

SUPPLEMENTARY INFORMATION:

Reasons for Dropouts

As described in the main text, the completer population consisted of 33 subjects in the JNJ-67953964 group and 35 placebo subjects. The reasons for dropout during double-blind treatment in the JNJ-67953964 group were: increase in depression symptoms (N=3); Hurricane Harvey prevented coming to the site and receiving study drug or led subject to have to leave town (N=2); subject unable to schedule visit within allowed time window (N=1); increase in anxiety symptoms (N=1); subject was lost to follow-up despite multiple attempts to contact (N=1); subject became pregnant (N=1); and subject had to start excluded medication for medical management of worsening of problem which predated study participation (N=1). The reasons for dropout in the placebo group were: increase in depression symptoms (N=3); subject was lost to follow-up despite multiple attempts to contact (N=2); increase in anxiety symptoms (N=1); subject dropped out due to developing back pain (N=1); and subject developed worsening of seasonal allergy symptoms and required an excluded medication (N=1).

A priori defined Quality Control Cutoff for the Probabilistic Reward Task

Quality control (QC) evaluations were performed blindly to Treatment Arm assignment and automatically using predefined QC cutoffs. Specifically, participants were excluded if any of the following QC were not met:

- 1) Less than 80 valid trials in each block (i.e., more than 20% outlier responses). Outlier responses were defined in two steps:
 - a. RT shorter than 150 ms or greater than 2,500 ms; and
 - b. log-transformed RT exceeding the participant's mean \pm 3SD.
- 2) less than 20 rich rewards or less than 6 lean rewards in each block;
- 3) rich-to-lean reward ratio < 2.0 in any block;

Additional Effort Expenditure for Rewards Task (EEfRT) Methods:

For all trials in the EEfRT, participants make repeated manual button presses within a short period of time. Each button press raises the level of a virtual “bar” viewed onscreen by the participant. Participants are eligible to win the money allotted for each trial if they raise the bar to the “top” within the prescribed time period. Each trial presents the subject with a choice between two levels of task difficulty, a ‘hard task’ and an ‘easy task.’ Successful completion of hard-task trials requires the subject to make 100 button presses, using the non-dominant little finger within 21 seconds, while successful completion of easy-task trials requires the subject to make 30 button presses, using the dominant index finger within 7 seconds. For easy-task trials, subjects are eligible to win the same amount, \$1.00, on each trial if they successfully complete the task. For hard-task choices, subjects are eligible to win higher amounts that vary per trial within a range of \$1.24 – \$4.30 (“reward magnitude”). Subjects are not guaranteed to win the reward if they complete the task; some trials are “win” trials, in which the subject receive the stated reward amount, while others are “no win” trials, in which the subject receives no money for that trial. To help subjects determine which trials are more likely to be win trials, subjects are provided with accurate probability cues at the beginning of each trial. Trials have three levels of probability: “high” 88% probability of being a win trial, “medium” 50% and “low” 12%. Probability levels always apply to both the hard task and easy task, and there are equal proportions of each probability level across the experiment. Each

level of probability appears once in conjunction with each level of reward value for the hard task. All subjects receive trials presented in randomized order.

Rationale for Including Baseline As a Covariate In Mixed Effects Models:

Baseline was included as a covariate in mixed effects models to address the problem that differences between groups in baseline values of the outcome measure can negatively affect the trajectories of different treatment arms. This issue is critical when analyzing longitudinal data for two or more distinct groups with mixed effects models.^{1,2} Including baseline as a covariate allows a comparison of the trajectories in the groups with the same baseline value for the outcome measure.² This is not achieved by the random intercept in the mixed effects models, which captures variations in overall tendencies that are not informed by known, measured differences between subjects at baseline.

