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1   **ABSTRACT**

2   Performance-based incentives tend to increase an individual's motivation,

3   resulting in enhancements in behavioral output. While much work has focused on

4   understanding how the brain's reward circuitry influences incentive motivated

5   performance, fewer studies have investigated how such reward representations act on

6   the motor system. Here we measured motor cortical excitability with transcranial

7   magnetic stimulation (TMS) while female and male human participants performed a

8   motoric incentive motivation task for prospective monetary gains and losses. We found

9   that individuals' performance increased for increasing prospective gains and losses.

10 While motor cortical excitability appeared insensitive to prospective loss, temporal

11 features of motor cortical excitability for prospective gains were modulated by an

12 independent measure of an individual's subjective preferences for incentive (i.e., loss

13 aversion). Those individuals that were more loss averse had a greater motor cortical

14 sensitivity to prospective gain, closer to movement onset. Critically, behavioral

15 sensitivity to incentive and motor cortical sensitivity to prospective gains were both

16 predicted by loss aversion. Furthermore, causal modeling indicated that motor cortical

17 sensitivity to incentive mediated the relationship between subjective preferences for

18 incentive and behavioral sensitivity to incentive. Together our findings suggest that

19 motor cortical activity integrates information about the subjective value of reward to

20 invigorate incentive motivated performance.

SIGNIFICANCE STATEMENT

Increasing incentives tend to increase motivation and effort. Using a motoric incentive motivation task and transcranial magnetic stimulation, we studied the motor cortical mechanisms responsible for incentive motivated motor performance. We provide experimental evidence that motor cortical sensitivity to incentive mediates the relationship between subjective preferences for incentive and incentive motivated performance. These results indicate that, rather than simply being a reflection of motor output, motor cortical physiology integrates information about reward value to motivate performance.

INTRODUCTION

We modulate our performance according to the rewards at stake. Larger stakes tend to increase motivation, which in turn elicits increased behavioral output (i.e., increased force exertion (Pessiglione et al., 2007; Kurniawan et al., 2010; Schmidt et al., 2012); and increased success rate during a skilled motor task (Chib et al., 2012, 2014)). Incentive motivation refers to the processes that convert higher reward expectancies into increased performance (Berridge, 2004). These processes include forming a subjective representation of prospective reward, which invigorates behavioral performance. The effects of incentive motivation on effortful exertion has been the topic of extensive investigation in psychology (Bolles, 1972; Bindra, 1974; Bolles and Fanselow, 1980), and, in more recent years, the field of cognitive neuroscience has begun to dissect how the brain's reward circuity influences motivated performance (Pessiglione et al., 2007; Talmi et al., 2008; Chib et al., 2012; Schmidt et

43 al., 2012). However, motivated performance is not only related to processing the

44 rewards at stake, but also how these reward representations influence activity in motor

45 cortex to result in behavioral performance. Despite the neural crosstalk between

46 motivation and motor processing during incentivized performance (Mogenson et al.,

47 1980; Bray et al., 2008; Talmi et al., 2008; Chib et al., 2014), the understanding of how

48 motor cortical excitability gives rise to incentive motivated performance is fairly limited.

49   Transcranial magnetic stimulation (TMS) provides precise timing to study how

50 motor cortical excitability is influenced by motivating stimuli. Freeman and colleagues

51 recently used TMS to demonstrate that stimuli predicting an appetitive juice reward (i.e.,

52 conditioned stimulus), paired with an instrumental response in extinction (i.e.

53 performance was not reward-contingent), served to increase motor cortical excitability

54 and responding; while stimuli predicting the absence of reward did not invoke increases

55 in motor excitability (Freeman et al., 2014). In a follow-up study, they found that

56 presentation of aversive stimuli inhibited motor evoked potentials during trials that did

57 not require instrumental responding (i.e. no-go trials) (Chiu et al., 2014). Together these

58 results illustrate that motivational information spills into the motor system, influencing

59 motor cortical excitability prior to execution.

