HHS Public Access

Author manuscript

J Clin Exp Neuropsychol. Author manuscript; available in PMC 2020 July 01.

Published in final edited form as:

J Clin Exp Neuropsychol. 2019 July ; 41(5): 512–529. doi:10.1080/13803395.2019.1585519.

The Titrated Monetary Incentive Delay Task: Sensitivity, Convergent and Divergent Validity, and Neural Correlates in an RDoC Sample

Sophie R. DelDonno[1], **Aimee Karstens**[1], **Brian Cerny**[2], **Leah R. Kling**[2], **Lisanne M. Jenkins**[3], **Jonathan P. Stange**[2], **Robin Nusslock**[4], **Stewart A. Shankman**[1], and **Scott A. Langenecker**[5,*]

[1]Department of Psychology, University of Illinois at Chicago

[2]Department of Psychiatry, University of Illinois at Chicago

[3]Department of Psychiatry and Behavioral Sciences, Northwestern University

[4]Department of Psychology, Northwestern University

[5]Department of Psychiatry, University of Utah

Abstract

Introduction: Neuropsychological tests are designed to assay brain function via performance measurements. Many tests corresponding to visual and motor cortex function have been validated. Tests probing reward circuitry, including the ventral striatum (VS), could benefit assessment of numerous neurological and psychiatric disorders in which reward or VS function is disturbed. The present study sought to examine convergent and divergent validity of our modified, titrated version of the Monetary Incentive Delay Task, such that it may in the future stand as a validated neuropsychological test for reward function.

Method: Participants were 132 individuals with a history of mood disturbance (HMD) and 43 healthy comparisons, ages 18–30. In addition to a standard neuropsychological battery and symptom measures, participants completed a modified version of the Monetary Incentive Delay task (T-MIDT) during fMRI, which involved a multi-stage titration procedure to incrementally increase or decrease the response window time per each participant's psychomotor speed and optimize individual performance.

Results: Across groups after titration, performance on the T-MIDT diverged from measures of processing speed, attention, spatial working memory, but not inhibitory control. Performance in the HMD group was differentially correlated with executive function measures before and after titration. The reward circuit (e.g., subcortical, insular, medial prefrontal) was activated during reward anticipation.

Conclusion: The present findings provide preliminary evidence that the T-MIDT measures a construct distinct from many executive functions and that individualized titration of the task

*Corresponding author: 501 Chipeta Way, Salt Lake City, UT 84108 E: s.langenecker@hsc.utah.edu.

Disclosure of Interest

The authors report no conflicts of interest.

parameters is critical in parsing reward from executive function. The T-MIDT correlated with residual mood symptoms in individuals with remitted depression or bipolar disorder, implying that behavioral or brain activation group differences are only to be observed in the active state of illness.

Keywords

reward circuit; neuropsychology; executive function; divergence; convergence

Neuropsychological tests are designed to estimate brain function through measurement of observable behavioral performance. Functional correlates of cortical areas (Desgranges et al., 1998; Fuster, 1988; Nielson et al., 2002), particularly in the left hemisphere (Hickok & Peoppel, 2000) and in the visual (Belliveau et al., 1991) and motor (Middleton & Strick, 2000) cortices, have been thoroughly investigated. However, although the functional neuroanatomy has been fairly well delineated for emotion (Phan et al., 2002) and reward (Koob, 1992; Kringelbach & Rolls, 2004; Haber & Knutson, 2010), there is a relative paucity of neuropsychological measures designed to probe these functions. Some examples of tests that have ventured into the domain of emotion include Iowa Gambling Test (Bechara et al., 2005), Advanced Clinical Solutions (Wechsler, 2009), and Mayer-Salovey-Caruso Emotional Intelligence Test (Mayer et al., 2003). These tests have begun to probe ventromedial prefrontal cortex (Fukui et al., 2005; Killgore et al., 2012) and anterior temporal (Killgore & Yurgelun-Todd, 2007) functions, in addition to integration of emotional and cognitive information (Dolcos et al., 2011; Killgore et al., 2013).

Although a few tasks have emerged in recent years to probe the function of some the reward circuit, more are needed to probe the circuit as a whole. The reward circuit includes the orbital and dorsal prefrontal cortices, dorsal anterior cingulate cortex (dACC), ventral pallidum, amygdala, ventral striatum (VS), and ventral tegmental area (Nestler & Carlezon, 2006; Haber & Knutson, 2010; Lutz & Widmer, 2014; Heshmati & Russo, 2015). The VS, which is considered part of the basal ganglia, is partly comprised of the nucleus accumbens (NAcc) (Parent & Hazrati, 1995; Di Martino et al., 2008). Identifying tasks that probe the function of the entire circuit or of each region is beyond the scope of this paper. Instead we will focus on the convergence of activation in a few key regions – dorsolateral prefrontal cortex (DLPFC), dACC, and VS – with behavioral performance.

Due to anatomical overlap, neuropsychological probes of the reward circuit and functioning might be relevant across some neurological and psychiatric diseases. For example, Parkinson's disease affects the basal ganglia (Berheimer et al., 1973) and Huntington's disease affects the striatum (Rosas et al., 2002; Vonsattel et al., 1998). It is possible that early signs of these diseases could be detected with tests that probe the affective/reward functions of the striatum and basal ganglia. In addition, potential use of neurodegeneration-slowing pharmacological agents to treat Parkinson's and Huntington's would require better proximal measures of functional changes (Schapira et al., 2014). Substance use disorders (Volkow et al., 2009), bipolar disorder (Caseras et al., 2013), and major depressive disorder (MDD; Epstein et al., 2006) are linked to core weaknesses in the functioning of the VS, perhaps within a broader reward and emotion processing network (Seeley et al., 2007).

Recent neuroimaging studies suggest that these broad networks can be measured using resting state fMRI (Kaiser et al., 2015; DelDonno et al., 2017), but the interpretation and application of findings of high or low connectivity are very much still in doubt. Although no single task can assess all aspects of reward processing and all functions of the reward circuit, it may be useful to identify tasks that could serve as a probe for anticipatory and responsiveness functions that involve the VS and reward circuit, towards developing a normative framework for the neuropsychological and functional neural correlates of these tasks.

Existing neuropsychological measures that are relevant to the diseases mentioned above probe executive function (EF), working memory, and processing speed (Elliot, 2003; Bearden et al., 2001; Hester & Garavan, 2004), but not reward circuit function. If a new measure is to be successful in probing anticipatory and responsiveness functioning of the reward circuit, it will need to be psychometrically distinct from the more well-known EF tasks. Ideally, such a test would be adapted to avoid confounds from individual differences in processing speed.

One potential candidate task for a reward circuit probe, which could be developed as a neuropsychological test, is the monetary incentive delay task (MIDT). The MIDT was originally developed by Knutson and colleagues (2000), based upon work by Schultz and colleagues (1996, 1997, 1998) and Breiter and colleagues (1996, 1997). Schultz and colleagues noted the influence of dopaminergic projections to the striatum and NAcc on addictive behavior and reward learning (Schultz et al., 1997). In non-human primate models, striatal and orbitofrontal neurons responded phasically to code reward prediction expectancy and error (Schultz et al., 1998). Breiter and colleagues concurrently observed that acute cocaine infusion in cocaine-dependent humans was correlated with robust, broad positive activation in the NAcc, striatum, basal forebrain, and other limbic structures important in memory and emotion (Breiter et al., 1997). Building upon this work, Knutson and colleagues developed a novel task to probe reward- and punishment-related responding in a small sample of healthy adults (Knutson et al., 2000). This monetary incentive delay task reliably activated striatal and mesial forebrain structures (Knutson et al., 2000), which had been identified in the work by Schultz, Breiter, and their respective colleagues.

Since the genesis of the MIDT, the task has been administered in a range of populations and diagnostic groups to assess reward responsiveness, i.e. anticipation of potential gains and losses. NAcc activation during anticipation of gains has been linked to positive affect, whereas insula activation during loss anticipation has been correlated with negative affect (Knutson & Heinz, 2015). In individuals with addiction or ADHD, increased NAcc activity during reward anticipation was related to decreased impulsivity (Knutson & Heinz, 2015). Blunted VS activity has been observed during reward anticipation in individuals with first-episode schizophrenia and during reward receipt in individuals with MDD (Knutson & Heinz, 2015). Findings from similar reward incentive tasks showed greater VS activity in individuals with bipolar disorder, relative to healthy comparisons (HC)s, during anticipation (Nusslock et al., 2012). There have also been some studies suggesting that VS activity is attenuated in individuals with substance use disorders (Balodis & Potenza, 2015) or a

positive family history of alcohol abuse (Andrews et al., 2011). Overall, there is evidence that the MIDT probes VS activity in a range of psychiatric disorders.

The capacity of the MIDT to reveal clinically meaningful group differences at the behavioral level is less clear. Many studies do not find (e.g. Knutson et al., 2001; Knutson et al., 2008; Andrews et al., 2011; Balodis & Potenza, 2015) or may not report group behavioral differences on the MIDT (e.g. Knutson et al., 2000; Patel et al., 2013). However, there is evidence to suggest that it is possible to detect behavioral differences in reward processing. Individuals with euthymic bipolar disorder and remitted depression failed to acquire a response bias towards reward during the Probabilistic Reward learning Task (Pizzagalli et al., 2008a; Pizzagalli et al., 2008b). We previously reported that participants with current MDD earned less money on the MIDT and reported lower trait reward responsiveness, relative to HCs (DelDonno et al., 2015). In that prior study, we adapted the design of the original MIDT to dissociate psychomotor and reward function (DelDonno et al., 2015). To achieve this dissociation, we created a procedure to track performance (accuracy and reaction time) in each run of the task and manually adjust (increase or decrease) the response window based on each individual's performance in the preceding run, thereby titrating the task per each participant's psychomotor speed. By accounting for individual differences in psychomotor speed, the titration procedure should have optimized, and relatively equalized, all participants' performance. The persistence of group differences after titration suggested that the titrated MIDT may be a clinically sensitive measure of reward function at the behavioral level for individuals in the active phase of MDD.