Further, achieving the goal of comparing trajectories between groups related to the same baseline value of the outcome conforms to the recommendations of the European Medicines Agency (EMA) who state in their “Guideline on Adjustment for Baseline Covariates in Clinical Trials” that when there is an association between baseline values and the outcome, adjustment for that difference generally improves the efficiency of the analysis and avoids conditional bias.³

The approach taken of including baseline as a covariate is also in keeping with the specific recommendation of the EMA: “If a baseline value of a continuous primary outcome measure is available, then this should usually be included as a covariate.”³

Results of Analysis Carried Out Without Controlling for Baseline Values:

Analyses were repeated for the primary and key secondary outcomes where statistically significant effects of treatment were found (SHAPS). A statistically significant treatment (JNJ-67953964 vs placebo) by time effect was found for the primary outcome measure (mean ventral striatal activation in anticipation of gain) when analysis when mixed-effects model analysis was carried out without controlling for baseline mean ventral striatal activation in anticipation of gain centered about its mean as a covariate ($F=1.9$; $p<0.027$). A statistically significant effect was not found when the mixed-effects model analysis was repeated for the SHAPS without controlling for baseline SHAPS score centered about its mean ($F=0.48$; $p=0.31$).

Consideration of the Relative Size of the VAS Anhedonia Scale JNJ-67953964 vs. Placebo Effect:

The VAS Anhedonia scale was among the exploratory clinical measures included in this study. While there was a tendency for greater improvement with JNJ-67953964 than placebo on the VAS anhedonia scale (difference between post-treatment and baseline mean: JNJ-67953964-1.27 cm; Placebo-1.01 cm) associated with an effect-size of 0.3, this was not statistically significant in this study, which was powered to detect relatively larger effect-sizes we anticipated for the primary imaging outcome measure. The relatively smaller effect-size seen with the VAS scale than the SHAPS and TEPS is surprising in light of the

history of VAS scales being relatively sensitive measures. However, the effect-size seen with the VAS anhedonia is consistent with the relatively smaller effect-sizes seen with the SHAPS and TEPS than the neuroimaging measures and further supports the hypothesis discussed above that the neuroimaging measures are likely to be associated with larger effects possibly because they are closer to the direct biological effects of the drug than the clinical measures.

Factors Related to Why We Did Not Find a Significant Effect for the Planned Analysis for the PRT Data:

There are a number of factors related to why we did not find a significant effect for the planned Treatment Arm x Block x Time interaction effect but did find a significant Treatment Arm x Time effect. In retrospect, our planned PRT analysis was based on a hypothesis of 3-way interaction involving Treatment Arm (KOR, Placebo), Block (block 1, block 2), and Time (pre-treatment, post-treatment) which we now believe was a suboptimal approach to analyzing our data. There are two reasons for this assessment. First, subject burden time limitations prevented us from implementing the 3-block version of the PRT, which has been used by over 50 groups worldwide in over 40 publications, and has been reliably found to induce systematic increases in response bias over the three blocks among healthy controls (typically, manifested as a main effect of Block for response bias). Instead, we used a 2-block version. Unfortunately, analyses of independent samples performed after we had decided on the analysis strategy for this study show that response bias does not increase as

much across blocks in the 2-block version of the PRT as in the 3-block version, thereby decreasing the chances that we would find a significant effect on the planned Treatment Arm by Block by Time Interaction.⁴ Second, prior studies using the PRT in MDD had found a main effect of Group (rather than a Group x Block interaction), due to overall (i.e., averaged across blocks) response bias in MDD patients relative to healthy controls² and differences in response bias have been reported to differentiate depressed patients and those with severe anhedonia from healthy controls.⁵⁻⁸ In retrospect, this would have been a more appropriate choice of planned analysis than the 3-way interaction.

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Supplementary Table 1
Baseline Characteristics of the Analysis Sub-Cohorts: All Subjects