60   Studies of binary choice have also used TMS to study the dynamics of motor

61 excitability prior to action selection. This work has shown that motor cortical activity

62 builds in the time period before a choice cue is presented and that excitability increases

63   as function of the value of the chosen option (Duque and Ivry, 2009; Klein et al., 2012;

64   Klein-Flügge et al., 2013). From these results it has been suggested that action

65   selection during choice entails a competition, within motor-related areas, in which motor

66   cortical excitability integrates reward value to drive a motor response. Furthermore, it

67   was found that during binary choice of risky options, motor excitability was best

68   described by chosen and unchosen subjective value (i.e., accounting for prospect

69   theoretic measures) (Klein-Flügge and Bestmann, 2012). These studies suggest that

70   the dynamics of motor excitability captures the value of reward during simple choice.

71   However, it is not known how subjective preferences for incentives might influence

72   motor cortical excitability to drive incentive motivated performance.

73   The aim of this study was to investigate the role of motor cortical excitability on

74   incentive motivation, and how these cortical processes interact with representations of

75   subjective value to result in motivated performance. We hypothesized that the sensitivity

76   of motor excitability to incentive would be predictive of an individual's motivated

77   performance. This hypothesis has its basis in previous TMS studies that found that

78   motor cortical excitability, measured prior to instrumental responding, was modulated in

79   response to conditioned stimuli that previously predicted appetitive and aversive

80   outcomes (Chiu et al., 2014; Freeman et al., 2014; Freeman and Aron, 2016). We also

81   hypothesized that motor cortical excitability would be related to an independent

82   behavioral measure of subjective preferences for incentive. This hypothesis has its

83   basis in previous TMS studies which found that motor cortical excitability reflected

84   subjective chosen and unchosen values during binary choice (Klein-Flügge and

85   Bestmann, 2012); and neuroimaging studies that found that the functional connectivity

86   between reward regions and motor cortex, during instrumental responding for reward,

87   was modulated by behavioral measures of subjective preferences (Chib et al., 2012,

88   2014). Specifically, our previous behavioral and neuroimaging studies (Chib et al., 2012,

89   2014) found that incentives associated with successful task performance are initially

90   encoded as a potential gain; and, when actually performing a task, individuals encode

91   the potential loss that would arise from failure. Given these findings, we predicted that

92   subjective feelings of loss, instantiated by a measure of loss aversion, would be

93   predictive of incentive motivated performance and motor cortical excitability.

94   **MATERIALS AND METHODS**

95   **Experimental Design and Statistical Analyses**

96   All participants were right handed and prescreened to exclude those with a prior

97   history of neurological or psychiatric illness. The Johns Hopkins Medical Institute

98   Institutional Review Board approved this study, and all participants gave informed

99   consent. Using an effect size from our previous study examining the relationship

100 between incentive motivated performance and neural sensitivity to value ($r = 0.70$,

101 $95\% \; CI \; [0.40, 0.88]$) (Chib et al., 2012), a significance of < 0.05 with a power goal of at

102 least 0.80, a power analysis indicated that we would need at least 13 subjects to

103 reproduce this effect. We aimed to collect data from 20 participants, to account for the

104 possibility of attrition, exclusion due to lack of task compliance, or mis-estimation of the

105 subjective reward preference data. In the end, nineteen participants (mean age, 20; age

106 range, 18-23; twelve females, seven males) were recruited and took part in the

107   experiment. Each participant performed the motor task and a behavioral choice

108   paradigm to characterize subjective preferences for incentive (i.e., loss aversion and

109   risk aversion). One participant was excluded from the final analysis because of atypical

110   choices during the subjective reward preference task (i.e. rejection of all gambles with

111   potential losses).

112   All analyses were conducted in Matlab2018a with the exception of the hierarchal

113   Bayesian modeling for subjective reward preference analysis (described below).

114   Hierarchical linear models were implemented to test population-level effects on subject-

115   level estimates, implemented in Matlab using *fitglme*, with no covariance matrix

116   restrictions. Analyses that examined population-level exertion report effects of slope on

117   subject-level z-scored mean force exertion. Analyses that examined the sub-population

118   motor cortical findings used ANOVAs of hierarchical linear models to evaluate the 2-way

119   interaction of timing and reward subjectivity. Subject-level parameters were estimated

120   from general linear models (described below), implemented in Matlab using *fitglm*.