The present study had three aims. First, we aimed to establish convergent validity of our Titrated Monetary Incentive Delay Task (T-MIDT). We conducted a preliminary analysis in the HMD group with self-report measures of reward-responsiveness and anhedonia because we lacked existing neuropsychological measures of reward function for which normative data have been collected. We predicted that positive correlations between amount of money won in the task and reward-responsiveness would be stronger in the titrated runs, compared to the pre-titrated runs. We also expected that we would observe broad reward circuit activation (see distributed circuit description above) during reward anticipation and that activation in reward-related regions of interest (ROIs) would correspond with performance in the titrated runs.

Second, we sought to establish divergence of reward anticipation, as measured by the T-MIDT, from working memory, set-shifting, attention, and inhibitory control, as well as processing speed. Although previous studies support "hot" emotional decision-making and "cool" cognitive control components to EF (Hongwanishkul et al., 2005; Brock et al., 2009; Roiser & Sahakian, 2013, no studies to our knowledge have directly examined possible construct overlap/separation between reward processing and neuropsychological measures of EF. Additionally, while the MIDT is routinely administered with a variable response window adjusted per each participant's reaction time in a practice run (Knutson et al., 2000; Knutson et al., 2001; Andrews et al., 2011; Balodis & Potenza, 2015), no studies to our knowledge have continued the titration process past the practice run or evaluated the influence of a titration procedure such as ours on performance. Accordingly, we examined pre- and post-titrated money earned in relation to each other and the divergent validity

measures. We expected that, after titration, the divergence from EF measures would be clearer, i.e., that there would be decreased positive or non-significant correlations between amount of money won and measures of attention, working memory, and inhibitory control.

Third, we intended to evaluate the sensitivity of the MIDT in detecting group differences between individuals with a remitted mood disorder and healthy comparisons. Considering that previous research that has failed to find behavioral group differences, we did not expect the HMD and HC groups to perform differently. We did expect to see group differences in reward circuit activation during the win anticipation trials of the T-MIDT, but made no predictions as to the direction of those differences given the mixed results in the literature.

Method

Participants

Participants were recruited from the community in Chicago, Illinois. Participants were 175 adults aged 18–30 years old with no chronic or serious medical conditions. There were 132 participants with a history of any mood disorder (HMD), who had experienced at least one week or more of mood disturbance in the past. Mood disturbance could include diagnoses of MDD, bipolar disorder, mood NOS categories, and other presentations of those disorders with subthreshold duration. Of those in the HMD group, 105 (80%) individuals met full or subthreshold DSM-5 criteria for past MDD, 21 (16%) individuals met full or subthreshold criteria for past bipolar I disorder, and 6 (5%) individuals met full or subthreshold criteria for past bipolar II disorder. The large majority of individuals with HMD were enrolled in the remitted/euthymic phase of illness, scoring 8 or below on the Hamilton Rating Scale for Depression (Ham-D). However, 11% (n = 14) of the HMD sample had Ham-D scores ranging from 9 to 21 at the time of enrollment. Comorbid anxiety disorders were permitted for enrollment in the HMD group; 4% of the HMD group scored from 17 to 23 on the Hamilton Anxiety Rating Scale, indicating moderate anxiety. All HMD participants had Young Mania Rating Scale scores less than 8 at the time of enrollment. Those with stable psychotherapy and/or pharmacological treatment over four weeks prior to enrollment were eligible. If potential participants were currently using psychostimulants, benzodiazepines, sleep aids, or pain medications as needed, they were asked to refrain from taking medications one day before and the day of any study visits. HCs (n = 43) had no history of mood disturbance and no personal or family history of any psychiatric problems.

Exclusion criteria were active substance abuse in the last month or dependence in the last two years; changes in psychotherapy/treatment within the last month (e.g. new provider, new treatment); current antipsychotic medication use; history of psychosis outside of severe manic episodes; chronic or serious medical conditions known to affect cognitive functioning and/or mood, such as diabetes mellitus, seizures, Cushing’s disease, or an organic brain syndrome due to closed head injury; history of a developmental disability, neurocognitive disorder, or traumatic brain injury; an active suicidal plan or history of serious suicide attempt in the last six months; and contraindications for fMRI.

Table 1 reports participant demographics and clinical characteristics.

Forty-five participants opted out of or did not complete the fMRI visit. The subset of the sample with fMRI consisted of 37 HCs and 93 with HMD (17 history of bipolar, 76 history of MDD).

Procedure

All study procedures were approved by the University of Illinois at Chicago Institutional Review Board. Individuals who responded to recruitment materials were contacted by phone for an eligibility screening. During the phone screening conducted by a trained research assistant, participants heard a detailed description of the study and were given the chance to ask questions. If eligible and interested, participants were invited to the laboratory for a baseline assessment. After obtaining informed consent and confirming eligibility (approximately 30–45 minutes), participants completed a 2.5-hour baseline clinical assessment. In the clinical assessment, a trained Masters-level clinician conducted a version of the Structured Clinical Interview for DSM-IV (SCID; First et al., 1995) that was modified to provide a dimensional, rather than categorical, assessment of symptoms and diagnosis, in the spirit of RDoC. A small subset of participants at the start of the study were diagnosed using the Diagnostic Interview for Genetic Studies (DIGS; Nurnberger et al., 1994), prior to switching to the dimensional SCID. The SCID or DIGS interview confirmed current remitted/euthymic status and included a review of each participant's past mood episodes, such that we were able to retrospectively confirm a diagnosis of a past mood disorder.

At baseline, a masters-level clinician also conducted the Hamilton Depression Rating Scale (HAM-D; Hamilton, 1960), Hamilton Anxiety Rating Scale (HAM-A; Hamilton, 1959), and Young Mania Rating Scale (YMRS, Young et al., 1978) with each participant. A verbal IQ estimate was obtained (Shipley et al., 2009). Participants then completed an ordered battery of self-report questionnaires and EF tasks. All participants performed the T-MIDT task, described below, during the neuropsychological battery. A subset of participants performed the task again during fMRI.

Participants were compensated $250 for completion of the intake procedures and neuropsychological battery, with the opportunity to win up to an additional $52 based upon performance on the computerized reward task.

Measures

Reward

Titrated monetary incentive delay task (T-MIDT).: The MIDT was a 24-minute reward-processing task in which participants responded to a simple visual stimulus (target) with an index-finger button-press within a predefined response window. The present task was modified from the original task (Knutson et al., 2000). The task was presented in E-Prime (Version 2.0, Psychology Software Tools Inc., Pittsburgh PA, USA). There were three types of trials: win, neutral, and loss trials. At the beginning of each trial, the type of trial upcoming and amount of money at stake was indicated by a cue: "win $5" or "win $0.20" in a red circle, "don't lose $5" or "don't lose $0.20" in a blue square, or "no money at stake" in a green triangle. The cue then disappeared and, after a variable delay, a white square (the target) flashed on the screen. The length of time of the variable delay and target totaled 1000

ms for each trial (see next paragraph for more details). Upon seeing the target, participants were instructed to press the button as quickly as possible within the response window in order to win $0.20 or $5 (on win trials) or avoid losing $0.20 or $5 (on loss trials). On neutral trials, no money was at stake, no matter how quickly participants responded; however, participants were instructed to respond as quickly as possible even on neutral trials. After the target disappeared, participants received feedback as to whether they won or lost money. The three types of trials yielded nine possible outcomes: small win ($0.20 or none earned), big win ($5 or none earned), small loss (none lost or -$0.20), big loss (none lost or -$5), or no money at stake ($0). The inter-trial interval (ITI) was jittered, ranging from 2000–6000 ms with an average duration of 4000 ms. The task consisted of four runs of 25 trials each (5 per type) and lasted about 24 minutes (6 minutes per run). The order of trial types was randomized within each run. The task was administered during the fMRI scan. An example trial showing the timing of the task is presented in Figure 1.

Before completing runs 1–4, participants completed a 25-trial baseline run outside of the scanner. Besides acquainting participants with the task, the purpose of the baseline run (with a fixed 250 ms response time) was to measure each participant's reaction time (RT) to the target stimulus and then titrate the in-scanner task to that individualized response window. For example, if a participant's average RT to the target during the baseline run were 220 ms with a standard deviation (SD) of 30 ms, the response window for run 1 would be set to 265 ms (mean plus 1.5*SD). The variable delay time was then calculated by subtracting the response window time from 1000 ms. Titration adjustments were also made after the first and second runs of the task based upon number of correct responses, which was tracked by the experimenter and kept blind to the participant. Response window durations were either increased or decreased by .5 SD of the baseline average RT if accuracy was below 50% or above 80%, respectively. Participants were told that only their performance on runs three and four would count towards their total earnings (up to $52 more than the base compensation) and that no money would be taken away if their final performance was below $0. The individual titration process was aimed to result in each participant achieving 50–80% accuracy on the task. Titration also standardized the task by removing the effect of each participant's individual psychomotor ability.

Snaith-Hamilton Pleasure Scale (SHAPS).: The SHAPS (Snaith et al., 1995) assessed anhedonia, or the ability to experience pleasure, within the last several days.

Cognitive ability

Shipley Institute of Living Scale.: This scale (Zachary et al., 1985) provided a self-report estimate of verbal IQ based on vocabulary knowledge.

Executive functioning

Parametric Go/No-Go Stop Task (PGNGS).: The PGNGS (Langenecker et al., 2007) was developed by our group to measure sustained attention, set shifting, and response inhibition. The task involved responding as quickly and accurately as possible to letters rapidly presented on a computer screen, while inhibiting prepotent responses to certain targets that repeat and static non-targets. There were two conditions: two target and three target. There

were three levels in each condition: Go, in which the participant hit a button whenever the target letters appeared; Go/no-go, in which the participant hit a button whenever the target letters appeared but not when the target letters were presented in a repeating order; and Go/stop, in which the participant hit a button whenever the target letters appeared but not if a stop sign appeared immediately after the target. The task yielded eight main outcome variables that reflected the percentage of correct responses and correct inhibitions across conditions and levels. The PGNGS has demonstrated good construct validity and retest reliability in healthy and depressed samples (Langenecker et al., 2007; Votruba & Langenecker, 2013; Peters et al., 2015).