Variable	ITT Population N=89	As Treated Population N=86	Per Protocol Population N=86	Completers Population N=68
Mean Age in Years (SD)	39.5 (13.2)	39.5 (13.0)	39.5 (13.0)	40.0 (13.6)
Gender - %Female	62.9	62.8	62.8	58.8
Race				
%Caucasian	67.8	67.9	67.9	67.2
%African American	20.7	21.4	21.4	22.4
%Asian	3.4	2.4	2.4	3.0
%American Indian/Alaskan Native	1.1	1.2	1.2	0.0
%More Than One Race	6.9	7.1	7.1	7.5
Ethnicity - %Hispanic Origin	11.6	12.0	12.0	11.9
Mean BMI (SD)	28.7 (6.2)	28.9 (6.2)	28.9 (6.2)	29.1 (6.0)
Mean Weight (lbs) (SD)	180.6 (41.9)	182.2 (41.5)	182.2 (41.5)	184.6 (40.4)
Mean Baseline fMRI Ventral Striatal Activation in MID Task in Anticipation of Gain Contrasted with No-incentive Trials (SD)**	0.63 (0.8) (N=88)	0.63 (0.9) (N=85)	0.64 (0.8) (N=44)	0.57 (0.8) (N=67)
Mean Maximum Baseline fMRI Ventral Striatal Activation in MID Task (SD) in Anticipation of Gain Contrasted with No-Incentive Trials (SD)	2.70 (1.2) (N=88)	2.71 (1.2) (N=85)	2.71 (1.2) (N=85)	2.66 (1.1) (N=67)
Mean Baseline fMRI Ventral Striatal Activation in MID Task in Anticipation of Loss Contrasted with No-incentive Trials (SD)	0.33 (0.7) (N=88)	0.34 (0.7) (N=85)	0.34 (0.7) (N=85)	0.30 (0.7) (N=67)
Mean Maximum Baseline fMRI Ventral Striatal Activation in MID Task (SD) in Anticipation of Loss Contrasted with No-incentive Trials (SD)	2.19 (1.0) (N=88)	2.19 (1.0) (N=85)	2.19 (1.0) (N=85)	2.16 (1.0) (N=67)
Mean Baseline PRT Change in Response Bias from Block 1 to Block 2 (SD)*	0.04 (0.2) (N=67)	0.04 (0.2) (N=67)	0.04 (0.2) (N=67)	0.04 (0.2) (N=55)
Mean Baseline SHAPS (SD)*	34.9 (7.4) (N=88)	34.8 (7.5)	34.8 (7.5)	34.5 (6.8)
Mean Baseline PRT Response Bias (averaged across blocks) (SD)	0.11 (0.03) (N=67)	0.11 (0.03) (N=67)	0.11(0.03) (N=67)	0.12 (0.1) (N=55)
Mean Baseline EEfRT (SD)	0.36 (0.2) (N=83)	0.37 (0.2) (N=81)	0.37 (0.2) (N=81)	0.37 (0.2) (N=63)
Mean Baseline TEPS Anticipatory Subscore (SD)	29.4 (5.7) (N=88)	29.4 (5.7)	29.4 (5.7)	29.6 (5.9)
Means Baseline TEPS Consummatory Subscore (SD)	26.2 (4.4) (N=88)	26.3 (4.5)	26.3 (4.5)	26.3 (4.6)
Mean Baseline VAS Anhedonia (SD)	3.26 (2.2) (N=88)	3.24 (2.2)	3.24 (2.2)	3.25 (2.1)
Mean Baseline Resting State EEG Delta Current Density in Rostral Anterior Cingulate (SD)	74.0 (78.6) (N=81)	74.8 (79.4) (N=79)	74.8 (79.4) (N=79)	77.7 (84.6) (N=64)
Mean Baseline HAM-D (SD)	15.6 (5.6)	15.4 (5.6)	15.4 (5.6)	14.9 (5.3)
Mean Baseline HAM-A (SD)	15.5 (6.2)	15.5 (6.2)	15.5 (6.2)	14.9 (6.2)
Mean Baseline CGI-S (SD)	3.9 (0.5)	3.9 (0.6)	3.9 (0.6)	3.9 (0.5)
Mean Baseline CPFQ (SD)	26.3 (6.1)	26.2 (6.1)	26.2 (6.1)	25.4 (5.8)

Note: When N's are less than at top of column it reflects missing data for that variable

Supplementary Table 2: Baseline Characteristics of the JNJ-67953964 and Placebo Groups in Analysis Sub-Cohorts

