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FMRI INVESTIGATION OF INTERTEMPORAL DISCOUNTING IN SCHIZOPHRENIA

by

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A DISSERTATION

Submitted to the graduate faculty of The University of Alabama at Birmingham,
In partial fulfillment of the requirements for the degree of
Doctor of Philosophy

BIRMINGHAM, ALABAMA

2011

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FMRI INVESTIGATION OF INTERTEMPORAL DISCOUNTING IN SCHIZOPHRENIA

KATHY B. AVSAR

PSYCHOLOGY (BEHAVIORAL NEUROSCIENCE)

ABSTRACT

Schizophrenia is most recognizable by positive symptoms of hallucinations and delusions, but the cognitive deficits and negative symptoms contribute more to functional deficits. The delay discounting (DD) task, with choices between a small immediate reward and a larger delayed reward, tapping into both executive function and reward processing, may prove useful in identifying cognitive and reward processing abnormalities relevant to schizophrenia. In the present study, we used the discounting parameter, k, to assess whether patients with schizophrenia preferred more immediate rewards than healthy controls. We used a model fit statistic, R^2, as a measure of choice consistency, quantified using a non-linear regression of participants' responses. Using functional magnetic resonance imaging (fMRI), we investigated group differences between patients with schizophrenia and controls in blood oxygen level-dependent (BOLD) responses to DD decisions in general. In addition, we investigated neural responses to delay discounting decisions varying in difficulty. Compared to controls, patients were more inconsistent in their pattern of responses and exhibited greater DD. However, the difference in DD disappeared when analysis was limited to patients who were consistent in their task performance. Controls, matched on performance and demographics to the consistent patients, displayed greater activation in executive function and reward areas in response to task trials compared to control trials. Compared to

controls, consistent patients displayed greater activation to the task relative to the control trials in left insular and temporal cortices and in the precuneus. In response to hard DD trials, controls, when compared to patients, showed more activation in areas associated with executive function, such as the inferior frontal gyrus and the dorsal anterior cingulate cortex. In response to both hard and easy trials, controls showed more activation than consistent patients in the inferior parietal lobule and the ventral striatum. Patients unable to perform the task consistently, when compared to controls, showed greater activation to the DD task in the precuneus and posterior cingulate cortex. In general, patients with schizophrenia appear to have regions of hypoactivation contributing to executive function and reward processing deficits, in addition to hyperactivation in areas associated with resting state and conflict monitoring.

DEDICATION

To those with schizophrenia and their families…

ACKNOWLEDGMENTS

Where to begin? There were so many who contributed to the continuation of my education and in turn to this project. While I may not be able to include the many individual teachers along the way (who I regrettably failed to thank at the time), I would like to recognize and express my gratitude to “The Teacher”. I would like to acknowledge and thank that exceptional group of dedicated professionals who contributed to the rise in my curiosity; I am eternally grateful to the instructors who consistently engaged me and spent the extra time to lead me along a path to many wonderful moments of “aha” and “discovery”. To all of you, I express my deepest and sincerest gratitude.

I am deeply grateful to my mentor, Dr. Lahti, for her patience (and her lack of patience whenever necessary), for her willingness to let me hang myself and then her willingness to help me remove the rope. She provided a space to think and explore and an endless stream of data to examine. I was fortunate to stumble into her lab in the initial year and able to watch the exponential growth that she managed over the next four years. During my first year, Luke Stoeckel assisted me in analyzing my first fMRI data set and Mark Bolding got me through my first exposure to MATLAB. Meredith Reid entered the lab, followed by David White. Together we figured out the magnet, E-Prime, IFIS, STROOP and behavioral data. Some of us decided that we really did not want to understand behavioral data and moved on to MRS and DTI, while others became engrossed with prediction error and delay discounting. We ran participants, gathered data, trained undergraduates and each other. I was incredibly fortunate to have lab partners who were incredibly smart and patient and who immediately recognized the benefits of

collaboration. I learned a great deal through osmosis and being in their vicinity. During my third year, Thadeus Koontz rotated through the lab with his endless stream of questions and what if's. Nina Kragulijac, Nathan Hutcheson, Muriah Wheelock and Jennifer Hadley entered, challenged and supported me through my last year when I was extremely cranky and uncommunicative.

From the initial urge to learn how to become a scientist, there were Drs. Weller, Cox and Cook providing me with encouragement and direction. Dr. Weller spent countless hours correcting drafts with patience and plenty of red ink. She was tireless in her commitment to my success as a student and a scientist. Drs. Cox and Cook provided statistical instruction and humor to guide my efforts through the maze of assumptions, t-tests, p-values and ANOVAs to arrive at significant results. Dr. Visscher joined my committee and UAB late in my process, but brought a passion and excitement alongside her helpful feedback and suggestions. I thank all my committee members for being engaged in my project and thereby creating a supportive learning environment.

This work was supported in part by the Behavioral Neuroscience Graduate Program in Psychology and the Department of Psychiatry and Behavioral Neurobiology. I thank the head of my department, Dr. Randich, for his support, along with all my peers who supported me with laughter and/or tears through seminars and occasionally beer and pizza.

On a more personal level, I have to thank my sister, and my niece and nephews for their assistance in keeping the grass around my house at a manageable level, providing jokes and bringing a certain amount of levity to my somber demeanor when I needed it most. I thank both my sons and daughter for tolerating my absence in their lives

for almost a decade as I endeavored to return to school. I thank the many patients who came through the lab with courage and trust. Their strength and determination to deal with schizophrenia and its effects on their lives and their families gave me strength and determination to continue. I put in many hours trying to understand the disorder in hopes that I might contribute an incremental piece in the schizophrenia puzzle.

And, from beginning to end, the love of my life, Sadri, encouraged, ridiculed, threatened, cajoled, and supported me in every way possible to go back to school. He cooked, cleaned, made countless trips to Costco, fed the cats and me. On numerous occasions, I would look up to find him standing in the door of my cave with a tray of some delightful concoction that fed my body and soul. To keep himself occupied, midway through, he went so far as to return to school, driving three hours every other weekend to Atlanta, so that he would be out of the house so that I would have one less distraction. He was patient and selfless in his understanding that I had very little time to share. He provided me with understanding and support in numerous ways to ensure my success. I will never be able to thank him enough for this gift of time.

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A BEHAVIORAL AND fMRI INVESTIGATION OF DELAY DISCOUNTING IN SCHIZOPHRENIA

STOCHASTIC DELAY DISCOUNTING PERFORMANCE ASSOCIATED WITH ABERRANT RESPONSE TIMES AND HYPERACTIVATION IN PATIENTS WITH SCHIZOPHRENIA COMPARED TO HEALTHY CONTROLS

ACRONYMS AND ABBREVIATIONS

ANOVA	Analysis of variance
BOLD	Blood oxygen level-dependent
dACC:	Dorsal anterior cingulate cortex
DD	Delay discounting
DR	Delayed reward
FDR	False discovery rate
fMRI	Functional magnetic resonance imaging
GLM	General linear model
IR	Immediate reward
k	Discounting parameter
MPRAGE	Magnetization-prepared rapid gradient-echo
R^2	Model fit
SMC	Sensorimotor control
TE	Echo Time
TR	Repetition Time

INTRODUCTION

Schizophrenia is a debilitating psychiatric disorder found in approximately 1% of the population.[1] Although the more recognizable positive symptoms, such as hallucinations and delusions, are controlled to a large degree with antipsychotic medication, the negative symptoms, such as anhedonia and amotivation, and the cognitive deficits, such as problem solving and working memory deficits (aspects of executive function), are not. Yet, it is the negative symptoms and the cognitive deficits that tend to be more indicative of poor functional outcomes[2] such as poor job tenure[3,4] and quality of life.[5] Researchers have suggested that the reward system is impaired in patients with schizophrenia,[6-13] and this impairment may be a contributing factor to the negative symptoms such as anhedonia and amotivation[14,15] and to poor functional outcomes.[16] Other researchers[17] have suggested that it is an interaction between the reward system and executive function, in both subcortical and cortical regions,[18,19] that leads to the functional disabilities present in schizophrenia.

The executive function system involves multiple regions such as areas of prefrontal and parietal cortices and basal ganglia that provide processing for complex goal-directed behavior.[20] Decision-making requires the active maintenance of goal relevant information and adaption to a changing environment by ignoring information not relevant to goals.[21] Studies suggest that when tasks that require cognitive control are used, activation in medial and lateral prefrontal cortex serves to monitor performance,[22] while dorsolateral cortex is involved in rule-based performance that requires working memory.[23] Numerous studies point to cognitive impairment and executive dysfunction in patients with schizophrenia.[20,24-29] Deficits in patients include reduced ability to maintain

attention to relevant stimuli,[30,31] deficits in learning[32-34] and deficits on both verbal[5,35,36] and visuospatial working memory tasks.[28,37] These deficits lead to disorganization and the inability to complete sequential tasks.[38]

The reward system involves multiple regions, such as the substantia nigra, ventral tegmental area, the ventral striatum, the medial prefrontal cortex and the orbitofrontal cortex,[39] embedded within a cortico-basal ganglia network that provides motivation to support behaviors that result in positive outcomes.[40] Positive reinforcement for goal-directed behavior occurs due to reward regions responding through learning and association to secondary rewards and directly to primary rewards.[41,42] Aspects of reward processing, including reward anticipation and delivery,[9,43-45] attribution of salience,[6] reinforcement learning,[46] and prediction error,[47,48] have been found abnormal in those with schizophrenia.

Behavioral and electrophysiological studies of the reward system suggest that the relative and subjective nature of rewards necessitates the inclusion of sensory, emotional and cognitive evaluation in determining the value of a reward.[49,50] It may be the inefficiency of cortical and striatal regions, in conjunction with abnormal interaction between executive function areas in the frontal cortex and reward areas in the striatum and midbrain, that underlies patients' inability to maintain goal-directed behavior.[17,51] Barch and Dowd[17] proposed a model of schizophrenia that suggested that abnormalities in goal-directed behavior occur in patients due to deficits in the interaction between executive function and reward processing areas. Interactions between neural correlates of reward prediction in the substantia nigra/ventral tegmental area with hedonics in the striatum and orbitofrontal cortex, with a valuation system in the orbitofrontal cortex and

anterior cingulate cortex where cost versus benefit information is integrated with action plans provided by the dorsolateral prefrontal cortex, are necessary when making decisions. Optimal choices when making decisions that involve intertemporal, or delay, discounting (DD) require an ability to forego the receipt of an immediate reward in order to receive a larger reward in the future. The DD task, used in both human and animal studies,[52-55] requires an analysis of the cost of waiting versus the subjective difference in value between an immediate and a delayed reward.

Only a few studies have investigated goal-directed behavior in patients with schizophrenia and have found mixed results,[56-59] with DD abnormalities being less significant after taking into account cognitive deficits that are so prevalent in schizophrenia.[60] There have been no studies where groups were matched on smoking or consistent performance, or functional imaging studies investigating brain activation patterns during DD in patients with schizophrenia. The primary objective of this project was to use fMRI during a DD task to investigate differences in neural activation while patients with schizophrenia and healthy controls matched on age, parental socioeconomic status and smoking status performed the task.

Manuscript 1 – In the study described here, we performed a behavioral study of DD in healthy controls and patients who were not significantly different in age, gender, parental socioeconomic status or smoking. We also used fMRI to compare neural responses during hard and easy trials during a DD task in healthy controls and patients with schizophrenia. Participants in this study were limited to those who performed the task consistently, reducing the heterogeneity of the patient group and promoting behavioral

responses matched to the controls. Matched groups also allowed us to investigate whether differences in brain activation to the DD task occurred when performance did not differ.

Manuscript 2 – The purpose of this study was to determine how controls and patients with schizophrenia who were able to perform the DD task in a consistent manner differed from those patients with schizophrenia who could not perform the DD task consistently. Using demographic data, behavioral and cognitive measures and functional data acquired during imaging, we hypothesized that cognitive deficits would contribute to poor DD task performance and that functional activation would be even less than we found in the consistent controls and patients.

A BEHAVIORAL AND FMRI INVESTIGATION OF DELAY DISCOUNTING IN PATIENTS WITH SCHIZOPHRENIA AND CONTROLS MATCHED ON PERFORMANCE

by

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Submitted to Archives of General Psychiatry

Format adapted for dissertation

ABSTRACT

Background: Schizophrenia is associated with a reduced ability to set meaningful goals to reach desired outcomes, an aspect of executive function, as well as deficits in reward processing. The delay discounting (DD) task has proven useful in revealing cognitive and reward deficits in particular groups.

Objective: To compare delay discounting in patients with schizophrenia and healthy controls and to use fMRI during the task to compare brain activation in the two groups.

Design: Cross-sectional study comparing patients with schizophrenia to healthy controls.

Setting: Behavioral data were collected at the Neuroimaging and Translational Research Laboratory, and neuroimaging data were collected at the Functional Neuroimaging Laboratory at the Civitan International Research Center, at the University of Alabama at Birmingham (UAB).

Participants: We recruited patients with DSM-IV schizophrenia or schizoaffective disorder from the outpatient psychiatric clinics at the University of Alabama at Birmingham (n=34) and healthy control participants (n=21) from the community who did not differ significantly in age, sex, parental socioeconomic status, or smoking status.

Main Outcome Measures: We measured the rate of discounting, *k*, and DD response consistency, R^2. Only functional neuroimaging data from participants meeting a minimum level of consistency were retained. The fMRI analyses compared activation in patients (n=14) and controls (n=14) on the contrast of task vs. control trials and on contrasts related to trial difficulty.

Results: Overall, patients with schizophrenia showed greater delay discounting than did control participants. However, these group differences disappeared when comparisons were limited to those who performed the task consistently. In the fMRI analyses, patients with schizophrenia showed reduced patterns of activation to the task compared to the healthy controls in widespread regions, including putative executive function and reward areas and increased activation in the precuneus, posterior cingulate and temporal cortices.

Conclusions: The functional neuroimaging results are consistent with those of previous studies showing deficits in the neural substrates of decision-making and reward in those with schizophrenia.

Keywords: delay discounting, schizophrenia, fMRI, intertemporal discounting, executive function, subjective value, neuroimaging, reward system

INTRODUCTION

Schizophrenia is a complex mental illness with functional deficits contributing to the long-term cost of the illness. Amotivation, or the inability to set and maintain goal-directed behavior, is one aspect of schizophrenia that likely contributes to the long-term disability associated with the illness.[1,2] Goal-directed behavior, as an aspect of executive function, involves selecting some future outcome and making choices that best serve reaching that goal. Patients with schizophrenia have neural abnormalities associated with executive function[3-8] and reward system function.[9-20] Barch and Dowd[21] and others[10,22,23] have proposed that deficits in patients' ability to integrate emotional information from the limbic system and value information from orbitofrontal cortex with functioning of executive processing regions of the lateral prefrontal cortex result in abnormal value representation, leading to functional deficits in goal-directed behavior.

Delay discounting (DD) is an empirical construct based on the observation that as delays to receiving rewards increase, the valuation of rewards decreases, resulting in a preference for smaller, but more immediate rewards.[24-34] In other words, a future reward must be of greater nominal value to be more attractive over an immediate reward. Tapping into the economic aspect of decision-making that weighs the relative values of rewards is considered a key aspect of the DD paradigm.[35] The rate at which an individual discounts future rewards, or the reduction in the valuation of the reward per unit of time, is indexed by the discounting parameter, *k*, with *k*'s of greater magnitude indicating greater delay discounting.[36,37] A second, albeit understudied aspect of the DD paradigm is

the degree of inconsistency in individual choices,[38] quantified in this study with the model fit parameter, R^2.

Previous behavioral studies have reported greater DD of money in patients with schizophrenia.[1,39] Heerey and colleagues[39] found that greater discounting in patients was positively correlated with deficits in working memory and *inversely* correlated with the presence of negative symptoms such as avolition and anhedonia. These results emphasize the role that executive function and emotion play in patients' ability to determine the value of rewards. Patients appear to have difficulty in integrating cognitive and affective information to derive subjective value when making decisions.[40] Understanding the neural bases of abnormal value representation and aberrant behavioral choices in those with schizophrenia could lead to interventions to improve decision-making and goal-directed behavior in schizophrenia.

While the exact role and interaction of neural circuits subserving DD are debated, most agree that lateral prefrontal and parietal cortices, in conjunction with the striatum and cingulate gyrus, contribute to the evaluation of decisions.[33,41-43] For example, based on their functional magnetic resonance imaging (fMRI) studies of DD, McClure et al[44] suggested that short term impulsive choices are driven by the limbic system, whereas all decisions, and, in particular, more difficult decisions are subserved by the frontoparietal system. In one of the few studies to investigate DD trial difficulty, Marco-Pallarés et al[45] found that medial prefrontal/anterior cingulate cortex was activated during DD trials requiring more difficult decisions, presumably when conflict arose from the similarity in subjective value between the two choices. However, in the reverse contrast, during easier DD trials, activation occurred in widespread regions, including limbic areas such as the

insula, the ventromedial prefrontal cortex and ventral striatum, and in temporal and parietal cortices.[45]

The goals of the present study were to investigate the aberrant DD behavior and to determine whether the neural correlates of DD were also abnormal in those with schizophrenia when compared to controls. We utilized a modified DD task[36,37] requiring participants to choose in a series of trials between small immediate rewards and larger delayed rewards. We first determined a participant-specific discounting rate, *k,* on a DD task during a laboratory session. This was done in order to choose a magnet DD task appropriate for someone with that discounting rate, ensuring that each participant chose approximately equal numbers of immediate and delayed choice trials during scanning. This procedure reduced the possible confounding effect of differences in performance between groups. In addition to measuring *k*, we used the model fit (R^2) of choices to evaluate the degree of participants' inconsistent performance. We hypothesized that an inability of patients to incorporate the objective reward value with the length of the delay in valuation across trials of variable difficulty would result in performance that is more inconsistent. Groups were matched on age, sex, parental socioeconomic status and smoking, as DD is affected by these variables.[46-54] We contrasted all DD trials to control trials to investigate the broader decision-making circuit activated in previous DD studies,[44,45,55,56] and suggested by Barch and Dowd's model[21] as a contributing factor to deficits in motivation and drive in schizophrenia. Based on that model, we hypothesized that, when compared to controls, patients would fail to engage a broad decision-making circuit (ventral striatum, medial prefrontal, anterior cingulate, posterior cingulate,

prefrontal and parietal cortices), as shown by reduced activation to DD trials when contrasted to SMC trials during the DD task.

In addition, we investigated activation on DD trials with choices of relatively similar value (difficult trials), trials of relatively dissimilar value (easy trials), and the activation differences between them, contrasts thought to tap into the executive function network during the more difficult trials, and to tap into limbic regions during the easy trials.[44,45,57] We hypothesized that patients, in contrast to controls, would show reduced activation during the more difficult DD trials of similar value in the executive function networks, that is, lateral and medial prefrontal cortex, anterior cingulate cortex and medial prefrontal cortex, and reduced activation during easier trials of dissimilar value in the reward system, that is, the substantia nigra/ventral tegmental area, the ventral striatum and the orbitofrontal cortex.

METHODS

PARTICIPANTS

Thirty-four patients with DSM-IV[58] schizophrenia or schizoaffective disorder were recruited from the outpatient psychiatric clinics at the University of Alabama at Birmingham. Diagnoses were established using participants' medical records and the Diagnostic Interview for Genetic Studies.[59] Twenty-one healthy controls, not significantly different from the patient group on age, sex, parental socioeconomic status, sex and smoking were recruited by advertisements in flyers and the University

newspaper. Exclusion criteria were major medical conditions, substance abuse within the past six months, previous serious head injury, a neurological disorder, previous loss of consciousness, pregnancy and ferromagnetic material in the body. Healthy controls were excluded for any significant Axis I diagnosis. The Institutional Review Board of the University of Alabama at Birmingham approved the study, and all participants gave written informed consent. Before signing consent, each patient completed an Evaluation to Sign Consent Form, a form probing the patient's understanding of important aspects of the protocol.

General cognitive function of all participants was characterized by the Repeatable Battery of Neuropsychological Status (RBANS).[60] The Brief Psychological Rating Scale (BPRS)[61] and its positive (conceptual disorganization, hallucinatory behavior, and unusual thought content) and negative (emotional withdrawal, motor retardation, and blunted affect) subscales were used to assess mental status and symptom severity in the patient group. Participants received compensation of $92-$99 for their participation in the study.

DELAY DISCOUNTING TASK

We trained participants on the laboratory version of the DD task, modified from Kirby et al,[36] and used the laboratory session to estimate each participant's rate of discounting (*k* value). This step allowed us to choose an appropriate DD task to use during imaging that was based on each participant's specific *k* (eAppendix contains task instructions**;** eTable1contains the list of 10 DD tasks available for the imaging session). Participants

viewed the 108 trials of the task on a computer monitor. Of those trials, 96 trials were divided equally between eight trial k values and, hence, eight levels of discounting difficulty, interspersed with 12 sensorimotor control (SMC) trials (**Figure 1**). For any given trial k, IR (value of the immediate reward), DR (value of the delayed reward), and D (the delay in days) were related to each other according to the formula, IR=DR/(1+*k*D), from Mazur and Coe.[25] As an indicator of difficulty and temporal preference, a trial k that matched a participant's *k* would create the greatest conflict in choosing an immediate or delayed reward. The eight levels of trial difficulty ranged from a trial k of .0004, for which almost all participants would prefer to receive the reward immediately, to a trial k of 0.25, for which almost all participants would prefer to receive the delayed reward (eTable 2). We entered the percentages of immediate choices and the corresponding trial k values in an exponential discounting model and performed a non-linear regression analysis to determine a participant-specific *k.* In addition, the coefficient of determination, R^2, was calculated to provide a quantitative measure of response pattern consistency and/or task involvement.[62] Participants whose responses were more inconsistent would have a lower R^2.

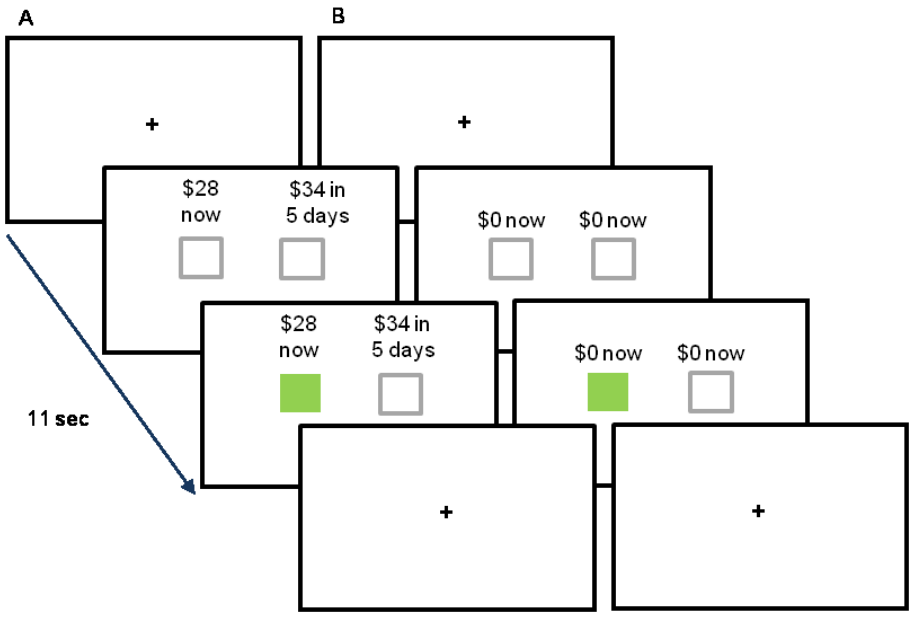

Figure 1. Delay discounting task. (A) Delay discounting task trial; (B) Sensorimotor control trial. All trials were 11 seconds in duration, with the initial fixation cross presented for 2, 4 or 6 seconds followed by two grey boxes paired with (A) the choice of an immediate or a delayed hypothetical monetary reward ($28 now or $34 in 5 days, an implied k of .041) or (B) the no choice option. Participants had the remainder of the 11-second trial (9, 7 or 5 seconds) to indicate their preference by pressing a button on the side corresponding to their choice. The box under the choice turned green, indicating the response. A return of the fixation cross indicated the start of the next trial.

DELAY DISCOUNTING TASK DURING SCANNING SESSION

Immediately following the laboratory session, participants were taken to the magnet for the scanning session. With the exception of the number of trials and distribution of trial k's, the magnet DD task was identical to the laboratory DD task. Each of 10 possible magnet tasks included five trial types based on trial k's, which ranged from difficult to easy and encouraged an overall equal number of immediate and delayed reward choices (See eTable 1 for details). Based on the laboratory results, a magnet task was chosen with

a target k (middle trial k value) nearest to the participant's specific *k*. Of the five trial types, the three trial types with a trial k nearest to the participant's *k* (referred to as hard trials) were the most difficult and produced approximately equal numbers of immediate and delayed reward choices. The two trial types with a trial k most distant from the participant's *k* were the easiest trials, on which either immediate or delayed choices predominated (referred to as easy immediate and easy delayed trials); that is, the subjective value between the two choices was dramatically different. For the scanning session, the DD task consisted of four runs of 40 trials, each with 30 task trials divided equally between the five trial k levels, and 10 SMC trials, on which participants arbitrarily made a left or right button response. During the fMRI scanning session, participants viewed the stimuli via a mirror mounted on the head coil adjusted to show the visual display in the scanner using IFIS-SA (Integrated Functional Imaging System). The participants viewed the 160 trials in four 7:24 minute runs, for a total scanning time of 29:36.

SCANNING SEQUENCES

Structural and functional scans were acquired on a Siemens Allegra head-only 3 T magnet with a single-channel circularly polarized no-tune transmit/receive head coil. We immobilized the participant's head with foam pads. We acquired a high-resolution anatomical T1-weighted image using a magnetization-prepared rapid gradient-echo (MPRAGE) sequence. An echo planar imaging (EPI) sequence with a 2.2s repetition time (TR) and 30 ms echo time (TE) was used to acquire 30 interleaved 4.0 mm axial slices, 1

mm gap, with a 70-degree flip angle during the task. The field of view was 24 x 24 cm^2. These acquisition parameters resulted in 3.8 x 3.8 x 4.0 mm voxels. E-Prime software (version 1.2; Psychology Software Tools, Pittsburgh, Pennsylvania) running on an IFIS-SA system was used to control stimulus delivery and to record responses and reaction times.

DATA ANALYSIS

Behavioral Measures. Two measures of DD, $\log_{10}(k)$ and the ratio of immediate to delayed choices, as well as the R^2 values from the laboratory session and the imaging session, were entered into analyses of variance (ANOVA) to compare the groups. Due to the positively skewed distribution of *k* values, we used a logarithmic (Base 10) transformation to normalize the distribution.[63,64] Reaction time data were analyzed to assess differences across level of trial difficulty using a mixed-design ANOVA, with a within-subject factor of trial type (easy immediate, hard immediate, hard target k, hard delayed, easy delayed, sensorimotor control) and a between-subject factor of group (healthy controls, patients). When Mauchly's assumption of sphericity[65] was violated, a Greenhouse-Geisser correction[66] was applied. To investigate the relationship between DD, cognitive function and symptoms, the log transformed *k*, RBANS and BPRS were entered into a bivariate correlation analysis. An alpha level of .05 was used as the statistical threshold.

Functional Data. We visually inspected functional and anatomical images for excessive movement, anatomical abnormalities and image artifacts with Osirex Dicom Viewer, as a first step in quality control. The preprocessing of functional and anatomical images was carried out using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/software/spm8/) running under the MATLAB platform. Functional images were reoriented with respect to the anterior-posterior commissure. Slices were corrected for differences in acquisition times using slice time-correction. Participant movement was corrected using a least squares method of realignment of the functional time series data to a mean functional image using a rigid-body transformation to produce six parameter estimates, and ArtRepair[67] was used to correct movement artifacts by interpolating between slices when movement exceeded 0.5 mm per TR. Data with movement greater than 2 mm per 40 trial run were not used in analyses. Each participant's anatomical scan was co-registered to the SPM canonical MNI template (Montreal Neurological Institute, Montreal, Canada) initially using linear rigid body registration. Although not adequate for normalization, this initial registration placed the images in adequate alignment such that normalization using the diffeomorphic image registration algorithm model (DARTEL)[68] was possible. The structural images were then normalized using DARTEL to produce a flow field. Using this flow field, functional images were coregistered to each participant's anatomical image in MNI space prior to first-level analysis.

Statistical analysis of the preprocessed functional images was conducted for each participant using the general linear model (GLM) to detect areas where changes in BOLD response were correlated with stimulus presentation and response. Individual responses were modeled using a variable epoch approach, where the reaction times for trials were

modeled using a boxcar epoch,[69] to create a more physiologically sound model, with onset vectors that corresponded to the presentation of the stimulus and duration vectors that corresponded to the length of time the participant required to make a decision. Onset vectors were divided into two conditions based on trial difficulty (hard, easy) and two conditions based on temporal preference (immediate, delayed). In addition, vectors that corresponded to the onset of SMC trials were included in the design matrix (also with reaction time as duration vector). Each regressor of interest was convolved with the canonical hemodynamic response function followed by a time derivative that allowed for temporal variance in the BOLD response. Cognitive subtraction[70,71] was used to contrast brain activations to all task trials>SMC trials, hard>easy trials and easy>hard trials to produce statistical parametric contrast images to be carried into second-level random effects, within- and between-group analyses. To resolve an obtained interaction between group and difficulty (see results), we obtained parameter estimates from hard trials>baseline (baseline being activation to the fixation cross presented between trials, not explicitly modeled in the GLM) and easy trials>baseline from each participant, from a mask of the cluster showing the interaction. Finally, we also performed whole-brain group comparisons from the contrasts, hard trials>baseline and easy trials>baseline.

In both within- and between- group analyses, we used a cluster level threshold determined within SPM8 to maintain the false discovery rate (FDR) =.05.[72-74] We maintained a FDR of .05 but adjusted the voxel level p-value based on past results; within group, we used $P<.001$ & between-group used $P<.05$ with two exceptions. We had hypothesized that the hard versus easy contrast would result in greater activation in putative executive function regions. Not finding the expected activation in those regions

led to reducing *P*-value to $P<.05$ for the within-group analyses to investigate how difficulty influenced activation. In addition, in the between-group analyses of hard trials versus baseline and easy trials versus baseline, we used a voxel level $P<.001$.

Further analyses, based on R^2 values, were done to investigate neural responses that correlated with consistent choices. For the task>SMC trials contrast, we included the variables of Group, mean centered Fischer transformed *R* primes (*R'*)[75] and Group x *R'* interaction in a multiple regression analysis of the contrast maps of task>SMC trials. When a significant Group x *R'* interaction was found, regions of interest masks were created for all of the voxels within the clusters using MarsBar[76] and then used to extract the mean beta values from each participant's task>SMC results. Within-group correlations were then calculated in SPSS.

RESULTS

BEHAVIORAL RESULTS

Demographic data and clinical and cognitive assessments[59,60] for all study participants recruited are presented in **Table 1**. One healthy control and two patients were unable to tolerate the scanning environment. Participants were also excluded from the imagining analyses for image artifact (1 patient), excessive motion (2 healthy controls, 5 patients), and poor behavioral data (4 healthy controls, 12 patients). **Table 2** contains demographic characteristics of only those participants who were included in the imaging analyses

(n=14 in each group). In an independent samples t-test of log-transformed *k* values obtained during the laboratory session, healthy controls (n=21) had a lower discounting rate than patients (n=34)(t[53]=-3.44, P=.001), indicating greater preferences for the immediate reward in the patient group (see eFigure 1 for histograms of log-transformed *k*).