Trail Making Test.: The Trail Making Test (Tombaugh, 2004) contains two subtests. In Trails A, a measure of processing speed, participants drew lines connecting a display of numbers on a page in order as quickly as they could. In Trails B, which measures set-shifting, participants drew lines connecting a display of alternating numbers and letter in order (i.e., 1-A-2-B-3-C, etc.). Raw scores (time in number of seconds to complete the task) were the outcome variable. We opted to use raw scores rather than T scores because of the narrow age and educational range in the sample.

Stroop Color-Word Interference.: The Stroop task (Stroop, 1935) is a classic measure of verbal inhibitory control. In the color-word interference trial, which measures inhibition and set-shifting, participants viewed a sheet with color words that are printed in an incongruent ink color (e.g., “red” is printed in blue), and they were instructed to ignore the prepotent response of reading the word and instead identify the ink color. T-scores were used in the present analyses.

Wechsler Adult Intelligence Scale Digit Span.: Digit Span (Wechsler, 1997) is a well-recognized measure of attention and working memory. During this task, participants heard increasingly long strings of numbers and were instructed to repeat them back exactly. In the forward condition, the string was to be repeated in the same order it was presented. In the backward condition, the string was to be repeated in the backwards order that it was presented. Although norms do not exist for the separate components of the test, the forward and backward scaled scores were used in the present analyses.

Cambridge Neuropsychological Test Automated Batteries (CANTAB) Spatial Working Memory.: This subtest of the CANTAB (Fray et al., 1996) is a computerized task requiring retention and manipulation of spatial information in working memory. The participant was required to find blue tokens in a series of displayed boxes and use these tokens to fill up an empty column while not returning to the boxes that previously housed blue tokens. Each box disappeared once it was selected, resulting in the search being ordered by each individual’s choices. There were three conditions: four-, six-, and eight-box. Performance was measured as the number of errors made during each condition.

Personality and symptoms

Behavioral Inhibition System/Behavioral Activation System Scales (BIS/BAS).: The BIS/BAS (Carver & White, 1994) measured the personality traits behavioral inhibition and

behavioral activation. Three of the four subscales were used: behavioral inhibition (BIS), reward-responsiveness (BAS-RR), and drive (BAS-D). Higher scores indicate higher levels of the trait.

Beck Anxiety Inventory (BAI).: The BAI (Steer & Beck, 1997) assessed broad anxiety symptoms over the last week.

Beck Depression Inventory (BDI).: The BDI (Beck et al., 1997) assessed depressive symptoms over the last two weeks.

fMRI acquisition

Scans were acquired on a GE Discovery scanner using parallel imaging with ASSET and T2* gradient-echo axial echo planar imaging sequence (44 3mm thick slices, TE = 22.2 ms; TR = 2000 ms; 143 TRs total; flip angle = 90°; FOV = 22; matrix = 64 × 64). High-resolution T1 anatomic scans were obtained for spatial normalization.

fMRI preprocessing

Functional images underwent slice-timing corrections with SPM8 (http://www.fil.ion.ucl.ac.uk/spm/doc/) and motion correction algorithms with FSL (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/). During pre-processing, images were visually inspected for motion greater than 1.5 mm across more than three TRs; no subjects were removed from the present analyses based upon this motion check. Structural and functional images were co-registered and then the co-registered T1-MPRAGE underwent spatial normalization (DARTEL to MNI template). The resulting normalization matrix was then applied to the slice-time-corrected, movement corrected, time series data and smoothed with a 5 mm Gaussian kernel. Resulting T2* images contained were 2 mm isotropic voxels.

Statistical and ROI analyses for fMRI data

A contrast of interest was created by subtracting neutral trial activation from win trial activation (W-N). This contrast was based upon win trial activation, which encompassed the anticipation of potential wins using the canonical hemodynamic response function in SPM8 (without derivatives), irrespective of subsequent performance. A between-groups ANOVA was conducted with W-N activation as the dependent variable; covariates of no interest were age, sex, and the average standard deviations of pitch, roll, and yaw translations. Cluster extent was determined based upon 1000 Monte Carlo simulations in the bug-fixed 3dClustSim tool (Cox et al., 2016), resulting in a joint threshold of height and extent ($p < .005$, extent of 464 mm^3). The Monte Carlo approach was intended to balance Type I and Type II error. A gray matter mask was applied and whole brain alpha of .01 was achieved.

We built ROIs for the following regions based on MNI coordinates reported in relevant meta-analyses: right VS (12, 10, −6) and left VS (−12, 10, −6; Bartra, McGuire, & Kable, 2013), dACC (0, 18, 49; Lieberman & Eisenberger, 2015), and right DLPFC (40, 32, 30) and left DLPFC (−40, 32, 30; Owen et al., 2005). Each ROI, built using the marsbar toolbox in SPM8, was spherical with an 8mm radius. We then extracted the data from each ROI for each participant.

We ran the fMRI analyses with and without the individuals in the HMD group with Ham-D scores over 8, which revealed no significant differences in the pattern of results. We therefore present the results with all individuals included.

Statistical analyses for behavioral data

To reduce multiple comparisons stemming from the multi-variable PGNGS task, we entered the eight outcome variables into a maximum-likelihood factor analysis with direct oblimin rotation and a maximum of 25 iterations. Direct oblimin is a type of oblique rotation, which allows the factors to correlate (Costello & Osborne, 2005). We chose oblique rotation because the outcome variables from the task were correlated, and therefore forcing an orthogonal factor solution would be inaccurate (Costello & Osborne, 2005). Three factors emerged: percentage of correct responses to targets at the go/no-go level across both conditions (GNG percent hits), percentage of correct responses to targets at the go/stop level across both conditions (go-stop percent hits), and percentage of correct inhibited responses at the go/no-go and go/stop levels across both conditions (no-go and stop percent correct inhibition).

Factor analysis with the same parameters as above was also conducted on the three outcomes variables from the CANTAB spatial working memory task, yielding a single factor for the combined errors committed during all three conditions.

To assess divergence and convergence of the reward and EF tasks, we computed Pearson's *r* correlation coefficients between the variables of interest in each task. We used data from the T-MIDT performed outside the scanner for the analyses related to divergence, convergence, and clinical/personality variables (Tables 2–5).

There were no significant differences in the pattern of results when individuals in the HMD group with Ham-D scores above 8 were removed. We therefore present the results with all individuals included.

Results

Divergence of reward and executive function measures

AMW in the practice run (prior to any titration) was positively correlated with set-shifting on the Color-Word Stroop ($r(157) = .21$, $p = .01$) and negatively correlated with speed on Trails A ($r(143) = -.21$, $p = .01$) and spatial working memory on the CANTAB ($r(168) = -.16$, $p = .03$). Amount of money won (AMW) in the fully titrated runs (runs 3 and 4) of the T-MIDT was positively correlated with inhibitory control as measured by the PGNGS task ($r(169) = .18$, $p = .02$) and Stroop Color-Word test ($r(157) = .21$, $p = .01$) but not significantly correlated with IQ ($r(161) = .02$, $p = .85$), Trails A time ($r(141) = .21$, $p = .01$), Trails B time ($r(141) = -.07$, $p = .41$), the difference between Trails A and B times ($r(141) = -.07$, $p = .41$), Forward Span working memory ($r(157) = .14$, $p = .09$), Backward Span working memory ($r(157) = .04$, $p = .60$), CANTAB ($r(168) = -.08$, $p = .28$), GNG hits ($r(169) = .12$, $p = .12$), or Go-Stop hits ($r(169) = -.05$, $p = .56$). Accuracy on win trials in the fully titrated runs of the T-MIDT was significantly positively correlated with correct inhibitions in the PGNGS ($r(168) = .21$, $p = .01$) and Stroop Color-Word score ($r(156) = .21$,

$p = .01$), but not significantly correlated with estimated IQ ($t(160) = .09$, $p = .28$), Trails A time ($t(142) = -.14$, $p = .10$), Trails B time ($t(140) = -.11$, $p = .19$), the difference between Trails A and B times ($t(140) = -.08$, $p = .34$), Forward Span ($t(156) = .14$, $p = .09$), Backward Span ($t(156) = -.01$, $p = .93$), CANTAB ($t(167) = -.06$, $p = .47$), GNG hits ($t(168) = .13$, $p = .08$), and Go-Stop hits ($t(168) = -.10$, $p = .22$). Accuracy on loss trials in the T-MIDT titrated runs was significantly correlated with Forward Span ($t(156) = .18$, $p = .02$), correct inhibitions on the PGNGS task ($t(168) = .26$, $p = .001$), and Stroop Color-Word ($t(156) = .18$, $p = .03$), but not significantly correlated with estimated IQ ($t(160) = .08$, $p = .29$), Trails A time ($t(142) = -.10$, $p = .37$), Trails B time ($t(140) = -.11$, $p = .21$), the difference between Trails A and B times ($t(140) = -.08$, $p = .22$), Backward Span ($t(156) = .10$, $p = .22$), CANTAB ($t(167) = -.12$, $p = .12$), GNG hits ($t(168) = .09$, $p = .27$), and Go-Stop hits ($t(168) = -.10$, $p = .21$). Accuracy on neutral trials of the titrated T-MIDT runs was correlated with Stroop Color-Word ($t(156) = .19$, $p = .02$), but not significantly with estimated IQ ($t(160) = .01$, $p = .88$), Trails A time ($t(142) = -.12$, $p = .15$), Trails B time ($t(140) = -.05$, $p = .54$), the difference between Trails A and B times ($t(140) = -.03$, $p = .77$), Forward Span ($t(156) = .05$, $p = .55$), Backward Span ($t(156) = .07$, $p = .42$), CANTAB ($t(167) = -.08$, $p = .30$), GNG hits ($t(168) = .04$, $p = .61$), Go-Stop hits ($t(168) = -.06$, $p = .45$), or correct inhibitions in the PGNGS task ($t(168) = .02$, $p = .83$). See Table 2 for full correlation matrix.