Variable	ITT Population		As Treated Population		Per Protocol Population		Completers Population	
	JNJ N=45	Placebo N=44	JNJ N=43	Placebo N=43	JNJ N=43	Placebo N=43	JNJ N=34	Placebo N=34
Mean Age in Years (SD)	40.7 (13.3)	38.2 (13.0)	41.3 (13.0)	37.8 (12.9)	41.3 (13.0)	37.8 (12.9)	40.3 (13.8)	39.8 (13.5)
Gender - %Female	64.4	61.4	65.1	60.5	65.1	60.5	61.8	55.9
Race								
%Caucasian	70.5	65.1	71.4	64.3	71.4	64.3	70.6	63.6
%African American	22.7	18.6	23.8	19.0	23.8	19.0	23.5	21.2
%Asian	2.3	4.7	0.0	4.8	0.0	4.8	0.0	6.1
%American Indian/Alaskan Native	0.0	2.3	0.0	2.4	0.0	2.4	0.0	0.0
%More Than One Race	4.5	9.3	4.8	9.5	4.8	9.5	5.9	9.1
Ethnicity - %Hispanic Origin	11.6	11.6	12.2	11.9	12.2	11.9	11.8	12.1
Mean BMI (SD)	29.4 (6.4)	28.0 (5.9)	29.7 (6.4)	28.0 (6.0)	29.7 (6.4)	28.0 (6.0)	29.9 (6.1)	28.4 (5.9)
Mean Weight (lbs) (SD)	180.9 (43.7)	180.3 (40.6)	184.2 (42.3)	180.2 (41.1)	184.2 (42.3)	180.2 (41.1)	184.5 (39.8)	184.7 (41.5)
Mean Baseline fMRI Ventral Striatal Activation in MID Task in Anticipation of Gain Contrasted with No-incentive Trials (SD)**	0.63 (0.9) (N=44)	0.64 (0.8) (N=44)	0.63 (0.9) (N=42)	0.64 (0.8) (N=43)	0.63 (0.9) (N=42)	0.64 (0.8) (N=43)	0.58 (0.9) (N=33)	0.57 (0.7) (N=34)
Mean Maximum Baseline fMRI Ventral Striatal Activation in MID Task (SD) in Anticipation of Gain Contrasted with No-Incentive Trials (SD)	2.66 (1.2) (N=44)	2.73 (1.2) (N=44)	2.71 (1.2) (N=42)	2.71 (1.2) (N=43)	2.71 (1.2) (N=42)	2.71 (1.2) (N=43)	2.69 (1.2) (N=33)	2.63 (1.1) (N=34)
Mean Baseline fMRI Ventral Striatal Activation in MID Task in Anticipation of Loss Contrasted with No-incentive Trials (SD)	0.29 (0.8) (N=44)	0.36 (0.7) (N=44)	0.32 (0.8) (N=42)	0.36 (0.7) (N=43)	0.32 (0.8) (N=42)	0.36 (0.7) (N=43)	0.30 (0.8) (N=33)	0.30 (0.6) (N=34)
Mean Maximum Baseline fMRI Ventral Striatal Activation in MID Task (SD) in Anticipation of Loss Contrasted with No-incentive Trials (SD)	2.15 (1.2) (N=44)	2.23 (0.9) (N=44)	2.16 (1.1) (N=42)	2.21 (0.9) (N=43)	2.16 (1.1) (N=42)	2.21 (0.9) (N=43)	2.20 (1.2) (N=33)	2.13 (0.8) (N=34)
Mean Baseline PRT Change in Response Bias from Block 1 to Block 2 (SD)*	0.02 (0.2) (N=30)	0.05 (0.2) (N=37)	0.02 (0.2) (N=30)	0.05 (0.2) (N=37)	0.02 (0.2) (N=30)	0.05 (0.2) (N=37)	0.05 (0.2) (N=24)	0.03 (0.2) (N=31)
Mean Baseline SHAPS (SD)*	36.4 (8.5) (N=44)	33.4 (5.9) (N=44)	36.4 (8.6)	33.3 (5.9)	36.4 (8.6)	33.3 (5.9)	35.4 (8.1)	33.6 (5.2)
Mean Baseline PRT Response Bias (averaged across blocks) (SD)	0.11 (0.03) (N=30)	0.11 (0.03) (N=37)	0.11 (0.03) (N=30)	0.11 (0.03) (N=37)	0.11 (0.03) (N=30)	0.11 (0.03) (N=37)	0.11 (0.1) (N=24)	0.11 (0.1) (N=31)
Mean Baseline EEfRT (SD)	0.35 (0.2) (N=42)	0.38 (0.2) (N=41)	0.35 (0.2) (N=41)	0.38 (0.2) (N=40)	0.35 (0.2) (N=41)	0.38 (0.2) (N=40)	0.36 (0.2) (N=32)	0.38 (0.2) (N=31)
Mean Baseline TEPS Anticipatory Subscore (SD)	29.3 (5.7) (N=44)	29.5 (5.6) (N=44)	29.4 (5.7)	29.4 (5.7)	29.4 (5.7)	29.4 (5.7)	29.5 (5.9)	29.6 (5.8)
Means Baseline TEPS Consummatory Subscore (SD)	26.3 (4.4)	26.1 (4.4) (N=44)	26.4 (4.5)	26.1 (4.5)	26.4 (4.5)	26.1 (4.5)	26.4 (4.6)	26.1 (4.6)