Table 1. Demographic Data, Clinical and Behavioral Measures[a]

Variable	Healthy Controls (n=21)	Patients (n=34)	*P*
Age, years	37.24±12.41 (23-61)	36.41±12.61 (20-61)	.97
Sex[b]	11 Men; 10 Women	25 Men; 9 Women	.095
Parental SES[c]	6.94±4.59	6.75±4.91	.91
Smoking[d]	.42±.51	.64±.62	.171
RBANS[e]			
Total Index	92.70±13.30	74.29±10.34	<.001
Immediate Memory	96.85±12.90	78.65±13.66	<.001
Visuospatial	92.80±18.33	77.48±17.60	.004
Language	94.10±14.11	87.52±11.07	.069
Attention	95.80±18.79	83.68±13.11	.009
Delayed Memory	95.58±11.20	72.42±19.59	<.001
BPRS			
Total		32.35±8.74	
Positive		6.12±3.63	
Negative		4.76±2.18	
Delay Discounting			
Log of Lab *k*	-1.77±.77	-1.02±.80	.001
Lab R^2	.94±.05	.72±.29	.001
Log of Imaging *k*[f]	-1.71±.84	-.89±1.13	.006
Imaging R^2[g]	.84±.19	63±.36	.007

Abbreviations: RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; BPRS, Brief Psychiatric Rating Scale; *k*, discounting parameter; R^2, discounting model fit.
[a]Values are expressed as mean ± SD unless otherwise indicated.
[b]Values are expressed as number of individuals.
[c]Score determined by Diagnostic Interview for Genetic Studies (1-18 score); lower score signifies higher socioeconomic status (SES); data not available for 8 healthy controls and 7 patients.
[d]Value is expressed in packs per day (PPD).
[e]RBANS data not available for 1 healthy control and 3 patients.
[f]Imaging *k* represents data from healthy controls (n=20) and patients (n=28).
[g]R^2 represents data from healthy controls (n=20) and patients (n=31).

Table 2. Demographic Data and Clinical and Behavioral Measures for Subgroups of Consistent Responders used in fMRI Analyses

Variable	Healthy Controls (n=14)	Patients (n=14)	*P*
Age, years	34.07±10.82	36.50 ± 13.17	.60
Sex	8 Men; 6 Women	10 Men; 4 Women	.35
Parental SES[a]	6.10±4.68	5.92 ± 4.68	.93
Smoking	.27 PPD	.59 PPD	.09
RBANS[b]			
Total Index	95.69±10.84	77.93±10.52	<.001
Immediate Memory	97.15±11.57	82.64±13.39	.001
Visuospatial	96.62±15.69	80.50±18.55	.031
Language	96.46±14.65	91.36±7.11	.198
Attention	98.46±16.52	83.43±16.29	.040
Delayed Memory	98.00±5.98	77.79±19.27	.001
BPRS			
Total		32.57±9.75	
Positive		6.64±3.95	
Negative		4.93±2.27	
Delay Discounting			
Log of Lab *k*	-1.86±.71	-1.66±.49	.382
Lab R^2	.96±.03	.89±.12	.065
Log of Imaging *k*	-1.91±.66	-1.70±.66	.402
Imaging R^2	.91±.05	.91±.10	.992

Conventions same as in Table 1 except where noted.
[a]Data not available for 4 healthy controls and 1 patient.
[b]RBANS data not available for 1 healthy control.

The R^2 values, or model fit, for healthy controls and patients for the laboratory and imaging DD sessions are shown in **Figure 2.** Healthy controls had significantly higher R^2 values, indicating greater consistency, than patients both during the laboratory session ($F_{1, 53}$=11.78; P=.001) and the imaging session ($F_{1, 49}$=6.19; P=.02). Examination of patients' R^2 values obtained during imaging revealed a quasi-bimodal distribution of values, with one group of patients displaying R^2 values similar to those of healthy controls and the other group showing very low values, suggesting an inability to make consistent choices. Based on this distribution, we used a model fit criterion of R^2>.60 to determine which participants would be retained in the fMRI analyses. Three healthy controls and 13 patients failed to meet this criterion and were not included in the fMRI

analyses. The fourth healthy control was excluded due to poor behavioral data; that is, failing to respond to the SMC trials. An independent samples t-test of the 14 healthy controls and the 14 patients that met criteria (in addition to having imaging data of adequate quality) did not show a significant difference between the groups in either R^2 (.9136±.05, .9134±.10) or log-transformed k (-1.91±.71, -1.70±.49), corresponding to approximate k values of .012 and .020, respectively, obtained during the imaging session.

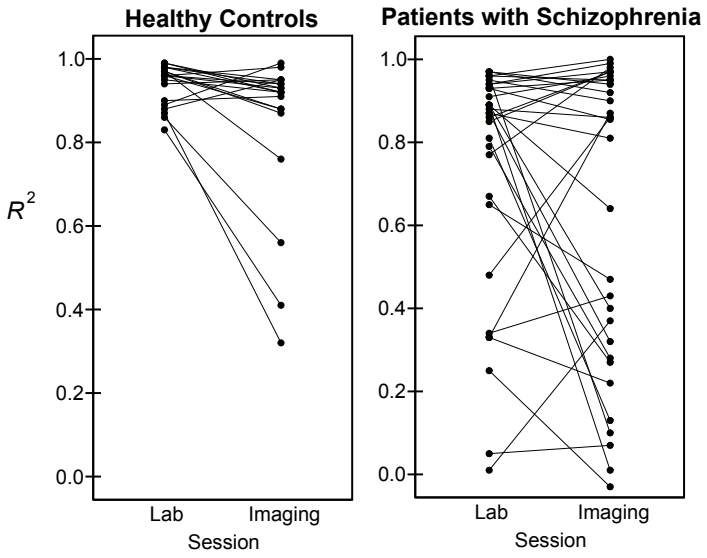

Figure 2. Model fit (R^2) values during estimation of discounting parameters, k values, during the laboratory session and the imaging session for healthy controls and patients with schizophrenia.

To verify that our method of establishing a participant's discounting rate during the laboratory session produced the expected response pattern during the imaging session, we determined the percentage of immediate reward preferences in the healthy controls at

varying trial k's during scanning. Their choices were as follows: 96% preference for the easy immediate trials, 67% for hard immediate trials, 50% for hard target k trials, 36% for hard delayed trials, and 9% for easy delayed trials. In the consistent patients, their choices were as follows: 89% preference for the easy immediate trials, 62% for hard immediate trials, 46% for hard target k trials, 33% for hard delayed trials and 14% for easy delayed trials (see graph in eFigure 2). The only significant between-group difference was for the easy immediate trials, where patients preferred the immediate reward less often than controls (P=.049; other trial types, P>.35). These patterns showed that, as expected, as the k for trials became higher, our participants exhibited correspondingly fewer choices for the immediate reward.

The distributions of mean response times for patients and controls for each of the trial types based on choice difficulty are shown in **Figure 3**. Response times were different across trial difficulty ($F_{4, 104}$= 6.68, P<.001, ε=.667), and patients' responses were slower than those of controls ($F_{1, 26}$=4.32, P<.05). In controls, response times were significantly longer for the three hard trial types than the two easy trial types (P<.05). Patients, however, failed to show this pattern, as their response times did not differ significantly between hard and easy trials. Response times were significantly shorter for SMC trials than task trials in both groups (P <.001). Results from the between-group analysis revealed that controls had faster response times than patients to easy immediate trials ($F_{1,26}$=10.27, P=.004), easy delayed trials ($F_{1, 26}$=6.76, P=.015), and to SMC trials ($F_{1,26}$=29.01, P=.001). However, response times on the more difficult trials did not differ significantly between groups (immediate, $F_{1,26}$= 1.196, P=.18; target k, $F_{1,26}$= 2.237,

P=.15; delayed, $F_{1,26}$= .984, *P*=.33) (see eTable 3 for means and standard deviations of response times).

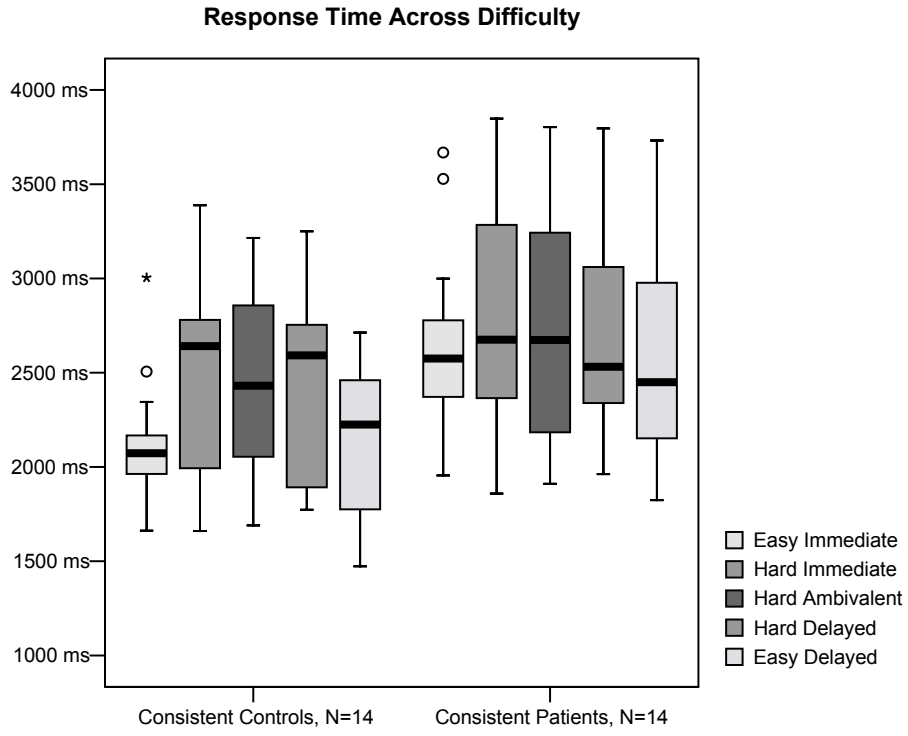

Figure 3. Box plots of response times for consistent controls and consistent patients. °indicates outliers with values between 1.2 and 3 box lengths from upper or lower edge of box; *indicates extreme cases with values more than 3 box lengths from upper or lower edge of box.

To investigate the relationships between DD, cognitive function and symptom severity, we used the laboratory DD $\log_{10}(k)$, the total and subscale RBANS scores as measures of cognitive function, and the BPRS score as a measure of symptom severity in an ANOVA. Among all participants, DD was negatively correlated with total RBANS

(Pearson's r[51]=-.44, P=.001), immediate memory (r[51]=-.29, P<.05), visuospatial construction (r[51]=-.36, P<.01), language (r[50]=-.41, P<.01) and delayed memory (r[50]=-.41, P<.01). Discounting was not significantly correlated with attention (r[51]=-.07, P=.61). That is, participants with higher scores on all cognitive tests except for attention discounted less. However, when we looked at the groups individually, these correlations were not significant in the healthy controls (r[20]<.34; P>.15) or in patients (r[31]<.29; P>.12), with the exception of language (r[31]=-.410; P<.05); that is, patients who scored higher on the language section of the RBANS discounted less steeply. Discounting was not significantly correlated in patients with BPRS total or subscales (in all cases, $|r[34]| < .25$; P>.17).

IMAGING RESULTS

The initial comparison of interest was activation to all DD trials versus the SMC trials. Within-group results are presented in supplementary material eTable 4, and between-group results are presented in **Table 3** and **Figure 4.** For the within-group results (eFigure 3), the controls showed qualitatively more widespread activation to the task than did patients, including more activation in putative executive function areas (inferior and middle frontal gyri, medial wall/dorsal anterior cingulate cortex, and inferior parietal lobule). In the between-group analysis (**Table 3**), greater activation in the healthy controls (**Figure 4**, red) occurred in widespread regions including the inferior frontal gyrus; medial wall, including the middle cingulate gyrus and supplementary motor area; parietal cortex extending into occipital cortex (not shown), and subcortically, in the

ventral striatum and thalamus. By contrast, greater activation in the patient group (**Figure 4**, blue) was found in the region of the insula extending into the frontal opercuum, superior temporal gyrus, and in a more posterior and dorsal medial wall cluster that included the precuneus and the posterior and middle cingulate gyrus (not shown).

Table 3. Between-group Results for Task>SMC Trials[1]

Brain Regions[2]	Cluster[3]	Voxels[4]	x[5]	y	z	t	*P*[6]
Controls(Task>SMC)>Patients(Task>SMC)							
Frontal Cortex-Left	1366		-48	16	29	3.98	0.015
Inferior Frontal Gyrus		289					
Parietal/Occipital Cortex-Right	1161		30	-50	47	4.98	0.022
Inferior Parietal Lobule		428					
Angular Gyrus		132					
Supramarginal Gyrus		52					
Precuneus		72					
Superior Occipital Gyrus		133					
Parietal/Occipital Cortex-Left	1651		-42	-41	48	3.70	0.007
Superior Parietal Lobule		234					
Inferior Parietal Lobule		821					
Angular Gyrus		140					
Middle Occipital Gyrus		172					
Medial Wall/Dorsal ACC[7]	1298		2	18	59	3.66	0.015
Supplementary Motor Area,R[8]		538					
Supplementary Motor Area,L[8]		375					
Middle Cingulate Gyrus-R		56					
Middle Cingulate Gyrus-L		111					
Thalamus/Basal Ganglia	1627		4	3	0	3.60	0.007
Thalamus-L		255					
Thalamus-R		247					
Ventral Striatum-L		249					
Pallidum-L		69					
Midbrain		360					
Patients(Task>SMC)>Controls(Task>SMC)							
Insula/Adjacent Cortex-Left	1347		-12	-32	18	4.40	0.027
Insula		279					
Superior Temporal Gyrus		80					
Rolandic Operculum		451					
Postcentral Gyrus		61					
Supramarginal Gyrus		66					
Medial Wall/Dorsal ACC	1556		-8	-62	48	4.04	0.022
Precuneus-R		602					
Precuneus-L		646					
Middle Cingulate Gyrus-R		172					
Posterior Cingulate Gyrus-R		54					

[1]Comparisons for the healthy controls (N=14) and patients with schizophrenia (N=14), contrasting greater activation to the task trials than to the SMC trials.
[2]Identification of activation according to the WFU Pickatlas.
[3]Cluster extent.
[4]Number of voxels within region identified by WFU Pickatlas; voxel size: 1.5 mm.
[5]x, y and z coordinates in MNI space for most significant voxel within the cluster.
[6]FDR corrected for cluster.
[7]Dorsal ACC, dorsal anterior cingulate cortex.
[8]Cluster may also extend into the Pre-Supplementary Motor Area, not recognized by the WFU Pickatlas.

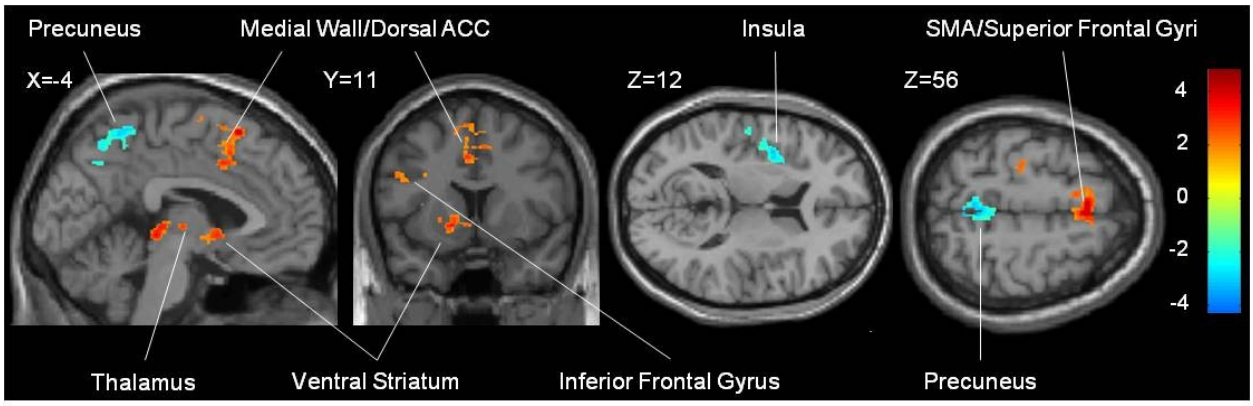

Figure 4. Between-group results for activation to task>SMC trials revealed more activation in controls (red) in the inferior frontal gyrus and medial areas of the prefrontal cortex and subcortically in the striatum and thalamus. Patients (blue) had more activation than controls in the precuneus and insula (P<.05, FDR corrected). Color bar indicates t-values; x, y, z, = MNI coordinates.

Additional contrasts of interest were related to DD trial difficulty. Although the within-group analyses of activation to hard>easy trials were not significant in controls or in patients, the reverse contrast of easy>hard trials revealed significant results in both groups. For the within-group analysis of activation for the contrast of easy>hard trials, control participants exhibited activation in widespread areas including the middle temporal gyrus, insula, and middle cingulate gyrus (eTable 5). Analysis of the patient group revealed that they, too, showed more activation to easy than hard trials, with activation in the superior and middle frontal gyri, middle temporal cortex, middle and posterior cingulate gyri and inferior parietal cortex (eTable 5). Comparing groups for difference in activation to easy versus hard trials (**Table 4; Figure 5)** revealed an interaction between group and difficulty, with a cluster of activation extending from

lateral frontal regions such as the superior and middle frontal gyri, into medial wall locations such as the anterior and middle cingulate gyrus and the supplementary motor area, and parietal locations such as inferior parietal cortex (not shown).

Table 4. Between-group Results for Trial Difficulty[1]

Brain Regions	Cluster	Voxels	x	y	z	t	*P*
Frontal Cortex-Right	6010		22	-2	54	5.06	<0.001
Superior Frontal Gyrus		297					
Middle Frontal Gyrus		259					
Precentral Gyrus		275					
Frontal Cortex-Left							
Superior Frontal Gyrus		417					
Middle Frontal Gyrus		382					
Medial Wall/Dorsal ACC							
Superior Medial Frontal Gyrus-R		220					
Superior Medial Frontal Gyrus-L		319					
Supplementary Motor Area-R		679					
Anterior Cingulate Gyrus-R		213					
Anterior Cingulate Gyrus-L		60					
Middle Cingulate Gyrus-R		35					
Middle Cingulate Gyrus-L		294					
Parietal Cortex-Left							
Inferior Parietal Lobule		326					
Postcentral Gyrus		175					

[1]Differential activation between the healthy controls (n=14) and patients with schizophrenia (n=14), contrasting trial difficulty. For controls>patients, contrast is hard>easy; for patients>controls, contrast is easy>hard.
Other conventions as in Table 3.

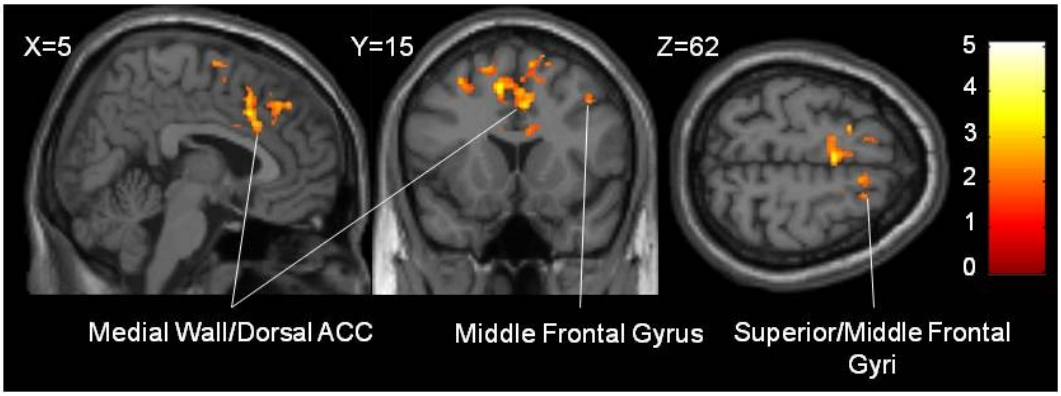

Figure 5. An interaction occurred between difficulty and group. Images above show the regions where activation differences occurred between groups when hard trials were contrasted to easy trials, *P*<.05, FDR corrected. Other conventions as in Figure 4.

The Group x Difficulty interaction led to the post hoc, between-group analyses of activation to hard trials exclusively and easy trials exclusively (**Figure 6**). In both, hard>baseline (top row) and easy>baseline (bottom row), controls had greater activation than patients subcortically in the basal ganglia and cortically, in the inferior frontal, anterior cingulate, and posterior parietal cortices. Activation to the easier trials (**Figure 6,** bottom row) was again greater in controls than patients in similar areas of the basal ganglia and parietal cortex, but not in the lateral or medial frontal areas seen activated for the more difficult trials (**Table 5**). Patients showed no areas of greater activation than controls.

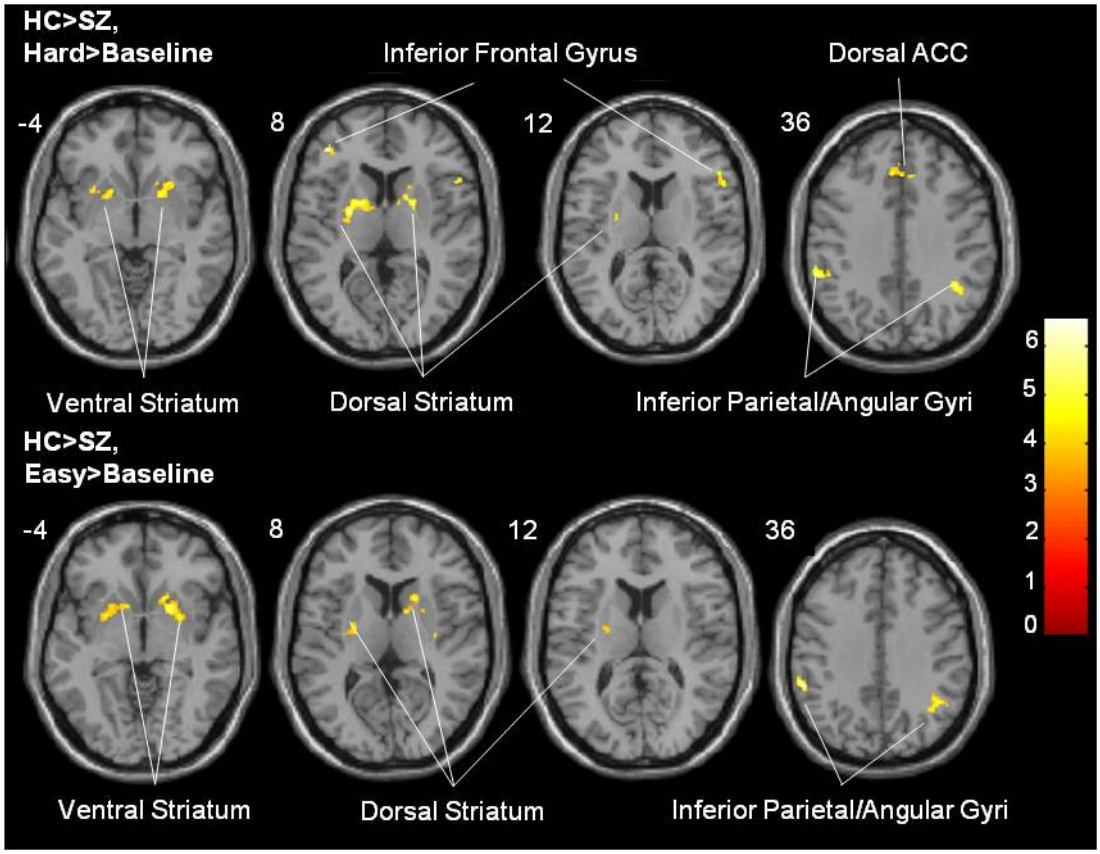

Figure 6. Between-group results of activation to hard trials (top row) and easy trials (bottom row) revealed that more activation occurred in controls regardless of trial difficulty. Controls exhibited more activation than patients in the inferior frontal and dorsal anterior cingulate cortex (ACC) during hard trials, regions expected to contribute more during difficult decisions, in addition to more activation in the striatum and parietal cortex, expected to contribute during all decisions. The results survived a voxel-level intensity threshold uncorrected $P<.001$, with a minimum cluster size to maintain a FDR of .05. There were no regions of greater activation in patients at that threshold. The MNI z coordinate is given. Other conventions as in Figure 4.

Table 5. Between-group Results for Hard & Easy Trials

Brain Regions	Cluster	Voxels	x	y	z	t	*P*
Controls(Hard)>Patients(Hard)[1]							
Frontal Cortex-Right	76		54	18	9	5.01	.04
Inferior Frontal Gyrus		56					
Precentral Gyrus		20					
Frontal Cortex-Left	74		-40	42	8	6.14	.04
Inferior Frontal Gyrus		68					
Parietal Cortex-Right	289		39	-48	35	5.68	<.001
Inferior Parietal Gyrus		199					
Angular Gyrus		64					
Parietal Cortex-Left	281		-42	-45	39	5.53	.001
Inferior Parietal Gyrus		241					
Supramarginal Gyrus		33					
Medial Wall/Dorsal ACC-Left	140		-6	32	35	4.77	.004
Superior Medial Frontal Gyrus		118					
Middle Cingulate Gyrus		19					
Basal Ganglia/Insula-Right	333		21	1	8	5.83	.013
Putamen, dorsal, ventral		208					
Caudate, dorsal, ventral		25					
Lateral Globus Pallidus		16					
Insula		17					
Basal Ganglia-Left	407		-20	1	5	6.11	<.001
Putamen, dorsal		328					
Lateral Globus Pallidus		22					
Controls(Easy)>Patients(Easy)[2]							
Parietal Cortex-Right	211		44	-54	36	5.93	<.001
Angular Gyrus		106					
Inferior Parietal Lobule		94					
Parietal Cortex-Left	89		-57	-39	36	6.70	.034
Supramarginal Gyrus		59					
Inferior Parietal Lobule		30					
Basal Ganglia/Limbic-Right	816		33	-5	2	6.53	<.001
Putamen, dorsal, ventral		609					
Caudate, dorsal, ventral		95					
Amygdala		20					
Basal Ganglia-Left	626		-16	6	-10	6.59	<.001
Putamen, ventral		537					
Caudate, ventral		15					

[1]Comparisons for the healthy controls (n=14) and patients with schizophrenia (n=14), contrasting activation to hard trials.
[2]Comparisons for the healthy controls (n=14) and patients with schizophrenia (n=14), contrasting activation to easy trials.
Other conventions as in Table 3.

In order to elucidate the interaction between group and difficulty, a functionally defined mask was created of the significant between-group difference, and then used to extract mean beta values from the individual contrast maps for hard trials versus baseline (fixation) and for easy trials versus baseline. A graph of the interaction (**Figure 7**) suggested that both controls and patients had greater activity to the easy trials than to the hard trials, with patients exhibiting a greater difference in activation due to trial difficulty.

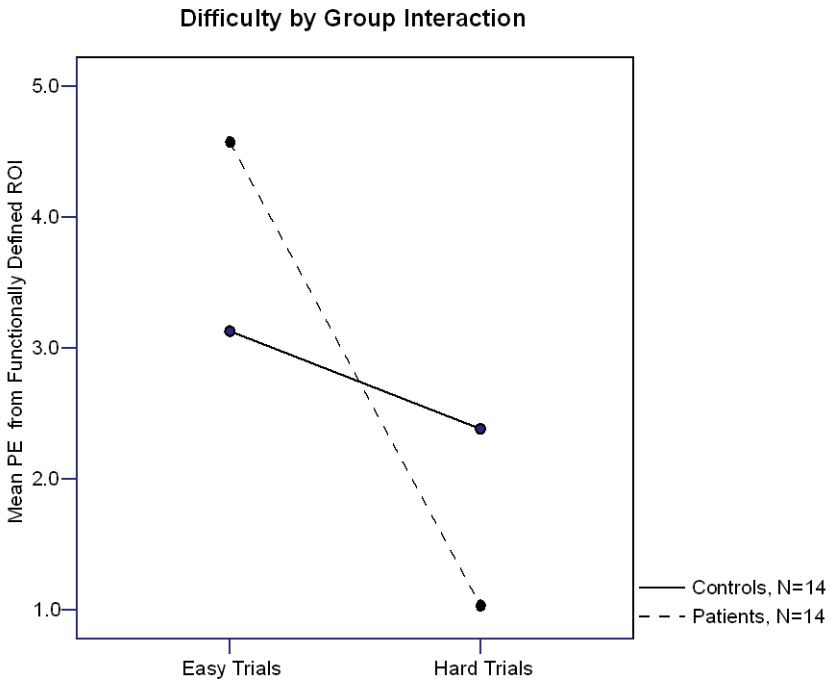

Figure 7. Mean parameters estimates extracted from each participant's contrast maps for hard trials and easy trials using a functionally defined region of interest mask using the between-group results for hard versus easy trials.

The regression analysis performed in SPM8, using the transformed R^2 values, or *R'*, as the covariate with the contrast of task>SMC revealed a significant group x *R'* interaction in the superior and middle frontal gyri; insula; anterior cingulate cortex, extending into the Supplementary Motor Area; precuneus and midbrain **(Figure 8)**. Follow-up analyses in SPSS using the mean beta values extracted from the functionally-defined mask showed significant positive correlations between activation and *R'* in the controls and significant negative correlations in the patients. **Table 6** contains the cluster extent and MNI coordinates for the most significant voxels.

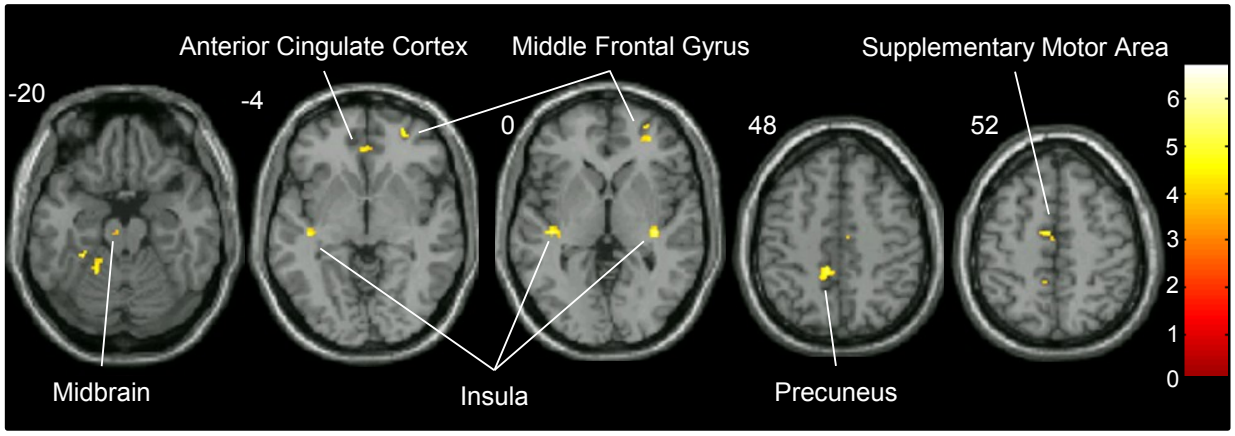

Figure 8. Group x *R*' interaction revealed activation from the contrast of DD task trials>SMC trials that was positively correlated with *R*' in controls (n=14) and negatively correlated in patients (n=14). Activations displayed survived a voxel-level intensity threshold uncorrected *P*<.001, with a minimum cluster size to maintain a FDR corrected value of .05. Other conventions as in Figure 6.

Table 6. Group x R' Interaction[a]

Brain Regions	Cluster	Voxels	x	y	z	t	*P*
Frontal Cortex-Right	117		28	52	-3	5.14	0.013
Superior Frontal Gyrus		30					
Middle Frontal Gyrus		66					
Insular Region-Right	251		36	-24	0	6.11	<0.001
Insula		92					
Superior Temporal Gyrus		54					
Precentral Gyrus		16					
Insular Region-Left	207		-42	-23	-3	6.44	0.011
Insula		112	-33	-32	23	5.00	0.049
Superior Temporal Gyrus		31					
Temporal Cortex-Left	78		-36	-45	-21	5.84	0.049
Fusiform Gyrus		67					
Transverse Temporal Gyrus	123	52	-28	-30	12	5.15	0.011
Superior Temporal Gyrus		23					
Medial Wall/Dorsal ACC	101		2	40	-7	6.27	0.02
Anterior Cingulate Gyrus-R		48					
Medial Frontal Gyrus-R		99					
Supplementary Motor Area-L	123		-6	-8	53	4.75	0.011
Medial Frontal Gyrus-L		66					
Parietal Cortex-Left	129		-9	-39	45	6.15	0.011
Precuneus		89					
Postcentral Gyrus		22					
Brainstem-Left	102		-3	-20	-22	5.41	0.02
Midbrain		49					
Pons		53					
Cerebellum-Left	83		-20	-47	-18	4.69	0.046

[a]fMRI activation during the contrast of task trials>SMC trials positively correlated with R' in healthy controls and negatively correlated with R' in patients.
Other conventions as in Table 3.