Group behavioral differences

We examined correlations between the pre-titration and post-titration T-MIDT runs and EF measures separately by group (Table 3). Correlations that were significant across groups (reported above) were found to be driven by either the HC or HMD group. Before titration, the HC group showed significant positive correlations between AMW and IQ ($t(38) = .33$, $p = .04$) and between AMW and Stroop Color-Word ($t(37) = .37$, $p = .02$). After titration, the correlation between AMW and Stroop was significant for the HMD group ($t(118) = .21$, $p = .02$) but not HC group ($t(37) = .18$, $p = .28$). In only the HMD group before titration, AMW was significantly correlated with Trails A speed ($t(106) = -.25$, $p = .01$) and CANTAB spatial working memory ($t(125) = -.21$, $p = .02$). After titration, AMW was significantly correlated with GNG hits in the HC group ($t(39) = .32$, $p = .04$) but not HMD group ($t(128) = .06$, $p = .53$). After titration, AMW was significantly correlated with correct inhibition on the PGNGS ($t(128) = .17$, $p = .05$) in the HMD group but not HC group ($t(39) = .16$, $p = .31$).

As expected, there were no performance differences on the T-MIDT between the HMD and HC groups. Specifically, on AMW in the baseline run, the HC group ($M = 14.65$, $SD = 8.17$) and HMD group ($M = 14.59$, $SD = 8.29$) did not differ, $t(172) = .04$, $p = .97$. On AMW in the two fully titrated runs, the HC group ($M = 41.89$, $SD = 9.28$) and HMD group ($M = 39.69$, $SD = 10.74$) did not differ, $t(172) = 1.20$, $p = .23$.

Convergence of T-MIDT and clinical measures in HMD group

Looking at the HMD group alone, some symptom and trait measures were significantly associated with T-MIDT variables (Table 4). AMW in the titrated runs was negatively correlated with self-reported anxiety ($t(130) = -.21$, $p = .02$) and depression symptoms

($r(87) = -.25$, $p = .02$). Self-reported anxiety was also negatively correlated with accuracy for win trials ($r(129) = -.18$, $p = .04$) and loss trials ($r(129) = -.18$, $p = .05$) during the titrated runs.

BAS-RR showed a non-significant positive correlation with AMW in the titrated runs, $r(125) = .14$, $p = .13$. In contrast, BAS-RR was positively correlated with win trial accuracy during the titrated runs , $r(124) = .18$, $p = .05$. Posthoc Spearman's correlations with each item in the BAS-RR subscale revealed that an item about feeling energized upon obtaining something desired ($r(123) = .25$, $p = .01$) and an item about feeling excited about an opportunity to get something appealing ($r(123=4) = .18$, $p = .04$) were significantly correlated with win trial accuracy (Table 5). SHAPS was not related to AMW in the pre-titrated ($r(86) = .06$, $p = .58$) or titrated ($r(86) = .05$, $p = .65$) runs of the T-MIDT.

fMRI

Across groups, during the anticipation of win trials compared to neutral, we observed five clusters of increased activation in many reward circuit and related regions, including the DLPFC, middle frontal gyrus, ACC, thalamus, pallidum, amygdala, hippocampus, VS, caudate, insula, subthalamic nucleus substantia nigra, and supplementary motor area (Figure 2). We observed 16 clusters of decreased activation in the superior, middle, and inferior temporal gyri; fusiform gyrus; superior, middle, and inferior frontal gyri; lingual gyrus; middle and superior occipital gyri; cuneus; and supramarginal gyrus.

There were no regions in which the HMD group showed greater activation than the HC group. The HC group showed greater activation in the anterior cerebellum and the postcentral gyrus, compared to the HMD group.

BOLD signal values extracted from the ROIs were not correlated with the T-MIDT behavioral indices (Table 6).

Discussion

The present study sought to establish the divergent and convergent validity of the T-MIDT, which was modified from a widely used probe of NAcc BOLD response. We also evaluated the sensitivity of the T-MIDT in detecting group differences between those with a history of mood disturbance and healthy comparisons. Our results suggest that, once individual differences in psychomotor speed have been controlled for, the T-MIDT taps into a reward construct that is largely distinct from processing speed and EF abilities. We did not observe group differences in T-MIDT performance; however, residual depression and anxiety symptoms were negatively related to performance in the T-MIDT in the HMD group. In support of the validity of the task as a reward circuit probe, increased activation in the reward circuit was observed during anticipation of monetary gains.

Our results provide preliminary support for convergent validity of the T-MIDT as a measure of reward processing. Specifically, trait reward responsiveness (BAS-RR) was positively correlated with accuracy for the win trials in the titrated runs in the HMD group. In a posthoc analysis of this finding, two of five items that make up the measure of trait reward

responsiveness were correlated with win trial accuracy. These items both referred to the exciting, energizing experience of obtaining something desirable. The non-correlated items had more to do with the sustained rewarding experience of achievement or positive events occurring. Considering the nuanced differences between these sets of items, the T-MIDT may converge more with state reward responsiveness than long-term or trait reward responsiveness. With further examination and corroboration, these items alone could be used as screening items in clinical practice to predict reward-related behavior, which could be useful for treatment selection (e.g. choosing behavioral activation). State anhedonia in the HMD group, as measured by the SHAPS, was not correlated with any runs in the T-MIDT or accuracy for any type of trial, which may suggest a lack of convergence or that these measures assess different aspects of reward processing.

Intra-task convergence was demonstrated with win accuracy, loss accuracy, and titrated AMW showing moderate-to-strong positive correlations with each other, in each group. These correlations were slightly weaker in the HMD compared to HC group, which may represent impairment in reward function that did not resolve for some with HMD, even in the absence of symptoms, or may point to a scar of illness. Neutral trial accuracy generally showed a poorer pattern of correlation with other T-MIDT variables..

Divergent validity was demonstrated by lack of correlation between the T-MIDT and performance on most of the standard neuropsychological tests, including IQ and processing speed. Prior to or early in titration, the T-MIDT was correlated with measures of processing speed, attention, estimated IQ, spatial working memory, and inhibition. Divergence emerged most clearly after the task parameters had been titrated to control for each individual's psychomotor speed. In the HMD group, self-reported anxiety and depression were correlated with amount won and accuracy in only the titrated runs of the T-MIDT, suggesting that residual symptoms influence reward processing after psychomotor ability is adjusted for. The relationship between symptoms and titrated T-MIDT performance underscores the divergent validity of the task, in that residual psychiatric symptoms influence reward processing more than EF abilities do. The T-MIDT may be particularly useful for objectively assessing reward processing in active mood disorders and other populations apart from psychomotor speed, which is also often impaired (Rock et al., 2013).

Surprisingly, in the sample as a whole, there were modest correlations between T-MIDT and inhibition measures. Reward processing and inhibitory control represent distinct, but associated functions, particularly across development (Sergeant et al., 2003), with inhibitory control developing later in adolescence relative to reward functions (Geier et al., 2009). Both reward processing and inhibition similarly involve a level of expectancy and are relevant to decision-making and execution processes that depend on prefrontal (e.g., orbitofrontal cortex) and subcortical (e.g., striatum) structures (Schoenbaum et al., 2009, Schoenbaum et al., 2011). Considering the divergence of reward processing with the EF measures other than inhibition, we assert that reward and executive function do appear to be distinct. Our data are not definitive or conclusive, but reveal a low association of T-MIDT with inhibition and not other measures of EF.

Amount won during the titrated runs of the T-MIDT was positively correlated with two measures of inhibitory control. These results are in line with previous research showing that reward incentive improves response inhibition (Geier et al., 2009). During a task in which participants could earn money by inhibiting a saccade towards a peripheral cue, both adolescents and adults had faster inhibitory responses (eye movement away from the cue) during reward incentive trials compared to neutral (Geier et al., 2009). Considered alongside the present results, there may be a bidirectional relationship between inhibitory control capacity and reward responsiveness. There may also be a developmental component to this, as suggested by a previous finding that adolescents, but not adults, exhibited fewer inhibitory errors during reward trials compared to neutral, indicating that adolescents may be more sensitive to reward modulation of inhibitory control or that adults may have been already performing at the optimal level (Geier et al., 2009). Looking to the ADHD literature, there is a lack of consensus on whether children with ADHD are hypo- or hyper-sensitive to reward, but it is clear that children with ADHD experience both reward dysfunction and inhibitory control deficits (Sergeant et al., 2003), further underscoring the potential connections between reward and inhibition.

We did not observe group differences on T-MIDT performance, which is in line with many previous studies that have not found behavioral differences between mood disorder and HC groups (Knutson et al., 2001; Knutson et al., 2008; Andrews et al., 2011; Nusslock et al., 2012; Balodis & Potenza, 2015). We propose that, although the T-MIDT may be sensitive to behavioral deficits in participants in the active phase of MDD (DelDonno et al., 2015), the task may not detect or there may not be behavioral reward responsiveness deficits in individuals in the remitted or euthymic phase of illness (e.g. Nusslock, et al., 2012).

Examining the divergence between T-MIDT and EF measures did reveal some group patterns. Relationships between T-MIDT and EF variables were not always consistent when looking across HC and HMD versus at each group separately, which may be a limitation caused by the relatively small sample size for HCs ($n = 46$). In HCs, estimated IQ was moderately positively correlated with AMW in the pre-titrated runs and with loss trial accuracy in the titrated runs of the T-MIDT. This relationship suggests that elements of this task modestly tap into intellectual abilities for HCs, but not for HMDs; in other words, in mood disorder samples, the T-MIDT may provide a measure of reward processing unadulterated by effects of IQ.

Individual differences in psychomotor speed on the T-MIDT were controlled by the titration procedure, more so in the HMD group than HC group. This effect was demonstrated by increased divergence between EF tests with processing speed elements (Trails A, Digit Span, Go-stop and No-go percent correct, and Stroop Color-Word) and AMW in the post-titration T-MIDT runs, relative to pre-titration. Specifically, before titration the magnitude of the correlations between these EF tests and AMW differed modestly between the HMD and HC groups, whereas after titration the magnitude and direction of correlations became more similar between groups. This pattern suggests that, for individuals in the remitted state of MDD, it is important to adjust task parameters for individual differences in processing speed when assessing reward anticipation functioning. Of course, these differences are statistically

minor, but the clinical interpretation of the task becomes clearer and possibly invariant across groups. Future studies with larger samples can test this more explicitly.

