from an intercept, β_0, a parameter for the potential Gain presented in the gambles, β_1, and a parameter for a potential Loss presented in the gambles, β_2. The variable α represents the curvature of the value function.

Behavioral loss aversion (λ) was then calculated as: $\lambda = -ß_2/ß_1$

where β_2 and β_1 are the unstandardized regression coefficients for the loss and gain variables, respectively.[6]

The Subject Level analysis permitted the use of linear regressions to further explore the relationship between loss aversion and the covariates of age, IQ, income BIMPS, SPSRQ, BIS/BAS and DOSPERT total scores. Kolmogorov-Smirnov tests, scatterplots and residual analyses were used to help assess nonlinearity of the relationship and the appropriateness of the assumptions of normality for loss aversion and constant variance of the outcome for each predictor value. Where these assumptions are violated, transformations (e.g., natural log) were used.

Multiple linear regression models to assess the effects of the predictor variables on loss aversion were developed, incorporating age, IQ and income as covariates. Independent variables correlated with lambda at a level of $r = 0.2$ or greater were entered step-wise into the models after the covariates.

Interactions between covariates were also evaluated. The coefficient of determination (R^2) will be used to assess how much of the variation in λ was accounted for by the regression equations. Multicollinearity between continuous predictors (i.e., age, BIMPS, SPSRQ, BIS/BAS and DOSPERT scores) was assessed by the coefficient of determination between predictors and the variance inflation factor (VIF).

The second analysis was the **"Representative Agent"** analysis. In this approach, the responses of all depressed subjects are pooled into one set, and those of all the healthy control subjects are pooled into another. Representative agent models in economics assume that all decision-makers in a group are identical. For this analysis, the Representative Agent approach results in a single lambda for the Depressed subjects as a whole, and the Healthy control subjects as a whole. The regression equation for this model is:

$$\text{Log}\,[P/(1-P)] = B_i + \beta_{G1}\,\text{Gain}^{\alpha} + \beta_{L1}\,\text{Loss}^{\alpha} + \beta_{G2}\,\text{Gain}^{\alpha} + \beta_{L2}\,\text{Loss}^{\alpha}$$

Where Group 1 = Healthy controls and Group 2 = Depressed.

B_i is a dummy variable to represent each of the 43 subjects with analyzable data.

β_{G1} is the parameter for the slope of the utility curve in the realm of gains for healthy controls, and β_{L1} is the slope of the utility curve in the realm of losses for this group. β_{G2} and β_{L2} are the corresponding parameters for the Depressed group.

The Representative Agent model analysis produced 361 potential models from the dataset. Selection of the best model was determined from the method developed by Hirotsugu Akaike of "an information criterion" (AIC), a measure that compares the relative goodness of fit of multiple statistical models of a dataset. [29] The Akaike method aims to assess the relative amount of

information lost when a model is used to represent the observed data. Lower AIC values reflect lower amounts of lost information, and thus indicate the most accurate model.

Analyses were conducted using SPSS version 17.0 (SPSS Inc.,Chicago, Illinois, USA) and plots were made using JMP version 9 (SAS Institute, Inc.).

RESULTS

Subjects

Twenty-one MDD subjects and 25 HC subjects consented to participate in the study. Nineteen MDD and 24 HC subjects completed the required visits and the fMRI task. One subject in each group was unable to complete the fMRI session due to scheduling difficulties.

Table 1 compares the demographic and clinical characteristics of the participants. The demographic features of the two groups were comparable. No differences were statistically significant between the two groups at baseline, though the HC group had an average household income roughly 50% greater than the Depressed group. As expected, the Depressed group had substantially higher scores on both self-rated and clinician-rated measures of depression and anxiety.

Personality Questionnaires

The mean scores for impulsivity (BIS) and sensitivity to punishment (SP) were both significantly greater in the MDD than in the HC group. All other personality measures did not differ (see **Table 2**)

Loss Aversion: Lambda

Subject Level Analysis:

Figure 3 demonstrates the distribution of lambda using the Subject Level analysis among all subjects. Kolmorgorv-Smirnov testing did not indicate a non-normal distribution. The distributions of lamda by group are presented in **Figure 4.** The mean lambda for the two groups was significantly different (HC: 1.64 ± 0.78, MDD: 1.19 ± 0.49, p=.032). However, these results appeared to be influenced by 2 outliers, one in each group. After removal of these two outliers, the means were no longer significantly different (HC: 1.53 ± 0.55, MDD: 1.25 ± 0.41, p=.085). The alpha values between the two groups did not differ (Healthy control: 0.67 ± .40; Depressed: 0.55 ± 0.50, p = .41)

To examine whether any of the demographic variables were correlated with the primary outcome, lambda, Pearson correlation coefficients were calculated for age, IQ and income. No variable was significantly correlated with the lambda. Nevertheless, because these variables were a priori considered to impact decision-making variables, they were included in subsequent models to control for their effects. Correlations with lambda for clinical and questionnaire variables are shown in **Table 3.**

Separate multiple linear regression models were explored for the Healthy control and Depressed subjects, and a final model was constructed with all subjects included. For the models for the Healthy controls, and the model for all subjects combined, no variables significantly contributed to the models. However, for Depressed subjects, impulsivity, risk-taking and depression severity all significantly contributed to the coefficient of determination **(Table 4).** .