DISCUSSION

To our knowledge, this is the first study comparing the neural circuits engaged during a delay discounting task between patients with schizophrenia and healthy controls. Behaviorally, there were several principle findings. Overall, patients were more likely to choose immediate rewards and had greater DD than healthy controls. A key measure was the behavioral inconsistency, as indexed by R^2, measured during performance of the task. Patients were less able to perform the task consistently, with a quasi-bimodal distribution of R^2 values. Patients with lower R^2 made fewer choices that conformed to our model of DD (or stochastic performance) on trials of comparable value than those with higher R^2. Although we found a steeper rate of discounting in the overall patient group than in controls, this difference disappeared when we limited the analysis to those with consistent performance. Both within- and between-group differences in reaction times indicated that patients were less able to modulate their behavior based on trial difficulty. Better cognitive function in all participants was related to lower DD.

The principal findings for the fMRI results were reduced activation overall to the task in the patients with schizophrenia. Both between- and within-group whole brain analyses showed that patients exhibited reduced activation to the DD task compared to healthy controls. Patterns of activation to the difficult DD trials, that is, those of relatively similar value, revealed that controls engaged more of the executive function network, in lateral and medial frontal regions, in addition to parietal regions and the basal ganglia, than did patients. Patterns of activation to the easy DD trials, those of relatively dissimilar values, revealed that controls still engaged more of the subcortical and parietal areas than did patients, but not the lateral and medial frontal regions activated during the more

difficult trials. The regression analysis of activation and *R*' revealed that activity in multiple regions (midbrain, anterior cingulate cortex, precuneus, middle frontal gyrus, insula and superior temporal gyrus) in healthy controls was positively correlated with consistent performance, whereas in patients with schizophrenia, it was negatively correlated.

BEHAVIORAL RESULTS

BEHAVIORAL RESULTS

Overall, patients discounted more steeply than healthy controls. In this study, we used how well participants' choices fit a discounting model as a measure of cognitive performance and found inconsistent performance during scanning in approximately half of the patients. Importantly, group differences in DD disappeared when we limited our analyses to the subgroups of patients and controls that performed the task consistently. In two previous behavioral studies of DD in patients with schizophrenia, Heerey et al[1,39] reported steeper discounting in patients than in controls and a relationship between steeper discounting and episodic and working memory deficits in patients. Heerey and colleagues, however, did not systematically investigate performance consistency as we did, although they excluded some patients based on inconsistent responses and lack of variability in responses.[1,39] The inconsistent performance we identified may be related to deficits in the maintenance of goal-directed behavior. If goal-directed behavior is dependent on consistent performance, then accurate and consistent calculation of the

relative value between behaviors, that is, deciding which behaviors contribute more to reaching goals, would be essential. If patients have difficulty in calculating subjective value consistently or staying on task, then this might contribute to their inability to set and reach meaningful goals. *Clearly, this behavioral inconsistency indexes an important aspect of abnormal decision-making in schizophrenia. Broadly, this abnormality could be linked to the inability to sustain goal-directed behaviors often seen in patients.*

Both within- and between-group differences in reaction times indicated that patients were less able to modulate their behavior based on task difficulty. In contrast to controls, who took less time to respond to the easy than to the difficult trials, patients were generally slower to respond to both type of trials. Clearly, fast, impulsive decisions cannot explain the previously discussed choice inconsistency. Others[77-79] have also observed abnormal reaction time modulation in schizophrenia in response to task difficulty. Deficits in conflict monitoring[80-82] during decisions might lead to an inability to make compensatory adjustments, such as increased response times, as tasks become more difficult.

Overall, better cognitive function in all participants was related to lower DD, but in the individual groups, only better performance on the language section of the RBANS, tapping into semantic fluency, was correlated with lower DD in the patient group. Unlike Heerey et al,[1] we did not find a relationship between working memory deficits and DD in this group of patients. Neither did we find a relationship between DD and negative symptoms that had been found in a previous schizophrenia study[39] and between DD and anhedonia in healthy college students.[83]

fMRI RESULTS

As in previous fMRI studies investigating DD, controls in our study utilized an extended network that included cortical (frontal, medial and parietal) and subcortical regions (ventral striatum and thalamus) during the performance of the DD task. Previous fMRI studies of DD have reported activation in the medial prefrontal cortex, posterior cingulate and ventral regions of the striatum during DD decisions,[42,44,84-88] although the exact role each region plays in DD is still controversial. McClure et al.[44] have argued that choices for sooner rewards and/or more emotional choices are driven by the limbic system, more specifically the ventral striatum, interconnected regions of the prefrontal cortex (medial and orbitofrontal), posterior cingulate cortex and posterior hippocampus. . Activation in dorsolateral and ventrolateral prefrontal cortex, lateral orbitofrontal cortex, the Supplementary Motor Area and intraparietal sulcus occurred during all trials requiring a decision. Hariri and colleagues[89] found that the preference for an immediate reward during a DD task outside the scanner was correlated with ventral striatum activity to both positive and negative feedback during a monetary reward task in the scanner. This preference for immediate rewards also positively correlated with activity in the medial prefrontal cortex and negatively correlated with activity in the dorsolateral prefrontal cortex and lateral orbitofrontal cortex. Kable and Glimcher[42,43] and others[33,90] have proposed that activity in the ventral striatum, medial prefrontal cortex and posterior cingulate tracks the subjective value of rewards,[42] that is, the value given to a choice that

is unique to the individual. However, additional regions are also likely to contribute to subjective valuation, as behavioral and electrophysiological studies of the reward system suggest that the relative and subjective nature of rewards necessitates the inclusion of sensory, emotional and cognitive evaluation in determining the value of rewards.[91,92] Thus, performance on the DD task is likely to result from the integration of information originating from multiple brain regions.

We first compared the groups on all DD trials versus SMC trials, a contrast thought to tap into a broad decision-making circuit. In this contrast, the within-group analysis revealed that while healthy controls exhibited a more extensive BOLD response during task performance than patients, activation in patients occurred in similar regions. The between-group analysis, however, revealed that patients had significantly less activation in inferior frontal, medial frontal, and parietal/occipital cortices, as well as in thalamus and ventral striatum. Importantly, these abnormalities were found in the face of matched performance. The results of a recent meta-analysis have shown that, in healthy controls, executive tasks in general engage a distributed neural network, prominently including these frontal regions, and others such as the parietal cortex, as well as the thalamus, and that patients fail to engage this network to the same extent as healthy controls.[5] Abnormal prefrontal function, including of the dorsolateral,[93,94] ventrolateral[95-97] and medial[98-100] frontal cortex, is one of the most frequently reported abnormalities in schizophrenia and is thought to underlie dysfunction of cognitive processes sustained by these regions,[101,102] such as working memory,[40,93,94,103,104] episodic memory,[101,105-107] and conflict monitoring.[80,100,108] Our results are in agreement with these findings. On the other hand, in the contrast of activation to the DD task greater than SMC trials, greater

activation in the patients occurred in more limited regions of the left insula extending into the frontal operculum and superior temporal gyrus, and in more posterior and dorsal medial wall locations that included the precuneus and posterior and middle cingulate cortex. These results suggest that the failure in these patients to engage the extended neural circuit to the same extent as healthy controls may be offset by engaging other areas, perhaps in a compensatory manner.

Literature on the role of the ventral striatum in reward is extensive.[45,89,109-111] The reward system involves multiple regions that interact to support behaviors that result in positive outcomes. These regions include the substantia nigra, ventral tegmental area, the ventral striatum, medial prefrontal cortex and orbitofrontal cortex.[112] Previous fMRI studies have found increased ventral striatum activation during easier DD trials,[45] when more immediate rewards were available and when received rewards were unexpected. Decreased activation has been found when expected rewards were not received.[113] In schizophrenia, abnormal modulation of the ventral striatum has been identified in tasks tapping into different aspects of reward processing, including reward anticipation and delivery,[13,96,114,115] attribution of salience,[9] reinforcement learning,[116] and prediction error,[113,117] although results from the prediction error studies have been mixed.[118] In addition, as discussed previously, studies of decision-making suggest that subjective valuation of choices, such as in the DD task, taps into a neural network that includes ventral striatum, medial frontal, and posterior cingulate cortex. In this regard, our finding of differences in ventral striatal and medial frontal activation between the groups is noteworthy.

In addition, we compared the groups based on task difficulty, a comparison thought to tap more into executive function. We did not identify any regions more significantly activated to hard>easy trials in the control or patient groups. Previous studies that investigated difficulty in relation to DD reported activation in the medial prefrontal cortex[45] (uncorrected for multiple comparisons), dorso- and ventrolateral prefrontal and lateral orbital cortex[44] (no direct whole brain contrast of difficult to easy trials); and inferior and middle frontal gyri (regions of interest), medial prefrontal cortex and dorsal anterior cingulate cortex[37] to difficult DD decisions. Using a corrected threshold in a whole brain analysis may have limited our findings. Interestingly though, in our study, the contrast of easy greater than hard trials revealed widespread cortical activation in both groups, similar to results reported by Marco-Pallarés et al.[45] In an investigation using contrasts similar to ours, Marco-Pallarés and colleagues found greater activation in only one region, medial prefrontal cortex, to the more difficult trials compared to the easier trials, whereas in the reverse contrast, they reported more activation in multiple regions, to the easier trials compared to the more difficult trials, corresponding to our within-group results such as the middle temporal cortex, insula, middle cingulate gyrus, and parietal cortex.[45]

We identified an interaction between groups and trial difficulty in regions of the superior frontal cortex, anterior and middle cingulate cortex and medial frontal cortex. In these regions, both controls and patients showed greater BOLD response to the easy trials than to the hard trials, with patients exhibiting the greatest difference in response in relation to trial difficulty. When the hard and easy trials were analyzed separately, patients showed less activation in ventral and dorsal striatum and inferior parietal cortex

to both types of trials. In addition, during the hard, but not the easy, trials, patients had less activation in the lateral and medial frontal cortices. These results underscore abnormal modulation of medial frontal cortex with trial difficulty, as well as decreased engagement of the prefrontal network during the more difficult trials, in patients with schizophrenia.

Other studies examining task difficulty in schizophrenia have reported reduced activation in the striatum and insula/opercular cortex during tasks requiring temporal differentiation,[119] the absence of increased activation in the dorsolateral prefrontal cortex and thalamus to increased task difficulty during an antisaccade task,[120] increased activation in the dorsolateral prefrontal cortex during working memory tasks when performance was matched,[121] decreased activation in ventrolateral prefrontal cortex and visual processing areas during a visual discrimination task, again with matched performance,[97] and increased and decreased activation of the anterior cingulate cortex associated with task difficulty (for review see Adams and David[122]).

Finally, in the regression analysis using all task> SMC trials with *R'*, we found significant interactions between more consistent task performance and group in several regions, including the midbrain, anterior cingulate cortex, precuneus, middle frontal gyrus, insula, and superior temporal gyrus. Thus, even though these patients performed the DD task with similar R^2 and k as controls, important differences in brain activation, encompassing cortical and subcortical networks, have been identified. These results shed light into neural networks associated with patients' proclivity for inconsistent choices. Middle frontal involvement is in line with the finding of Heerey and colleagues, relating abnormal discounting to working memory abnormalities.[1] As discussed above, the

anterior cingulate cortex and precuneus are components of a network whose activity correlates with subjective value during delayed choice.[123] In addition, abnormalities in the midbrain would indicate that dopamine and reward are relevant to the inconsistent responding, and abnormalities in the insula could implicate an emotional aspect linked to choice inconsistency.

STUDY LIMITATIONS

The patients in this study were on stable doses of antipsychotic medications that may influence the BOLD signal.[124] However, understanding neural activity and behavior in the context of the medicated patient is important to obtaining clues pointing to better cognitive therapies. Only consistent patients were included in the imaging study; thus, the imaging data may not generalize to all subjects with schizophrenia, although they provide important clues as to brain regions related to consistent choices in schizophrenia.

CONCLUSIONS

Our data point to local and specific disrupted neural activation in patients with schizophrenia, such as abnormal neural modulation of the dorsal anterior cingulate cortex with trial difficulty, as well as the lack of more widespread engagement of the distributed network during DD performance seen in the control participants. As a group, patients with schizophrenia showed a steeper rate of discounting and less consistent behavior; however, even in the subgroup of patients matched with controls on discounting and

consistency, we found reduced activation in cortical and subcortical regions. Postmortem[125-127] and imaging studies[5] have provided abundant evidence for neural abnormalities in those with schizophrenia in multiple cortical and subcortical regions, as well as white matter abnormalities.[128-130] These abnormalities are likely to affect the fine-tuning of local and projection neural networks, thus severely compromising the integration of cognitive functions. Patients appear to lack an integrated neural response when making decisions. These results suggest that abnormal value representation and aberrant behavioral choices, such as the behavioral inconsistencies in the overall patient group, are related to the lack of contributions from multiple regions.

ACKNOWLEDGMENTS

This work was supported by research funds from a University of Alabama Health Services Foundation General Endowment Fund Scholar Award. We want to thank Luke Stoeckel for his assistance in the initial phase of the experiment, Muriah Wheelock, Nathan Hutchenson, Mark Bolding and Jenifer Hadley for their assistance on data management and data processing, Debbie Lowman for her recruitment expertise and all our participants who so graciously took part in this project.

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Supplementary Online Content

Avsar KB, Cox JE, Weller RE, Reid MA, White DM, Lahti AC. A Behavioral and fMRI Investigation of Delay Discounting in Patients with Schizophrenia and Controls Matched on Performance.

eAppendix. Details about DD task administration and data analyses.

eTable 1. Estimating a participant-specific *k*.

eTable 2. Tasks available during scanning.

eTable 3. Response times for different trial types.

eTable 4. Within-group results for task>SMC trials.

eTable 5. Within-group results for easy>task trials.

eFigure 1. Histograms of the distribution of the $\log_{10}(k)$ values from the laboratory session.

eFigure 2. Graph showing the number of immediate reward preferences.

eFigure 3. Within-group results from the whole brain analysis of task>SMC.

This supplementary material has been provided by the authors to give readers additional information about their work.

Instructions to participants.

> Participants were told that the purpose of the experiment was to choose between two hypothetical reward amounts. One of the amounts would always be available immediately, and the other choice would only be available after a delay. An explicit instruction was also given to select based on their preference and not on what they might think someone else would want them to choose. Participants were told that during the lab session they would be making 108 choices and during the magnet session 160 choices, broken up into four blocks. We told participants that they would receive $92-$99 for their participation on an unrelated task. They were also told that all choices were unrelated and to not attempt to plan ahead. For some of the trials, they were instructed that they would see the same choices on the left and right sides and to arbitrarily choose (sensorimotor control). Participants indicated their choice using a button press on the corresponding side.

Using data obtained during the laboratory session, a participant who exhibited the pattern of responses in **eTable1** had a *k* of .036 with a model fit or R^2 of .99, indicating that the model explained 99% of the variance in the participant's responses, or that the participant's responses fit the model consistently. Using task #8 from eTable 2 with a Target k of 0.041 during imaging would provide choices that varied in difficulty while promoting an equal number of immediate and delayed preferences. We analyzed the participant's choices during the initial fMRI run to ensure an approximately equal number of immediate and delayed reward choices. If the participant made more immediate reward choices, we shifted to a task with a larger target *k* to encourage more delayed choices, and vice versa (see **eTable 2**). By evaluating responses during the initial run (**eTable 1**), we were able to adjust the task, as necessary, to promote more optimal responding.

eTable 1. Estimating a participant-specific *k*

Trial *k*[a]	% IR Choices[b]
.0004	100
.001	100
.0025	100
.006	100
.01	75
.041	42
.1	17
.25	0

Abbreviations: *k*, discounting parameter; IR, immediate reward.
[a]Trial k*'s* from laboratory version of the DD task
[b]Values expressed as the percentage of responses indicating an immediate reward preference.

eTable 2. Tasks available during scanning[a]

Difficulty	Reward Preference	*#1*	*#2*	*#3*	*#4*	*#5*	*#6*	*#7*	*#8*	*#9*	*#10*
Easy	Immediate	0.0004	0.0007	0.0007	0.001	0.0018	0.0025	0.0033	0.006	0.011	0.028
Hard	Immediate	0.001	0.0018	0.0025	0.0033	0.006	0.011	0.016	0.028	0.041	0.1
Hard	Target k[b]	0.0018	0.0025	0.0033	0.006	0.011	0.016	0.028	0.041	0.07	0.17
Hard	Delayed	0.0025	0.0033	0.006	0.011	0.016	0.028	0.041	0.07	0.1	0.25
Easy	Delayed	0.011	0.016	0.028	0.041	0.07	0.1	0.17	0.25	0.25	1

[a]Values in table are trial k's used in each of the 10 possible magnet tasks.
[b]Target k where participants were ambivalent about receiving the immediate or delayed reward.

eTable 2 contains the ten tasks available for the scanning session with an trial k for each trial type. The task with a target k most closely matching the subject-specific *k* would optimize responses from participants so they would choose approximately an equal number of immediate and delayed rewards during scanning.

Mean response times as a function of trial difficulty are listed in **eTable 3**. Both groups required more time to respond to the task trials than to the SMC trials. Controls also required more time to respond to the harder trials, while patients did not benefit from the easier trials, taking as long to respond to the easy trials as to the hard trials.

eTable 3. Response times for different trial types

	Healthy Controls	Patients	Between	
Trial Type	**Mean ± SD**	**Mean ± SD**	**$F_{1,26}$**	**P**
Easy immediate	2122 ± 329[a]	2638 ± 504[a]	**10.27**	**.004**
Hard immediate	2443 ± 509[b]	2729 ± 582[a]	1.92	.18
Target k	2437 ± 466[b]	2750 ± 628[a]	2.24	.15
Hard delayed	2481 ± 526[b]	2679 ± 532[a]	.98	.33
Easy delayed	2103 ± 425[a]	2569 ± 518[a]	**6.76**	**.015**
SMC	863 ± 114[c]	1226 ± 225[b]	**29.001**	**<.001**

SMC, sensorimotor control trials; within each group, trial types with different superscripts are significantly different (P < .05). Bold indicates a significant between-group difference.

eTable 4 contains the results for the within-group analysis of activation to task>SMC trials, and **eTable 5** contains the results for the within-group analysis of activation to easy>hard trials. For the fMRI analyses, three healthy controls and 13 patients failed to meet the criterion of R^2>.60 and were not included. In addition, we excluded imaging data from 2 controls and 5 patients for excessive motion.

eTable 4. Within-group results for activation to task>SMC trials[1]

Brain Regions[2]	Cluster[3]	x[4]	y	z	t	*P*[5]
Controls						
Frontal Cortex-Right						
Middle Frontal Gyrus	281	51	42	14	8.86	<0.001
Inferior Frontal Gyrus	239	52	12	29	7.65	<0.001
Inferior Frontal Gyrus	103	31	22	-1	5.58	0.001
Frontal Cortex-Left						
Inferior Frontal Gyrus	638	-48	16	29	8.79	<0.001
Parietal/Occipital-Right						
Inferior Parietal Lobule	190	32	-47	39	9.01	<0.001
Middle Occipital Gyrus	930	18	-90	-3	8.52	<0.001
Parietal/Occipital-Left						
Inferior Parietal Lobule	264	-27	-53	47	8.99	<0.001
Inferior Parietal Lobule	92	-42	-42	48	7.46	0.002
Middle Occipital Gyrus	1282	-32	-84	0	10.48	<0.001
Temporal Cortex-Left						
Inferior Temporal Gyrus	184	-46	-54	-9	6.57	<0.001
Medial Wall/Dorsal ACC						
Medial Frontal Gyrus	621	0	19	50	7.0	<0.001
Anterior Cingulate-R	94	3	36	32	7.58	0.002
Precuneus-R	306	26	-63	42	7.5	<0.001
Precuneus-L	81	-21	-60	47	6.22	0.004
Thalamus/Basal ganglia						
Thalamus/Striatum	45	-6	-29	-3	6.1	0.034
Thalamus/Striatum	40	4	-29	-3	5.98	0.047
Cerebellum-Left						
Cerebellum	57	-8	-77	-37	7.48	0.016
Cerebellum	55	-3	-72	-27	4.86	0.017
Patients						
Frontal Cortex-Right						
Inferior Frontal Gyrus	51	33	21	0	6.36	0.010
Parietal/Occipital-Right						
Middle Occipital Gyrus	114	22	-96	10	8.97	<0.001
Parietal/Occipital-Left						
Middle Occipital Gyrus	43	-39	-86	-4	10.26	0.019
Middle Occipital Gyrus	323	-26	-87	0	9.22	<0.001
Medial Wall						
Medial Frontal Gyrus	54	-6	19	45	6.28	0.009
Cuneus	40	14	-95	8	7.35	0.023
Precuneus	73	33	-71	35	12.71	0.002
Cerebellum-Left						
Cerebellum	123	-3	-69	-27	11.65	<0.001

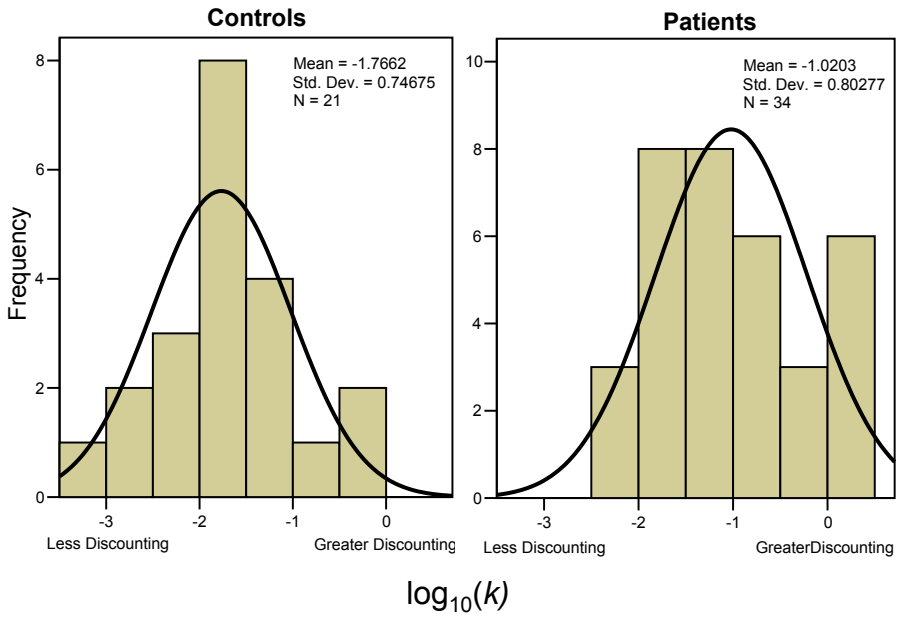
[1]Within-group results for the healthy controls (n = 14) and patients with schizophrenia (n = 14), contrasting greater activation to the DD task trials than to the SMC trials.
[2]Labeling of activation according to WFU Pickatlas.
[3]Cluster Extent.
[4]x, y and z coordinates in MNI space of most significant voxel within the cluster.
[5]False discovery rate adjusted p for cluster.

eTable 5. Within-group results for easy>hard trials[1]

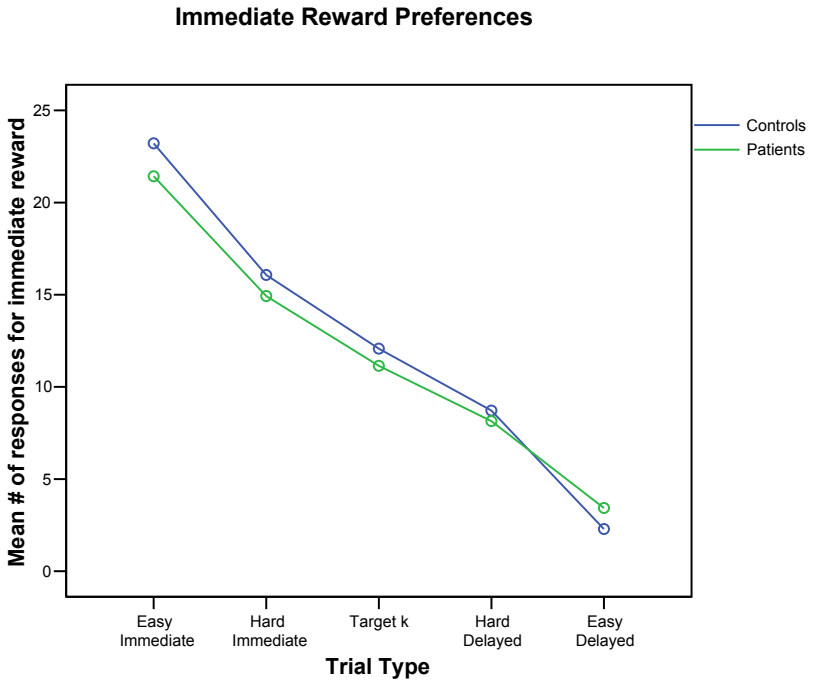
Brain Regions	Cluster[1]	x	y	z	t	*P*
Controls						
Parietal/Occipital-Right						
Angular Gyrus	1292	38	-71	45	4.97	0.014
Parietal/Occipital-Left						
Superior Occipital Gyrus	1402	-16	-81	30	6.65	0.011
Temporal Cortex-Right						
Middle Temporal Gyrus	2124	64	-29	-3	7.26	0.001
Insula/Temporal Cortex-Left						
Middle Temporal Gyrus	2396	-66	-32	30	5.75	0.001
Insula	2036	-33	-5	11	5.99	0.001
Fusiform Gyrus	1014	-38	-74	-19	5.20	0.030
Medial Wall/Dorsal ACC						
Middle Cingulate Gyrus-R	1217	8	-30	38	4.85	0.015
Cerebellum-Right	1241	22	-81	-16	5.19	0.015
Cerebellum-Left	1030	-15	-75	-40	6.70	0.03
Patients						
Frontal Cortex-Right						
Middle Frontal Gyrus	4178	28	18	48	5.12	0.001
Frontal Cortex-Left						
Superior Frontal Gyrus	876	-18	31	48	5.00	0.027
Precentral Gyrus	2047	-14	-11	33	6.09	0.001
Parietal/Occipital-Right						
Inferior Parietal Lobule	1830	38	-42	48	5.12	0.001
Middle Occipital Gyrus	1036	36	-78	12	5.54	0.017
Temporal Cortex-Left						
Middle Temporal Gyrus	900	-45	-48	8	3.87	0.026
Medial Wall/Dorsal ACC						
Middle Cingulate Gyrus-R	1210	4	-36	39	4.54	0.008
Posterior Cingulate-R	1584	21	-59	5	4.91	0.002
Cuneus-R	911	3	-81	15	5.13	0.026

[1]Within-group analysis of the healthy controls (N=14) and patients with schizophrenia (N=14), contrasting difficulty. No activation survived the corrected threshold for hard>easy trials. Other conventions as in eTable 4.

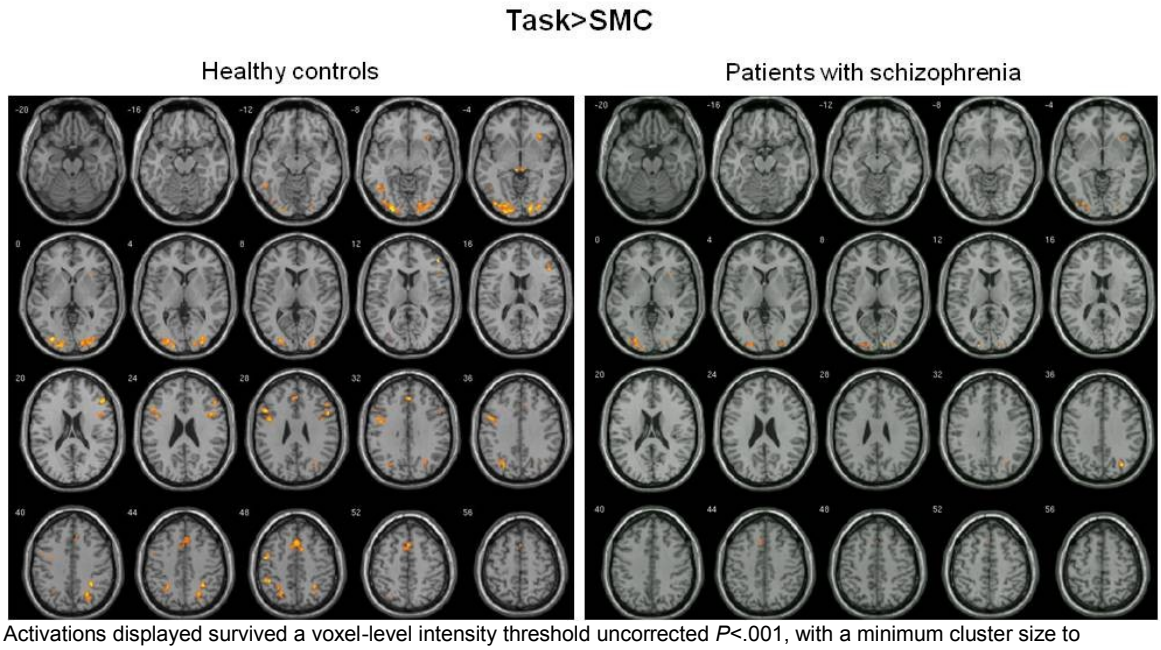
eFigure 1. Histograms of the distribution of the $\log_{10}(k)$ values from the laboratory session.



eFigure 2. Graph showing the number of immediate reward preferences.



eFigure 3. Within-group results from the whole brain analysis of activation to task>SMC trials.



Activations displayed survived a voxel-level intensity threshold uncorrected *P*<.001, with a minimum cluster size to maintain a FDR of .05.

INCONSISTENT DELAY DISCOUNTING PERFORMANCE ASSOCIATED WITH ABERRANT RESPONSE TIMES AND HYPERACTIVATION IN PATIENTS WITH SCHIZOPHRENIA COMPARED TO HEALTHY CONTROLS

by

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In Preparation for Archives of General Psychiatry

Format adapted for dissertation

Abstract:

Background: Previously, we compared behavioral performance and neural activation to delay discounting task>sensorimotor (SMC) trials of patients with schizophrenia with controls who did not differ in delay discounting when matched on consistent performance. A subgroup of patients whose performance was more erratic and inconsistent was not included.

Objective: To compare delay discounting in consistent controls, consistent patients and inconsistent patients and to use fMRI during the task to compare brain activation in response to task trials versus SMC trials in the three groups.

Design and Setting: We collected behavioral and fMRI data while participants performed a delay discounting task requiring decisions between receiving hypothetical small immediate rewards or larger delayed rewards. The behavioral data were collected at the Neuroimaging and Translational Research Laboratory, Birmingham, AL; fMRI data were collected at the University of Alabama at Birmingham (UAB) Functional Neuroimaging Laboratory at the Civitan International Research Center.

Participants: We recruited patients with DSM-IV schizophrenia or schizoaffective disorder from the outpatient psychiatric clinics at the University of Alabama at Birmingham Center (n=35) and healthy control participants (n=21) from the community who did not differ significantly on age, parental socioeconomic status or smoking.

Main Outcome Measures: The rate of discounting, k, model fit, R^2, the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)[101] and the Brief Psychiatric Rating Scale (BPRS)[102] were collected during the laboratory session. For each participant, we used discounting results from the laboratory session to choose a version of the discounting task that optimized behavioral responses during the acquisition of functional imaging data. The fMRI analysis compared the activation in consistent controls (n=14), consistent patients (n=14) and inconsistent patients (n=9) on the contrast of task versus SMC trials.

Results: Overall, inconsistent patients did not differ significantly from consistent patients with schizophrenia on RBANS or BPRS, although subscale scores were lower on delayed memory and language. In comparison to controls, inconsistent patients displayed greater activation when we contrasted task to SMC trials in the precuneus and posterior and middle cingulate cortex, whereas, in comparison to consistent patients, they displayed greater activation in the superior frontal and superior medial frontal gyri. Neither consistent controls nor consistent patients exhibited more activation than inconsistent patients to the contrast of task greater than SMC trials.