The imaging data provided evidence of the task's validity as a reward circuit probe. Despite the behavioral performance metrics not being correlated with BOLD response in key reward regions, we observed that the win anticipation component of the task robustly activated the reward circuit, which is consistent with the design of the original task (Knutson et al., 2000) and regions purported to be functionally associated with reward anticipation (Haber & Knutson, 2010; Heshmati & Russo, 2015). We also observed increased in activation frontal, parietal, and subcortical regions that would not be considered part of the core reward circuit. These findings are in line with a meta-analysis examining brain regions activated during reward processing (Liu et al., 2011). This meta-analysis identified a core reward network, as well as a number of frontal, supplementary motor area, and parietal regions activated during reward anticipation. Further research, perhaps using a connectivity approach, is needed to better understand these findings.

Interestingly, we did not observe reward circuit activation differences between groups, which could suggest that the blunted reward circuit activation typically seen in active MDD patients normalized in the remitted state, relative to HCs. In contrast to what would be expected based on previous reports, activation in the VS and other key ROIs was not significantly correlated with the behavioral indices of the task. It may be that although the reward anticipation phase of the T-MIDT robustly elicits broad reward circuit activation, performance metrics do not reflect activation in any single region. Moreover, the neural process of anticipation of reward (displayed in Figure 2) and the motoric response within a fixed window (reflected in Table 6) need not be related to each other. The former could pertain to the desire for engagement in process of winning, while the latter could relate to visual perception and efficiency of motoric action. Nonetheless, the observed lack of correlation between performance and ROI activation fails to support the use of the T-MIDT as a probe of neural signal in specific regions of the reward circuit.

We note some limitations of the current study. First, examining convergent and divergent validity across individuals with and without a history of mood disorders could diminish the clarity of the results. However, assuming a full dimensionality to reward processing across normal and abnormal levels of functioning is consistent with NIMH's Research Domain Criteria initiative and highlights individual differences. Second, convergent validity may have been under-assessed, as participants completed only one objective measure of reward function, although we did include clinically relevant self-reports of state anhedonia and trait reward responsiveness for preliminary evaluation of convergent validity in the HMD group. Third, the T-MIDT did not detect behavioral differences between the HC and HMD groups. Our group previously published findings from a different sample in which actively depressed individuals won significantly less money on the T-MIDT than remitted depressed individuals and healthy controls (DelDonno et al., 2015). Considering our previous findings together with the current results, we posit that the T-MIDT is a clinically sensitive measure for individuals with active psychiatric symptoms, but is unlikely to detect differences in currently euthymic individuals. Fourth, there was an unbalanced distribution by race in the two groups, with fewer African Americans and more Asian Americans in the HC group

relative to the HMD group. Fifth, due to a change in study protocol, a subset of participants were diagnosed at baseline using the DIGS, whereas the majority of participants underwent the dimensional SCID interview. Although this change introduces a slight confound in diagnosis, all diagnoses were reviewed and confirmed by another masters- or Ph.D.-level clinician.

To date, tasks that measure reward processing in humans have not been validated in normative samples for clinical use or used a titration approach to control for other forms of processing speed and EF. Future work should further examine the diagnostic and prescriptive value of this measure in psychiatric and related disorders that commonly involve deficits in reward processing (e.g., ADHD, addiction). Prospective work in these groups may help to determine whether this measure of reward processing predicts treatment response. For the purposes of creating norms for the T-MIDT, future research with a larger sample could examine sex and age differences on the T-MIDT and how sex and age might moderate divergence and convergence from EF measures. Future studies with larger samples could more broadly and prospectively address a multitrait, multimethod matrix of reward functioning.

Overall, the present findings indicate that the T-MIDT taps into a reward processing function that is divergent from executive function, save for inhibitory control. These findings also highlight the importance of individually titrating task parameters to reduce confounding effects of individual differences in psychomotor speed. The current data suggest that reward responsiveness, as measured by the T-MIDT, might be considered a distinct process from EF and warrants further development as a neuropsychological probe. In terms of the imaging results, our data support the use of the T-MIDT as a neural probe of reward circuit activation during reward anticipation. Our data provide only weak evidence of the T-MIDT as a clinically sensitive behavioral probe of reward responsiveness, given the lack of group differences in performance and modest relationships between residual clinical symptoms and performance. We also did not observe a correlation between behavioral performance and BOLD response in any given reward circuit ROI, suggesting that the T-MIDT is not a sensitive probe of neural activation in isolated brain regions.

Two clinically relevant findings emerged: the two groups differed in their patterns of correlations between T-MIDT and EF measures, and residual mood and anxiety symptoms were correlated with T-MIDT performance in the HMD group. These two findings are particularly important considering that neuropsychologists often report frustration in evaluating the effect of symptoms upon performance in clinical patients. With further psychometric validation in a broader age range and variety of psychiatric and neurological illnesses, it is conceivable that the T-MIDT could provide useful clinical information if given as part of a neuropsychological battery.

Acknowledgements

This work was supported by the National Institute of Mental Health under Grant MH 101487 (SAL, SRD, LMJ, JPS, LRK).

References

Andrews MM, Meda SA, Thomas AD, Potenza MN, Krystal JH, Worhunsky P, … & Pearlson GD (2011). Individuals family history positive for alcoholism show functional magnetic resonance imaging differences in reward sensitivity that are related to impulsivity factors. Biological psychiatry, 69(7), 675–683. [PubMed: 21126735]

Balodis IM, & Potenza MN (2015). Anticipatory reward processing in addicted populations: a focus on the monetary incentive delay task. Biological psychiatry, 77(5), 434–444. [PubMed: 25481621]

Bartra O, McGuire JT, & Kable JW (2013). The valuation system: a coordinate-based meta-analysis of BOLD fMRI experiments examining neural correlates of subjective value. Neuroimage, 76, 412–427. [PubMed: 23507394]

Bearden CE, Hoffman KM, & Cannon TD (2001). The neuropsychology and neuroanatomy of bipolar affective disorder: a critical review. Bipolar disorders, 3(3), 106–150. [PubMed: 11465675]

Bechara A, Damasio H, Tranel D, & Damasio AR (2005). The Iowa Gambling Task and the somatic marker hypothesis: some questions and answers. Trends in cognitive sciences, 9(4), 159–162. [PubMed: 15808493]

Beck AT, Steer RA, & Brown GK (1996). Beck depression inventory-II. San Antonio, 78(2), 490–8.

Belliveau JW, Kennedy DN, McKinstry RC, Buchbinder BR, Weisskoff R, Cohen MS, … & Rosen BR (1991). Functional mapping of the human visual cortex by magnetic resonance imaging. Science, 254(5032), 716–719. [PubMed: 1948051]

Bernheimer H, Birkmayer W, Hornykiewicz O, Jellinger K, & Seitelberger F 1. (1973). Brain dopamine and the syndromes of Parkinson and Huntington Clinical, morphological and neurochemical correlations. Journal of the neurological sciences, 20(4), 415–455. [PubMed: 4272516]

Breiter HC, Berke JD, Kennedy WA, Rosen BR, and Hyman SE 1996 Activation of striatum and amygdala during reward conditioning: An FMRI study. NeuroImage 3:S220.

Breiter HC, Gollub RL, Weisskoff RM, Kennedy DN, Makris N, Berke JD, Goodman JM, Kantor HL, Gast-friend DR, Riorden JP, Mathew RT, Rosen BR, and Hyman SE 1997 Acute effects of cocaine on human brain activity and emotion. Neuron 19:591–611. [PubMed: 9331351]

Brock LL, Rimm-Kaufman SE, Nathanson L, & Grimm KJ (2009). The contributions of 'hot'and 'cool' executive function to children's academic achievement, learning-related behaviors, and engagement in kindergarten. Early Childhood Research Quarterly, 24(3), 337–349.

Carver CS, & White TL (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS Scales. Journal of personality and social psychology, 67(2), 319.

Caseras X, Lawrence NS, Murphy K, Wise RG, & Phillips ML (2013). Ventral striatum activity in response to reward: differences between bipolar I and II disorders. American Journal of Psychiatry, 170(5), 533–541. [PubMed: 23558337]

Costello AB, & Osborne JW (2005). Best practices in exploratory factor analysis: Four recommendations for getting the most from your analysis. Practical assessment, research & evaluation, 10(7), 1–9.

DelDonno SR, Weldon AL, Crane NA, Passarotti AM, Pruitt PJ, Gabriel LB, … & Heitzeg MM (2015). Affective personality predictors of disrupted reward learning and pursuit in major depressive disorder. Psychiatry research, 230(1), 56–64. [PubMed: 26319737]

Desgranges B, Baron JC, & Eustache F (1998). The functional neuroanatomy of episodic memory: the role of the frontal lobes, the hippocampal formation, and other areas. Neuroimage, 8(2), 198–213. [PubMed: 9740762]

Di Martino A, Scheres A, Margulies DS, Kelly AMC, Uddin LQ, Shehzad Z, … & Milham MP (2008). Functional connectivity of human striatum: a resting state FMRI study. Cerebral cortex, 18(12), 2735–2747. [PubMed: 18400794]

Dolcos F, Iordan AD, & Dolcos S (2011). Neural correlates of emotion–cognition interactions: A review of evidence from brain imaging investigations. Journal of Cognitive Psychology, 23(6), 669–694. [PubMed: 22059115]

Eklund A, Nichols TE, & Knutsson H (2016). Cluster failure: why fMRI inferences for spatial extent have inflated false-positive rates. Proceedings of the National Academy of Sciences, 113(28), 7900–7905.

Elliott R (2003). Executive functions and their disorders: Imaging in clinical neuroscience. British medical bulletin, 65(1), 49–59. [PubMed: 12697616]

Epstein J, Pan H, Kocsis JH, Yang Y, Butler T, Chusid J, … & Silbersweig DA (2006). Lack of ventral striatal response to positive stimuli in depressed versus normal subjects. American Journal of Psychiatry, 163(10), 1784–1790. [PubMed: 17012690]

First MB, Spitzer RL, Gibbon MWJB, & Williams JB (1995). Structured clinical interview for DSM-IV axis I disorders. New York: New York State Psychiatric Institute.