	(N=44)							
Mean Baseline VAS Anhedonia (SD)	2.93 (2.1) (N=44)	3.59 (2.2) (N=44)	2.86 (2.1)	3.63 (2.2)	2.86 (2.1)	3.63 (2.2)	3.00 (2.2)	3.50 (2.0)
Mean Baseline Resting State EEG Delta Current Density in Rostral Anterior Cingulate (SD)	73.0 (97.1) (N=43)	75.2 (51.6) (N=38)	73.8 (98.0) (N=42)	76.0 (52.0) (N=37)	73.8 (98.0) (N=42)	76.0 (52.0) (N=37)	75.0 (104.7) (N=34)	80.7 (55.3) (N=30)
Mean Baseline HAM-D (SD)	16.3 (5.2)	14.8 (5.9)	16.0 (5.2)	14.8 (6.0)	16.0 (5.2)	14.8 (6.0)	14.7 (4.7)	15.0 (6.0)
Mean Baseline HAM-A (SD)	16.0 (5.8)	15.1 (6.6)	15.8 (5.7)	15.1 (6.7)	15.8 (5.7)	15.1 (6.7)	14.2 (5.2)	15.6 (7.2)
Mean Baseline CGI-S (SD)	3.9 (0.6)	4.0 (0.5)	3.9 (0.6)	4.0 (0.5)	3.9 (0.6)	4.0 (0.5)	3.8 (0.5)	4.0 (0.5)
Mean Baseline CPFQ (SD)	27.2 (6.4) (N=44)	25.4 (5.7) (N=44)	27.1 (6.4)	25.4 (5.8)	27.1 (6.4)	25.4 (5.8)	25.9 (5.9)	24.9 (5.7)

*JNJ = JNJ-67953964; Note: When N's are less than at top of column it reflects missing data for that variable

Supplementary Table 3. Site Effects on Outcomes Variables (ITT Population)