Conclusions: The functional neuroimaging results are similar to those of previous studies showing less task-induced deactivation in patients with schizophrenia.

Keywords: delay discounting, schizophrenia, fMRI, intertemporal discounting, executive function, subjective value, neuroimaging, reward system, default mode network, conflict monitoring

INTRODUCTION

Schizophrenia is a heterogeneous disorder, with patients exhibiting a wide range of symptoms and functional outcomes. The positive symptoms of delusions and hallucinations are typically most prominent and used in the diagnosis. However, it is cognitive deficits, which occur due to deterioration in function during a prodromal period prior to onset, that contribute most to functional outcomes.[3] These deficits are less likely to be affected by treatment than the more visible positive symptoms.[4] Understanding the neural abnormalities underlying the functional deficits is necessary to understanding how domains disrupted in the illness may be improved. One domain disrupted in the illness, related to an inability to maintain goal-directed behavior, results in the inability to set and reach meaningful long-term goals.[5] In order to maintain goal-directed behavior, a goal must be selected and then maintained, while making decisions that contribute to reaching that goal at some point in the future. An integration of executive function and reward processing is necessary for goal selection and maintenance of goal-directed behavior. Widespread neural abnormalities, both morphological[6] and functional (for review see Mizenberg[7]), are reported in schizophrenia in regions associated with executive function[8-11] and reward processing.[12-18] Understanding how neural abnormalities may disrupt the integration of information between executive function and the reward system offers a window into better understanding of functional deficits in schizophrenia.

Goal-directed behavior requires choosing between alternative behaviors that may require short-term sacrifice for long-term gain, similar to choices in delay discounting paradigms. Delay discounting requires a decision between a small immediate reward and

a larger delayed reward.[19,20] Greater willingness to wait for larger rewards in delay discounting is associated with better cognition and executive functioning.[21] Performance in delay discounting requires holding alternate rewards in working memory, then inhibiting the desire for the immediate reward.[22] Previous studies of DD in schizophrenia found that discounting in patients was related to memory "fitness", that is, those with better memory scores discounted less.[23] Some researchers found that increasing cognitive load by taxing working memory during delay discounting tasks in healthy controls increased the selection of immediate rewards,[22] while others found that increasing cognitive load during delay discounting resulted in more inconsistent performance, rather than increased impulsivity.[24] Franco-Watkins and colleagues[24] reported that using a letter generation task to tax executive processing during the delay discounting task resulted in a greater number of choices that did not relate to previous choices; that is, inconsistent performance.

Most studies using the discounting paradigm estimate a discounting parameter, *k*, to index impulsivity (e.g. see[23,25,26]). The delay discounting parameter is the rate at which an individual discounts future rewards, with larger *k*'s indicating greater discounting.[19,27] Few studies have used the delay discounting task to understand choice behavior in the context of reasoned decisions; that is, decisions that relate to previous choices, or consistency.[28] Luo and colleagues[28] used the discounting parameter to predict preferences for immediate or delayed rewards, then measured how closely actual preferences matched predicted preferences. In other words, they examined how stochastic choices were with the probabilistic discounting model predicted by the participant's *k*. Using a task with choices tailored to increase ambivalence in participants, Luo and colleagues found that

participants who made more stochastic choices exhibited greater activation in the left insula and left inferior frontal gyrus than participants who made less stochastic choices when choosing the larger delayed reward rather than the smaller immediate reward. They argued that participants who were more inconsistent did not rely as strongly on an algorithm when making decisions, therefore requiring greater activation in more executive function regions when choosing the larger delayed reward.

In our initial investigation,[29] we used regression analysis to estimate an individual's discounting parameter (k) and obtain a model-fit statistic (R^2) to measure consistency. This procedure allowed analysis of groups well matched on consistent performance during the delay discounting task. Patients with schizophrenia, when compared to controls not significantly different on demographic variables that included smoking, had greater delay discounting. However, when the subset of patients with schizophrenia that exhibited inconsistent choices, that is, lower R^2 values during the delay discounting task, were removed from the patient group, there were no differences in the rate of discounting between the controls and patients. Additionally, when compared to consistent controls, consistent patients failed to show the same modulation of response times with trial difficulty.

In light of the quasi-bimodal distribution of R^2 values, we limited the fMRI analysis in the previous study to healthy controls and patients whose R^2 values were greater than .60, indicative of consistent choices, which had the effect of matching groups on performance. Controls showed the expected activation to the task trials versus SMC trials in the ventral striatum, thalamus, precuneus and putative executive function areas such as prefrontal, dorsal anterior cingulate and inferior parietal cortex, as found in

previous fMRI studies of delay discounting.[30-34] However, compared to consistent controls, consistent patients showed reduced fMRI activation in cortical (including the inferior frontal gyrus; medial wall, including dorsal anterior cingulate, middle cingulate and supplementary motor area; and parietal cortex extending into occipital cortex) and subcortical (in the ventral striatum and thalamus) regions during delay discounting task versus control task performance. In addition, we found increased fMRI activation in consistent patients in lateral (left insula and temporal cortex) and medial (precuneus and posterior cingulate cortex) cortical regions during task performance, which we suggested might be compensatory.

In the current study, we now focus on comparing three groups; consistent controls and consistent patients who performed the task as expected, with R^2 values greater than .60, and inconsistent patients, who performed the task inconsistently, with R^2 values less than .60. The main purpose of this study was to identify factors associated with or arising from inconsistency in patients. Heerey and colleagues reported that working memory deficits in patients with schizophrenia were related to greater delay discounting,[35] and more severe negative symptoms were related to less discounting.[23] Therefore, we hypothesized that the inconsistent patients would score lower on cognitive tests and/or exhibit fewer negative symptoms. Based on fMRI results from our previous study,[29] we predicted that inconsistent patients would show similar patterns of reduced activation of the decision-making circuit (lateral prefrontal, medial prefrontal, posterior cingulate, parietal and anterior cingulate cortices and ventral striatum) that we had found in the consistent patients, just to a greater degree.

METHODS

PARTICIPANTS

Participants were 56 individuals recruited from the University of Birmingham (UAB) area. Using the diagnoses of DSM-IV[36] schizophrenia or schizoaffective disorder established using participants' medical records and the Diagnostic Interview for Genetic Studies,[37] 35 patients were recruited from UAB outpatient psychiatric clinics. We recruited the 21 healthy controls from the community using flyers and advertisements in the University newspaper. Exclusion criteria were major medical conditions, substance abuse within the past six months, previous serious head injury, a neurological disorder, previous loss of consciousness, pregnancy and ferromagnetic material in the body. The study was approved by the Institutional Review Board of the University of Alabama at Birmingham, and all participants gave written informed consent. Participants received compensation between $92-99, depending on performance on an unrelated task in the magnet. For more detailed demographics of those participants not included here, see Avsar et al.[29]

We used the Repeatable Battery of Neuropsychological Status (RBANS)[1] to measure general cognitive function in all participants and the Brief Psychological Rating Scale (BPRS)[2] in patients to measure positive (conceptual disorganization, hallucinatory behavior, and unusual thought content) and negative (emotional withdrawal, motor retardation, and blunted affect) mental status and symptoms.

DELAY DISCOUNTING TASK

We used a modified DD tasks[26,38] that consisted of 108 trials during the laboratory session and 160 trials during the imaging session.[29] The 108 trials from the laboratory session were subdivided equally between eight trial k values (.0004, .001, .0025, .006, .016, .041, .1, .25) and sensorimotor control (SMC) trials (see **Figure 1**). We included the SMC trials during the laboratory session to familiarize participants with the procedure for the imaging session. The SMC trials required an arbitrary left or right button press to a non-evaluative decision between $0 now and $0 now. The 12 trials at each trial k consisted of a choice between a unique combination of an immediate reward (IR), ranging from $1 to $73, and a delayed reward (DR), ranging from $28 to $86, with delays (D) ranging from 1 to 116 days. The choices were produced for the eight trial k's by adjusting reward values and delays using the hyperbolic function, IR=DR/(1+kD).[27] Individuals normally prefer the IR when the trial k is small, with a decreasing IR preference as trial k's become larger. As trial k's become larger, participants make a decreasing percentage of choices for the IR until nearly all choices are for the DR. For example, most individuals will choose the IR when given a choice between $29 now and $30 in 86 days (trial k of .0004) and the DR when given a choice between $67 now and $83 in 1 day (trial k of .25). If trial k equals participant's *k,* responses for IR approach 50%, and the choice is most difficult because the IR and DR have equal subjective values. The more distant the trial k, either smaller or larger, is from the participant's *k*, the easier the decision between the IR and DR.

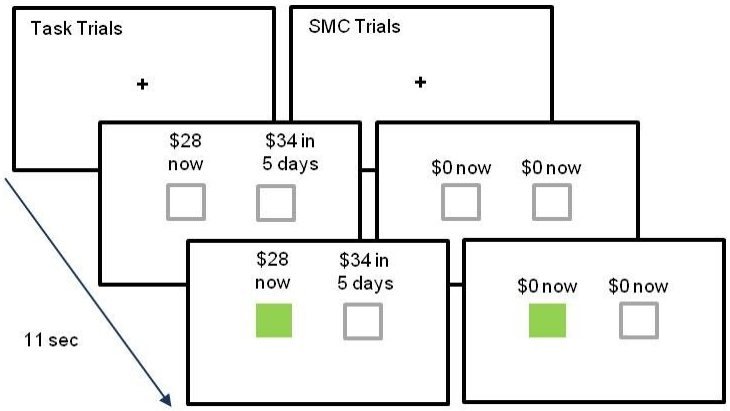


Figure 1. Delay discounting task trials and sensorimotor control trials required a left or right button press to indicate preference for the immediate or delayed choice.

The percentages of IR preferences at each trial k were entered into a non-linear regression using an exponential model to calculate an individual discounting parameter, ie, the participant's *k*. The calculation also produced a model fit statistic, R^2, used as an index of consistency which provided a measurement of how well the participant's responses fit the expected pattern of decreasing preferences for the IR as trial k increased. We used R^2 to divide groups into consistent (R^2>.60) and inconsistent (R^2<.60) participants.

The 160 trials from the imaging session were subdivided into 120 trials equally divided between five trial k values (see **Table 1**) and 40 SMC trials. Using a task with trial k values centered near the participant's *k* promoted an overall equivalent number of IR and DR preferences during the scanning session. The five trial types ranged from the smallest k (easy immediate) to the largest k (easy delayed), with the three trial k's nearest the participant's *k* being the most difficult (hard immediate, hard ambivalent, hard

delayed). As the magnitude of trial k increased, the percentage of choices for the IR decreased. Participants indicated their choice by a corresponding left or right button press.

Table 1. Trial k's Available During Imaging

Easy Immediate	Hard Immediate	Hard Ambivalent	Hard Delayed	Easy Delayed
0.0004	0.001	**0.0018**	0.0025	0.011
0.0007	0.0018	**0.0025**	0.0033	0.016
0.0007	0.0025	**0.0033**	0.006	0.028
0.001	0.0033	**0.006**	0.011	0.041
0.0018	0.006	**0.011**	0.016	0.07
0.0025	0.011	**0.016**	0.028	0.1
0.0033	0.016	**0.028**	0.041	0.17
0.006	0.028	**0.041**	0.07	0.25
0.011	0.041	**0.07**	0.1	0.25

Matching the participant's *k* determined during the laboratory session to the nearest trial k in the hard ambivalent category during imaging promoted an overall equivalent number of IR and DR choices.

IMAGING DATA ACQUISITION

We used a Siemens Allegra head-only 3T magnet with a single-channel circularly polarized no-tune transmit/receive head coil to acquire a high-resolution anatomical T1-weighted image, using a magnetization-prepared rapid gradient-echo (MPRAGE) sequence. Functional images using an echo planar imaging (EPI) sequence with a 2.2s repetition time (TR) and 30 ms echo time (TE) were used to acquire 30 interleaved 4.0 mm axial slices, 1 mm gap, with a 70-degree flip angle during the task. The field of view was 24 x 24 cm^2. The task was presented on a mirror attached to the head coil, using E-

Prime software (version 1.2; Psychology Software Tools, Pittsburgh, Pennsylvania) running on an IFIS-SA system. For additional details, see Avsar et al.[29]

DATA ANALYSIS

Behavioral Measures. Transformed discounting parameters, $\log_{10}(k,)$ and the model-fit statistic, R^2, from the laboratory session and the imaging session were entered into analyses of variance (ANOVA) to compare the three groups. Reaction time data were analyzed to assess differences across levels of trial difficulty using a mixed-design ANOVA, with a within-subject factor of trial type (easy immediate trials, hard trials, easy delayed trials) and a between-subject factor of group (consistent controls, consistent patients, inconsistent patients). Post hoc tests, using Fisher's Least Significant Difference tests, were conducted to compare groups when the omnibus indicated significant group differences. Greenhouse-Geisser estimates were used to correct for sphericity deviations.[39]

Functional Data. Data were preprocessed (slice-timing correction, movement correction using least squares with interpolation between slices using ArtRepair[40] when movement exceeded 0.5 mm per TR; data discarded if in excess of 2 mm per 40 trial run) under the SPM8 software package (Wellcome Department Imaging Neuroscience, London UK). See Avsar et al (submitted) for further details. We used a general linear model (GLM) with a variable epoch approach[41] with regressors that corresponded to the presentation of the stimulus and duration vectors that corresponded to the length of time participants

required to make decisions. We included two regressors of interest in the GLM, task trials and SMC trials, convolved with the canonical hemodynamic response function, followed by a time derivative that allowed for temporal variance in the BOLD response and a high pass filter implemented in a mixed model to account for within- and between-subject variability.

Individual-subject GLMs were created to estimate parameters for the contrasts of task trials versus SMC trials. In within-group analyses, we used voxel-wise $P<.001$ and a cluster level threshold to maintain a false discovery rate (FDR) of .05.[42,43] For between-group tests, we used voxel-wise, $P<.05$ and maintained the FDR of .05.

RESULTS

BEHAVIORAL RESULTS

Demographic data and clinical and cognitive assessments[1,37] for study participants included in this study who performed the task are presented in **Table 2**. During the laboratory session, 21 controls and 27 patients exhibited consistent performance; that is, their pattern of responses fit our model with an R^2 greater than .60 on the DD task. Of those, 17 controls and 16 patients were able to perform the task consistently, with R^2 values>.60, during the scanning session, and 12 patients were unable to meet the performance criterion, with R^2 values<.60. **Figure 2** shows the distribution of consistency scores for the laboratory and imaging session. Of the 12 patients that exhibited inconsistent performance during the imaging session, 8 had been able to perform the task

consistently during the initial laboratory session but were then unable to maintain performance during the imaging session. One patient who had been inconsistent during the laboratory session performed consistently during the imaging session.

Table 2. Demographic Data, Clinical and Behavioral Measures for Participants who were Consistent or Inconsistent During Laboratory Session

Variable	Consistent Controls (n=21)	Consistent Patients (n=27)	Inconsistent Patients (n=8)	$F_{2,52}$	*P*
Age, years[a]	37 ± 3	39 ± 2	32 ± 4	.10	.38
Gender[b]	11 Men; 10 Women	18 Men; 9 Women	7 Men; 1 Women	4.50	.03
Parental SES[c]	6.94 ± 1.11	6.85 ± 1.05	8.60 ± 2.11	.26	.77
Smoking[d]	.42 ± .11	.63 ± .11	.52 ± .32	.60	.47
RBANS[e]					
Total Index	92.70 ± 2.97[f]	74.92 ± 2.18[g]	67.50 ± 3.74[g]	15.76	<.001
Immediate Memory	95.85 ± 3.04[f]	78.04 ± 2.88[g]	77.00 ± 3.76[g]	9.86	<.001
Visuospatial	92.80 ± 4.10[f]	78.08 ± 3.45[g]	72.00 ± 7.49[g]	5.13	.01
Language	94.10 ± 3.16[f]	89.46 ± 1.65[f]	77.00 ± 6.60[g]	4.42	.012
Attention	95.80 ± 4.02[f]	81.27 ± 3.14[g]	86.83 ± 3.89[fg]	3.77	.019
Delayed Memory	95.58 ± 2.57[f]	74.85 ± 3.83[g]	58.50 ± 6.03[h]	14.38	<.001
BPRS[i]					
Total		32.96 ± 1.73	30.63 ± 2.60		.51
Positive		6.15 ± .72	6.13 ± 1.12		.99
Negative		4.67 ± .42	5.00 ± .78		.71
Delay Discounting					
$Log_{10}(k)$	-1.68 ± .15[f]	-1.20 ± .14[f]	-.34± .27[g]	10.70	<.001
Lab R^2	.94 ± .01[f]	.86 ± .02[g]	.24 ± .06[h]	169.83	<.001

Abbreviations: RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; BPRS, Brief Psychiatric Rating Scale; *k*, discounting parameter; R^2, discounting model fit.
[a]Values are expressed as mean ± standard error unless otherwise indicated.
[b]Values are expressed as number of individuals and chi^2 used to test for gender difference .
[c]Parental socioeconomic status (SES) was determined by Diagnostic Interview for Genetic Studies (1-18 score); lower score signifies higher socioeconomic status; data not available for 8 healthy controls and 7 patients.
[d]Value is expressed in packs per day (PPD).
[e]RBANS data not available for 1 healthy control, 1 consistent patient and 2 inconsistent patients.
[f,g,h]Scores with different superscripts are significantly different between the groups (P<.05).
[i]t-tests.

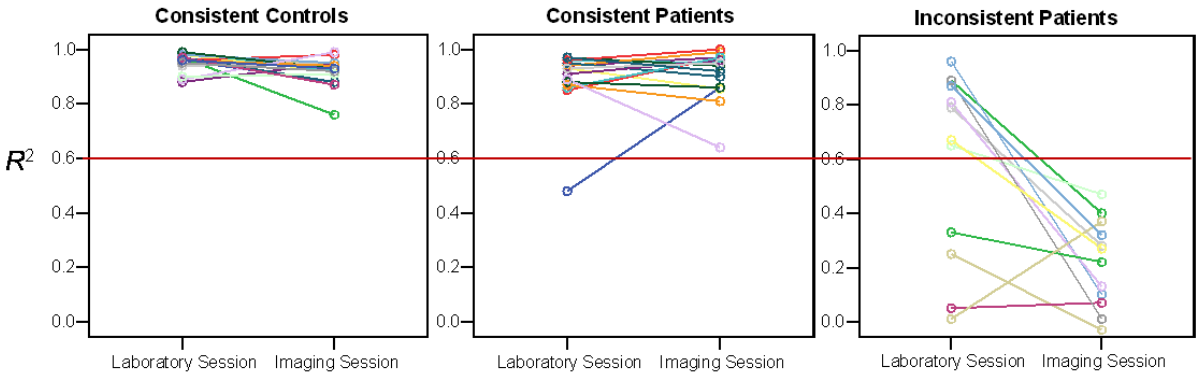


Figure 2. Model fit statistics, R^2, during performance of DD task in laboratory and imaging sessions for consistent controls, consistent and inconsistent patients with schizophrenia. Red line at .6 is the minimum criterion used for consistent performance.

Table 3 contains demographic characteristics and behavioral results for those participants with quality imaging data that were included in the fMRI analyses. Seven controls were not included in the imaging analyses; two controls exceeded movement criterion, three were inconsistent during the imaging session, one did not respond to SMC trials and one was unable to tolerate the scanner. Twelve patients were not included in the imaging analyses; three patients exceeded movement criterion, three made fewer than 15% IR choices, four made more than 85% IR choices, and two were unable to tolerate the scanner. The seven participants who showed too little variability in their choices were likely not engaged in the task and just choosing, by and large, all immediate or all delayed rewards. While the overall ANOVA showed significant between-group differences on $\log_{10}(k)$ values obtained during the laboratory session and imaging session, post hoc analyses revealed that in both instances, it was the inconsistent patients that had

a higher rate of discounting than consistent controls and consistent patients, who were not significantly different.

Table 3. Demographic Data, Clinical and Behavioral Measures for Participants who were Consistent or Inconsistent During Imaging Session

Variable	Consistent Controls (n=14)	Consistent Patients (n=14)	Inconsistent Patients (n=9)	$F_{2,34}$	*P*
Age, years	34 ± 3	37 ± 3	41 ± 3	.74	.48
Gender	8 Men; 6 Women	10 Men; 4 Women	7 Men; 2 Women	2.78	.096
Parental SES[a]	6.46 ± 4.93	6.00 ± 1.24	8.50 ± 1.67	.81	.45
Smoking	.27 ± .11[d]	.59 ± .14[de]	.81 ± .28[e]	2.53	.10
RBANS[b]					
Total Index	95.69 ± 3.0[d]	77.93 ± 2.81[e]	73.88 ± 2.573[e]	23.43	<.001
Immediate Memory	97.15 ± 3.09[d]	82.64 ± 3.58[e]	77.00 ± 5.67[e]	10.53	.003
Visuospatial	96.62 ± 4.35[d]	80.50 ± 4.96[e]	77.63 ± 2.81[e]	6.99	.013
Language	96.46 ± 4.06[d]	91.36 ± 1.90[d]	88.25 ± 4.10[d]	3.95	.26
Attention	98.46 ± 4.58[d]	83.43 ± 4.35[e]	84.88 ± 2.89[de]	6.92	.03
Delayed Memory	98.00 ± 1.73[d]	77.79 ± 5.15[e]	69.50 ± 6.56[f]	14.80	.001
BPRS[c]				$F_{1,21}$	
Total		32.57 ± 2.60	31.67 ± 2.71	.05	.82
Positive		6.61 ± 1.06	5.56± 1.42	.37	.54
Negative		4.93 ± .61	4.67 ± .83	.07	.80
Delay Discounting				$F_{2,34}$	
$Log_{10}(k)$	-1.91 ±.18[d]	-1.70 ± .18[d]	-.02 ± .24[e]	143.30	<.001
Imaging R^2	.92 ± .01[d]	.91 ± .03[d]	.26 ± .05[e]	20.74	<.001

Conventions same as in Table 2 except where noted.
[a]Data not available for 4 consistent controls, 1 consistent patient and 2 inconsistent patients.
[b]RBANS data not available for 1 healthy control and 1 inconsistent patient.

ANOVA revealed expected group differences on RBANS between controls and both patient groups with some exceptions (**Tables 2 & 3**). For both laboratory and imaging sessions, the RBANS language scores were not significantly different between consistent controls and consistent patients. Patients inconsistent during the laboratory session did not differ from consistent controls on the RBANS attention subscale. For the

participants included in the imaging analyses, there was no significant difference between any groups on the language subscale. For both sessions, consistent controls scored higher on the delayed memory subscale than consistent patients who scored higher than inconsistent patients scored. The patient groups were not different on BPRS total scores, or on positive and negative subscales of the BPRS.

Due to the poorer model fit, R^2, making the discounting parameter, (k), less reliable for inconsistent patients, we compared the percentage of IR choices in the three groups across trial k values in a mixed ANOVA for laboratory and imaging sessions. Results indicated percentages were different across trial k's ($F_{7, 238}$= 98.30, P<.001, ε=.367) and across groups ($F_{2, 34}$= 8.78, P=.001), with a significant interaction ($F_{14, 238}$= 5.58, P<.001, ε=.367). During the laboratory session, inconsistent responders choose the IR more often than consistent controls and consistent patients on trials with k .016, .041, .1 and .25 (P<.01) (see **Figure 3**). During the imaging session, percentages were, again, different across trial k's ($F_{4, 136}$=5.58, P<.001, ε=.667), but not different across groups ($F_{2, 34}$=2.45, P=.10), although a significant interaction ($F_{8, 136}$=8.84, P<.001, ε=.667) occurred between group and trial type **(Figure 4**). With trial k's centered on the participant's *k,* making the task more difficult, post hoc analyses using Fischer's LSD showed that inconsistent patients chose the IR on easy immediate trials less often than consistent controls (P=.02) and more often on easy delayed trials than consistent controls and consistent patients (P<.001). Consistent controls (N=14) and consistent patients (N=14) showed similar preferences, while the inconsistent responders (N=9) showed less modulation of their responses across the varying trial types, as expected for a group with higher k's.

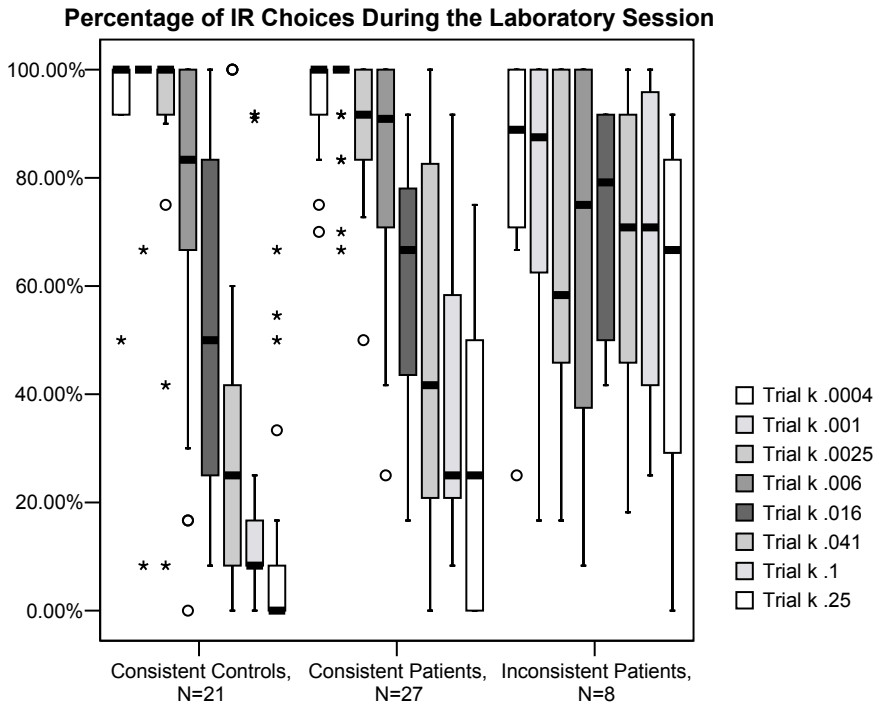


Figure 3. Box plots of decreasing percentage of immediate reward (IR) choices during the laboratory session as trial k increased in all three groups. °indicates outliers with values between 1.2 and 3 box lengths from upper or lower edge of box; *indicates extreme cases with values more than 3 box lengths from upper or lower edge of box.

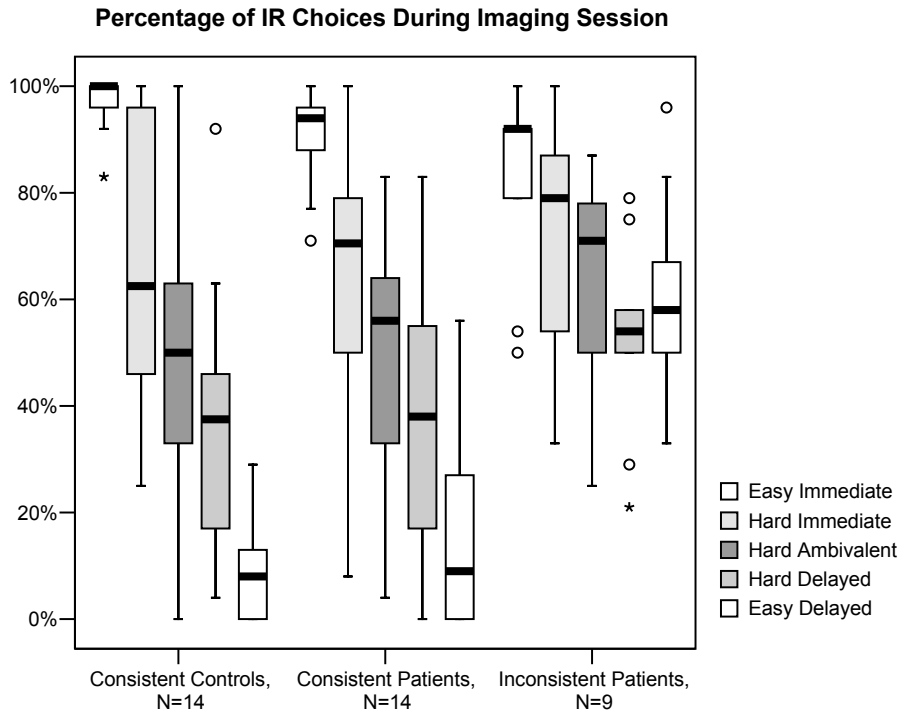


Figure 4. Box plots of decreasing percentage of immediate reward (IR) choices during the imaging session for different trial types in all three groups. Conventions as in Figure 3.

In the mixed-design ANOVA of response times, with a within-subject factor of trial type (easy immediate, easy delayed and hard trials) and between-subject factor of group (consistent controls, consistent patients and inconsistent patients), results indicated that response times were different across trial types ($F_{2, 26}$=7.12, P=.003), marginally different across groups ($F_{2, 34}$=2.92, P=.06), with a group by trial interaction, meaning that the groups responded differently across trial types ($F_{4, 68}$=4.54, P=.003). **Figure 5** shows the mean response times of the groups for different trial types during the imaging session. The within-group analyses showed that consistent controls varied their response times according to the trial difficulty ($F_{2, 26}$=7.12, P=.003), while consistent patients did

not. Response times also varied in the inconsistent patients ($F_{2,16}$=4.51, P=.03). Pairwise comparisons revealed that consistent controls responded slower to the hard trials than to the easy immediate trials ($F_{1,34}$=14.16, P<.001) and the easy delayed trials ($F_{1,34}$=11.96, P<.001), while inconsistent patients responded slower to the easy delayed trials than to the hard trials ($F_{1,34}$=11.96, P<.001). As previously reported, consistent controls responded more quickly than consistent patients when making easy immediate choices ($F_{1,34}$=3.96, P.054) and when making easy delayed choices ($F_{1,34}$=5.17, P=.03) and more quickly than inconsistent patients when responding to the easy delayed trials ($F_{1,34}$=4.44, P<.05). Response times were significantly shorter for SMC trials than task trials in all three groups (P<.001).