A generalized linear model was developed, using Group as a fixed effect and the clinical and questionnaire variables as random effects. The model that explained the greatest level of variance included impulsivity and risk-taking, and identified and interaction effect between group and risk-taking **(Table 5).** Risk taking alone had no effect on loss aversion, but there was an interaction effect, in which depressed subjects with greater risk-taking contributed to higher levels of loss aversion.

Representative Agent Analysis

The model that generated the smallest AIC (AIC = 6218). The loss aversion values for the two groups using this analysis were nearly identical (Healthy controls: $\lambda = 1.365$; Depressed: $\lambda = 1.338$, p = n.s.).

DISCUSSION

This analysis identified no significant differences in loss aversion between healthy control volunteers and patients suffering from active major depression. Although the Subject Level analysis indicated a difference that might have clinical significance, exclusion of outliers removed the significance of this effect. Loss aversion values determined using a representative agent model were nearly identical between the groups. Thus, the primary hypothesis of this analysis was not supported.

The multiple regression model of the depressed subjects only identified effects for impulsivity, risk-taking and severity of depression on loss aversion. Specifically, lower impulsivity and greater risk-taking and greater depression severity all predicted lower levels of loss aversion. Impulsivity and risk-taking also predicted loss aversion in the generalized linear model using all subjects. This model suggested that group membership may affect loss aversion, if the personality variables of impulsivity and risk-taking are taken into account.

The AIC used to select the best model for the data is based only on the relative superiority of one model over others. It does not provide an absolute measure of how well the data fit the model, so therefore does not test the differences between groups in terms of a classic null hypothesis. However, the insignificant differences between the estimated lambdas for the two groups suggests the groups have essentially identical levels of loss aversion.

Representative Agent models have been challenged for ignoring potential concerns about aggregating individuals, particularly when significant differences between individuals of a group exist and which may impact the decisions being examined. [30] In the current analysis, other factors, such as impulsivity or depression severity (as suggested by the Subject-level analysis), may have been important contributors to differences in loss aversion.

The interaction effect identified in the generalized linear model suggests that the effect of risk-taking on loss aversion is dependent upon mood state. Specifically, healthy controls who report higher

levels of risk-taking appear to remain mindful of downside risk in making financial decisions under uncertainty, whereas risk-taking Depressed patients appear to lose this inhibition. This finding suggests that depressed patients, particularly those who generally endorse a more risk-taking approach to life, may be at particularly susceptible to poor decision-making when depressed.

There are a number of limitations to this study that may have contributed to Type II error. First, the relatively small number of subjects may have limited the power to detect actual differences between the groups, though the very small differences between the groups using the Representative Agent analysis strongly suggests there is no meaningful difference. Second, it is possible that the Healthy control sample was not representative of all non-depressed patients. Our findings of lambda values of 1.3 – 1.5 in this sample is consistent with this interpretation. Most studies of loss aversion in general populations find lambda values of 1.8-2.25. Had the Healthy controls in this sample had lambda values in this range, the differences from the Depressed subjects would have been significant. Healthy controls in this sample may have been more likely to have low levels of loss aversion, in that they were willing to enter a clinical study with some minimal risk to themselves (MRI, emotional stress). Unmeasured levels of altruism may have impacted loss aversion and willingness to participate, thus providing a confound to the results. Moreover the Healthy control sample had higher than average IQ, and lower impulsivity than population norms, which may have also contributed to the lower-than-expected lambda values for this sample.

In conclusion, the results of this study suggest that, as a group, patients with MDD do not have levels of loss aversion that differ from non-depressed individuals. The possibility that MDD occurring in some individuals with specific personality characteristics may lead to adverse decision-making warrants further exploration. In addition, other sources of alterations in decision-making in depression should be explored, such as discounting rates and risk aversion.