Fukui H, Murai T, Fukuyama H, Hayashi T, & Hanakawa T (2005). Functional activity related to risk anticipation during performance of the Iowa Gambling Task. Neuroimage, 24(1), 253–259. [PubMed: 15588617]

Fuster JM (1988). Prefrontal cortex In Comparative neuroscience and neurobiology (pp. 107–109). Birkhäuser Boston.

Geier CF, Terwilliger R, Teslovich T, Velanova K, & Luna B (2009). Immaturities in reward processing and its influence on inhibitory control in adolescence. Cerebral cortex, 20(7), 1613–1629. [PubMed: 19875675]

Haber SN, & Knutson B (2010). The reward circuit: linking primate anatomy and human imaging. Neuropsychopharmacology, 35(1), 4–26. [PubMed: 19812543]

Heshmati M, & Russo SJ (2015). Anhedonia and the brain reward circuitry in depression. Current behavioral neuroscience reports, 2(3), 146–153. [PubMed: 26525751]

Hester R, & Garavan H (2004). Executive dysfunction in cocaine addiction: evidence for discordant frontal, cingulate, and cerebellar activity. Journal of Neuroscience, 24(49), 11017–11022. [PubMed: 15590917]

Hickok G, & Poeppel D (2000). Towards a functional neuroanatomy of speech perception. Trends in cognitive sciences, 4(4), 131–138. [PubMed: 10740277]

Hongwanishkul D, Happaney KR, Lee WS, & Zelazo PD (2005). Assessment of hot and cool executive function in young children: Age-related changes and individual differences. Developmental neuropsychology, 28(2), 617–644. [PubMed: 16144430]

Kaiser RH, Andrews-Hanna JR, Wager TD, & Pizzagalli DA (2015). Large-scale network dysfunction in major depressive disorder: a meta-analysis of resting-state functional connectivity. JAMA psychiatry, 72(6), 603–611. [PubMed: 25785575]

Killgore WD, & Yurgelun-Todd DA (2007). Neural correlates of emotional intelligence in adolescent children. Cognitive, Affective, & Behavioral Neuroscience, 7(2), 140–151.

Killgore WD, Weber M, Schwab ZJ, DelDonno SR, Kipman M, Weiner MR, & Rauch SL (2012). Gray matter correlates of Trait and Ability models of emotional intelligence. Neuroreport, 23(9), 551–555. [PubMed: 22546702]

Killgore WD, Schwab ZJ, Tkachenko O, Webb CA, DelDonno SR, Kipman M, … & Weber M (2013). Emotional intelligence correlates with functional responses to dynamic changes in facial trustworthiness. Social neuroscience, 8(4), 334–346. [PubMed: 23802123]

Knutson B, Adams CM, Fong GW, & Hommer D (2001). Anticipation of increasing monetary reward selectively recruits nucleus accumbens. Journal of Neuroscience, 21(16), RC159–RC159. [PubMed: 11459880]

Knutson B, Bhanji JP, Cooney RE, Atlas LY, & Gotlib IH (2008). Neural responses to monetary incentives in major depression. Biological psychiatry, 63(7), 686–692. [PubMed: 17916330]

Knutson B, & Heinz A (2015). Probing psychiatric symptoms with the monetary incentive delay task. Biological psychiatry, 77(5), 418–420. [PubMed: 25645271]

Knutson B, Westdorp A, Kaiser E, & Hommer D (2000). FMRI visualization of brain activity during a monetary incentive delay task. Neuroimage, 12(1), 20–27. [PubMed: 10875899]

Koob GF (1992). Drugs of abuse: anatomy, pharmacology and function of reward pathways. Trends in pharmacological sciences, 13, 177–184. [PubMed: 1604710]

Kringelbach ML, & Rolls ET (2004). The functional neuroanatomy of the human orbitofrontal cortex: evidence from neuroimaging and neuropsychology. Progress in neurobiology, 72(5), 341–372. [PubMed: 15157726]

Lieberman MD, & Eisenberger NI (2015). The dorsal anterior cingulate cortex is selective for pain: Results from large-scale reverse inference. Proceedings of the National Academy of Sciences, 112(49), 15250–15255.

Liu X, Hairston J, Schrier M, & Fan J (2011). Common and distinct networks underlying reward valence and processing stages: a meta-analysis of functional neuroimaging studies. Neuroscience & Biobehavioral Reviews, 35(5), 1219–1236. [PubMed: 21185861]

Lutz K, & Widmer M (2014). What can the monetary incentive delay task tell us about the neural processing of reward and punishment. Neuroscience and Neuroeconomics, 3, 33–35.

Mayer JD, Salovey P, Caruso DR, & Sitarenios G (2003). Measuring emotional intelligence with the MSCEIT V2. 0. Emotion, 3(1), 97. [PubMed: 12899321]

Middleton FA, & Strick PL (2000). Basal ganglia output and cognition: evidence from anatomical, behavioral, and clinical studies. Brain and cognition, 42(2), 183–200. [PubMed: 10744919]

Mirenowicz J, and Schultz W 1996 Preferential activation of midbrain dopamine neurons by appetitive rather than aversive stimuli. Nature 379:449–451. [PubMed: 8559249]

Nestler EJ, & Carlezon WA (2006). The mesolimbic dopamine reward circuit in depression. Biological psychiatry, 59(12), 1151–1159. [PubMed: 16566899]

Nielson KA, Langenecker SA, & Garavan H (2002). Differences in the functional neuroanatomy of inhibitory control across the adult life span. Psychology and aging, 17(1), 56. [PubMed: 11931287]

Nurnberger JI, Blehar MC, Kaufmann CA, York-Cooler C, Simpson SG, Harkavy-Friedman J, … & Reich T (1994). Diagnostic interview for genetic studies: rationale, unique features, and training. Archives of general psychiatry, 51(11), 849–859. [PubMed: 7944874]

Nusslock R, Almeida JR, Forbes EE, Versace A, Frank E, LaBarbara EJ, … & Phillips ML (2012). Waiting to win: elevated striatal and orbitofrontal cortical activity during reward anticipation in euthymic bipolar disorder adults. Bipolar disorders, 14(3), 249–260. [PubMed: 22548898]

Owen AM, McMillan KM, Laird AR, & Bullmore E (2005). N-back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. Human brain mapping, 25(1), 46–59. [PubMed: 15846822]

Parent A, & Hazrati LN (1995). Functional anatomy of the basal ganglia. I. The cortico-basal ganglia-thalamo-cortical loop. Brain Research Reviews, 20(1), 91–127. [PubMed: 7711769]

Patel KT, Stevens MC, Meda SA, Muska C, Thomas AD, Potenza MN, & Pearlson GD (2013). Robust changes in reward circuitry during reward loss in current and former cocaine users during performance of a monetary incentive delay task. Biological psychiatry, 74(7), 529–537. [PubMed: 23778289]

Phan KL, Wager T, Taylor SF, & Liberzon I (2002). Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. Neuroimage, 16(2), 331–348. [PubMed: 12030820]

Pizzagalli DA, Goetz E, Ostacher M, Iosifescu DV, & Perlis RH (2008a). Euthymic patients with bipolar disorder show decreased reward learning in a probabilistic reward task. Biological psychiatry, 64(2), 162–168. [PubMed: 18242583]

Rock PL, Roiser JP, Riedel WJ, & Blackwell AD (2013). Cognitive impairment in depression: a systematic review and meta-analysis. Psychological Medicine, 1–12. 10.1017/S0033291713002535

Pizzagalli DA, Iosifescu D, Hallett LA, Ratner KG, & Fava M (2008b). Reduced hedonic capacity in major depressive disorder: evidence from a probabilistic reward task. Journal of psychiatric research, 43(1), 76–87. [PubMed: 18433774]

Roiser JP, & Sahakian BJ (2013). Hot and cold cognition in depression. CNS spectrums, 18(3), 139–149. [PubMed: 23481353]

Rosas HD, Liu AK, Hersch S, Glessner M, Ferrante RJ, Salat DH, … & Fischl B (2002). Regional and progressive thinning of the cortical ribbon in Huntington's disease. Neurology, 58(5), 695–701. [PubMed: 11889230]

Schapira AH, Olanow CW, Greenamyre JT, & Bezard E (2014). Slowing of neurodegeneration in Parkinson's disease and Huntington's disease: future therapeutic perspectives. The Lancet, 384(9942), 545–555.

Schultz W, Dayan P, and Montague PR 1997 A neural substrate of prediction and reward. Science 275:1593–1599. [PubMed: 9054347]

Schultz W, Tremblay L, and Hollerman JR 1998 Reward prediction in the primate basal ganglia and frontal cortex. Neuropharmacology 37:421–429. [PubMed: 9704983]

Schoenbaum G, Roesch MR, Stalnaker TA, & Takahashi YK (2009). A new perspective on the role of the orbitofrontal cortex in adaptive behaviour. Nature Reviews Neuroscience, 10(12), 885 10.1038/nrn2753 [PubMed: 19904278]

Schoenbaum G, Takahashi Y, Liu T-L, & McDannald MA (2011). Does the orbitofrontal cortex signal value? Annals of the New York Academy of Sciences, 1239(1), 87–99. 10.1111/j.1749-6632.2011.06210.x [PubMed: 22145878]

Sergeant JA, Geurts H, Huijbregts S, Scheres A, & Oosterlaan J (2003). The top and the bottom of ADHD: a neuropsychological perspective. Neuroscience & Biobehavioral Reviews, 27(7), 583–592. [PubMed: 14624803]

Seeley WW, Menon V, Schatzberg AF, Keller J, Glover GH, Kenna H, … & Greicius MD (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. Journal of Neuroscience, 27(9), 2349–2356. [PubMed: 17329432]

Snaith RP, Hamilton M, Morley S, Humayan A, Hargreaves D, & Trigwell P (1995). A scale for the assessment of hedonic tone the Snaith-Hamilton Pleasure Scale. The British Journal of Psychiatry, 167(1), 99–103. [PubMed: 7551619]

Steer RA, & Beck AT (1997). Beck Anxiety Inventory.