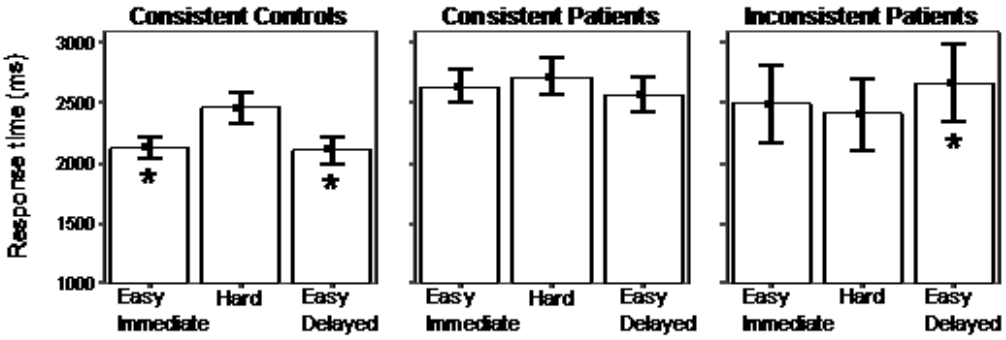
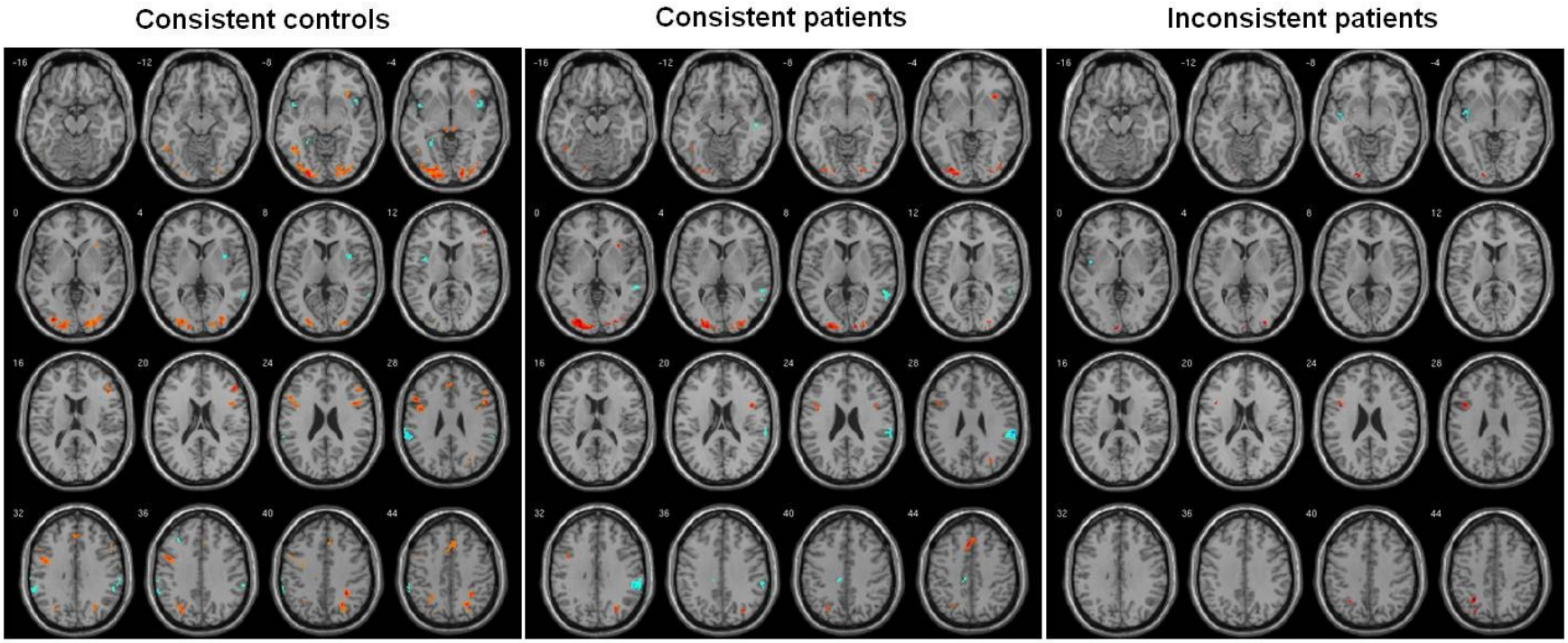


Figure 5. Comparison of mean response times for easy immediate trials, hard trials and easy delayed trials. Error bars show mean ± 1 standard error. *indicates within-group difference, P<.05.

IMAGING RESULTS

fMRI analysis were limited to consistent controls (n=14), and consistent (n=14) and inconsistent (n=9) patients with good quality imaging data. Consistent controls, in general, showed more extensive activation to the task than consistent patients, while both consistent groups showed more extensive activation than exhibited by inconsistent patients. Within-group task>SMC contrasts (**Figure 6,** red=task>SMC; blue=SMC>task) revealed qualitatively less BOLD response in inconsistent patients. The limited activation during task performance in inconsistent patients (**Table 4**) occurred in a small region in the left frontal cortex and areas in the left parietal and occipital cortices. **Table 5** shows the between-group comparisons of inconsistent patients versus consistent controls and consistent patients. In both between-group analyses, the inconsistent patients exhibited greater activation to the task than controls and patients. The greater activation in inconsistent patients compared to consistent controls was in posterior medial wall regions such as the precuneus, middle and posterior cingulate and calcarine cortex (**Table 5; Figure 7**). To clarify the group difference, we extracted mean parameter estimates from the individual contrasts of task>SMC in all three groups using functionally defined masks of clusters that were more activated in inconsistent patients than in consistent controls (**Figure 8 & 9**). In both clusters, increased activation in inconsistent patients and decreased activation in consistent controls led to the greater activation seen in the comparison. Parameter estimates for consistent patients are included for comparison.



Red, task>SMC trials; Blue, SMC>task trials.

Figure 6. Within-group results of activation to DD task>SMC trials in red and activation to SMC>task trials in blue for consistent controls, consistent patients, and inconsistent patients, shown on axial slices from ventral to dorsal. Numbers are for MNI x coordinate. Voxel-level intensity threshold uncorrected, *P*<.001, with a minimum cluster size to maintain a FDR of .05.

Table 4. Within-group Results for Inconsistent Patients for Activation to Task>SMC Trials[1]

Brain Regions[2]	Cluster[3]	Voxels[4]	x[5]	y	z	t	*P*[6]
Frontal Cortex-Left	113		-44	11	27	7.94	<.001
Inferior Frontal Gyrus		110					
Parietal Cortex-Right	54		27	-60	50	6.00	.019
Superior Parietal Lobule		28					
Precuneus		25					
Parietal Cortex-Left	49		-28	-54	44	8.86	.023
Inferior Parietal Lobule		19					
	36		-27	-72	45	6.92	.049
Superior Parietal Lobule		17					
Occipital Cortex-Right	46		30	-89	3	7.15	.025
Middle Occipital Gyrus		46					
Occipital Cortex-Left	36		-4	-98	5	8.65	.049
Cuneus		34					
	91		-15	-93	-4	8.39	.001
Calcarine Cortex		42					
Inferior Occipital Gyrus		20					
Lingual Gyrus		17					

[1]Within-group contrast (N=9) of activation to the task trials>SMC trials.
[2]Identification of activation according to WFU Pickatlas.
[3] Cluster-extent threshold to maintain a FDR of *P*.05.
[4]Number of voxels within region identified by WFU Pickatlas; voxel size: 1.5 mm^3.
[5]x, y and z coordinates in MNI space of most significant voxel within the cluster.
[6]False discovery rate adjusted *P* for cluster. Voxel-level intensity threshold uncorrected, *P*<.001, with a minimum cluster size to maintain a FDR of .05.

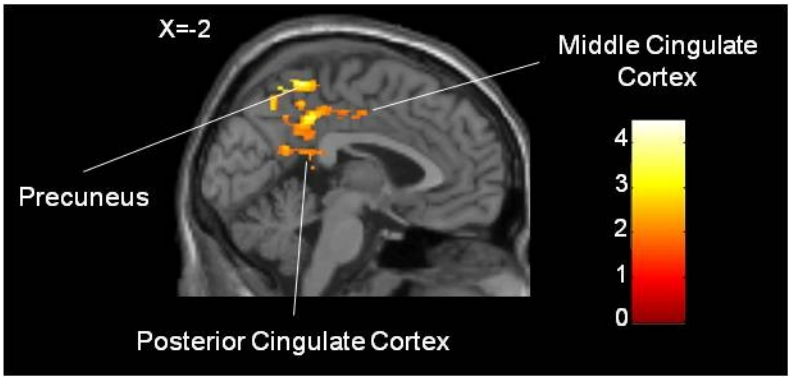


Figure 7. Between-group results for activation to task>SMC trials revealed more activation occurred in inconsistent patients (N=9) when compared to consistent controls (N=14) in the precuneus and posterior and middle cingulate cortex. Voxel-level intensity threshold uncorrected *P*<.05, with a minimum cluster size to maintain a FDR of .05. No regions were more activated in the consistent controls than in the inconsistent patients.

Table 4. Within-group Results for Inconsistent Patients for Activation to Task>SMC Trials[1]

Brain Regions[2]	Cluster[3]	Voxels[4]	x[5]	y	z	t	*P*[6]
Frontal Cortex-Left	113		-44	11	27	7.94	<.001
Inferior Frontal Gyrus		110					
Parietal Cortex-Right	54		27	-60	50	6.00	.019
Superior Parietal Lobule		28					
Precuneus		25					
Parietal Cortex-Left	49		-28	-54	44	8.86	.023
Inferior Parietal Lobule		19					
	36		-27	-72	45	6.92	.049
Superior Parietal Lobule		17					
Occipital Cortex-Right	46		30	-89	3	7.15	.025
Middle Occipital Gyrus		46					
Occipital Cortex-Left	36		-4	-98	5	8.65	.049
Cuneus		34					
	91		-15	-93	-4	8.39	.001
Calcarine Cortex		42					
Inferior Occipital Gyrus		20					
Lingual Gyrus		17					

[1]Within-group contrast (N=9) of activation to the task trials>SMC trials.
[2]Identification of activation according to WFU Pickatlas.
[3]Voxel-forming threshold, *P*<.001 with cluster-extent threshold to maintain a FDR, *P*.05.
[4]Number of voxels within region identified by WFU Pickatlas; voxel size: 1.5 mm^3.
[5]x, y and z coordinates in MNI space of most significant voxel within the cluster.
[6]False discovery rate adjusted *P* for cluster. Voxel-level intensity threshold uncorrected *P*<.001, with a minimum cluster size to maintain a FDR of .05.

Table 5. Between-group Results for Activation to Task>SMC Trials[1]

Brain Regions	Cluster	Voxels	x	y	z	t	*P*[3]
Inconsistent Patients(Task>SMC)>Consistent Controls(Task>SMC)							
Medial Wall/Parietal Cortex	2213		32	-41	58	4.50	.001
Middle Cingulate Gyrus-Bilateral		56					
Precuneus-Bilateral		902					
Superior Parietal Lobule-Bilateral		345					
Medial Wall/Parietal/Occipital Cortex	3048		-4	-42	41	4.34	<.001
Postcentral Gyrus		83					
Precuneus-Bilateral		652					
Middle Cingulate Gyrus-Bilateral		544					
Posterior Cingulate Gyrus-Bilateral		297					
Cuneus-Right		251					
Calcarine Area-Bilateral		445					
Superior Occipital Gyrus		30					
Lingual Gyrus-Right		121					
Inconsistent Patients(Task>SMC)>Consistent Patients(Task>SMC)							
Frontal/Parietal Cortex-Left	1713		-33	24	46	4.20	0.01
Superior Frontal Gyrus		443					
Middle Frontal Gyrus		391					
Superior Medial Frontal		164					
Supplementary Motor Area[2]		142					
Precentral Gyrus		331					
Postcentral Gyrus		44					

[1]Between-group comparisons for the inconsistent patients (N=9), consistent controls (N=14) and consistent patients (N=14), contrasting greater activation to the task trials than to the SMC trials. Neither consistent controls nor consistent patients exhibited greater activation than inconsistent patients to the task>SMC trials.
[2]Cluster may also extend into the Pre-Supplementary Motor Area, not recognized by the WFU Pickatlas.
[3]Voxel-level intensity threshold uncorrected *P*<.05, with a minimum cluster size to maintain a FDR of .05. Other conventions as in Table 3.

Inconsistent patients showed greater activation than consistent patients in more frontal areas, such as the left superior and middle frontal gyri, and more medially in the superior medial frontal and supplementary motor area, near the location of the pre-SMA[45,46] (**Table 5; Figure 10**). Mean parameter estimates (**Figure 11**) were extracted from the individual contrasts of task>SMC in all three groups using a functionally-defined mask of the cluster that was more activated in inconsistent patients than in consistent patients (**Figure 10 &11**). The opposite contrasts of activation to task trials

greater than SMC trials in consistent controls or consistent patients greater than the inconsistent patients were not significant.

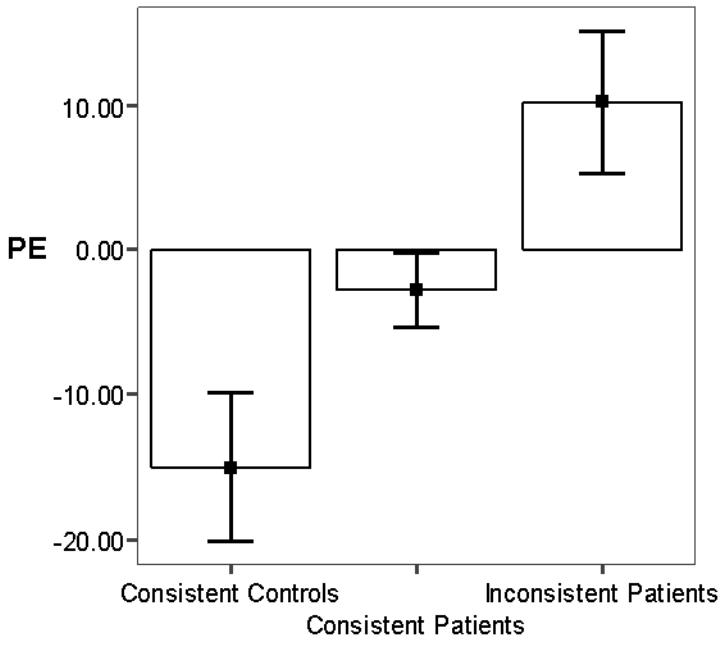


Figure 8. Mean parameter estimates (PE) extracted using the functionally defined mask of group difference for inconsistent patients (task>SMC) > consistent controls (task>SMC) for the cluster with peak voxel at MNI coordinates, -4, -42, 41 located on the medial wall. Error bars show means ± standard error.

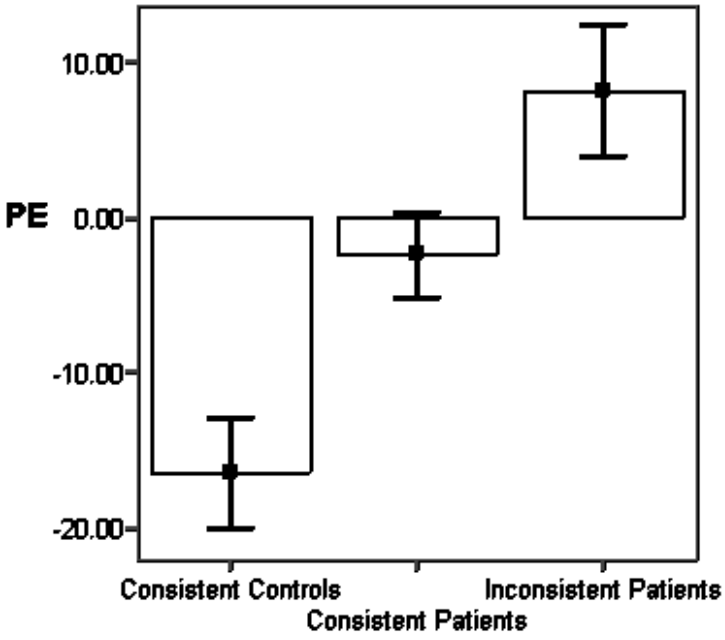


Figure 9. Mean parameter estimates (PE) extracted using functionally-defined mask of group difference for inconsistent patients (task>SMC) > consistent controls (task>SMC) for the cluster with peak voxel at MNI coordinate, 32, -41, 58 in the parietal cortex. Conventions as in Figure 8.

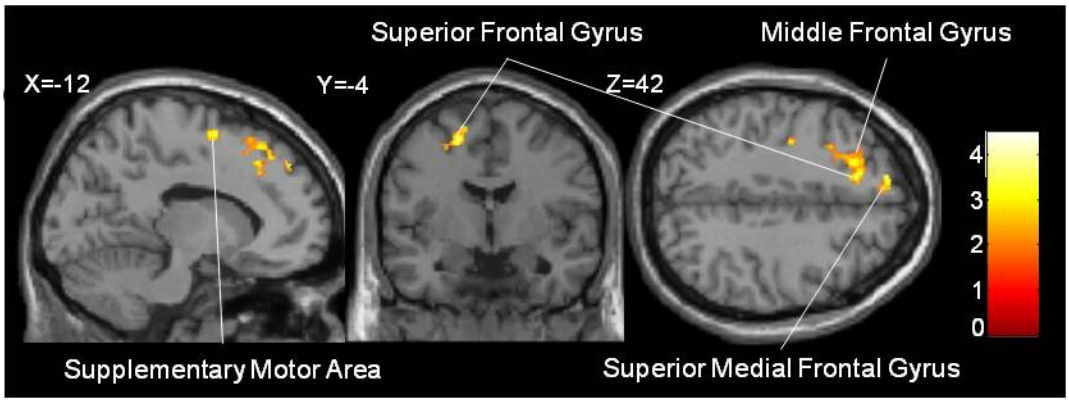


Figure 10. Between-group results for activation to task>SMC trials revealed more activation occurred in inconsistent patients (N=9) when compared to consistent patients in the supplementary motor area, superior frontal and superior medial frontal gyri. *P*<.05.

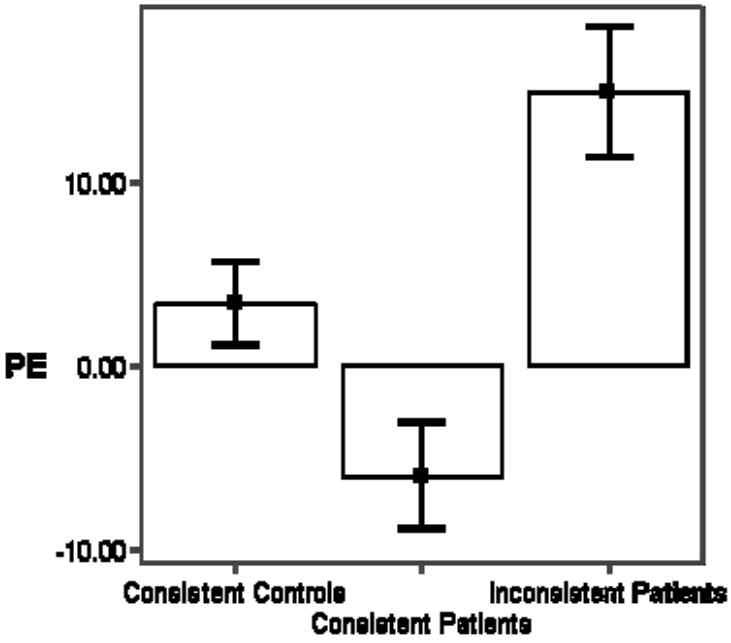


Figure 11. Mean parameter estimates extracted using functionally-defined mask of group difference for inconsistent patients (task>SMC) > consistent patients (task>SMC) for the cluster with peak voxel at MNI coordinates -33, 24, 46 in the middle frontal gyrus. Conventions as in Figure 8.

In our initial investigation,[29] we found that, overall, patients had greater delay discounting, or were more likely to choose immediate rewards, although it was striking that this difference disappeared when we limited the analysis to those with consistent performance. In the present study, inconsistent patients preferred immediate rewards more often than consistent controls or patients. Here we investigated how the consistent controls and consistent patients differed from the inconsistent patients and what might be associated with their IR preference and inconsistent performance. While, in general, inconsistent patients were not significantly different from consistent patients on RBANS or BPRS, their scores were lower on the delayed memory index of the RBANS. Heerey et al[23] previously found that, in patients, better memory was correlated with less discounting. We previously found that consistent patients were slower on easier trials than consistent controls, with less modulation of response times between hard and easy trials.[29] Inconsistent patients showed an abnormal pattern of response times between hard and easy trials. In the previous fMRI results, consistent controls exhibited more activation to task>SMC trials in multiple regions when compared to consistent patients,[29] while, surprisingly, in the current study, the between-group brain analyses showed more activation to the task in the inconsistent patients when compared to consistent controls and to consistent patients. Although the inconsistent patients appeared to have less activation in the within-group analyses, the between-group analyses showed that inconsistent patients exhibited more activation to the DD task in the middle and posterior cingulate than controls and more activation in inferior and middle frontal gyri than consistent patients. These results will be discussed in relation to previous delay discounting studies and other fMRI findings in schizophrenia.

BEHAVIORAL RESULTS

We did not find significant differences between the patient groups on RBANS total or BPRS scores, although inconsistent patients, in general had lower RBANS scores than consistent patients. Patients unable to perform the task consistently during the laboratory session scored more similar to the controls on the attention portion of the RBANS than consistent patients. However, patients who were consistent in both the laboratory and magnet sessions scored higher and more similarly to controls on the language portion of the RBANS, tapping into semantic fluency, than inconsistent patients. Language tends to be one area of preserved function in schizophrenia, and RBAN scores are often higher on that index.[46] RBANS scores for the delayed memory were lower in patients who were inconsistent during laboratory and imaging sessions. The decreased performance in patients from the laboratory session to the imaging session was striking. During the laboratory session, 27 patients were able to perform the task in a way that matched our model, but almost half of those were unable to do as well later during the imaging session. Centering the task on the participant's *k*, theoretically, should have increased the proportion of difficult trials and contributed to the decline in performance. Although patients may have found the magnet environment more stressful and stress, known to exacerbate psychiatric illnesses[47] may also have been a contributing factor in the decline.

We did not find a difference in BPRS scores between patient groups. Heerey and colleagues[23] had found an inverse relationship between negative symptoms and delay

discounting; that is, patients with more negative symptoms tended to prefer immediate rewards less often than those with fewer negative symptoms. In the inconsistent patients, preferences for the IR and response times were abnormal. In contrast to the consistent patients, who were similar to controls during the laboratory and magnet session in their preference for the IR, inconsistent patients chose the IR more often on trials when the DR choice should have been more prevalent. However, during the imaging session, with trial k's centered on the participant's *k*, thus making the task more difficult, inconsistent patients actually chose fewer IR on trials with the smaller k's and more IR on trials with the larger k's, exhibiting more aberrant behavior. In addition, response times did not differ between easy and hard trials in consistent or inconsistent patients. *These finding suggest that while some patients with schizophrenia may be more impulsive, preferring immediate rewards, aberrant decisions also contribute to greater discounting and may be linked more closely to an inability to adapt and adjust behavior to more difficult tasks or to an more stressful environment.*

IMAGING RESULTS

In our previous study,[29] similar to results of other fMRI studies of DD that used a comparable contrast of task trials versus control trials,[30-34]controls exhibited activation in an extended network that included the ventral striatum, thalamus, precuneus, and putative executive function areas such as prefrontal, dorsal anterior cingulate and inferior parietal cortex. Previously, a between-group comparison of consistent patient and control groups revealed that consistent patients had significantly less activation than consistent controls

in inferior frontal, dorsal anterior cingulate, posterior parietal and superior occipital cortices, as well as in ventral striatum and thalamus, with over-activation of left inferior insula and temporal cortices, which we interpreted as compensatory.[29] More activation also occurred in the consistent patients, when compared to the controls, in the precuneus and middle and posterior cingulate, near the areas where greater activation was found in the inconsistent patients in this study. Compensatory activation has been reported previously when patient groups were matched on performance (for examples see[8,48,49]).

However, in the present study, in which groups were not matched on performance, the between-group analysis of all DD task trials versus SMC trials revealed that inconsistent patients exhibited more activation than consistent controls. Based on their inconsistent performance, these areas of over-activation were not (successfully) compensatory. Investigation of the regions of activation differences between controls and the inconsistent patients revealed that, in consistent controls, the regions were deactivated during the task, whereas the regions were activated in inconsistent patients. In contrast to the inconsistent patients, beta values from consistent patients fell in an intermediate position between consistent controls and inconsistent patients.

Our inconsistent patients showed activation of the precuneus and posterior cingulate cortex during the task trials when contrasted to SMC trials, in contrast to consistent controls, who showed deactivation. One area of abnormal activation in inconsistent patients, the precuneus, is reportedly involved in a wide range of integrated tasks, while also exhibiting a high resting state metabolism and deactivating during cognitive tasks that are goal oriented or are part of the default mode network (for review see[50]). Greater activation in the inconsistent patients, or rather, the lack of deactivation

present in consistent controls, may suggest that an inability to redirect resources from the precuneus to more lateral task-oriented parietal and frontal cortices was a contributing factor in performance deficits. In an fMRI study, Jeong and Kubicki[51] and others[52] have reported less task-induced deactivation in patients with schizophrenia during tasks, with the suggestion that adequate task performance required deactivation of regions associated with the default mode network, in addition to activation of task-related regions. In contrast, Harrison and colleagues[53] reported more task-induced deactivation of midline cortical regions that included the precuneus, in schizophrenia, but unlike as in controls, there was no correlation between the degree of deactivation and task performance. An alternative explanation for greater activation in the precuneus and posterior cingulate in those unable to perform the task consistently is that because they experience difficulty in doing the task, they might experience more conflict-related activity.[54] More speculative is the possibility that the lack of deactivation of the precuneus leads to fewer resources directed toward the task, i.e., less focused activation of the decision-making circuit, resulting in more conflict-related activation in the posterior cingulate.

The inconsistent patients also showed more activation in comparison to consistent patients in the superior and middle frontal cortices. Abnormal prefrontal activation in schizophrenia is one of the most replicated findings, with reports of hyper- and hypo-activation associated with fluctuating task difficulty and performance (for review see [55]). In an fMRI study that specifically looked at stochasticity related to inconsistency, Luo et al[28] found that, counterintuitively, more activation occurred in the prefrontal regions in their participants who were more stochastic in their responses during a delay discounting task. They suggested that stochastic performance was due to the lack of algorithms or

rules when making decisions. In such instances, decisions were more difficult and required more input from regions associated with executive function. More activation in the inconsistent patients than consistent patients may reflect inefficient processing related to the inability to consistently perform the task. Inconsistent patients showed more activation in the precuneus, middle and posterior cingulate gyri than consistent controls and more activation in superior and middle frontal cortices than consistent patients.

STUDY LIMITATIONS

We previously reported on patients who performed the task as well as controls. Here we wanted to understand and identify variables that contributed to the inconsistent performance in this subgroup of patients with schizophrenia. However, we recognize that our fMRI results are confounded by performance differences between groups. Might these performance differences be because inconsistent patients were simply not engaged in the task? The difference in response times between task trials and SMC trials suggests that the inconsistent patients were attempting to perform the task. Another limitation is that inconsistent patients had higher rates of smoking than the consistent controls though they did not differ from the consistent patients. Another limitation is that patients in this study were on stable doses of antipsychotic medications, which may influence the BOLD signal.[56] However, understanding neural activity and behavior in the medicated patient is important to obtaining clues pointing to better cognitive therapies. We limited this study to those participants who attempted the task. Participants were excluded from the functional analyses if they exhibited too little variability in their choices. Thus, the imaging data may not generalize to all participants, although exclusionary criteria were

relatively liberal. Finally, the small number of patients in the inconsistent patient group is problematic, but the findings of activation differences are consistent and support previous studies investigating schizophrenia.[51] It should also be noted that decisions involving a delay, while dependent on value calculations, are also related to a wide range of factors such as hyperexcitability, behavioral disinhibition, and higher order cognitive functions.[57]

CONCLUSIONS

The inconsistent performance on delay discounting identified by lower R^2 values in inconsistent patients may be related to and a contributing factor to deficits in the maintenance of goal-directed behavior in those with schizophrenia. If goal-directed behaviors are dependent on consistent performance, then accurate and consistent calculation of the relative values between different behaviors, that is, deciding which behaviors contribute more to reaching goals, would be essential. If patients have difficulty in calculating value consistently, then this might contribute to their inability to set and reach meaningful goals. *This study also demonstrated that poor performance on the DD task is associated with higher activity in the precuneus and middle and posterior cingulate cortex in those patients who performed inconsistently. Taken with the results from our previous study,[29] these findings suggest that an abnormal pattern of deactivation in the precuneus, in conjunction with abnormal activation of decision-making networks, contributes to cognitive deficits in schizophrenia.*

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SUMMARY

In summary, we found that compared to controls, patients with schizophrenia were more inconsistent and had greater discounting of hypothetical money on a delay discounting task. The DD differences disappeared when we limited our analysis to only those patients who were consistent during the task. Compared to controls, patients were more aberrant in their response times with no increase in response time with task difficulty that was seen in controls. In our neuroimaging study, we found reduced activation in both reward and executive function regions in patients with schizophrenia who were consistent in their performance when compared to controls with similar performance during the DD tasks. Controls, when compared to the consistent patients, exhibited more activation to the task trials versus SMC trials during DD decisions in a broad circuit that included reward processing and executive function areas thought to provide an integrated response. Consistent patients exhibited more activation than controls to DD task trials versus SMC trials in a limited region of left insular and temporal cortices, perhaps compensatory in nature. We found an interaction between group and DD trial difficulty, where patients showed a greater difference in activation between easy and hard trials, but less activation to hard trials or easy trials, separately, than controls. Patients with schizophrenia appear to have difficulty in integrating information or modulating their behavior in response to changing task difficulty. Inconsistent patients showed greater activation to DD task trials versus SMC trials in the precuneus and posterior cingulate cortex than controls, suggestive of the "default mode"

failing to deactivate, contributing to more activation in areas associated with conflict monitoring.

CONCLUSIONS

Optimal performance during a DD task likely requires an integration of higher order cognitive function with motivational desire for immediate rewards; that is, lateral areas of the prefrontal and parietal cortices providing executive control, with reward processing of ventral striatal and ventral tegmental areas providing motivation. It is likely that integrating information necessary for higher order cognitive function with motivational desire requires coordinated activation and deactivation to modulate behavior for optimal performance during DD. Patients with schizophrenia appear to have regions of hypoactivation contributing to executive function and reward processing deficits, in addition to hyperactivation in areas associated with resting state and conflict monitoring. These results support a hypothesis, that proposes that deficits in goal-directed behavior found in schizophrenia may be related to the lack of an integrated response of multiple cortical and striatal regions.

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APPENDIX A

IRB APPROVAL FORM

Project Revision/Amendment Form

Form version: October 28, 2010

In MS Word, click in the white boxes and type your text; double-click checkboxes to check/uncheck.

- **Federal regulations require IRB approval before implementing proposed changes. See Section 14 of the IRB Guidebook for Investigators for additional information.**
- **Change means any change, in content or form, to the protocol, consent form, or any supportive materials (such as the Investigator's Brochure, questionnaires, surveys, advertisements, etc.). See Item 4 for more examples.**

1. Today's Date	04/29/11

2. Principal Investigator (PI)

Name (with degree)	Adrienne C. Lahti, M.D.	**Blazer ID**	alahti
Department	Psychiatry & Behavioral Neurobiology	**Division (if applicable)**	
Office Address	501G Sparks Center	**Office Phone**	996-6776
E-mail	alahti@uab.edu	**Fax Number**	975-4879

Contact person who should receive copies of IRB correspondence (Optional)

Name	David White	**E-Mail**	dw2777@uab.edu
Phone	996-9813	**Fax Number**	975-4879
Office Address (if different from PI)			

3. UAB IRB Protocol Identification

3.a. Protocol Number	F080108002
3.b. Protocol Title	Response to Probabilistic and Delayed Reward in Schizophrenia, Schizoaffective Disorder, and Healthy Volunteers - an fMRI Study

3.c. Current Status of Protocol—Check ONE box at left; provide numbers and dates where applicable

- ☐ **Study has not yet begun** — **No participants, data, or specimens have been entered.**
- ☒ **In progress, open to accrual** — **Number of participants, data, or specimens entered:** 56
- ☐ **Enrollment temporarily suspended by sponsor**
- ☐ **Closed to accrual, but procedures continue as defined in the protocol (therapy, intervention, follow-up visits, etc.)**
  - **Date closed:**
  - **Number of participants receiving interventions:**
  - **Number of participants in long-term follow-up only:**
- ☐ **Closed to accrual, and only data analysis continues**
  - **Date closed:**
  - **Total number of participants entered:**

4. Types of Change

Check all types of change that apply, and describe the changes in Item 5.c. or 5.d. as applicable. To help avoid delay in IRB review, please ensure that you provide the required materials and/or information for each type of change checked.

- ☐ **Protocol revision (change in the IRB-approved protocol)**
  In Item 5.c., if applicable, provide sponsor's protocol version number, amendment number, update number, etc.
- ☐ **Protocol amendment (addition to the IRB-approved protocol)**
  In Item 5.c., if applicable, provide funding application document from sponsor, as well as sponsor's protocol version number, amendment number, update number, etc.
- ☒ **Add or remove personnel**
  In Item 5.c., include name, title/degree, department/division, institutional affiliation, and role(s) in research, and address whether new personnel have any conflict of interest. See "Change in Principal Investigator" in the IRB Guidebook if the principal investigator is being changed.
  - ☐ **Add graduate student(s) or postdoctoral fellow(s) working toward thesis, dissertation, or publication**
    In Item 5.c., (a) identify these individuals by name; (b) provide the working title of the thesis, dissertation, or publication; and (c) indicate whether or not the student's analysis differs in any way from the purpose of the research described in the IRB-approved HSP (e.g., a secondary analysis of data obtained under this HSP).
- ☐ **Change in source of funding; change or add funding**
  In Item 5.c., describe the change or addition in detail, include the applicable OGCA tracking number(s), and provide a copy of the application as funded (or as submitted to the sponsor if pending). Note that some changes in funding may require a new IRB application.