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TABLES

Table 1. Demographic and Clinical Variables

Characteristic	Controls	Depressed	P-value
Means (SD)			
Age (yrs)	33.7 (11.4)	37.6 (11.0)	.268
Income ($1,000)	48.4 (34.3)	30.5 (21.1)	.054
IQ	119 .4 (11.0)	114.2 (12.6)	.152
Medians (Range)			
HAM-Depression	0 (0-4)	23 (18-31)	<.001
BDI	0 (0-6)	22 (13-43)	<.001
HAM-Anxiety	0 (0-10)	18 (8-29)	<.001

BDI: Beck Depression Inventory; HAM-Anxiety: Hamilton Rating Scale for Anxiety; HAM-Depression: Hamilton Rating Scale for Depression; IQ: Intelligence quotient.

Table 2.

Personality questionnaire results in healthy control and depressed subjects.

Questionnaire	Controls	MDD	P-value
Means (SD)			
BAS_Reward	13.3 (2.4)	14.0 (3.5)	.499
SPSRQ - Reward	9.1 (3.5)	10.7 (3.1)	.150
DOSPERT Total	97.9 (20.3)	96.3 (31.0)	.843
SPSRQ - Punishment	5.4 (4.5)	15.3 (5.4)	<.001
Barratt Total Impulsivity	51.7 (6.6)	67.2 (11.6)	<.001
Medians (Range)			
BIS_Inhibition	18 (11-21)	19 (15-26)	.321
BAS_Drive	11 (5-14)	11 (6-16)	.986
BAS_Fun	12 (8-14)	12 (8-16)	.555

BAS: Behvioral Activation Scale; BIS: Behavioral Inhibition Scale; DOSPERT: Domain Specific Risk-Taking Scale; SPSRQ: Sensitivity to Punishment and Reward Questionnaire.

Table 3.

Correlations of predictor variables with loss aversion using the Subject Level Analysis

	Healthy Controls		Depressed		Combined	
Variable	r	p	r	p	r	p
Barratt Total Impulsivity	.37	.08	.39	.11	.05	.77
BIS	-.24	.26	-.12	.63	-.23	.15
DOSPERT Total	.22	.32	-.33	.18	-.03	.83
BAS_Fun	.20	.35	.47	.05	.29	.07
BAS_Drive	.11	.61	.29	.24	.17	.29
BDI	-.10	.66	.21	.40	-.30	.06
HAM -Anxiety	.09	.70	.20	.43	-.19	.23
SPSRQ Punishment	-.16	.45	.06	.81	-.25	.12

BAS: Behvioral Activation Scale; BDI: Beck Depression Inventory; BIS: Behavioral Inhibition Scale; DOSPERT: Domain Specific Risk-Taking Scale; HAM-Anxiety: Hamilton Rating Scale for Anxiety; SPSRQ: Sensitivity to Punishment and Reward Questionnaire.

Table 4. Multiple regression model for Depressed subjects only.

Model	Variables	R	R-square	R-square Change	F	Sig.
1.	Income, Age, IQ	.136	.018	.018	.09	.966
2.	1. + Impulsivity	.411	.169	.150	.66	.631
3.	2. + Risk Taking	.699	.489	.320	2.30	.111
4.	3. + Beck Depression	.803	.644	.156	3.32	.041

	Unstandardized Coefficients		Standardized Coefficient		
	B	Std. Error	β	t	Sig.
Impulsivity	.033	.009	.821	3.80	.003
Risk Taking	-.008	.003	-.591	-2.92	.014
Beck Depression	-.024	.011	-.486	-2.19	.051

Table 5. Generalized linear model for all subjects

Model	-Log Likelihood	L-R Chi Sq	DF	p
Difference	6.89	13.78	4	.008
Full	22.88			
Reduced	29.77			

	Coefficients		Chi Sq	p
	B	Std. Error		
(Intercept)	1.004	.424	5.23	.022
Impulsivity	.024	.008	7.78	.005
GROUP	-.684	.193	10.94	.0009
Risk Taking	-.001	.003	.03	.861
Group x Risk Taking	-.012	.006	4.07	.044

FIGURES

Figure 1. The value function curve and its hypothesized change in patients with major depressive disorder.