121   Correlations were reported with Pearson coefficients and 95% confidence intervals

122   generated by 10000 iteration bootstrapping. Additionally, standardized regressions were

123   used for the mediation analysis and the completely standardized indirect effect size was

124   bootstrapped to measure mediation (Preacher and Kelley, 2011).

125 **Experimental Setup and Brain Stimulation**

126   Participants sat in a chair and held a force transducer (LMD300, Futek) between

127 the thumb and forefinger of their right hand. During the experiment, participants rested

128 their head in a custom-built gantry. The gantry minimized head-movements across trials

129 and ensured accurate brain stimulator placement. An armrest ensured consistent

130 positioning of the arm across trials. Visual stimuli were presented using MATLAB 2014a

131 and Psychtoolbox-3 (Brainard, 1997; Kleiner et al., 2007).

132   To record motor evoked potentials elicited from TMS, surface electromyographic

133 electrodes were placed on the first dorsal interosseous (FDI) muscle; and these signals

134 were recorded, amplified, and filtered (Bortec Biomedical). To elicit motor evoked

135 potentials, we delivered TMS using a 70mm figure-eight coil (Magstim) to the optimal

136 scalp position over the left motor cortex. To ensure accurate and precise placement of

137 the TMS coil throughout the experiment, we used a frameless neuronavigation system

138 (Brainsight, Rouge Research) and coregistered participants' heads to a default

139 Talairach template provided in the Brainsight software suite. The coil was placed

140 tangentially on the scalp with the handle pointing backward and laterally at a 45 degree

141 angle away from the midline, perpendicular to the central sulcus.

142   We first coregistered participants' heads to a standard magnetic resonance

143 image in the neuronavigation system. Then we identified the optimal area for eliciting

144 MEPs in the resting FDI. The optimal M1 location was defined as the site in which we

145 could elicit a localized motor response at a minimal intensity. At this location we

146 determined the resting motor threshold, defined as the minimum TMS intensity that

147 evoked a motor evoked potential (MEP) of 50 microvolts in 5 of 10 trials in the FDI of

148 the right hand (Pascual-Leone et al., 1994; Rossini et al., 1994). A deviation of more

149 than 3 mm or 15 degrees resulted in the experimenter repositioning the coil during the

150 intertrial interval and trials with sub-threshold MEP magnitude were excluded from

151 analysis.

152   The stimulation timings presented in this experiment (50 ms and 150 ms) were

153 informed by a number of previous studies that examined how motor cortical excitability

154 evolves in the time period between presentation of a 'Go' cue and movement, and were

155 chosen to probe the early and late stages of motor preparation (Chen and Hallett, 1999;

156 Leocani et al., 2000; Duque and Ivry, 2009; Klein-Flügge and Bestmann, 2012;

157 Hortobágyi et al., 2017). Specifically, our stimulation times were meant to capture motor

158 cortical excitability in the first half of reaction time (since RTs are usually in range of 200

159 to 300 ms), while minimizing the influence of motor cortical stimulation on performance

160 (e.g., motor quickening). We focused on two stimulation times to ensure we sampled

161 enough trials at each incentive level and stimulation time to maximize the possibility of

162 obtaining behavioral and motor cortical effects. Similar variably timed, single pulse TMS

163 paradigms have been used to study the neural processing of different types of affective

164 processes (Pitcher et al., 2007, 2012; Klein-Flügge and Bestmann, 2012; Klein-Flügge

165 et al., 2013).

166   To control between participants and conditions, the stimulus intensity was

167   calibrated on a per subject basis during the calibration phase. For this procedure, TMS

168   pulse intensity was adjusted such that pulses delivered 50ms following the 'Go' cue

169   elicited a 1mV MEP. The stimulation intensity was fixed to this value for the remainder

170   of the experiment (i.e., the same intensity was used on 50ms and 150ms trials during

171   familiarization and incentivized phases, described below). This procedure was similar to

172   those previously used to study motor cortical excitability (Stefan et al., 2004; Vallence et

173   al., 2013). To generate this baseline MEP level, the first 30 trials of the unincentivized

174   phase (described below) involved only TMS pulses 50ms following the 'Go' cue and the

175   experimenter monitored the elicited MEPs to target 1mV. Additionally, the initial

176   stimulator intensity was set to 120% of a participant's resting motor threshold.