☐ **Add or remove performance sites**
In Item 5.c., identify the site and location, and describe the research-related procedures performed there. If adding site(s), attach notification of permission or IRB approval to perform research there. Also include copy of subcontract, if applicable. If this protocol includes acting as the Coordinating Center for a study, attach IRB approval from any non-UAB site added.

☐ **Add or change a genetic component or storage of samples and/or data component—this could include data submissions for Genome-Wide Association Studies (GWAS)**
To assist you in revising or preparing your submission, please see the IRB Guidebook for Investigators or call the IRB office at 934-3789.

☐ **Suspend, re-open, or permanently close protocol to accrual of individuals, data, or samples (IRB approval to remain active)**
In Item 5.c., indicate the action, provide applicable dates and reasons for action; attach supporting documentation.

☐ **Report being forwarded to IRB (e.g., DSMB, sponsor or other monitor)**
In Item 5.c., include date and source of report, summarize findings, and indicate any recommendations.

☐ **Revise or amend consent, assent form(s)**
Complete Item 5.d.

☐ **Addendum (new) consent form**
Complete Item 5.d.

☐ **Add or revise recruitment materials**
Complete Item 5.d.

☐ **Other (e.g., investigator brochure)**
Indicate the type of change in the space below, and provide details in Item 5.c. or 5.d. as applicable.
Include a copy of all affected documents, with revisions highlighted as applicable.

▶

5. Description and Rationale

In Item 5.a. and 5.b, check Yes **or** No **and see instructions for** Yes **responses.**
In Item 5.c. and 5.d, describe—and explain the reason for—the change(s) noted in Item 4.

☒Yes ☐No **5.a. Are any of the participants enrolled as normal, healthy controls?**
If yes, describe in detail in Item 5.c. how this change will affect those participants.

☐Yes ☒No **5.b. Does the change affect subject participation, such as procedures, risks, costs, location of services, etc.?**
If yes, FAP-designated units complete a FAP submission and send to fap@uab.edu. Identify the FAP-designated unit in Item 5.c.
For more details on the UAB FAP, see www.uab.edu/cto.

5.c. Protocol Changes: In the space below, briefly describe—and explain the reason for—all change(s) to the protocol.

▶ We are amending the HSP in order to name Kathy Avsar as a co-principal investigator. She is currently listed as staff able to obtain consent and work on other aspects of the study not directly related to participants. Due to needed power for publication, we are having to recruit more participants than originally anticipated, which has changed our recruitment goals from 30 patients with schizophrenia or schizoaffective disorder and 30 matched healthy controls to 45 patients with schizophrenia or schizoaffective disorder and 45 matched healthy controls.

updated SICF

5.d. Consent and Recruitment Changes: In the space below,
(a) describe all changes to IRB-approved forms or recruitment materials and the reasons for them;
(b) describe the reasons for the addition of any materials (e.g., addendum consent, recruitment); and
(c) indicate either how and when you will reconsent enrolled participants or why reconsenting is not necessary (not applicable for recruitment materials).

Also, indicate the number of forms changed or added. For new forms, provide 1 copy. For revised documents, provide 3 copies:
- **a copy of the currently approved document (showing the IRB approval stamp, if applicable)**
- **a revised copy highlighting all proposed changes with "tracked" changes**
- **a revised copy for the IRB approval stamp.**

▶

Signature of Principal Investigator ____ Date 4/29/14

FOR IRB USE ONLY

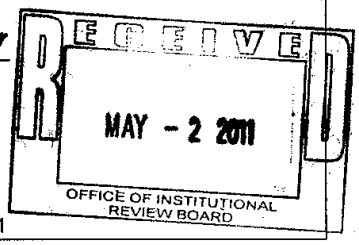
☐ Received & Noted ☑ Approved Expedited* ☐ To Convened IRB

6 Clutholen MD May 4, 2011
Signature (Chair, Vice-Chair, Designee) Date

DOLA 10-27-10 only increase in N

Change to Expedited Category Y / N / NA

*No change to IRB's previous determination of approval criteria at 45 CFR 46.111 or 21 CFR 56.111



APPENDIX B

PHONE INTERVIEW

Screener Initials: _____ Reviewer Initials/Date: _____

SCREENING INTERVIEW

Name (first, middle, last):_____

Date(s) and Time(s) of contact(s):_____

Phone (H): _____ Is this your permanent phone number? **Y N**

(W): _____(Fax?)_____

Email/ Alternate phone: _____

Mailing Address:_____

Sex: M F

Hello, may I speak with _____ please? my name is _____, and I'm calling on behalf of the UAB Department of Psychiatry. We are conducting an important research study. If you are eligible for the study and complete the tasks involved, you will receive up to $150 as an appreciation of your participation.

Now let me tell you a little more about the study. The fMRI (functional Magnetic Resonance Imaging) and MRS (Magnetic Resonance Spectroscopy) studies are designed to help research scientists and physicians better understand what parts of the brain are

used for memory and judgment. Would you be willing to answer a couple of questions to see if you might qualify for this study?

Yes

No [Terminate]

To participate in the study, you will need to spend about 2-4 hours with a professional clinician to answer some questions to make sure you qualify for the study. We would also like to collect a small sample of your blood (about 3 tablespoons) for scientific research reasons. The blood draw is optional and will not exclude you from participation in our study. The last phase will involve taking fMRI/MRS images of your brain while you perform cognitive tasks, which will take approximately two hours. Women who are pregnant cannot participate in this study. Also, women of child-bearing potential who wish to participate, will be required to take a urine-based pregnancy test on the day the fMRI and MRS scans are performed.

SC1. Would you like to participate in this study?

Yes

No [Terminate]

Great. Thank you for agreeing to participate in this important research. Now let me ask you some questions to determine if you are eligible for the study. You have the right to skip any questions you don't want to answer. All of your answers will be kept confidential.

These questions will take approximately 15 minutes to answer.

SC2. How old are you? _____

Is the individual less than, or equal to, 18 years old? Y (EXCLUDE) N

[OTHER SCREENING QUESTIONS]

---

1. Do you have any vision problems that could make it difficult for you to see words or small objects on a computer screen a foot away from you? **Y (EXCLUDE) N**

---

2. Do you have any physical problems that make it difficult for you to move your hands or arms? **Y (EXCLUDE)** **N**

---

3. Do you have any metal objects in your body **Y (EXCLUDE)** **N**

Do you weigh over 300 pounds? **Y (EXCLUDE)** **N**

---

4. Have you ever bumped or hit your head resulting in a concussion or loss of consciousness?

Y **N**

If yes:

- Were you unconscious? **Y** **N**
- Did you or anyone else notice any change in your personality after this occurred?

  Y (EXCLUDE) ***N***
- Did you experience any depression or other mood changes after it occurred?

  Y (EXCLUDE) ***N***
- Did you have any continuing brain or nerve symptoms resulting from the accident, such as severe memory loss lasting more than 1 week, or muscle weakness?

  Y (EXCLUDE) **N**
- Did you have any tests, like neuroimaging (CT Scan or MRI) or EEG, which showed any abnormalities? **Y (EXCLUDE)** **N**

---

5. Have you ever been told by a doctor that you have had any of the following neurological problems or diseases:

o Alzheimer's Disease	**Y (EXCLUDE)**	**N**
o Brain tumor	**Y (EXCLUDE)**	**N**
o Blindness	**Y (EXCLUDE)**	**N**
o Huntington's Disease	**Y (EXCLUDE)**	**N**
o Multiple Sclerosis	**Y (EXCLUDE)**	**N**
o Quadraplegia	**Y (EXCLUDE)**	**N**
o Parkinson's	**Y (EXCLUDE)**	**N**
o Seizure disorder (since age 18)	**Y (EXCLUDE)**	**N**
o Stroke (cerebral vascular accident)	**Y (EXCLUDE)**	**N**
o Tardive dyskinesia	**Y (EXCLUDE)**	**N**

---

6. Have you ever had any of the following medical diagnoses or conditions:

o Cirrhosis	**Y (EXCLUDE)**	**N**
o Hepatic encephalopathy	**Y (EXCLUDE)**	**N**
o Kidney failure	**Y (EXCLUDE)**	**N**
o Lupus	**Y (EXCLUDE)**	**N**

---

7. Have you ever seen a professional, such as a psychiatrist or mental health worker, for emotional problems, your nerves, or the way you were feeling or acting?

Y **N**

If yes: Have you ever been told that you had any of the following?

o Schizophrenia	**Y (EXCLUDE)**	**N**
o Any other disorder with the term "schizo" in it?	**Y (EXCLUDE)**	**N**
o Voices	**Y (EXCLUDE)**	**N**
o Visions	**Y (EXCLUDE)**	**N**
o Delusions	**Y (EXCLUDE)**	**N**
o Paranoia or paranoid	**Y (EXCLUDE)**	**N**

- Psychotic disorder or psychosis **Y (EXCLUDE) N**
- **Other:**_____

NOTE: Some of the above terms are not official "diagnoses" but are some phrases that people might use to describe relevant experiences.

8. In the past month, have you been admitted to a hospital because of problems with your mood, emotions, or how you were acting? **Y (EXCLUDE) N**

---

9. In the last 6 months, have you received electro-convulsive treatment (ECT, shock treatments)?
   Y (EXCLUDE) N

---

10. In the past month, have you received an **INCREASE** in any medications you are prescribed for your nerves or for any emotional or mental problems? **Y (EXCLUDE) N**

---

11. Have you ever had a drink of alcohol? **Y N**
    If yes:

    In the last 6 months, have you sought or received treatment for a drinking problem?

    Y (EXCLUDE) N

---

12. Have you ever used any drugs to feel good or high, or to feel more active or alert, or when they were not prescribed to you? Or, have you ever used a prescribed drug in larger quantities or for longer than prescribed?
    If yes:

What drugs: _____

Period of time: _____

In the last 6 months, have you sought or received treatment for a drug problem?

Y (EXCLUDE) N

---

13. How many years were you in school?
    a. 8 years (through eighth grade)
    b. 9 – 12 years (including high school graduates)
    c. 12 – 16 years (some college, and including college graduates)
    d. 16 – 16+ years (post-graduate work)

---

14. How do you define your race?
    a. Caucasian (white)
    b. African American (black)
    c. Asian
    d. Hispanic or Latino
    e. Other

---

15. What were the occupations of your parents?

Mother: _____

Father: _____

---

16. Do you smoke cigarettes?
If yes:

How many packs do you smoke per day? _____

(record exact answer)

IF EXCLUDED, DISCONTINUE THE INTERVIEW AND SAY: These are all the questions we will need to ask you. Thank you for your time and participation in our research program; however based on your responses you do not meet criteria for your being a participant in our study. However we thank you for your time and appreciate your willingness to help us in our research. Do you have any further questions of me? **If not thank you and Good Bye.**

IF NOT EXCLUDED, SAY: It looks like you are eligible to participate in this study. The next stage will involve coming to the study site for an interview, and take a memory and judgment test. We also request you allow us to obtain a small amount of your blood (approximately 3-tablespoons), but this is not required for study participation.

13. Would you like to participate? Yes___ No___ (If no, be sure to thank caller .)

If YES, SAY: Thank you for agreeing to participate in this important study. A study staff member will be in touch with you within the next 7 days to schedule an appointment.

What are the days and times that are best for contacting you by phone?

1)_____ between _____ and _____

2)_____between _____and _____

3)_____between _____and _____

Over

Thank you for agreeing to participate in this important study. To refresh your memory of what we talked about, the study will require that you complete an interview that may take 2-3 hours, a computer assisted test that may take 1-2 hours, and provide a sample of your blood. The blood draw is optional and will not disqualify you from participating in our study. The last phase of the study will involve having fMRI and MRS images taken of your brain while you perform cognitive tasks. In total, you may expect to spend 4-5 hours with a clinician and 2 hours in the fMRI/MRS machine.

Thank you for your time today. Someone will be in touch with you in the near future.

[READ IF NECESSARY]: If you have questions about this study, you may call Dr. Adrienne Lahti at University of Alabama at 205-996-7171. If you have any questions about your rights as a study participant, you may contact Ms. Sheila Moore, Director of the Office of the Institutional Review Board for Human Use, University of Alabama at Birmingham. Ms Moore can be reached at 205-934-3789 or 1-800 -822-8816, press the option for an operator/attendant and ask for extension 4-3789 between the hours of 8:00 a.m. and 5:00 p.m. CT, Monday through Friday.

APPENDIX C

LAB AND MAGNET TASKS

Laboratory Task

Lab task							
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
1	$20 now	$50 in 94 days	0.016	55	$30 now	$31 in 83 days	0.0004
2	$34 in 5 days	$28 now	0.041	56	$0 now	$0 now	
3	$54 in 96 days	$52 now	0.0004	57	$74 in 69 days	$72 now	0.0004
4	$49 now	$60 in 2 days	0.1	58	$0 now	$0 now	
5	$32 now	$76 in 86 days	0.016	59	$55 in 58 days	$52 now	0.001
6	$4 now	$36 in 80 days	0.1	60	$35 in 1 day	$30 now	0.25
7	$73 in 70 days	$71 now	0.0004	61	$18 now	$78 in 81 days	0.041
8	$8 now	$84 in 95 days	0.1	62	$2 now	$53 in 102 days	0.25
9	$38 in 90 days	$31 now	0.0025	63	$56 in 28 days	$48 now	0.006
10	$36 now	$55 in 88 days	0.006	64	$67 now	$80 in 78 days	0.0025
11	$63 now	$76 in 5 days	0.041	65	$56 in 9 days	$49 now	0.016
12	$78 in 83 days	$72 now	0.001	66	$49 now	$50 in 51 days	0.0004
13	$37 in 37 days	$30 now	0.1	67	$31 now	$34 in 39 days	0.0025
14	$12 now	$60 in 98 days	0.041	68	$0 now	$0 now	
15	$0 now	$0 now		69	$60 in 76 days	$3 now	0.25
16	$78 in 10 days	$67 now	0.016	70	$68 now	$81 in 12 days	0.016
17	$46 now	$72 in 94 days	0.006	71	$36 in 85 days	$8 now	0.041
18	$30 in 86 days	$29 now	0.0004	72	$59 in 74 days	$7 now	0.1
19	$31 now	$79 in 97 days	0.016	73	$32 now	$35 in 38 days	0.0025
20	$67 now	$83 in 1 day	0.25	74	$61 in 60 days	$53 now	0.0025
21	$73 now	$75 in 68 days	0.0004	75	$54 in 11 days	$46 now	0.016
22	$0 now	$0 now		76	$50 now	$61 in 1 day	0.25
23	$86 in 99 days	$69 now	0.0025	77	$50 now	$62 in 6 days	0.041
24	$0 now	$0 now		78	$52 in 79 days	$23 now	0.016
25	$62 in 2 days	$51 now	0.1	79	$24 now	$37 in 90 days	0.006
26	$37 in 82 days	$16 now	0.016	80	$74 in 68 days	$68 now	0.001
27	$49 now	$59 in 82 days	0.0025	81	$29 now	$36 in 97 days	0.0025
28	$32 now	$33 in 78 days	0.0004	82	$64 now	$79 in 6 days	0.041
29	$51 in 50 days	$50 now	0.0004	83	$9 now	$81 in 80 days	0.1
30	$48 now	$58 in 1 day	0.25	84	$77 in 99 days	$3 now	0.25
31	$86 in 3 days	$67 now	0.1	85	$37 in 2 days	$31 now	0.1
32	$0 now	$0 now		86	$29 now	$32 in 17 days	0.006
33	$79 in 97 days	$72 now	0.001	87	$50 now	$58 in 27 days	0.006
34	$0 now	$0 now		88	$41 in 88 days	$17 now	0.016
35	$31 now	$38 in 6 days	0.041	89	$51 now	$58 in 55 days	0.0025
36	$0 now	$0 now		90	$76 in 103 days	$73 now	0.0004
37	$13 now	$58 in 84 days	0.041	91	$0 now	$0 now	
38	$75 in 88 days	$49 now	0.006	92	$26 now	$28 in 77 days	0.001
39	$75 in 87 days	$69 now	0.001	93	$7 now	$33 in 91 days	0.041
40	$69 now	$82 in 75 days	0.0025	94	$56 in 98 days	$51 now	0.001
41	$30 in 116 days	$1 now	0.25	95	$0 now	$0 now	
42	$77 in 25 days	$67 now	0.006	96	$23 now	$36 in 94 days	0.006
43	$37 in 20 days	$28 now	0.016	97	$34 in 76 days	$33 now	0.0004
44	$51 now	$53 in 39 days	0.001	98	$53 in 98 days	$51 now	0.0004
45	$54 in 80 days	$50 now	0.001	99	$35 in 61 days	$33 now	0.001
46	$32 now	$34 in 63 days	0.001	100	$0 now	$0 now	
47	$6 now	$61 in 92 days	0.1	101	$44 in 84 days	$2 now	0.25
48	$63 in 8 days	$48 now	0.041	102	$68 now	$79 in 1 day	0.25
49	$52 in 96 days	$33 now	0.006	103	$4 now	$81 in 77 days	0.25
50	$66 now	$82 in 2 days	0.1	104	$83 in 88 days	$68 now	0.0025
51	$75 in 98 days	$15 now	0.041	105	$31 now	$34 in 16 days	0.006
52	$32 now	$35 in 94 days	0.001	106	$36 in 1 day	$32 now	0.25
53	$45 now	$56 in 98 days	0.0025	107	$4 now	$39 in 88 days	0.1
54	$38 in 22 days	$28 now	0.016	108	$65 now	$74 in 23 days	0.006

Magnet Tasks

Target K 0.0018							
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
1	$26 now	$30 in 81 days	0.0018	41	$58 in 55 days	$51 now	0.0025
2	$0 now	$0 now		42	$0 now	$0 now	
3	$34 in 13 days	$30 now	0.011	43	$32 in 79 days	$28 now	0.0018
4	$18 now	$34 in 82 days	0.011	44	$73 now	$76 in 103 days	0.0004
5	$71 in 77 days	$69 now	0.0004	45	$0 now	$0 now	
6	$36 now	$72 in 90 days	0.011	46	$38 in 97 days	$35 now	0.001
7	$0 now	$0 now		47	$52 now	$54 in 96 days	0.0004
8	$69 now	$76 in 96 days	0.001	48	$79 in 97 days	$72 now	0.001
9	$0 now	$0 now		49	$0 now	$0 now	
10	$76 in 16 days	$65 now	0.011	50	$64 now	$73 in 13 days	0.011
11	$63 now	$71 in 50 days	0.0025	51	$35 in 96 days	$17 now	0.011
12	$74 in 86 days	$64 now	0.0018	52	$48 now	$55 in 84 days	0.0018
13	$29 in 83 days	$28 now	0.0004	53	$31 now	$34 in 39 days	0.0025
14	$0 now	$0 now		54	$75 in 97 days	$64 now	0.0018
15	$51 in 91 days	$42 now	0.0025	55	$0 now	$0 now	
16	$29 now	$30 in 86 days	0.0004	56	$31 now	$38 in 19 days	0.011
17	$0 now	$0 now		57	$0 now	$0 now	
18	$53 in 56 days	$46 now	0.0025	58	$57 in 91 days	$52 now	0.001
19	$27 now	$29 in 48 days	0.0018	59	$34 in 76 days	$33 now	0.0004
20	$34 now	$36 in 74 days	0.001	60	$0 now	$0 now	
21	$0 now	$0 now		61	$72 now	$78 in 88 days	0.001
22	$52 now	$56 in 75 days	0.001	62	$47 now	$54 in 13 days	0.011
23	$76 in 79 days	$67 now	0.0018	63	$77 in 80 days	$67 now	0.0018
24	$0 now	$0 now		64	$28 now	$54 in 84 days	0.011
25	$33 in 36 days	$30 now	0.0025	65	$0 now	$0 now	
26	$0 now	$0 now		66	$32 now	$34 in 79 days	0.001
27	$50 now	$51 in 50 days	0.0004	67	$44 now	$54 in 87 days	0.0025
28	$71 now	$73 in 70 days	0.0004	68	$75 in 55 days	$66 now	0.0025
29	$35 in 88 days	$32 now	0.001	69	$0 now	$0 now	
30	$0 now	$0 now		70	$64 now	$78 in 85 days	0.0025
31	$75 in 87 days	$69 now	0.001	71	$50 in 51 days	$49 now	0.0004
32	$62 now	$73 in 70 days	0.0025	72	$0 now	$0 now	
33	$53 in 98 days	$51 now	0.0004	73	$73 now	$75 in 68 days	0.0004
34	$49 now	$58 in 16 days	0.011	74	$32 in 52 days	$29 now	0.0018
35	$0 now	$0 now		75	$77 in 91 days	$38 now	0.011
36	$56 in 98 days	$51 now	0.001	76	$51 now	$55 in 78 days	0.001
37	$25 now	$51 in 93 days	0.011	77	$0 now	$0 now	
38	$34 in 94 days	$28 now	0.0025	78	$35 in 94 days	$34 now	0.0004
39	$53 in 47 days	$49 now	0.0018	79	$53 now	$58 in 56 days	0.0018
40	$46 now	$54 in 95 days	0.0018	80	$36 in 97 days	$29 now	0.0025

Target K 0.0018	(continued)						
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
81	$0 now	$0 now		121	$55 in 58 days	$48 now	0.0025
82	$19 now	$36 in 85 days	0.011	122	$29 now	$31 in 70 days	0.001
83	$30 now	$36 in 18 days	0.011	123	$0 now	$0 now	
84	$0 now	$0 now		124	$75 in 14 days	$65 now	0.011
85	$37 in 87 days	$30 now	0.0025	125	$54 now	$59 in 53 days	0.0018
86	$52 in 53 days	$46 now	0.0025	126	$0 now	$0 now	
87	$27 now	$28 in 91 days	0.0004	127	$81 in 86 days	78 now	0.0004
88	$35 in 46 days	$32 now	0.0018	128	$71 now	$74 in 98 days	0.0004
89	$0 now	$0 now		129	$80 in 81 days	$70 now	0.0018
90	$35 in 38 days	$32 now	0.0025	130	$47 now	$51 in 88 days	0.001
91	$49 now	$51 in 91 days	0.0004	131	$0 now	$0 now	
92	$60 now	$76 in 103 days	0.0025	132	$37 in 90 days	$32 now	0.0018
93	$50 now	$54 in 80 days	0.001	133	$36 in 83 days	$33 now	0.001
94	$0 now	$0 now		134	$0 now	$0 now	
95	$78 in 85 days	$75 now	0.0004	135	$47 now	$57 in 20 days	0.011
96	$30 now	$33 in 93 days	0.001	136	$29 now	$35 in 20 days	0.011
97	$0 now	$0 now		137	$39 in 41 days	$35 now	0.0025
98	$74 in 82 days	$68 now	0.001	138	$0 now	$0 now	
99	$79 in 92 days	$68 now	0.0018	139	$32 now	$33 in 78 days	0.0004
100	$0 now	$0 now		140	$38 in 90 days	$31 now	0.0025
101	$39 in 77 days	$36 now	0.001	141	$37 in 95 days	$18 now	0.011
102	$31 now	$32 in 89 days	0.0004	142	$70 now	$81 in 89 days	0.0018
103	$45 now	$56 in 98 days	0.0025	143	$0 now	$0 now	
104	$0 now	$0 now		144	$65 now	$74 in 52 days	0.0025
105	$69 now	$78 in 74 days	0.0018	145	$0 now	$0 now	
106	$53 in 17 days	$45 now	0.011	146	$49 now	$53 in 77 days	0.001
107	$0 now	$0 now		147	$74 in 98 days	$59 now	0.0025
108	$80 in 95 days	$39 now	0.011	148	$0 now	$0 now	
109	$30 now	$35 in 93 days	0.0018	149	$74 now	$81 in 92 days	0.001
110	$76 in 89 days	$70 now	0.001	150	$55 in 55 days	$54 now	0.0004
111	$0 now	$0 now		151	$80 in 92 days	$73 now	0.001
112	$71 now	$81 in 58 days	0.0025	152	$0 now	$0 now	
113	$58 in 74 days	$54 now	0.001	153	$33 now	$36 in 55 days	0.0018
114	$51 now	$59 in 91 days	0.0018	154	$55 in 89 days	$53 now	0.0004
115	$50 in 48 days	$46 now	0.0018	155	$30 now	$31 in 83 days	0.0004
116	$0 now	$0 now		156	$78 in 84 days	$41 now	0.011
117	$59 in 97 days	$29 now	0.011	157	$45 now	$55 in 85 days	0.0025
118	$52 now	$53 in 58 days	0.0004	158	$0 now	$0 now	
119	$70 now	$79 in 12 days	0.011	159	$55 in 89 days	$28 now	0.011
120	$74 in 69 days	$72 now	0.0004	160	$49 now	$58 in 98 days	0.0018

Target K 0.0025							
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
1	$28 now	$34 in 94 days	0.0025	41	$55 in 44 days	$48 now	0.0033
2	$0 now	$0 now		42	$0 now	$0 now	
3	$33 in 9 days	$29 now	0.016	43	$36 in 97 days	$29 now	0.0025
4	$14 now	$32 in 83 days	0.016	44	$71 now	$76 in 103 days	0.0007
5	$71 in 77 days	$67 now	0.0007	45	$0 now	$0 now	
6	$31 now	$75 in 91 days	0.016	46	$37 in 90 days	$32 now	0.0018
7	$0 now	$0 now		47	$51 now	$54 in 96 days	0.0007
8	$67 now	$77 in 80 days	0.0018	48	$79 in 92 days	$68 now	0.0018
9	$0 now	$0 now		49	$0 now	$0 now	
10	$78 in 10 days	$67 now	0.016	50	$65 now	$74 in 9 days	0.016
11	$65 now	$74 in 42 days	0.0033	51	$36 in 92 days	$15 now	0.016
12	$73 in 70 days	$62 now	0.0025	52	$44 now	$54 in 87 days	0.0025
13	$29 in 83 days	$27 now	0.0007	53	$31 now	$34 in 29 days	0.0033
14	$0 now	$0 now		54	$74 in 98 days	$59 now	0.0025
15	$54 in 89 days	$42 now	0.0033	55	$0 now	$0 now	
16	$28 now	$30 in 86 days	0.0007	56	$33 now	$38 in 10 days	0.016
17	$0 now	$0 now		57	$0 now	$0 now	
18	$50 in 41 days	$44 now	0.0033	58	$59 in 91 days	$51 now	0.0018
19	$30 now	$33 in 36 days	0.0025	59	$34 in 76 days	$32 now	0.0007
20	$32 now	$35 in 46 days	0.0018	60	$0 now	$0 now	
21	$0 now	$0 now		61	$69 now	$78 in 74 days	0.0018
22	$53 now	$58 in 56 days	0.0018	62	$45 now	$52 in 10 days	0.016
23	$71 in 50 days	$63 now	0.0025	63	$74 in 52 days	$65 now	0.0025
24	$0 now	$0 now		64	$20 now	$50 in 94 days	0.016
25	$35 in 28 days	$32 now	0.0033	65	$0 now	$0 now	
26	$0 now	$0 now		66	$29 now	$32 in 52 days	0.0018
27	$48 now	$51 in 88 days	0.0007	67	$42 now	$56 in 98 days	0.0033
28	$70 now	$73 in 70 days	0.0007	68	$71 in 38 days	$63 now	0.0033
29	$32 in 79 days	$28 now	0.0018	69	$0 now	$0 now	
30	$0 now	$0 now		70	$61 now	$78 in 85 days	0.0033
31	$74 in 86 days	$64 now	0.0018	71	$50 in 82 days	$47 now	0.0007
32	$59 now	$73 in 70 days	0.0033	72	$0 now	$0 now	
33	$53 in 98 days	$50 now	0.0007	73	$72 now	$75 in 68 days	0.0007
34	$47 now	$55 in 11 days	0.016	74	$34 in 39 days	$31 now	0.0025
35	$0 now	$0 now		75	$79 in 97 days	$31 now	0.016
36	$58 in 98 days	$49 now	0.0018	76	$49 now	$53 in 47 days	0.0018
37	$24 now	$58 in 88 days	0.016	77	$0 now	$0 now	
38	$36 in 97 days	$27 now	0.0033	78	$35 in 94 days	$33 now	0.0007
39	$53 in 56 days	$46 now	0.0025	79	$48 now	$55 in 58 days	0.0025
40	$42 now	$51 in 91 days	0.0025	80	$38 in 90 days	$29 now	0.0033

Target K 0.0025	(continued)						
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
81	$0 now	$0 now		121	$53 in 46 days	$46 now	0.0033
82	$17 now	$41 in 88 days	0.016	122	$27 now	$29 in 48 days	0.0018
83	$31 now	$37 in 11 days	0.016	123	$0 now	$0 now	
84	$0 now	$0 now		124	$81 in 12 days	$68 now	0.016
85	$34 in 94 days	$26 now	0.0033	125	$51 now	$58 in 55 days	0.0025
86	$51 in 40 days	$45 now	0.0033	126	$0 now	$0 now	
87	$26 now	$28 in 91 days	0.0007	127	$81 in 86 days	$76 now	0.0007
88	$35 in 38 days	$32 now	0.0025	128	$69 now	$74 in 98 days	0.0007
89	$0 now	$0 now		129	$81 in 58 days	$71 now	0.0025
90	$36 in 28 days	$33 now	0.0033	130	$46 now	$54 in 95 days	0.0018
91	$48 now	$51 in 91 days	0.0007	131	$0 now	$0 now	
92	$56 now	$74 in 98 days	0.0033	132	$38 in 90 days	$31 now	0.0025
93	$48 now	$55 in 84 days	0.0018	133	$35 in 93 days	$30 now	0.0018
94	$0 now	$0 now		134	$0 now	$0 now	
95	$78 in 85 days	$74 now	0.0007	135	$47 now	$54 in 9 days	0.016
96	$26 now	$30 in 81 days	0.0018	136	$30 now	$35 in 11 days	0.016
97	$0 now	$0 now		137	$33 in 30 days	$30 now	0.0033
98	$76 in 79 days	$67 now	0.0018	138	$0 now	$0 now	
99	$76 in 103 days	$60 now	0.0025	139	$31 now	$33 in 78 days	0.0007
100	$0 now	$0 now		140	$37 in 87 days	$29 now	0.0033
101	$36 in 55 days	$33 now	0.0018	141	$37 in 82 days	$16 now	0.016
102	$30 now	$32 in 89 days	0.0007	142	$64 now	$78 in 85 days	0.0025
103	$45 now	$58 in 88 days	0.0033	143	$0 now	$0 now	
104	$0 now	$0 now		144	$66 now	$75 in 41 days	0.0033
105	$66 now	$75 in 55 days	0.0025	145	$0 now	$0 now	
106	$59 in 9 days	$52 now	0.016	146	$46 now	$50 in 48 days	0.0018
107	$0 now	$0 now		147	$76 in 103 days	$57 now	0.0033
108	$76 in 86 days	$32 now	0.016	148	$0 now	$0 now	
109	$30 now	$37 in 87 days	0.0025	149	$70 now	$81 in 89 days	0.0018
110	$75 in 97 days	$64 now	0.0018	150	$55 in 75 days	$52 now	0.0007
111	$0 now	$0 now		151	$80 in 81 days	$70 now	0.0018
112	$71 now	$81 in 43 days	0.0033	152	$0 now	$0 now	
113	$59 in 53 days	$54 now	0.0018	153	$35 now	$39 in 41 days	0.0025
114	$45 now	$56 in 98 days	0.0025	154	$55 in 89 days	$52 now	0.0007
115	$52 in 53 days	$46 now	0.0025	155	$29 now	$31 in 83 days	0.0007
116	$0 now	$0 now		156	$77 in 84 days	$33 now	0.016
117	$52 in 83 days	$22 now	0.016	157	$40 now	$53 in 94 days	0.0033
118	$50 now	$53 in 77 days	0.0007	158	$0 now	$0 now	
119	$65 now	$79 in 13 days	0.016	159	$55 in 98 days	$21 now	0.016
120	$74 in 69 days	$71 now	0.0007	160	$45 now	$55 in 85 days	0.0025