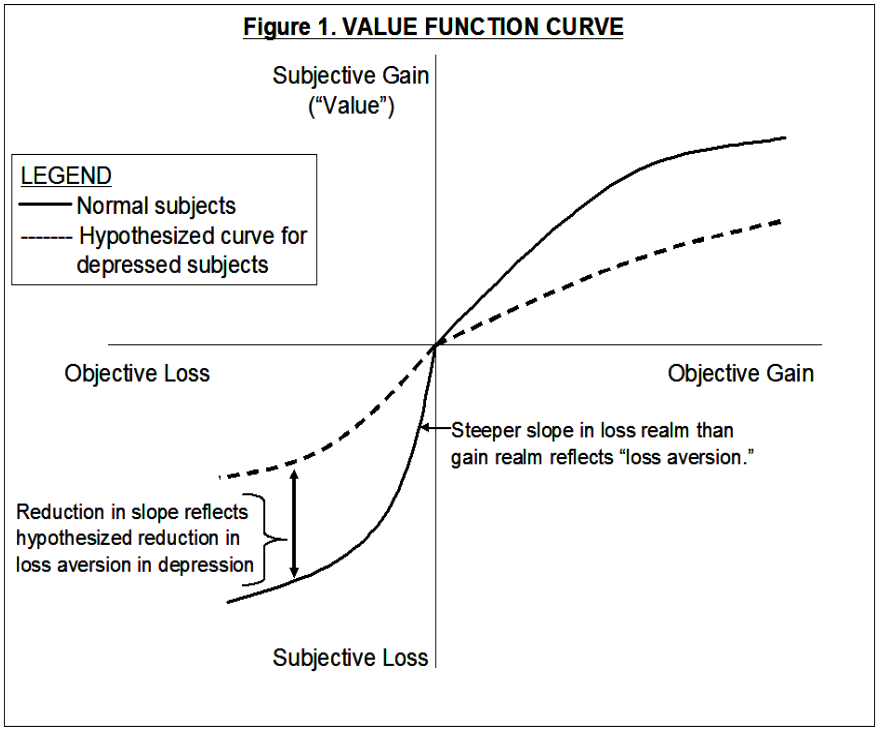

Figure 2. Schematic of the decision-making task used for the study.

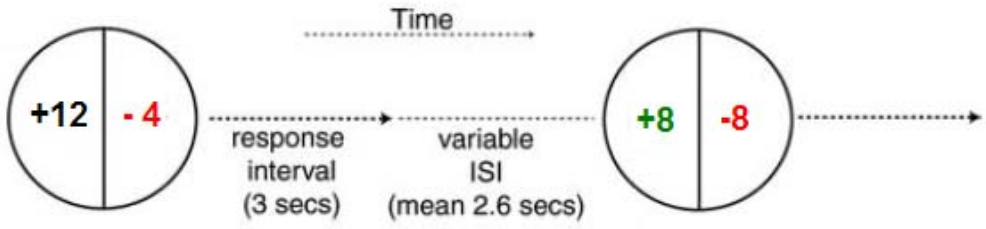

Figure 3. Histogram of loss aversion lambda values in total sample.

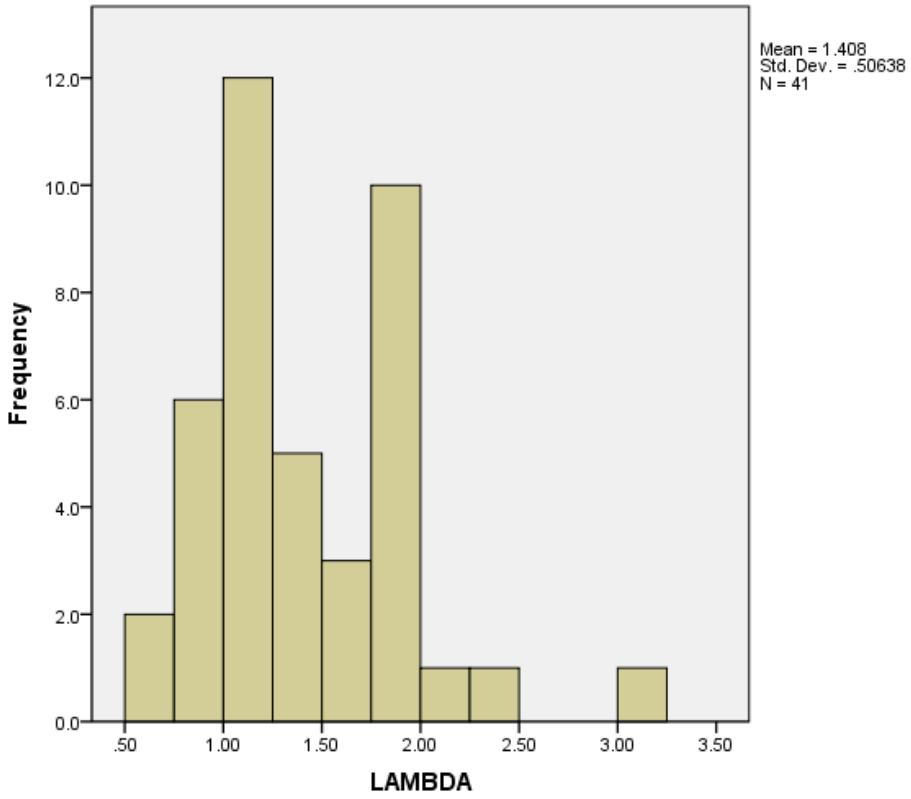

Figure 4. Individual and mean loss aversion values using the Subject Level Analysis