Variable	Site 1	Site 2	Site 3	Site 4	Site 5	Site 6	Site Effect*	SiteXTime Effect*	SiteXArmXTime Effect*
Mean fMRI Ventral Striatal Activation in MID Task in Anticipation of Gain Contrasted with No-incentive Trials	JNJ N=1 0.99 (N/A)	JNJ N=11 0.99 (0.73)	JNJ N=2 0.24 (1.0)	JNJ N=12 0.77 (0.87)	JNJ N=9 0.59 (0.90)	JNJ N=9 0.60 (0.81)	p=0.19 $\eta^2=0.02$ $\omega^2=0.00$	p=0.47 $\eta^2=0.01$ $\omega^2=0.0$	p=0.45 $\eta^2=0.01$ $\omega^2=-0.01$
	PCBO N=5 0.13 (0.72)	PCBO N=9 0.78 (0.81)	PCBO N=5 0.11 (0.96)	PCBO N=9 0.00 (0.81)	PCBO N=9 0.35 (0.90)	PCBO N=7 0.41 (0.82)			
Mean SHAPS	JNJ N=1 30.1 (N/A)	JNJ N=11 28.3 (5.0)	JNJ N=2 35.9 (4.9)	JNJ N=12 29.4 (4.5)	JNJ N=9 31.1 (4.8)	JNJ N=9 34.9 (5.4)	p=0.026 $\eta^2=0.04$ $\omega^2=0.03$	p=0.47 $\eta^2=0.01$ $\omega^2=0.00$	P=0.016 $\eta^2=0.04$ $\omega^2=-0.02$
	PCBO N=5 30.8 (4.7)	PCBO N=9 33.6 (4.8)	PCBO N=5 35.8 (4.7)	PCBO N=9 30.8 (4.8)	PCBO N=9 33.8 (5.1)	PCBO N=7 32.1 (4.8)			
Mean PRT Change in Response Bias from Block 1 to Block 2	JNJ N=1 0.40 (N/A)	JNJ N=5 -0.10 (0.16)	JNJ N=0 N/A (N/A)	JNJ N=9 0.06 (0.18)	JNJ N=5 -0.02 (0.16)	JNJ N=4 -0.03 (0.16)	p=0.35 $\eta^2=0.02$ $\omega^2=-0.01$	p=0.055 $\eta^2=0.08$ $\omega^2=-0.03$	p=0.11 $\eta^2=0.12$ $\omega^2=0.06$
	PCBO N=4 0.08 (0.16)	PCBO N=6 0.00 (0.17)	PCBO N=5 0.11 (0.16)	PCBO N=8 0.07 (0.17)	PCBO N=6 0.13 (0.17)	PCBO N=2 0.22 (0.17)			
Maximum fMRI Ventral Striatal Activation in MID Task in Anticipation of Gain Contrasted with No-incentive Trials	JNJ N=1 4.5 (N/A)	JNJ N=11 3.0 (0.93)	JNJ N=2 2.6 (1.2)	JNJ N=12 3.0 (1.1)	JNJ N=9 2.7 (1.1)	JNJ N=9 2.6 (0.99)	p=0.48 $\eta^2=0.02$ $\omega^2=0.00$	p=0.27 $\eta^2=0.01$ $\omega^2=0.00$	p=0.26 $\eta^2=0.03$ $\omega^2=0.01$
	PCBO N=5 1.8 (0.89)	PCBO N=9 2.3 (0.90)	PCBO N=5 1.4 (1.1)	PCBO N=9 2.2 (0.90)	PCBO N=9 3.1 (1.1)	PCBO N=7 2.6 (1.0)			
Mean fMRI Ventral Striatal Activation in MID Task in Anticipation of Loss Contrasted with No-incentive Trials	JNJ N=1 1.9 (N/A)	JNJ N=11 0.94 (0.66)	JNJ N=2 -0.2 (0.85)	JNJ N=12 0.68 (0.69)	JNJ N=9 0.54 (0.75)	JNJ N=9 0.64 (0.69)	p=0.056 $\eta^2=0.02$ $\omega^2=0.00$	p=0.21 $\eta^2=0.01$ $\omega^2=0.00$	p=0.11 $\eta^2=0.03$ $\omega^2=0.01$
	PCBO N=5 0.09 (0.40)	PCBO N=9 0.36 (0.60)	PCBO N=5 0.52 (0.80)	PCBO N=9 -0.49 (0.69)	PCBO N=9 0.24 (0.78)	PCBO N=7 0.01 (0.71)			
Maximum fMRI Ventral Striatal Activation in MID Task in Anticipation of Loss Contrasted with No-incentive Trials	JNJ N=1 4.4 (N/A)	JNJ N=11 3.1 (0.93)	JNJ N=2 1.5 (1.2)	JNJ N=12 2.7 (1.1)	JNJ N=9 2.5 (1.1)	JNJ N=9 2.5 (0.99)	p=0.25 $\eta^2=0.01$ $\omega^2=0.00$	p=0.34 $\eta^2=0.01$ $\omega^2=0.00$	p=0.23 $\eta^2=0.02$ $\omega^2=0.00$
	PCBO N=5 2.0 (0.60)	PCBO N=9 2.3 (0.99)	PCBO N=5 2.2 (1.2)	PCBO N=9 2.1 (0.99)	PCBO N=9 2.8 (1.1)	PCBO N=7 1.8 (1.0)			
Mean Baseline PRT Response Bias (averaged across blocks)	JNJ N=1 0.17 (N/A)	JNJ N=5 0.17 (0.13)	JNJ N=0 N/A (N/A)	JNJ N=9 0.19 (0.15)	JNJ N=5 0.18 (0.13)	JNJ N=4 0.05 (0.14)	p=0.02 $\eta^2=0.09$ $\omega^2=0.05$	p=0.15 $\eta^2=0.08$ $\omega^2=0.04$	p=0.41 $\eta^2=0.08$ $\omega^2=-0.01$
	PCBO N=4 0.08 (0.14)	PCBO N=6 0.09 (0.12)	PCBO N=5 0.25 (0.13)	PCBO N=8 0.03 (0.14)	PCBO N=6 0.01 (0.15)	PCBO N=2 0.00 (0.14)			