Target K 0.0033							
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
1	$27 now	$36 in 97 days	0.0033	41	$57 in 19 days	$51 now	0.006
2	$0 now	$0 now		42	$0 now	$0 now	
3	$32 in 5 days	$28 now	0.028	43	$38 in 90 days	$29 now	0.0033
4	$9 now	$33 in 98 days	0.028	44	$71 now	$76 in 103 days	0.0007
5	$71 in 77 days	$67 now	0.0007	45	$0 now	$0 now	
6	$21 now	$73 in 87 days	0.028	46	$38 in 90 days	$31 now	0.0025
7	$0 now	$0 now		47	$51 now	$54 in 96 days	0.0007
8	$65 now	$74 in 52 days	0.0025	48	$76 in 103 days	$60 now	0.0025
9	$0 now	$0 now		49	$0 now	$0 now	
10	$78 in 6 days	$67 now	0.028	50	$65 now	$79 in 8 days	0.028
11	$64 now	$74 in 27 days	0.006	51	$34 in 82 days	$10 now	0.028
12	$73 in 70 days	$59 now	0.0033	52	$42 now	$56 in 98 days	0.0033
13	$29 in 83 days	$27 now	0.0007	53	$29 now	$34 in 32 days	0.006
14	$0 now	$0 now		54	$76 in 103 days	$57 now	0.0033
15	$52 in 96 days	$33 now	0.006	55	$0 now	$0 now	
16	$28 now	$30 in 86 days	0.0007	56	$28 now	$38 in 12 days	0.028
17	$0 now	$0 now		57	$0 now	$0 now	
18	$56 in 28 days	$48 now	0.006	58	$56 in 98 days	$45 now	0.0025
19	$32 now	$35 in 28 days	0.0033	59	$34 in 76 days	$32 now	0.0007
20	$32 now	$35 in 38 days	0.0025	60	$0 now	$0 now	
21	$0 now	$0 now		61	$66 now	$75 in 55 days	0.0025
22	$48 now	$55 in 58 days	0.0025	62	$44 now	$54 in 8 days	0.028
23	$74 in 42 days	$65 now	0.0033	63	$75 in 41 days	$66 now	0.0033
24	$0 now	$0 now		64	$13 now	$50 in 98 days	0.028
25	$33 in 20 days	$29 now	0.006	65	$0 now	$0 now	
26	$0 now	$0 now		66	$31 now	$34 in 39 days	0.0025
27	$48 now	$51 in 88 days	0.0007	67	$35 now	$53 in 87 days	0.006
28	$70 now	$73 in 70 days	0.0007	68	$78 in 23 days	$69 now	0.006
29	$36 in 97 days	$29 now	0.0025	69	$0 now	$0 now	
30	$0 now	$0 now		70	$53 now	$81 in 89 days	0.006
31	$73 in 70 days	$62 now	0.0025	71	$50 in 82 days	$47 now	0.0007
32	$46 now	$73 in 98 days	0.006	72	$0 now	$0 now	
33	$53 in 98 days	$50 now	0.0007	73	$72 now	$75 in 68 days	0.0007
34	$48 now	$58 in 7 days	0.028	74	$34 in 29 days	$31 now	0.0033
35	$0 now	$0 now		75	$75 in 97 days	$20 now	0.028
36	$55 in 85 days	$45 now	0.0025	76	$46 now	$53 in 56 days	0.0025
37	$14 now	$52 in 96 days	0.028	77	$0 now	$0 now	
38	$32 in 96 days	$20 now	0.006	78	$35 in 94 days	$33 now	0.0007
39	$50 in 41 days	$44 now	0.0033	79	$46 now	$53 in 46 days	0.0033
40	$42 now	$54 in 89 days	0.0033	80	$35 in 83 days	$23 now	0.006

Target K 0.0033	(continued)						
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
81	$0 now	$0 now		121	$53 in 25 days	$46 now	0.006
82	$10 now	$37 in 95 days	0.028	122	$30 now	$33 in 36 days	0.0025
83	$30 now	$35 in 6 days	0.028	123	$0 now	$0 now	
84	$0 now	$0 now		124	$77 in 5 days	$68 now	0.028
85	$36 in 94 days	$23 now	0.006	125	$48 now	$55 in 44 days	0.0033
86	$55 in 22 days	$49 now	0.006	126	$0 now	$0 now	
87	$26 now	$28 in 91 days	0.0007	127	$81 in 86 days	76 now	0.0007
88	$36 in 28 days	$33 now	0.0033	128	$69 now	$74 in 98 days	0.0007
89	$0 now	$0 now		129	$81 in 43 days	$71 now	0.0033
90	$37 in 23 days	$33 now	0.006	130	$42 now	$51 in 91 days	0.0025
91	$48 now	$51 in 91 days	0.0007	131	$0 now	$0 now	
92	$49 now	$77 in 95 days	0.006	132	$37 in 87 days	$29 now	0.0033
93	$44 now	$54 in 87 days	0.0025	133	$37 in 87 days	$30 now	0.0025
94	$0 now	$0 now		134	$0 now	$0 now	
95	$78 in 85 days	$74 now	0.0007	135	$45 now	$51 in 5 days	0.028
96	$28 now	$34 in 94 days	0.0025	136	$29 now	$39 in 13 days	0.028
97	$0 now	$0 now		137	$38 in 27 days	$33 now	0.006
98	$71 in 50 days	$63 now	0.0025	138	$0 now	$0 now	
99	$74 in 98 days	$56 now	0.0033	139	$31 now	$33 in 78 days	0.0007
100	$0 now	$0 now		140	$38 in 88 days	$25 now	0.006
101	$39 in 41 days	$35 now	0.0025	141	$38 in 88 days	$11 now	0.028
102	$30 now	$32 in 89 days	0.0007	142	$61 now	$78 in 85 days	0.0033
103	$36 now	$55 in 88 days	0.006	143	$0 now	$0 now	
104	$0 now	$0 now		144	$68 now	$75 in 18 days	0.006
105	$63 now	$71 in 38 days	0.0033	145	$0 now	$0 now	
106	$56 in 11 days	$43 now	0.028	146	$46 now	$52 in 53 days	0.0025
107	$0 now	$0 now		147	$76 in 84 days	$51 now	0.006
108	$76 in 81 days	$23 now	0.028	148	$0 now	$0 now	
109	$26 now	$34 in 94 days	0.0033	149	$64 now	$78 in 85 days	0.0025
110	$74 in 98 days	$59 now	0.0025	150	$55 in 75 days	$52 now	0.0007
111	$0 now	$0 now		151	$81 in 58 days	$71 now	0.0025
112	$70 now	$80 in 25 days	0.006	152	$0 now	$0 now	
113	$58 in 55 days	$51 now	0.0025	153	$30 now	$33 in 30 days	0.0033
114	$45 now	$58 in 88 days	0.0033	154	$55 in 89 days	$52 now	0.0007
115	$51 in 40 days	$45 now	0.0033	155	$29 now	$31 in 83 days	0.0007
116	$0 now	$0 now		156	$79 in 92 days	$22 now	0.028
117	$59 in 90 days	$17 now	0.028	157	$38 now	$57 in 81 days	0.006
118	$50 now	$53 in 77 days	0.0007	158	$0 now	$0 now	
119	$63 now	$80 in 10 days	0.028	159	$53 in 84 days	$16 now	0.028
120	$74 in 69 days	$71 now	0.0007	160	$40 now	$53 in 94 days	0.0033

Target K 0.006							
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
1	$20 now	$32 in 96 days	0.006	41	$58 in 16 days	$49 now	0.011
2	$0 now	$0 now		42	$0 now	$0 now	.
3	$34 in 5 days	$28 now	0.041	43	$35 in 83 days	$23 now	0.006
4	$6 now	$32 in 99 days	0.041	44	$72 now	$79 in 97 days	0.001
5	$74 in 82 days	$68 now	0.001	45	$0 now	$0 now	.
6	$15 now	$75 in 98 days	0.041	46	$38 in 90 days	$29 now	0.0033
7	$0 now	$0 now	.	47	$51 now	$56 in 98 days	0.001
8	$65 now	$74 in 42 days	0.0033	48	$76 in 103 days	$57 now	0.0033
9	$0 now	$0 now	.	49	$0 now	$0 now	.
10	$79 in 6 days	$63 now	0.041	50	$63 now	$76 in 5 days	0.041
11	$64 now	$73 in 13 days	0.011	51	$35 in 90 days	$7 now	0.041
12	$73 in 98 days	$46 now	0.006	52	$35 now	$53 in 87 days	0.006
13	$31 in 70 days	$29 now	0.001	53	$29 now	$35 in 20 days	0.011
14	$0 now	$0 now	.	54	$76 in 84 days	$51 now	0.006
15	$51 in 93 days	$25 now	0.011	55	$0 now	$0 now	.
16	$32 now	$35 in 88 days	0.001	56	$31 now	$39 in 6 days	0.041
17	$0 now	$0 now	.	57	$0 now	$0 now	.
18	$54 in 13 days	$47 now	0.011	58	$56 in 98 days	$42 now	0.0033
19	$29 now	$33 in 20 days	0.006	59	$39 in 77 days	$36 now	0.001
20	$32 now	$35 in 28 days	0.0033	60	$0 now	$0 now	.
21	$0 now	$0 now	.	61	$66 now	$75 in 41 days	0.0033
22	$45 now	$51 in 40 days	0.0033	62	$46 now	$54 in 4 days	0.041
23	$74 in 27 days	$64 now	0.006	63	$75 in 18 days	$68 now	0.006
24	$0 now	$0 now	.	64	$12 now	$57 in 91 days	0.041
25	$34 in 13 days	$30 now	0.011	65	$0 now	$0 now	.
26	$0 now	$0 now	.	66	$31 now	$34 in 29 days	0.0033
27	$51 now	$55 in 78 days	0.001	67	$28 now	$54 in 84 days	0.011
28	$69 now	$75 in 87 days	0.001	68	$76 in 16 days	$65 now	0.011
29	$36 in 97 days	$27 now	0.0033	69	$0 now	$0 now	.
30	$0 now	$0 now	.	70	$39 now	$80 in 95 days	0.011
31	$73 in 70 days	$59 now	0.0033	71	$53 in 77 days	$49 now	0.001
32	$36 now	$72 in 90 days	0.011	72	$0 now	$0 now	.
33	$54 in 80 days	$50 now	0.001	73	$72 now	$78 in 88 days	0.001
34	$47 now	$57 in 5 days	0.041	74	$34 in 32 days	$29 now	0.006
35	$0 now	$0 now	.	75	$80 in 87 days	$18 now	0.041
36	$54 in 89 days	$42 now	0.0033	76	$44 now	$50 in 41 days	0.0033
37	$11 now	$53 in 89 days	0.041	77	$0 now	$0 now	.
38	$34 in 82 days	$18 now	0.011	78	$38 in 97 days	$35 now	0.001
39	$55 in 22 days	$49 now	0.006	79	$48 now	$56 in 28 days	0.006
40	$33 now	$52 in 96 days	0.006	80	$35 in 96 days	$17 now	0.011

Target K 0.006	(continued)						
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
81	$0 now	$0 now	.	121	$57 in 20 days	$47 now	0.011
82	$8 now	$36 in 85 days	0.041	122	$30 now	$33 in 30 days	0.0033
83	$28 now	$37 in 8 days	0.041	123	$0 now	$0 now	.
84	$0 now	$0 now	.	124	$82 in 4 days	$70 now	0.041
85	$36 in 85 days	$19 now	0.011	125	$51 now	$57 in 19 days	0.006
86	$53 in 17 days	$45 now	0.011	126	$0 now	$0 now	.
87	$30 now	$33 in 93 days	0.001	127	$80 in 92 days	73 now	0.001
88	$37 in 23 days	$33 now	0.006	128	$70 now	$76 in 89 days	0.001
89	$0 now	$0 now	.	129	$80 in 25 days	$70 now	0.006
90	$36 in 18 days	$30 now	0.011	130	$48 now	$55 in 44 days	0.0033
91	$47 now	$51 in 88 days	0.001	131	$0 now	$0 now	.
92	$41 now	$78 in 84 days	0.011	132	$38 in 88 days	$25 now	0.006
93	$40 now	$53 in 94 days	0.0033	133	$37 in 87 days	$29 now	0.0033
94	$0 now	$0 now	.	134	$0 now	$0 now	.
95	$81 in 92 days	$74 now	0.001	135	$49 now	$63 in 7 days	0.041
96	$26 now	$34 in 94 days	0.0033	136	$26 now	$35 in 9 days	0.041
97	$0 now	$0 now	.	137	$38 in 19 days	$31 now	0.011
98	$71 in 38 days	$63 now	0.0033	138	$0 now	$0 now	.
99	$77 in 95 days	$49 now	0.006	139	$34 now	$36 in 74 days	0.001
100	$0 now	$0 now	.	140	$37 in 95 days	$18 now	0.011
101	$36 in 28 days	$33 now	0.0033	141	$38 in 95 days	$8 now	0.041
102	$32 now	$34 in 79 days	0.001	142	$53 now	$81 in 89 days	0.006
103	$29 now	$59 in 97 days	0.011	143	$0 now	$0 now	.
104	$0 now	$0 now	.	144	$65 now	$75 in 14 days	0.011
105	$69 now	$78 in 23 days	0.006	145	$0 now	$0 now	.
106	$62 in 6 days	$50 now	0.041	146	$45 now	$58 in 88 days	0.0033
107	$0 now	$0 now	.	147	$77 in 91 days	$38 now	0.011
108	$77 in 93 days	$16 now	0.041	148	$0 now	$0 now	.
109	$23 now	$36 in 94 days	0.006	149	$61 now	$78 in 85 days	0.0033
110	$74 in 98 days	$56 now	0.0033	150	$58 in 74 days	$54 now	0.001
111	$0 now	$0 now	.	151	$81 in 43 days	$71 now	0.0033
112	$70 now	$79 in 12 days	0.011	152	$0 now	$0 now	.
113	$53 in 46 days	$46 now	0.0033	153	$33 now	$38 in 27 days	0.006
114	$38 now	$57 in 81 days	0.006	154	$57 in 91 days	$52 now	0.001
115	$53 in 25 days	$46 now	0.006	155	$33 now	$36 in 83 days	0.001
116	$0 now	$0 now	.	156	$78 in 81 days	$18 now	0.041
117	$58 in 84 days	$13 now	0.041	157	$28 now	$55 in 89 days	0.011
118	$52 now	$56 in 75 days	0.001	158	$0 now	$0 now	.
119	$66 now	$80 in 5 days	0.041	159	$60 in 98 days	$12 now	0.041
120	$76 in 96 days	$69 now	0.001	160	$36 now	$55 in 88 days	0.006

Target K 0.011							
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
1	$18 now	$34 in 82 days	0.011	41	$54 in 9 days	$47 now	0.016
2	$0 now	$0 now	.	42	$0 now	$0 now	.
3	$32 in 2 days	$28 now	0.07	43	$35 in 96 days	$17 now	0.011
4	$4 now	$33 in 98 days	0.07	44	$68 now	$79 in 92 days	0.0018
5	$76 in 79 days	$67 now	0.0018	45	$0 now	$0 now	.
6	$10 now	$79 in 102 days	0.07	46	$38 in 88 days	$25 now	0.006
7	$0 now	$0 now	.	47	$49 now	$58 in 98 days	0.0018
8	$68 now	$75 in 18 days	0.006	48	$77 in 95 days	$49 now	0.006
9	$0 now	$0 now	.	49	$0 now	$0 now	.
10	$80 in 2 days	$70 now	0.07	50	$64 now	$77 in 3 days	0.07
11	$65 now	$74 in 9 days	0.016	51	$34 in 82 days	$5 now	0.07
12	$72 in 90 days	$36 now	0.011	52	$28 now	$54 in 84 days	0.011
13	$29 in 48 days	$27 now	0.0018	53	$30 now	$35 in 11 days	0.016
14	$0 now	$0 now	.	54	$80 in 95 days	$39 now	0.011
15	$58 in 88 days	$24 now	0.016	55	$0 now	$0 now	.
16	$28 now	$32 in 79 days	0.0018	56	$30 now	$38 in 4 days	0.07
17	$0 now	$0 now	.	57	$0 now	$0 now	.
18	$55 in 11 days	$47 now	0.016	58	$55 in 88 days	$36 now	0.006
19	$30 now	$34 in 13 days	0.011	59	$36 in 55 days	$33 now	0.0018
20	$33 now	$37 in 23 days	0.006	60	$0 now	$0 now	.
21	$0 now	$0 now	.	61	$69 now	$78 in 23 days	0.006
22	$46 now	$53 in 25 days	0.006	62	$45 now	$54 in 3 days	0.07
23	$73 in 13 days	$64 now	0.011	63	$76 in 16 days	$65 now	0.011
24	$0 now	$0 now	.	64	$7 now	$54 in 104 days	0.07
25	$33 in 9 days	$29 now	0.016	65	$0 now	$0 now	.
26	$0 now	$0 now	.	66	$29 now	$34 in 32 days	0.006
27	$49 now	$53 in 47 days	0.0018	67	$20 now	$50 in 94 days	0.016
28	$64 now	$74 in 86 days	0.0018	68	$79 in 13 days	$65 now	0.016
29	$35 in 83 days	$23 now	0.006	69	$0 now	$0 now	.
30	$0 now	$0 now	.	70	$31 now	$79 in 97 days	0.016
31	$73 in 98 days	$46 now	0.006	71	$50 in 48 days	$46 now	0.0018
32	$31 now	$75 in 91 days	0.016	72	$0 now	$0 now	.
33	$55 in 84 days	$48 now	0.0018	73	$69 now	$78 in 74 days	0.0018
34	$43 now	$55 in 4 days	0.07	74	$35 in 20 days	$29 now	0.011
35	$0 now	$0 now	.	75	$78 in 81 days	$12 now	0.07
36	$57 in 81 days	$38 now	0.006	76	$48 now	$56 in 28 days	0.006
37	$7 now	$52 in 96 days	0.07	77	$0 now	$0 now	.
38	$32 in 83 days	$14 now	0.016	78	$37 in 90 days	$32 now	0.0018
39	$58 in 16 days	$49 now	0.011	79	$45 now	$53 in 17 days	0.011
40	$25 now	$51 in 93 days	0.011	80	$36 in 92 days	$15 now	0.016

Target K 0.011	(continued)						
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
81	$0 now	$0 now	.		$59 in 9 days	$52 now	0.016
82	$5 now	$36 in 95 days	0.07		$29 now	$33 in 20 days	0.006
83	$30 now	$36 in 3 days	0.07		$0 now	$0 now	.
84	$0 now	$0 now	.		$81 in 2 days	$71 now	0.07
85	$41 in 88 days	$17 now	0.016		$47 now	$57 in 20 days	0.011
86	$52 in 10 days	$45 now	0.016		$0 now	$0 now	.
87	$26 now	$30 in 81 days	0.0018		$80 in 81 days	70 now	0.0018
88	$36 in 18 days	$30 now	0.011		$64 now	$75 in 97 days	0.0018
89	$0 now	$0 now	.		$75 in 14 days	$65 now	0.011
90	$37 in 11 days	$31 now	0.016		$33 now	$52 in 96 days	0.006
91	$46 now	$54 in 95 days	0.0018		$0 now	$0 now	.
92	$33 now	$77 in 84 days	0.016		$37 in 95 days	$18 now	0.011
93	$35 now	$53 in 87 days	0.006		$36 in 94 days	$23 now	0.006
94	$0 now	$0 now	.		$0 now	$0 now	.
95	$81 in 89 days	$70 now	0.0018		$51 now	$58 in 2 days	0.07
96	$20 now	$32 in 96 days	0.006		$29 now	$35 in 3 days	0.07
97	$0 now	$0 now	.		$38 in 10 days	$33 now	0.016
98	$74 in 27 days	$64 now	0.006		$0 now	$0 now	.
99	$78 in 84 days	$41 now	0.011		$32 now	$35 in 46 days	0.0018
100	$0 now	$0 now	.		$37 in 82 days	$16 now	0.016
101	$38 in 27 days	$33 now	0.006		$39 in 87 days	$6 now	0.07
102	$29 now	$32 in 52 days	0.0018		$38 now	$77 in 91 days	0.011
103	$21 now	$55 in 98 days	0.016		$0 now	$0 now	.
104	$0 now	$0 now	.		$67 now	$78 in 10 days	0.016
105	$70 now	$79 in 12 days	0.011		$0 now	$0 now	.
106	$56 in 5 days	$41 now	0.07		$49 now	$55 in 22 days	0.006
107	$0 now	$0 now	.		$76 in 86 days	$32 now	0.016
108	$76 in 87 days	$11 now	0.07		$0 now	$0 now	.
109	$19 now	$36 in 85 days	0.011		$53 now	$81 in 89 days	0.006
110	$76 in 84 days	$51 now	0.006		$59 in 53 days	$54 now	0.0018
111	$0 now	$0 now	.		$80 in 25 days	$70 now	0.006
112	$68 now	$81 in 12 days	0.016		$0 now	$0 now	.
113	$57 in 19 days	$51 now	0.006		$31 now	$38 in 19 days	0.011
114	$28 now	$55 in 89 days	0.011		$59 in 91 days	$51 now	0.0018
115	$54 in 13 days	$47 now	0.011		$30 now	$35 in 93 days	0.0018
116	$0 now	$0 now	.		$80 in 92 days	$11 now	0.07
117	$56 in 81 days	$8 now	0.07		$22 now	$52 in 83 days	0.016
118	$53 now	$58 in 56 days	0.0018		$0 now	$0 now	.
119	$62 now	$79 in 4 days	0.07		$57 in 87 days	$8 now	0.07
120	$77 in 80 days	$67 now	0.0018		$29 now	$59 in 97 days	0.011

Target K 0.016							
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
1	$14 now	$32 in 83 days	0.016	41	$51 in 5 days	$45 now	0.028
2	$0 now	$0 now	.	42	$0 now	$0 now	.
3	$32 in 1 days	$29 now	0.1	43	$36 in 92 days	$15 now	0.016
4	$3 now	$33 in 98 days	0.1	44	$60 now	$76 in 103 days	0.0025
5	$71 in 50 days	$63 now	0.0025	45	$0 now	$0 now	.
6	$7 now	$79 in 102 days	0.1	46	$37 in 95 days	$18 now	0.011
7	$0 now	$0 now	.	47	$45 now	$55 in 85 days	0.0025
8	$65 now	$76 in 16 days	0.011	48	$78 in 84 days	$41 now	0.011
9	$0 now	$0 now	.	49	$0 now	$0 now	.
10	$80 in 1 days	$73 now	0.1	50	$64 now	$77 in 2 days	0.1
11	$65 now	$79 in 8 days	0.028	51	$34 in 82 days	$4 now	0.1
12	$75 in 91 days	$31 now	0.016	52	$20 now	$50 in 94 days	0.016
13	$33 in 36 days	$30 now	0.0025	53	$29 now	$39 in 13 days	0.028
14	$0 now	$0 now	.	54	$76 in 86 days	$32 now	0.016
15	$52 in 96 days	$14 now	0.028	55	$0 now	$0 now	.
16	$29 now	$36 in 97 days	0.0025	56	$29 now	$38 in 3 days	0.1
17	$0 now	$0 now	.	57	$0 now	$0 now	.
18	$58 in 7 days	$48 now	0.028	58	$55 in 89 days	$28 now	0.011
19	$29 now	$33 in 9 days	0.016	59	$39 in 41 days	$35 now	0.0025
20	$30 now	$36 in 18 days	0.011	60	$0 now	$0 now	.
21	$0 now	$0 now	.	61	$70 now	$79 in 12 days	0.011
22	$45 now	$53 in 17 days	0.011	62	$45 now	$54 in 2 days	0.1
23	$74 in 9 days	$65 now	0.016	63	$78 in 10 days	$67 now	0.016
24	$0 now	$0 now	.	64	$5 now	$54 in 104 days	0.1
25	$32 in 5 days	$28 now	0.028	65	$0 now	$0 now	.
26	$0 now	$0 now	.	66	$29 now	$35 in 20 days	0.011
27	$46 now	$53 in 56 days	0.0025	67	$13 now	$50 in 98 days	0.028
28	$62 now	$73 in 70 days	0.0025	68	$80 in 10 days	$63 now	0.028
29	$35 in 96 days	$17 now	0.011	69	$0 now	$0 now	.
30	$0 now	$0 now	.	70	$20 now	$75 in 97 days	0.028
31	$72 in 90 days	$36 now	0.011	71	$52 in 53 days	$46 now	0.0025
32	$21 now	$73 in 87 days	0.028	72	$0 now	$0 now	.
33	$54 in 87 days	$44 now	0.0025	73	$66 now	$75 in 55 days	0.0025
34	$42 now	$55 in 3 days	0.1	74	$35 in 11 days	$30 now	0.016
35	$0 now	$0 now	.	75	$78 in 81 days	$9 now	0.1
36	$59 in 97 days	$29 now	0.011	76	$49 now	$58 in 16 days	0.011
37	$5 now	$52 in 96 days	0.1	77	$0 now	$0 now	.
38	$33 in 98 days	$9 now	0.028	78	$38 in 90 days	$31 now	0.0025
39	$55 in 11 days	$47 now	0.016	79	$52 now	$59 in 9 days	0.016
40	$24 now	$58 in 88 days	0.016	80	$34 in 82 days	$10 now	0.028

Target K 0.016	(continued)						
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
81	$0 now	$0 now	.	121	$56 in 11 days	$43 now	0.028
82	$3 now	$36 in 95 days	0.1	122	$30 now	$34 in 13 days	0.011
83	$30 now	$36 in 2 days	0.1	123	$0 now	$0 now	.
84	$0 now	$0 now	.	124	$81 in 2 days	$68 now	0.1
85	$37 in 95 days	$10 now	0.028	125	$47 now	$54 in 9 days	0.016
86	$54 in 8 days	$44 now	0.028	126	$0 now	$0 now	.
87	$28 now	$34 in 94 days	0.0025	127	$81 in 58 days	71 now	0.0025
88	$37 in 11 days	$31 now	0.016	128	$59 now	$74 in 98 days	0.0025
89	$0 now	$0 now	.	129	$81 in 12 days	$68 now	0.016
90	$35 in 6 days	$30 now	0.028	130	$25 now	$51 in 93 days	0.011
91	$42 now	$51 in 91 days	0.0025	131	$0 now	$0 now	.
92	$22 now	$79 in 92 days	0.028	132	$37 in 82 days	$16 now	0.016
93	$28 now	$54 in 84 days	0.011	133	$36 in 85 days	$19 now	0.011
94	$0 now	$0 now	.	134	$0 now	$0 now	.
95	$78 in 85 days	$64 now	0.0025	135	$53 now	$58 in 1 days	0.1
96	$18 now	$34 in 82 days	0.011	136	$29 now	$35 in 2 days	0.1
97	$0 now	$0 now	.	137	$38 in 12 days	$28 now	0.028
98	$73 in 13 days	$64 now	0.011	138	$0 now	$0 now	.
99	$77 in 84 days	$33 now	0.016	139	$32 now	$35 in 38 days	0.0025
100	$0 now	$0 now	.	140	$38 in 88 days	$11 now	0.028
101	$38 in 19 days	$31 now	0.011	141	$39 in 87 days	$4 now	0.1
102	$31 now	$34 in 39 days	0.0025	142	$31 now	$79 in 97 days	0.016
103	$16 now	$53 in 84 days	0.028	143	$0 now	$0 now	.
104	$0 now	$0 now	.	144	$67 now	$78 in 6 days	0.028
105	$65 now	$79 in 13 days	0.016	145	$0 now	$0 now	.
106	$56 in 4 days	$40 now	0.1	146	$47 now	$54 in 13 days	0.011
107	$0 now	$0 now	.	147	$76 in 81 days	$23 now	0.028
108	$76 in 87 days	$8 now	0.1	148	$0 now	$0 now	.
109	$17 now	$41 in 88 days	0.016	149	$38 now	$77 in 91 days	0.011
110	$80 in 95 days	$39 now	0.011	150	$58 in 55 days	$51 now	0.0025
111	$0 now	$0 now	.	151	$75 in 14 days	$65 now	0.011
112	$68 now	$77 in 5 days	0.028	152	$0 now	$0 now	.
113	$57 in 20 days	$47 now	0.011	153	$33 now	$38 in 10 days	0.016
114	$21 now	$55 in 98 days	0.016	154	$56 in 98 days	$45 now	0.0025
115	$52 in 10 days	$45 now	0.016	155	$30 now	$37 in 87 days	0.0025
116	$0 now	$0 now	.	156	$80 in 92 days	$8 now	0.1
117	$56 in 81 days	$6 now	0.1	157	$17 now	$59 in 90 days	0.028
118	$48 now	$55 in 58 days	0.0025	158	$0 now	$0 now	.
119	$61 now	$79 in 3 days	0.1	159	$57 in 87 days	$6 now	0.1
120	$74 in 52 days	$65 now	0.0025	160	$22 now	$52 in 83 days	0.016

Target K 0.028							
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
1	$9 now	$33 in 98 days	0.028	41	$63 in 7 days	$49 now	0.041
2	$0 now	$0 now	.	42	$0 now	$0 now	.
3	$40 in 1 days	$34 now	0.17	43	$34 in 82 days	$10 now	0.028
4	$1 now	$30 in 116 days	0.17	44	$56 now	$74 in 98 days	0.0033
5	$74 in 42 days	$65 now	0.0033	45	$0 now	$0 now	.
6	$5 now	$76 in 86 days	0.17	46	$37 in 82 days	$16 now	0.016
7	$0 now	$0 now	.	47	$40 now	$53 in 94 days	0.0033
8	$67 now	$78 in 10 days	0.016	48	$77 in 84 days	$33 now	0.016
9	$0 now	$0 now	.	49	$0 now	$0 now	.
10	$95 in 3 days	$63 now	0.17	50	$63 now	$84 in 2 days	0.17
11	$63 now	$79 in 6 days	0.041	51	$44 in 84 days	$3 now	0.17
12	$73 in 87 days	$21 now	0.028	52	$13 now	$50 in 98 days	0.028
13	$35 in 28 days	$32 now	0.0033	53	$31 now	$39 in 6 days	0.041
14	$0 now	$0 now	.	54	$76 in 81 days	$23 now	0.028
15	$53 in 89 days	$11 now	0.041	55	$0 now	$0 now	.
16	$29 now	$38 in 90 days	0.0033	56	$25 now	$38 in 3 days	0.17
17	$0 now	$0 now	.	57	$0 now	$0 now	.
18	$54 in 4 days	$46 now	0.041	58	$55 in 98 days	$21 now	0.016
19	$28 now	$32 in 5 days	0.028	59	$33 in 30 days	$30 now	0.0033
20	$31 now	$37 in 11 days	0.016	60	$0 now	$0 now	.
21	$0 now	$0 now	.	61	$65 now	$79 in 13 days	0.016
22	$52 now	$59 in 9 days	0.016	62	$40 now	$54 in 2 days	0.17
23	$79 in 8 days	$65 now	0.028	63	$78 in 6 days	$67 now	0.028
24	$0 now	$0 now	.	64	$4 now	$60 in 91 days	0.17
25	$34 in 5 days	$28 now	0.041	65	$0 now	$0 now	.
26	$0 now	$0 now	.	66	$30 now	$35 in 11 days	0.016
27	$44 now	$50 in 41 days	0.0033	67	$12 now	$57 in 91 days	0.041
28	$59 now	$73 in 70 days	0.0033	68	$80 in 5 days	$66 now	0.041
29	$36 in 92 days	$15 now	0.016	69	$0 now	$0 now	.
30	$0 now	$0 now	.	70	$18 now	$78 in 81 days	0.041
31	$75 in 91 days	$31 now	0.016	71	$51 in 40 days	$45 now	0.0033
32	$15 now	$75 in 98 days	0.041	72	$0 now	$0 now	.
33	$56 in 98 days	$42 now	0.0033	73	$63 now	$71 in 38 days	0.0033
34	$40 now	$53 in 2 days	0.17	74	$39 in 13 days	$29 now	0.028
35	$0 now	$0 now	.	75	$75 in 97 days	$4 now	0.17
36	$52 in 83 days	$22 now	0.016	76	$47 now	$55 in 11 days	0.016
37	$4 now	$58 in 84 days	0.17	77	$0 now	$0 now	.
38	$32 in 99 days	$6 now	0.041	78	$37 in 87 days	$29 now	0.0033
39	$58 in 7 days	$48 now	0.028	79	$43 now	$56 in 11 days	0.028
40	$14 now	$52 in 96 days	0.028	80	$35 in 90 days	$7 now	0.041