Tombaugh TN (2004). Trail Making Test A and B: normative data stratified by age and education. Archives of clinical neuropsychology, 19(2), 203–214. [PubMed: 15010086]

Volkow ND, Fowler JS, Wang GJ, Baler R, & Telang F (2009). Imaging dopamine's role in drug abuse and addiction. Neuropharmacology, 56, 3–8. [PubMed: 18617195]

Vonsattel JPG, & DiFiglia M (1998). Huntington disease. Journal of neuropathology and experimental neurology, 57(5), 369. [PubMed: 9596408]

Wechsler D (2009). Advanced clinical solutions for the WAIS-IV and WMS-IV.

Young RC, Biggs JT, Ziegler VE, & Meyer DA (1978). A rating scale for mania: reliability, validity and sensitivity. The British Journal of Psychiatry, 133(5), 429–435. [PubMed: 728692]

Zachary RA, Crumpton E, & Spiegel DE (1985). Estimating WAIS-R IQ from the Shipley Institute of Living Scale. Journal of Clinical Psychology, 41(4), 532–540.

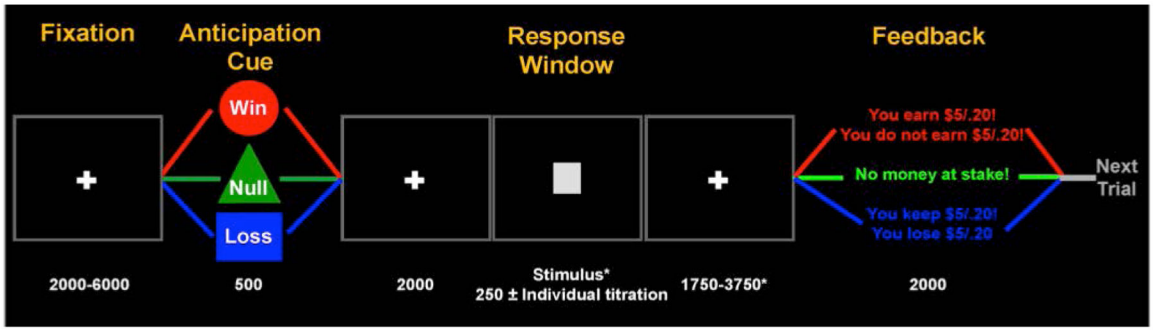

Figure 1.

Monetary incentive delay task design. A fixation cross was presented, followed by a cue indicating the type of upcoming trial. The fixation cross returned, followed by the response window individualized in length per each participant's baseline reaction time. Then after a jittered delay, participants received feedback on the outcome of the trial.

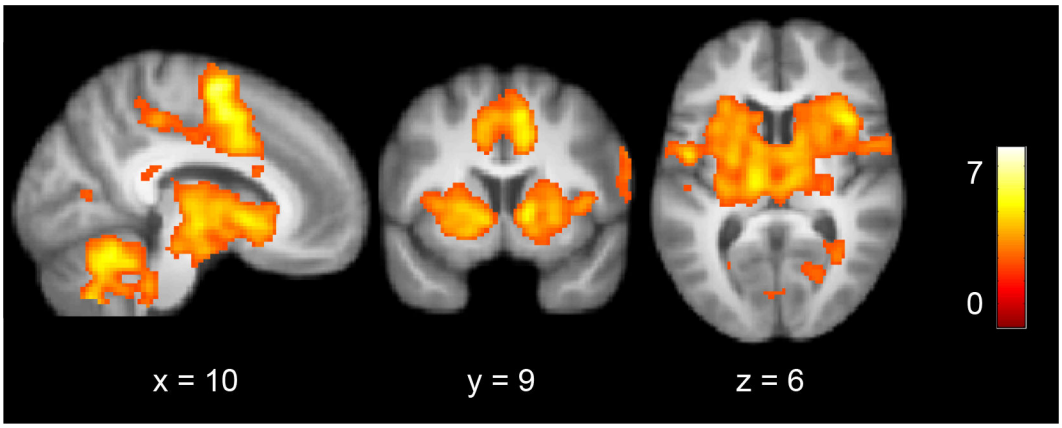

Figure 2.

Whole-brain activation during anticipation of win trials compared to neutral trials in the T-MIDT. Activation was observed in the VS, dACC, DLPFC, right anterior superior insula, and other subcortical reward circuit regions.

Table 1.

Demographics and clinical symptoms at diagnostic interview

	HC ***n*** **= 43**	**HMD** ***n*** **= 132**	***t/X²***	***p***	**All** ***n*** **= 189**
Age	22.59 (3.18)	23.25 (3.45)	−1.16	.25	23.09 (3.40)
% Female	60%	69%	.92	.37	67%
Education	14.84 (1.85)	14.74 (2.08)	.30	.77	14.77 (2.02)
Race			20.69	<.001	
African American/Black	5 (10.9%)	28 (19.6%)			33 (17.5%)
Asian	15 (32.6%)	10 (7.0%)			25 (13.2%)
Caucasian/White	21 (45.7%)	86 (60.1%)			107 (56.6%)
More than one	3 (6.5%)	8 (5.6%)			11 (5.8%)
Unknown	2 (4.3%)	11 (7.7%)			13 (6.9%)
Ethnicity			.06	.003	
Hispanic	7 (15.2%)	24 (16.8%)			31 (16.4%)
Not Hispanic	39 (84.8%)	119 (83.2%)			158 (83.6%)
Estimated IQ	106.56 (7.51)	106.93 (10.08)	−.22	.82	106.84 (9.49)
Ham-D	.51 (.87)	4.20 (4.33)	−8.54	<.001	3.29 (4.01)
Ham-A	1.02 (1.31)	5.19 (5.23)	−9.24	<.001	4.26 (4.95)
YMRS	.33 (.93)	2.17 (3.29)	−5.73	<.001	1.79 (2.92)

HC, healthy control; HMD, any mood disorder; Ham-D, Hamilton Depression Rating Scale (17-item); Ham-A, Hamilton Anxiety Rating Scale; YMRS, Young Mania Rating Scale.

Table 2.

Pearson's correlations between reward and executive function measures

Construct	Measure		AMW practice	AMW run 1	AMW run 2	AMW runs 3–4	Win trial accuracy runs 3–4	Loss trial accuracy runs 3–4	Neutral trial accuracy runs 3–4
Reward responsive-ness and drive	Titrated monetary incentive delay task	AMW practice	-	.21	.19	.33	.25	.32	.02
		p		.01	.01	.00	.00	.00	.80
		df		172	172	172	171	171	171
		AMW run 1	.21	-	.38	.29	.21	.23	.07
		p	.01		.00	.00	.01	.00	.35
		df	172		172	172	171	171	171
		AMW run 2	.19	.38	-	.53	.41	.54	.21 ^
		p	.01	.00		.00	.00	.00	.01
		df	172	172		172	171	171	139
		AMW runs 3–4	.33	.29	.53	-	.72	.81	.37 ^
		p	.00	.00	.00		.00	.00	.00
		df	172	172	172		171	171	139
		Win trial accuracy runs 3–4	.25	.21	.41	.72	-	.54	.24
		p	.00	.01	.00	.00		.00	.00
		df	171	171	171	171		171	171
		Loss trial accuracy runs 3–4	.32	.23	.54	.81	.54	-	.41 ^
		p	.00	.00	.00	.00	.00		.00
		df	171	171	171	171	171		139
		Neutral trial accuracy runs 3–4	.02	.07	.01	.11	.24	.10	-
		p	.80	.35	.87	.16	.00	.21	
		df	171	171	171	171	171	171	
Cognitive ability	Shipley	Estimated IQ	.15	.28	.20	.02	.09	.08	.01
		p	.06	.00	.01	.85	.28	.29	.88
		df	161	161	161	161	160	160	160
Processing speed	Trail Making Test	Trails A time (raw)	−.21	−.14	.001	−.06	−.14	−.08	−.12

Construct	Measure		AMW practice	AMW run 1	AMW run 2	AMW runs 3–4	Win trial accuracy runs 3–4	Loss trial accuracy runs 3–4	Neutral trial accuracy runs 3–4
		p	.01	.11	.99	.45	.10	.37	.15
		df	143	143	143	143	142	142	142
Set shifting		Trails B time (raw)	−.09	−.14	−.08	−.08	−.11	−0.11	−.05
		p	.26	.09	.35	.34	.19	.21	.54
		df	141	141	141	141	140	140	140
		Trails B minus A time (raw)	−.06	−.12	−.09	−.07	−.08	−.10	−.03
		p	.52	.16	.31	.41	.34	.22	.77
		df	141	141	141	141	140	140	140
Working memory	WAIS Digit Span	Forward span (scaled)	.05	.02	.15	.14	.14	.18	.05
		p	.56	.82	.06	.09	.09	.02	.55
		df	157	157	157	157	156	156	156
		Backward span (scaled)	.05	.10	.09	.04	−.01	.10	.07
		p	.55	.22	.26	.60	.93	.22	.42
		df	157	157	157	157	156	156	156
	CANTAB	Spatial working memory total errors	−.16	−.13	−.07	−.08	−.06	−.12	−.08
		p	.03	.08	.36	.28	.47	.12	.30
		df	168	168	168	168	167	167	167
Attention	Parametric Go/No-Go/Stop Test	GNG percent hits	.11	.19	.18	.12	.13	.09	.04
		p	.14	.02	.02	.12	.08	.27	.61
		df	169	169	169	169	168	168	168
Inhibitory control		Go-stop percent hits	−.11	−.21	−.08	−.05	−.10	−.10	−.06
		p	.15	.01	.28	.56	.22	.21	.45
		df	169	169	169	169	168	168	168
		No-go and Stop percent correct inhibition	.03	.17	.21	.18	.21	.26	.20 ^
		p	.69	.03	.01	.02	.01	.00	.02
		df	169	169	169	169	168	168	136
	Stroop	Color-Word (T)	.21	.12	.17	.21	.21	.18	.19
		p	.01	.13	.03	.01	.01	.03	.02

Construct	Measure		AMW practice	AMW run 1	AMW run 2	AMW runs 3–4	Win trial accuracy runs 3–4	Loss trial accuracy runs 3–4	Neutral trial accuracy runs 3–4
		df	157	157	157	157	156	156	156

AMW, amount won ($); WAIS, Wechsler Adult Intelligence Scale IV; GNG, go/no-go; CANTAB, Cambridge Neuropsychological Test Automated Battery.