TEPS Anticipatory Subscale	JNJ N=1 41.2 (N/A) PCBO N=5 31.3 (5.6)	JNJ N=11 37.4 (6.0) PCBO N=9 35.7 (6.3)	JNJ N=2 18.0 (7.5) PCBO N=5 30.3 (5.6)	JNJ N=12 31.5 (5.5) PCBO N=9 32.9 (5.7)	JNJ N=9 32.1 (6.3) PCBO N=9 29.2 (6.0)	JNJ N=9 28.4 (6.3) PCBO N=7 32.7 (6.3)	p=0.008 $\eta^2=0.04$ $\omega^2=0.03$	p=0.035 $\eta^2=0.01$ $\omega^2=0.00$	P=0.001 $\eta^2=0.04$ $\omega^2=0.03$
TEPS Consummatory Subscale	JNJ N=1 27.1 (N/A)	JNJ N=11 31.5 (4.6)	JNJ N=2 34.6 (5.9)	JNJ N=12 28.9 (4.5)	JNJ N=9 31.2 (5.1)	JNJ N=9 24.5 (5.1)	p=0.09 $\eta^2=0.02$ $\omega^2=0.01$	p=0.075 $\eta^2=0.01$ $\omega^2=0.00$	P=0.35 $\eta^2=0.00$ $\omega^2=0.00$
	PCBO N=5 30.2 (4.5)	PCBO N=9 28.1 (5.1)	PCBO N=5 26.2 (4.4)	PCBO N=9 28.8 (4.5)	PCBO N=9 24.0 (4.8)	PCBO N=7 25.5 (5.0)			
EEfRT	JNJ N=1 0.22 (N/A)	JNJ N=10 0.32 (0.13)	JNJ N=2 .45 (0.17)	JNJ N=11 0.49 (0.14)	JNJ N=9 0.34 (0.15)	JNJ N=9 0.52 (0.15)	p=0.055 $\eta^2=0.01$ $\omega^2=0.00$	p=0.022 $\eta^2=0.03$ $\omega^2=0.02$	P=0.42 $\eta^2=0.01$ $\omega^2=0.00$
	PCBO N=4 0.36 (0.16)	PCBO N=8 0.41 (0.12)	PCBO N=5 0.45 (0.18)	PCBO N=8 0.47 (0.15)	PCBO N=9 0.34 (0.15)	PCBO N=7 0.42 (0.13)			
VAS Anhedonia	JNJ N=1 5.4 (N/A)	JNJ N=11 5.2 (1.7)	JNJ N=2 1.4 (2.3)	JNJ N=12 3.6 (1.7)	JNJ N=9 4.7 (1.8)	JNJ N=9 3.3 (1.8)	p=0.055 $\eta^2=0.02$ $\omega^2=0.01$	p=0.022 $\eta^2=0.02$ $\omega^2=0.00$	P=0.42 $\eta^2=0.02$ $\omega^2=0.00$
	PCBO N=5 4.8 (1.6)	PCBO N=9 4.8 (1.8)	PCBO N=5 4.2 (1.8)	PCBO N=9 4.7 (1.8)	PCBO N=9 4.0 (1.8)	PCBO N=7 4.5 (1.9)			
Resting State EEG Delta Current Density in Rostral Anterior Cingulate	JNJ N=1 15.2 (N/A)	JNJ N=10 72.5 (84.7)	JNJ N=4 27.6 (160.1)	JNJ N=11 50.3 (88.9)	JNJ N=9 51.1 (115.5)	JNJ N=8 79.7 (107.2)	p=0.35 $\eta^2=0.04$ $\omega^2=0.02$	p=0.48 $\eta^2=0.03$ $\omega^2=0.01$	P=0.26 $\eta^2=0.02$ $\omega^2=0.00$
	PCBO N=5 220.2 (75.8)	PCBO N=8 55.0 (99.8)	PCBO N=4 76.5 (86.8)	PCBO N=9 44.6 (100.8)	PCBO N=7 25.5 (78.0)	PCBO N=5 76.9 (84.5)			
HAM-D	JNJ N=2 4.7 (5.1)	JNJ N=11 8.7 (4.3)	JNJ N=2 12.9 (5.5)	JNJ N=12 10.7 (4.5)	JNJ N=9 10.3 (4.8)	JNJ N=9 14.5 (4.5)	p=0.09 $\eta^2=0.01$ $\omega^2=0.00$	p=0.06 $\eta^2=0.02$ $\omega^2=0.01$	P=0.31 $\eta^2=0.01$ $\omega^2=0.00$
	PCBO N=5 10.8 (4.0)	PCBO N=9 9.2 (4.5)	PCBO N=5 12.9 (4.4)	PCBO N=9 8.2 (4.5)	PCBO N=9 14.2 (4.8)	PCBO N=7 12.2 (4.8)			
HAM-A	JNJ N=2 2.0 (5.4)	JNJ N=11 11.3 (4.6)	JNJ N=2 22.3 (5.9)	JNJ N=12 10.5 (4.8)	JNJ N=9 8.6 (5.1)	JNJ N=9 13.1 (4.8)	p=0.03 $\eta^2=0.01$ $\omega^2=0.00$	p=0.02 $\eta^2=0.02$ $\omega^2=0.01$	P=0.17 $\eta^2=0.01$ $\omega^2=0.00$
	PCBO N=5 8.8 (4.2)	PCBO N=9 10.2 (4.8)	PCBO N=5 14.0 (4.7)	PCBO N=9 7.4 (4.8)	PCBO N=9 12.7 (4.8)	PCBO N=7 11.7 (5.0)			
CGI-I	JNJ N=2 3.8 (1.2)	JNJ N=11 3.1 (1.0)	JNJ N=2 3.0 (1.1)	JNJ N=12 3.5 (1.0)	JNJ N=9 2.8 (0.9)	JNJ N=9 3.6 (0.9)	p=0.45 $\eta^2=0.02$ $\omega^2=0.01$	p=0.06 $\eta^2=0.03$ $\omega^2=0.00$	P=0.012 $\eta^2=0.06$ $\omega^2=0.02$