Target K 0.028	(continued)						
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
81	$0 now	$0 now	.	121	$62 in 6 days	$50 now	0.041
82	$2 now	$38 in 105 days	0.17	122	$29 now	$33 in 9 days	0.016
83	$29 now	$39 in 2 days	0.17	123	$0 now	$0 now	.
84	$0 now	$0 now	.	124	$89 in 2 days	$66 now	0.17
85	$36 in 85 days	$8 now	0.041	125	$45 now	$51 in 5 days	0.028
86	$57 in 5 days	$47 now	0.041	126	$0 now	$0 now	.
87	$27 now	$36 in 97 days	0.0033	127	$81 in 43 days	71 now	0.0033
88	$35 in 6 days	$30 now	0.028	128	$57 now	$76 in 103 days	0.0033
89	$0 now	$0 now	.	129	$77 in 5 days	$68 now	0.028
90	$37 in 8 days	$28 now	0.041	130	$24 now	$58 in 88 days	0.016
91	$42 now	$54 in 89 days	0.0033	131	$0 now	$0 now	.
92	$16 now	$77 in 93 days	0.041	132	$38 in 88 days	$11 now	0.028
93	$20 now	$50 in 94 days	0.016	133	$41 in 88 days	$17 now	0.016
94	$0 now	$0 now	.	134	$0 now	$0 now	.
95	$78 in 85 days	$61 now	0.0033	135	$37 now	$56 in 3 days	0.17
96	$14 now	$32 in 83 days	0.016	136	$27 now	$36 in 2 days	0.17
97	$0 now	$0 now	.	137	$35 in 9 days	$26 now	0.041
98	$74 in 9 days	$65 now	0.016	138	$0 now	$0 now	.
99	$79 in 92 days	$22 now	0.028	139	$33 now	$36 in 28 days	0.0033
100	$0 now	$0 now	.	140	$38 in 95 days	$8 now	0.041
101	$38 in 10 days	$33 now	0.016	141	$35 in 88 days	$2 now	0.17
102	$31 now	$34 in 29 days	0.0033	142	$20 now	$75 in 97 days	0.028
103	$12 now	$60 in 98 days	0.041	143	$0 now	$0 now	.
104	$0 now	$0 now	.	144	$63 now	$76 in 5 days	0.041
105	$63 now	$80 in 10 days	0.028	145	$0 now	$0 now	.
106	$54 in 2 days	$40 now	0.17	146	$45 now	$52 in 10 days	0.016
107	$0 now	$0 now	.	147	$80 in 87 days	$18 now	0.041
108	$79 in 91 days	$5 now	0.17	148	$0 now	$0 now	.
109	$10 now	$37 in 95 days	0.028	149	$31 now	$79 in 97 days	0.016
110	$76 in 86 days	$32 now	0.016	150	$55 in 44 days	$48 now	0.0033
111	$0 now	$0 now	.	151	$81 in 12 days	$68 now	0.016
112	$70 now	$82 in 4 days	0.041	152	$0 now	$0 now	.
113	$54 in 9 days	$47 now	0.016	153	$28 now	$38 in 12 days	0.028
114	$16 now	$53 in 84 days	0.028	154	$58 in 88 days	$45 now	0.0033
115	$54 in 8 days	$44 now	0.028	155	$26 now	$34 in 94 days	0.0033
116	$0 now	$0 now	.	156	$77 in 84 days	$5 now	0.17
117	$54 in 87 days	$3 now	0.17	157	$13 now	$58 in 84 days	0.041
118	$46 now	$53 in 46 days	0.0033	158	$0 now	$0 now	.
119	$58 now	$87 in 3 days	0.17	159	$57 in 98 days	$3 now	0.17
120	$75 in 41 days	$66 now	0.0033	160	$17 now	$59 in 90 days	0.028

Target K 0.041							
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
1	$6 now	$32 in 99 days	0.041	41	$58 in 2 days	$51 now	0.07
2	$0 now	$0 now		42	$0 now	$0 now	
3	$40 in 1 day	$32 now	0.25	43	$35 in 90 days	$7 now	0.041
4	$1 now	$30 in 116 days	0.25	44	$49 now	$77 in 95 days	0.006
5	$74 in 27 days	$64 now	0.006	45	$0 now	$0 now	
6	$3 now	$76 in 86 days	0.25	46	$38 in 88 days	$11 now	0.028
7	$0 now	$0 now		47	$38 now	$57 in 81 days	0.006
8	$67 now	$78 in 6 days	0.028	48	$79 in 92 days	$22 now	0.028
9	$0 now	$0 now		49	$0 now	$0 now	
10	$95 in 2 days	$63 now	0.25	50	$67 now	$84 in 1 day	0.25
11	$64 now	$77 in 3 days	0.07	51	$44 in 84 days	$2 now	0.25
12	$75 in 98 days	$15 now	0.041	52	$12 now	$57 in 91 days	0.041
13	$33 in 20 days	$29 now	0.006	53	$29 now	$35 in 3 days	0.07
14	$0 now	$0 now		54	$80 in 87 days	$18 now	0.041
15	$52 in 96 days	$7 now	0.07	55	$0 now	$0 now	
16	$23 now	$35 in 83 days	0.006	56	$25 now	$38 in 2 days	0.25
17	$0 now	$0 now		57	$0 now	$0 now	
18	$55 in 4 days	$43 now	0.07	58	$53 in 84 days	$16 now	0.028
19	$28 now	$34 in 5 days	0.041	59	$38 in 27 days	$33 now	0.006
20	$30 now	$35 in 6 days	0.028	60	$0 now	$0 now	
21	$0 now	$0 now		61	$63 now	$80 in 10 days	0.028
22	$43 now	$56 in 11 days	0.028	62	$43 now	$54 in 1 day	0.25
23	$79 in 6 days	$63 now	0.041	63	$76 in 5 days	$63 now	0.041
24	$0 now	$0 now		64	$2 now	$60 in 98 days	0.25
25	$32 in 2 days	$28 now	0.07	65	$0 now	$0 now	
26	$0 now	$0 now		66	$29 now	$39 in 13 days	0.028
27	$48 now	$56 in 28 days	0.006	67	$7 now	$54 in 104 days	0.07
28	$46 now	$73 in 98 days	0.006	68	$79 in 4 days	$62 now	0.07
29	$34 in 82 days	$10 now	0.028	69	$0 now	$0 now	
30	$0 now	$0 now		70	$12 now	$78 in 81 days	0.07
31	$73 in 87 days	$21 now	0.028	71	$55 in 22 days	$49 now	0.006
32	$10 now	$79 in 102 days	0.07	72	$0 now	$0 now	
33	$53 in 87 days	$35 now	0.006	73	$69 now	$78 in 23 days	0.006
34	$42 now	$53 in 1 day	0.25	74	$39 in 6 days	$31 now	0.041
35	$0 now	$0 now		75	$75 in 91 days	$3 now	0.25
36	$59 in 90 days	$17 now	0.028	76	$48 now	$58 in 7 days	0.028
37	$3 now	$58 in 84 days	0.25	77	$0 now	$0 now	
38	$33 in 98 days	$4 now	0.07	78	$38 in 88 days	$25 now	0.006
39	$54 in 4 days	$46 now	0.041	79	$50 now	$62 in 6 days	0.041
40	$11 now	$53 in 89 days	0.041	80	$34 in 82 days	$5 now	0.07

Target K 0.041	(continued)						
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
81	$0 now	$0 now		121	$56 in 5 days	$41 now	0.07
82	$1 now	$38 in 105 days	0.25	122	$28 now	$32 in 5 days	0.028
83	$26 now	$39 in 2 days	0.25	123	$0 now	$0 now	
84	$0 now	$0 now		124	$89 in 1 day	$71 now	0.25
85	$36 in 95 days	$5 now	0.07	125	$49 now	$63 in 7 days	0.041
86	$54 in 3 days	$45 now	0.07	126	$0 now	$0 now	
87	$20 now	$32 in 96 days	0.006	127	$80 in 25 days	$70 now	0.006
88	$37 in 8 days	$28 now	0.041	128	$51 now	$76 in 84 days	0.006
89	$0 now	$0 now		129	$82 in 4 days	$70 now	0.041
90	$36 in 3 days	$30 now	0.07	130	$14 now	$52 in 96 days	0.028
91	$33 now	$52 in 96 days	0.006	131	$0 now	$0 now	
92	$11 now	$80 in 92 days	0.07	132	$38 in 95 days	$8 now	0.041
93	$13 now	$50 in 98 days	0.028	133	$37 in 95 days	$10 now	0.028
94	$0 now	$0 now		134	$0 now	$0 now	
95	$81 in 89 days	$53 now	0.006	135	$37 now	$56 in 2 days	0.25
96	$9 now	$33 in 98 days	0.028	136	$29 now	$36 in 1 day	0.25
97	$0 now	$0 now		137	$38 in 4 days	$30 now	0.07
98	$79 in 8 days	$65 now	0.028	138	$0 now	$0 now	
99	$77 in 93 days	$16 now	0.041	139	$33 now	$37 in 23 days	0.006
100	$0 now	$0 now		140	$39 in 87 days	$6 now	0.07
101	$38 in 12 days	$28 now	0.028	141	$35 in 88 days	$2 now	0.25
102	$29 now	$34 in 32 days	0.006	142	$18 now	$78 in 81 days	0.041
103	$8 now	$57 in 87 days	0.07	143	$0 now	$0 now	
104	$0 now	$0 now		144	$70 now	$80 in 2 days	0.07
105	$66 now	$80 in 5 days	0.041	145	$0 now	$0 now	
106	$54 in 1 day	$43 now	0.25	146	$44 now	$54 in 8 days	0.028
107	$0 now	$0 now		147	$76 in 87 days	$11 now	0.07
108	$79 in 97 days	$3 now	0.25	148	$0 now	$0 now	
109	$8 now	$36 in 85 days	0.041	149	$20 now	$75 in 97 days	0.028
110	$76 in 81 days	$23 now	0.028	150	$57 in 19 days	$51 now	0.006
111	$0 now	$0 now		151	$77 in 5 days	$68 now	0.028
112	$71 now	$81 in 2 days	0.07	152	$0 now	$0 now	
113	$51 in 5 days	$45 now	0.028	153	$26 now	$35 in 9 days	0.041
114	$12 now	$60 in 98 days	0.041	154	$55 in 88 days	$36 now	0.006
115	$57 in 5 days	$47 now	0.041	155	$23 now	$36 in 94 days	0.006
116	$0 now	$0 now		156	$77 in 84 days	$4 now	0.25
117	$54 in 87 days	$2 now	0.25	157	$8 now	$56 in 81 days	0.07
118	$46 now	$53 in 25 days	0.006	158	$0 now	$0 now	
119	$58 now	$87 in 2 days	0.25	159	$57 in 91 days	$2 now	0.25
120	$75 in 18 days	$68 now	0.006	160	$13 now	$58 in 84 days	0.041

Target K 0.07							
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
1	$4 now	$33 in 98 days	0.07	41	$54 in 2 days	$45 now	0.1
2	$0 now	$0 now		42	$0 now	$0 now	
3	$40 in 1 day	$32 now	0.25	43	$34 in 82 days	$5 now	0.07
4	$1 now	$30 in 116 days	0.25	44	$41 now	$78 in 84 days	0.011
5	$76 in 16 days	$65 now	0.011	45	$0 now	$0 now	
6	$3 now	$76 in 86 days	0.25	46	$35 in 90 days	$7 now	0.041
7	$0 now	$0 now		47	$28 now	$55 in 89 days	0.011
8	$63 now	$79 in 6 days	0.041	48	$80 in 87 days	$18 now	0.041
9	$0 now	$0 now		49	$0 now	$0 now	
10	$95 in 2 days	$63 now	0.25	50	$67 now	$84 in 1 day	0.25
11	$73 now	$80 in 1 day	0.1	51	$44 in 84 days	$2 now	0.25
12	$79 in 102 days	$10 now	0.07	52	$7 now	$54 in 104 days	0.07
13	$36 in 18 days	$30 now	0.011	53	$29 now	$38 in 3 days	0.1
14	$0 now	$0 now		54	$78 in 81 days	$12 now	0.07
15	$52 in 96 days	$5 now	0.1	55	$0 now	$0 now	
16	$17 now	$35 in 96 days	0.011	56	$25 now	$38 in 2 days	0.25
17	$0 now	$0 now		57	$0 now	$0 now	
18	$55 in 3 days	$42 now	0.1	58	$57 in 91 days	$12 now	0.041
19	$28 now	$32 in 2 days	0.07	59	$35 in 20 days	$29 now	0.011
20	$28 now	$34 in 5 days	0.041	60	$0 now	$0 now	
21	$0 now	$0 now		61	$63 now	$76 in 5 days	0.041
22	$46 now	$54 in 4 days	0.041	62	$43 now	$54 in 1 day	0.25
23	$77 in 3 days	$64 now	0.07	63	$79 in 4 days	$62 now	0.07
24	$0 now	$0 now		64	$2 now	$60 in 98 days	0.25
25	$32 in 1 day	$29 now	0.1	65	$0 now	$0 now	
26	$0 now	$0 now		66	$31 now	$39 in 6 days	0.041
27	$45 now	$53 in 17 days	0.011	67	$5 now	$54 in 104 days	0.1
28	$36 now	$72 in 90 days	0.011	68	$77 in 2 days	$64 now	0.1
29	$32 in 99 days	$6 now	0.041	69	$0 now	$0 now	
30	$0 now	$0 now		70	$9 now	$78 in 81 days	0.1
31	$75 in 98 days	$15 now	0.041	71	$58 in 16 days	$49 now	0.011
32	$7 now	$79 in 102 days	0.1	72	$0 now	$0 now	
33	$59 in 97 days	$29 now	0.011	73	$70 now	$79 in 12 days	0.011
34	$42 now	$53 in 1 day	0.25	74	$35 in 3 days	$29 now	0.07
35	$0 now	$0 now		75	$75 in 91 days	$3 now	0.25
36	$53 in 89 days	$11 now	0.041	76	$50 now	$62 in 6 days	0.041
37	$3 now	$58 in 84 days	0.25	77	$0 now	$0 now	
38	$33 in 98 days	$3 now	0.1	78	$37 in 95 days	$18 now	0.011
39	$55 in 4 days	$43 now	0.07	79	$51 now	$58 in 2 days	0.07
40	$7 now	$52 in 96 days	0.07	80	$34 in 82 days	$4 now	0.1

Target K 0.07	(continued)						
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
81	$0 now	$0 now		121	$58 in 1 day	$53 now	0.1
82	$1 now	$38 in 105 days	0.25	122	$26 now	$35 in 9 days	0.041
83	$26 now	$39 in 2 days	0.25	123	$0 now	$0 now	
84	$0 now	$0 now		124	$89 in 1 day	$71 now	0.25
85	$36 in 95 days	$3 now	0.1	125	$41 now	$56 in 5 days	0.07
86	$56 in 4 days	$40 now	0.1	126	$0 now	$0 now	
87	$18 now	$34 in 82 days	0.011	127	$75 in 14 days	65 now	0.011
88	$36 in 3 days	$30 now	0.07	128	$38 now	$77 in 91 days	0.011
89	$0 now	$0 now		129	$80 in 2 days	$70 now	0.07
90	$36 in 2 days	$30 now	0.1	130	$13 now	$58 in 84 days	0.041
91	$28 now	$54 in 84 days	0.011	131	$0 now	$0 now	
92	$8 now	$76 in 87 days	0.1	132	$39 in 87 days	$6 now	0.07
93	$12 now	$60 in 98 days	0.041	133	$38 in 95 days	$8 now	0.041
94	$0 now	$0 now		134	$0 now	$0 now	
95	$80 in 95 days	$39 now	0.011	135	$37 now	$56 in 2 days	0.25
96	$8 now	$36 in 85 days	0.041	136	$29 now	$36 in 1 day	0.25
97	$0 now	$0 now		137	$35 in 2 days	$29 now	0.1
98	$80 in 5 days	$66 now	0.041	138	$0 now	$0 now	
99	$80 in 92 days	$11 now	0.07	139	$30 now	$34 in 13 days	0.011
100	$0 now	$0 now		140	$39 in 87 days	$4 now	0.1
101	$37 in 8 days	$28 now	0.041	141	$35 in 88 days	$2 now	0.25
102	$31 now	$38 in 19 days	0.011	142	$11 now	$76 in 87 days	0.07
103	$6 now	$56 in 81 days	0.1	143	$0 now	$0 now	
104	$0 now	$0 now		144	$68 now	$81 in 2 days	0.1
105	$71 now	$81 in 2 days	0.07	145	$0 now	$0 now	
106	$54 in 1 day	$43 now	0.25	146	$49 now	$63 in 7 days	0.041
107	$0 now	$0 now		147	$80 in 92 days	$8 now	0.1
108	$79 in 97 days	$3 now	0.25	148	$0 now	$0 now	
109	$5 now	$36 in 95 days	0.07	149	$18 now	$78 in 81 days	0.041
110	$77 in 93 days	$16 now	0.041	150	$54 in 13 days	$47 now	0.011
111	$0 now	$0 now		151	$82 in 4 days	$70 now	0.041
112	$61 now	$79 in 3 days	0.1	152	$0 now	$0 now	
113	$57 in 5 days	$47 now	0.041	153	$30 now	$38 in 4 days	0.07
114	$8 now	$57 in 87 days	0.07	154	$51 in 93 days	$25 now	0.011
115	$54 in 3 days	$45 now	0.07	155	$19 now	$36 in 85 days	0.011
116	$0 now	$0 now		156	$77 in 84 days	$4 now	0.25
117	$54 in 87 days	$2 now	0.25	157	$6 now	$57 in 87 days	0.1
118	$47 now	$57 in 20 days	0.011	158	$0 now	$0 now	
119	$58 now	$87 in 2 days	0.25	159	$57 in 91 days	$2 now	0.25
120	$73 in 13 days	$64 now	0.011	160	$8 now	$56 in 81 days	0.07

Target K 0.1							
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
1	$6 now	$56 in 81 days	0.1	41	$54 in 2 days	$40 now	0.17
2	$0 now	$0 now		42	$0 now	$0 now	
3	$40 in 0.5 days	$32 now	0.5	43	$33 in 98 days	$3 now	0.1
4	$1 now	$44 in 84 days	0.5	44	$31 now	$75 in 91 days	0.016
5	$78 in 10 days	$67 now	0.016	45	$0 now	$0 now	
6	$2 now	$75 in 91 days	0.5	46	$34 in 82 days	$5 now	0.07
7	$0 now	$0 now		47	$22 now	$52 in 83 days	0.016
8	$70 now	$80 in 2 days	0.07	48	$78 in 81 days	$12 now	0.07
9	$0 now	$0 now		49	$0 now	$0 now	
10	$54 in 0.5 days	$43 now	0.5	50	$67 now	$84 in 0.5 days	0.5
11	$63 now	$95 in 3 days	0.17	51	$38 in 105 days	$0.71 now	0.5
12	$76 in 87 days	$8 now	0.1	52	$8 now	$80 in 92 days	0.1
13	$35 in 11 days	$30 now	0.016	53	$25 now	$38 in 3 days	0.17
14	$0 now	$0 now		54	$39 in 87 days	$4 now	0.1
15	$58 in 84 days	$4 now	0.17	55	$0 now	$0 now	
16	$14 now	$32 in 83 days	0.016	56	$43 now	$54 in 0.5 days	0.5
17	$0 now	$0 now		57	$0 now	$0 now	
18	$53 in 2 days	$40 now	0.17	58	$54 in 104 days	$7 now	0.07
19	$29 now	$35 in 2 days	0.1	59	$37 in 11 days	$31 now	0.016
20	$28 now	$32 in 2 days	0.07	60	$0 now	$0 now	
21	$0 now	$0 now		61	$64 now	$77 in 3 days	0.07
22	$43 now	$55 in 4 days	0.07	62	$37 now	$56 in 1 day	0.5
23	$79 in 3 days	$61 now	0.1	63	$80 in 1 day	$73 now	0.1
24	$0 now	$0 now		64	$1 now	$60 in 98 days	0.5
25	$40 in 1 day	$34 now	0.17	65	$0 now	$0 now	
26	$0 now	$0 now		66	$30 now	$38 in 4 days	0.07
27	$65 now	$74 in 9 days	0.016	67	$4 now	$60 in 91 days	0.17
28	$21 now	$55 in 98 days	0.016	68	$84 in 2 days	$63 now	0.17
29	$33 in 98 days	$4 now	0.07	69	$0 now	$0 now	
30	$0 now	$0 now		70	$4 now	$75 in 97 days	0.17
31	$79 in 102 days	$10 now	0.07	71	$55 in 11 days	$47 now	0.016
32	$5 now	$76 in 86 days	0.17	72	$0 now	$0 now	
33	$50 in 94 days	$20 now	0.016	73	$65 now	$79 in 13 days	0.016
34	$25 now	$38 in 1 day	0.5	74	$36 in 2 days	$30 now	0.1
35	$0 now	$0 now		75	$77 in 84 days	$2 now	0.5
36	$52 in 96 days	$7 now	0.07	76	$45 now	$54 in 3 days	0.07
37	$1 now	$58 in 84 days	0.5	77	$0 now	$0 now	
38	$30 in 116 days	$1 now	0.17	78	$58 in 88 days	$24 now	0.016
39	$32 in 1 day	$29 now	0.1	79	$40 now	$56 in 4 days	0.1
40	$5 now	$52 in 96 days	0.1	80	$44 in 84 days	$3 now	0.17

Target K 0.1	(continued)						
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
81	$0 now	$0 now		121	$56 in 3 days	$37 now	0.17
82	$0.5 now	$30 in 116 days	0.5	122	$29 now	$35 in 3 days	0.07
83	$29 now	$36 in 0.5 days	0.5	123	$0 now	$0 now	
84	$0 now	$0 now		124	$87 in 1 day	$58 now	0.5
85	$38 in 105 days	$2 now	0.17	125	$53 now	$58 in 1 day	0.1
86	$54 in 2 days	$40 now	0.17	126	$0 now	$0 now	
87	$16 now	$37 in 82 days	0.016	127	$81 in 12 days	68 now	0.016
88	$38 in 3 days	$29 now	0.1	128	$33 now	$77 in 84 days	0.016
89	$0 now	$0 now		129	$81 in 2 days	$68 now	0.1
90	$39 in 2 days	$29 now	0.17	130	$8 now	$57 in 87 days	0.07
91	$31 now	$79 in 97 days	0.016	131	$0 now	$0 now	
92	$5 now	$79 in 91 days	0.17	132	$36 in 95 days	$3 now	0.1
93	$8 now	$56 in 81 days	0.07	133	$39 in 87 days	$6 now	0.07
94	$0 now	$0 now		134	$0 now	$0 now	
95	$76 in 86 days	$32 now	0.016	135	$42 now	$53 in 0.5 days	0.5
96	$5 now	$36 in 95 days	0.07	136	$26 now	$39 in 1 day	0.5
97	$0 now	$0 now		137	$36 in 2 days	$27 now	0.17
98	$79 in 4 days	$62 now	0.07	138	$0 now	$0 now	
99	$78 in 81 days	$9 now	0.1	139	$47 now	$54 in 9 days	0.016
100	$0 now	$0 now		140	$35 in 88 days	$2 now	0.17
101	$36 in 3 days	$30 now	0.07	141	$57 in 91 days	$1 now	0.5
102	$33 now	$38 in 10 days	0.016	142	$7 now	$79 in 102 days	0.1
103	$3 now	$54 in 87 days	0.17	143	$0 now	$0 now	
104	$0 now	$0 now		144	$66 now	$89 in 2 days	0.17
105	$45 now	$54 in 2 days	0.1	145	$0 now	$0 now	
106	$95 in 1 day	$63 now	0.5	146	$51 now	$58 in 2 days	0.07
107	$0 now	$0 now		147	$77 in 84 days	$5 now	0.17
108	$54 in 87 days	$1 now	0.5	148	$0 now	$0 now	
109	$4 now	$34 in 82 days	0.1	149	$11 now	$80 in 92 days	0.07
110	$76 in 87 days	$11 now	0.07	150	$59 in 9 days	$52 now	0.016
111	$0 now	$0 now		151	$81 in 2 days	$71 now	0.07
112	$58 now	$87 in 3 days	0.17	152	$0 now	$0 now	
113	$56 in 5 days	$41 now	0.07	153	$64 now	$77 in 2 days	0.1
114	$6 now	$57 in 87 days	0.1	154	$41 in 88 days	$17 now	0.016
115	$55 in 3 days	$42 now	0.1	155	$15 now	$36 in 92 days	0.016
116	$0 now	$0 now		156	$76 in 86 days	$2 now	0.5
117	$79 in 97 days	$2 now	0.5	157	$3 now	$57 in 98 days	0.17
118	$29 now	$33 in 9 days	0.016	158	$0 now	$0 now	
119	$71 now	$89 in 0.5 days	0.5	159	$35 in 88 days	$0.78 now	0.5
120	$52 in 10 days	$45 now	0.016	160	$5 now	$54 in 104 days	0.1

Target K 0.17							
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
1	$1 now	$30 in 116 days	0.17	41	$54 in1 day	$43 now	0.25
2	$0 now	$0 now		42	$0 now	$0 now	
3	$32 in 3 hours	$28 now	1	43	$35 in 88 days	$2 now	0.17
4	$0.33 now	$33 in 98 days	1	44	$20 now	$75 in 97 days	0.028
5	$78 in 6 days	$67 now	0.028	45	$0 now	$0 now	
6	$0.77 now	$79 in 102 days	1	46	$34 in 82 days	$4 now	0.1
7	$0 now	$0 now		47	$45 now	$51 in 5 days	0.028
8	$73 now	$80 in 1 day	0.1	48	$78 in 81 days	$9 now	0.1
9	$0 now	$0 now		49	$0 now	$0 now	
10	$77 in 5 hours	$64 now	1	50	$62 now	$79 in 7 hours	1
11	$63 now	$95 in 2 days	0.25	51	$34 in 82 days	$0.41 now	1
12	$75 in 97 days	$4 now	0.17	52	$40 now	$54 in 2 days	0.17
13	$37 in 95 days	$10 now	0.028	53	$25 now	$38 in 2 days	0.25
14	$0 now	$0 now		54	$76 in 86 days	$5 now	0.17
15	$58 in 84 days	$3 now	0.25	55	$0 now	$0 now	
16	$28 now	$32 in 5 days	0.028	56	$29 now	$35 in 5 hours	1
17	$0 now	$0 now		57	$0 now	$0 now	
18	$53 in 1 day	$42 now	0.25	58	$54 in 104 days	$5 now	0.1
19	$2 now	$38 in 105 days	0.17	59	$38 in 88 days	$11 now	0.028
20	$29 now	$32 in 1 day	0.1	60	$0 now	$0 now	
21	$0 now	$0 now		61	$64 now	$77 in 2 days	0.1
22	$42 now	$55 in 3 days	0.1	62	$51 now	$58 in 3 hours	1
23	$84 in 2 days	$63 now	0.17	63	$87 in 3 days	$58 now	0.17
24	$0 now	$0 now		64	$0.51 now	$54 in 104 days	1
25	$40 in1 day	$32 now	0.25	65	$0 now	$0 now	
26	$0 now	$0 now		66	$29 now	$38 in 3 days	0.1
27	$44 now	$54 in 8 days	0.028	67	$2 now	$60 in 98 days	0.25
28	$21 now	$73 in 87 days	0.028	68	$84 in1 day	$67 now	0.25
29	$33 in 98 days	$3 now	0.1	69	$0 now	$0 now	
30	$0 now	$0 now		70	$3 now	$75 in 91 days	0.25
31	$79 in 102 days	$7 now	0.1	71	$56 in 11 days	$43 now	0.028
32	$3 now	$76 in 86 days	0.25	72	$0 now	$0 now	
33	$50 in 98 days	$13 now	0.028	73	$65 now	$79 in 8 days	0.028
34	$43 now	$55 in 7 hours	1	74	$39 in 2 days	$29 now	0.17
35	$0 now	$0 now		75	$78 in 81 days	$1 now	1
36	$52 in 96 days	$5 now	0.1	76	$45 now	$54 in 2 days	0.1
37	$0.54 now	$52 in 96 days	1	77	$0 now	$0 now	
38	$30 in 116 days	$1 now	0.25	78	$33 in 98 days	$9 now	0.028
39	$56 in 3 days	$37 now	0.17	79	$3 now	$57 in 98 days	0.17
40	$40 now	$53 in 2 days	0.17	80	$44 in 84 days	$2 now	0.25

Target K 0.17	(continued)						
Trial #	Left choice	Right choice	ImplK of trial	Trial #	Left choice	Right choice	ImplK of trial
81	$0 now	$0 now		121	$56 in 2 days	$37 now	0.25
82	$0.37 now	$36 in 95 days	1	122	$29 now	$35 in 2 days	0.1
83	$30 now	$36 in 5 hours	1	123	$0 now	$0 now	
84	$0 now	$0 now		124	$80 in 3 hours	$70 now	1
85	$38 in 105 days	$1 now	0.25	125	$4 now	$60 in 91 days	0.17
86	$54 in1 day	$43 now	0.25	126	$0 now	$0 now	
87	$10 now	$34 in 82 days	0.028	127	$80 in 10 days	63 now	0.028
88	$40 in1 day	$34 now	0.17	128	$68 now	$77 in 5 days	0.028
89	$0 now	$0 now		129	$95 in 3 days	$63 now	0.17
90	$39 in 2 days	$26 now	0.25	130	$6 now	$57 in 87 days	0.1
91	$14 now	$52 in 96 days	0.028	131	$0 now	$0 now	
92	$3 now	$79 in 97 days	0.25	132	$38 in 3 days	$25 now	0.17
93	$6 now	$56 in 81 days	0.1	133	$39 in 87 days	$4 now	0.1
94	$0 now	$0 now		134	$0 now	$0 now	
95	$76 in 81 days	$23 now	0.028	135	$41 now	$56 in 9 hours	1
96	$3 now	$36 in 95 days	0.1	136	$30 now	$38 in 6 hours	1
97	$0 now	$0 now		137	$36 in1 day	$29 now	0.25
98	$79 in 3 days	$61 now	0.1	138	$0 now	$0 now	
99	$77 in 84 days	$5 now	0.17	139	$29 now	$39 in 13 days	0.028
100	$0 now	$0 now		140	$35 in 88 days	$2 now	0.25
101	$36 in 2 days	$30 now	0.1	141	$39 in 87 days	$0.44 now	1
102	$28 now	$38 in 12 days	0.028	142	$5 now	$79 in 91 days	0.17
103	$2 now	$54 in 87 days	0.25	143	$0 now	$0 now	
104	$0 now	$0 now		144	$71 now	$89 in 1 day	0.25
105	$66 now	$89 in 2 days	0.17	145	$0 now	$0 now	
106	$54 in 5 hours	$45 now	1	146	$53 now	$58 in 1 day	0.1
107	$0 now	$0 now		147	$77 in 84 days	$4 now	0.25
108	$80 in 92 days	$0.86 now	1	148	$0 now	$0 now	
109	$27 now	$36 in 2 days	0.17	149	$8 now	$80 in 92 days	0.1
110	$76 in 87 days	$8 now	0.1	150	$59 in 90 days	$17 now	0.028
111	$0 now	$0 now		151	$81 in 2 days	$68 now	0.1
112	$58 now	$87 in 2 days	0.25	152	$0 now	$0 now	
113	$56 in 4 days	$40 now	0.1	153	$3 now	$44 in 84 days	0.17
114	$40 now	$54 in 2 days	0.17	154	$53 in 84 days	$16 now	0.028
115	$58 in 84 days	$4 now	0.17	155	$30 now	$35 in 6 days	0.028
116	$0 now	$0 now		156	$76 in 87 days	$0.86 now	1
117	$57 in 87 days	$0.65 now	1	157	$2 now	$57 in 91 days	0.25
118	$48 now	$58 in 7 days	0.028	158	$0 now	$0 now	
119	$71 now	$81 in 3 hours	1	159	$56 in 81 days	$0.68 now	1
120	$79 in 92 days	$22 now	0.028	160	$3 now	$54 in 87 days	0.17