^ Significant only when MIDT neutral trial responses ≤ .5 are truncated

Table 3.

Pearson's correlations between reward and executive function measures by group

Construct	Measure		AMW practice		AMW runs 3–4		Win trial accuracy runs 3–4		Loss trial accuracy runs 3–4		Neutral trial accuracy runs 3–4	
			HMD	HC	HMD	HC	HMD	HC	HMD	HC	HMD	HC
Reward responsive-ness and drive	Titrated monetary incentive delay task	AMW practice	-		.32	.38	.24	.25	.32	.32	.04	−.02
		p			.00	.01	.01	.06	.00	.04	.69	.92
		df			129	41	128	41	128	41	128	41
		AMW run 1	.20	.26	.25	.41	.18	.32	.25	.12	.13	−.06
		p	.02	.09	.00	.01	.04	.04	.00	.44	.13	.73
		df	129	41	129	41	128	41	128	41	128	41
		AMW run 2	.18	.22	.48	.73	.35	.63	.55	.49	.06	−.08
		p	.04	.15	.00	.00	.00	.00	.00	.00	.53	.62
		df	129	41	129	41	128	41	128	41	128	41
		AMW runs 3–4	.32	.38	-		.71	.80	.81	.83	.21	.38 ^
		p	.00	.01			.00	.00	.00	.00	.02	.03
		df	129	41			128	41	128	41	128	31
		Win trial accuracy runs 3–4	.24	.29	.71	.80	-		.50	.68	.35	.37 ^
		p	.01	.06	.00	.00			.00	.00	.00	.04
		df	128	41	128	41			128	41	128	31
		Loss trial accuracy runs 3–4	.32	.32	.81	.83	.50	.68	-		.20	.51 ^
		p	.00	.04	.00	.00	.00	.00			.03	.00
		df	128	41	128	41	128	41			128	31
		Neutral trial accuracy runs 3–4	.04	−.02	.21	−.12	.35	−.01	.20	−.16	-	
		p	.69	.92	.02	.45	.00	.93	.03	.30		
		df	128	41	128	41	128	41	128	41		
Cognitive ability	Shipley	Estimated IQ	.11	.33	−.04	.29	.04	.29	.01	.42	−.02	.09
		p	.24	.04	.66	.07	.63	.07	.89	.01	.81	.569
		df	121	38	121	38	120	38	120	38	120	38

Construct	Measure		AMW practice		AMW runs 3–4		Win trial accuracy runs 3–4		Loss trial accuracy runs 3–4		Neutral trial accuracy runs 3–4	
			HMD	HC	HMD	HC	HMD	HC	HMD	HC	HMD	HC
Processing speed	Trail Making Test	Trails A time (raw)	−.25	−.12	−.06	−.07	−.13	−.16	−.05	−.18	−.15	−.07
		p	.01	.47	.57	.68	.19	.36	.59	.28	.13	.69
		df	106	35	106	35	105	35	105	35	105	35
Set shifting		Trails B time (raw)	−.07	−.21	−.03	−.32	−.05	−.42	−.07	−.33	−.05	−.08
		p	.48	.21	.80	.06	.64	.01	.51	.05	.61	.62
		df	104	35	104	35	103	35	103	35	103	35
		Trails B minus A time (raw)	−.02	−.18	−.02	−.31	−.02	−.38	−.07	−.28	−.02	−.07
		p	.81	.28	.87	.07	.86	.02	.49	.09	.85	.70
		df	104	35	104	35	103	35	103	35	103	35
Working memory	WAIS Digit Span	Forward span (scaled)	−.04	.30	.14	.13	.11	.25	.22	.06	−.04	.28
		p	.70	.06	.13	.43	.25	.12	.02	.70	.65	.09
		df	118	37	118	37	117	37	117	37	117	37
		Backward span (scaled)	−.03	.25	.03	.08	−.05	.14	.09	.11	−.04	.30
		p	.78	.13	.71	.64	.57	.38	.32	.49	.65	.07
		df	118	37	118	37	117	37	117	37	117	37
	CANTAB	Spatial working memory total errors	−.21	−.01	−.11	.03	−.05	−.06	−.18	.09	−.09	−.08
		p	.02	.93	.23	.86	.58	.69	.05	.55	.30	.61
		df	125	41	125	41	124	41	124	41	124	41
Attention	Parametric Go/No-Go/Stop Test	GNG percent hits	.09	.19	.06	.32	.05	.44	.03	.30	.19	−.08
		p	.30	.23	.53	.04	.56	.00	.72	.06	.23	.62
		df	128	39	128	39	127	39	127	39	127	39
Inhibitory control		Go-stop percent hits	−.12	−.08	−.04	−.04	−.13	.004	−.08	−.15	−.15	.11
		p	.17	.60	.63	.83	.16	.98	.37	.35	.09	.50
		df	128	39	128	39	127	39	127	39	127	39
		No-go and stop percent correct inhibition	.09	−.18	.17	.16	.22	.18	.26	.26	−.01	.46 ^
		p	.32	.27	.05	.31	.01	.27	.00	.10	.92	.01
		df	128	39	128	39	127	39	127	39	127	29
	Stroop	Color-Word (T)	.17	.37	.21	.18	.23	.11	.18	.21	.23 ^	.37 ^

Construct	Measure		AMW practice		AMW runs 3–4		Win trial accuracy runs 3–4		Loss trial accuracy runs 3–4		Neutral trial accuracy runs 3–4	
			HMD	HC	HMD	HC	HMD	HC	HMD	HC	HMD	HC
		p	.06	.02	.02	.28	.01	.53	.06	.21	.03	.05
		df	118	37	118	37	117	37	117	37	95	28

HC, healthy control; HMD, history of mood disorder; AMW, amount of money won; WAIS, Wechsler Adult Intelligence Scale IV; GNG, go/no-go; CANTAB, Cambridge Neuropsychological Test Automated Battery.

^ Significant only when MIDT neutral trial responses ≤ .5 are truncated.

Table 4.

Pearson's correlations between T-MIDT and clinical/personality variables in HMD group only

Measure	AMW practice	AMW run 1	AMW run 2	AMW runs 3–4	Win trial accuracy runs 3–4	Loss trial accuracy runs 3–4	Neutral trial accuracy runs 3–4
BAI	−.16	−.08	−.11	−.21	−.18	−.18	−.16
p	.07	.34	.21	.02	.04	.05	.70
df	130	130	130	130	129	129	129
BDI	−.08	−.17	−.15	−.25	−.16	−.17	−.08
p	.46	.12	.16	.02	.14	.11	.77
df	87	87	87	87	86	86	86
Behavioral Inhibition	.05	−.07	.06	−.07	.03	−.04	.07
p	.57	.47	.48	.43	.71	.68	.44
df	125	125	125	125	124	124	124
Reward Responsiveness	.01	.07	.05	.14	.18	.12	.01
p	.95	.46	.61	.13	.05	.19	.18
df	125	125	125	125	124	124	124
Drive	−.15	−.06	−.11	−.03	.03	−.07	−.15
p	.09	.49	.21	.71	.73	.47	.50
df	125	125	125	125	124	124	124
SHAPS	.06	−.01	.03	.05	−.02	.02	−.01
p	.58	.93	.78	.65	.87	.84	.43
df	86	86	86	86	85	85	85

BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory II; Behavioral Inhibition, Behavioral Inhibition System Scale; Reward Responsiveness, Behavioral Activation System Reward Responsiveness subscale; Drive, Behavioral Activation System Drive subscale; SHAPS, Snaith-Hamilton Pleasure Scale. Collected at time of neuropsychological assessment.

Table 5.

BAS-Reward Responsiveness Scale items and % win accuracy in runs 3 and 4 for HMD group only

	Strongly Disagree	Disagree	Agree	Strongly Agree	Spearman's rho	df	*p*
4. When I'm doing well at something I love to keep at it.	n = 3 70.0% (18.0)	n = 7 83.6% (11.4)	n = 40 86.3% (10.3)	n = 75 85.5% (11.7)	.08	123	.41
7. When I get something I want, I feel excited and energized.	n = 3 70.0% (18.0)	n = 5 86.0% (6.5)	n = 35 82.4% (11.1)	n = 81 87.1% (11.3)	.25	122	.01
14. When I see an opportunity for something I like I get excited right away.	n = 2 77.5% (17.7)	n = 15 81.0% (14.4)	n = 55 84.7% (11.0)	n = 53 87.4% (10.9)	.19	123	.04
18. When good things happen to me, it affects me strongly.	n = 4 87.5% (10.4)	n = 14 79.6% (13.8)	n = 63 85.8% (10.2)	n = 44 86.1% (12.5)	.14	123	.13
23. It would excite me to win a contest.	n = 4 82.5% (6.5)	n = 9 83.9% (16.0)	n = 42 85.7% (11.6)	n = 70 85.4% (11.3)	.02	123	.85

Table 6.

Pearson's correlations between brain activation during win anticipation (relative to neutral) and T-MIDT across groups

Region of Interest	MNI coordinates	AMW run 1	AMW run 2	AMW runs 3–4	Win trial accuracy runs 3–4	Neutral trial accuracy runs 3–4
Left VS	−12, 10, −6	.02	.02	.05	.11	.07
p		.83	.84	.59	.20	.46
Right VS	12, 10, −6	.05	.02	.01	.09	.11
p		.59	.81	.91	.32	.20
Left DLPFC	−40, 32, 30	−.04	−.12	−.08	.00	.03
p		.69	.17	.36	.96	.72
Right DLPFC	40, 32, 30	−.08	−.07	−.15	−.06	.08
p		.34	.45	.10	.49	.39
dACC	0, 18, 49	.07	.00	.03	.05	.14
p		.44	.97	.73	.59	.12

MNI, Montreal Neurological Institute; AMW, amount of money won ($); VS, ventral striatum; dACC, dorsal anterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex.

df = 126