	PCBO N=5 3.1 (0.9)	PCBO N=9 3.2 (0.9)	PCBO N=5 2.9 (0.9)	PCBO N=9 2.9 (0.9)	PCBO N=9 3.7 (0.9)	PCBO N=7 3.1 (1.1)			
CGI-S	JNJ N=2 2.8 (1.0)	JNJ N=11 3.1 (0.7)	JNJ N=2 3.5 (0.9)	JNJ N=12 3.3 (0.7)	JNJ N=9 2.8 (0.9)	JNJ N=9 3.4 (0.9)	p=0.35 $\eta^2=0.01$ $\omega^2=0.00$	p=0.32 $\eta^2=0.02$ $\omega^2=0.00$	P=0.43 $\eta^2=0.02$ $\omega^2=0.00$
	PCBO N=5 3.3 (0.7)	PCBO N=9 3.1 (0.6)	PCBO N=5 3.4 (0.7)	PCBO N=9 3.0 (0.6)	PCBO N=9 3.3 (0.9)	PCBO N=7 3.4 (0.8)			
CPFQ	JNJ N=1 17.6 (N/A)	JNJ N=11 19.7 (4.6)	JNJ N=2 24.5 (5.8)	JNJ N=12 22.5 (4.8)	JNJ N=9 17.8 (5.1)	JNJ N=9 24.0 (4.5)	p=0.20 $\eta^2=0.01$ $\omega^2=0.00$	p=0.27 $\eta^2=0.01$ $\omega^2=0.00$	P=0.075 $\eta^2=0.02$ $\omega^2=0.01$
	PCBO N=5 18.7 (4.0)	PCBO N=9 23.0 (4.5)	PCBO N=5 23.8 (4.5)	PCBO N=9 17.4 (4.5)	PCBO N=9 23.0 (4.8)	PCBO N=7 21.5 (4.8)			

Site columns contain baseline corrected least squared means (SD) at end of double-blind treatment from mixed effects models;

* η^2 and ω^2 are measures of effect-size for ANOVA effects. ω^2 is a relatively unbiased estimate for effect-size for ANOVA compared with η^2 and can be negative with a possible range from -1 to 1. Negative values occur when F is less than 1.^{9,10}