177   **Motor Task**

178   Participants first performed a calibration phase to determine their maximum

179   voluntary contraction (MVC) during an isometric pinch grip. This involved participants

180   maintaining their maximum pinch exertion for 4 seconds, on 3 consecutive trials, each

181   separated by a 5 second rest period. MVC was calculated as the maximum pinch force

182   exerted on the 3 calibration trials. Since we acquired each individual's MVC, we were

183   able to standardize difficulty, based on MVC ability, across participants.

184   The main experiment was divided into two phases: unincentivized and

185   incentivized (Figure 1). During both phases of the experiment participants performed an

186 isometric pinch exertion task. Participants were not instructed to grip on every trial and

187 were free to respond with grip force at their discretion (i.e., they could forgo exerting

188 effort if they were so inclined). This task was chosen because pinch grip isolates use of

189 the FDI muscle, which we targeted in our TMS procedure, to study the relationship

190 between incentive, motor excitability, and performance. TMS was performed on every

191 trial of each phase of the experiment. Participants were instructed that they would

192 receive a show-up fee of $15 dollars at the end of experiment in addition to any

193 earnings from their performance in the incentivized phase.

194   The unincentivized phase was comprised of 60 trials. At the beginning of each

195 trial, participants were presented a blue cursor that moved across the screen in

196 proportion to the amount of pinch exertion (Figure 1). Squeezing the force transducer

197 moved the cursor horizontally to the left, while relaxing caused the cursor to move right.

198 Participants were instructed to place the cursor in the start position ($\times$) for a random

199 amount of time (3–6 seconds). This start position corresponded to minimal pinch

200 exertion while still grasping the force transducer. During the task, a 'Go' cue and a

201 target line registered to 45% of MVC appeared on the screen. To successfully achieve

202 the task, participants had to exert pinch effort to move the cursor across the target line

203 within 0.5 seconds. At the end of a trial participants were shown a message indicating

204 their performance. Following the initial 30 trial TMS calibration epoch (described above),

205 the remaining 30 trials involved TMS delivered at either 50ms or 150ms after

206 presentation of the 'Go' cue, and visual feedback during exertion was withheld. This trial

207 epoch was meant to familiarize participants with the conditions of the main experimental

208 task. The stimulation times were evenly distributed across trials.

209 During the incentivized phase participants performed the isometric pinch exertion

210 task as described above, for varying amounts of monetary gain or loss. We did not

211 present participants with feedback of their hand cursor, or the effort target, in order to

212 allow them to reach the target effort level under their own implicit motivation. At the

213 beginning of the experiment, participants were given an endowment of $20 in cash,

214 separate from their show-up fee, and were told that at the end of the experiment, one

215 trial would be selected randomly and a payment made according to their performance

216 on that trial. Participants were told that their $20 endowment was given to them so that

217 they could pay any eventual losses at the end of the experiment. This payout

218 mechanism ensured that trials had significant monetary consequences and that

219 participants evaluated each trial independently. Participants performed trials for a range

220 of incentives (i.e. $\pm$ $0, $10, $20). Each incentive level was presented randomly 30

221 times for a total of 180 trials, with an equal balance of conditions for TMS pulse timing

222 (i.e. 50ms TMS pulse; 150ms TMS pulse). Importantly, +$0 and -$0 conditions did not

223 differ in their objective value, but only their framing (i.e. "Win $0" and "Lose $0"). At the

224 beginning of each trial, participants were shown a message indicating the amount of

225 incentive for which they were playing. They then performed the motor task, with the

226 same success criteria as during the unincentivized phase. At the end of the experiment,

227 a single trial was selected at random and participants were paid based on their

228 performance on that trial.

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229   To summarize, our task had several important features: 1) During the

230 incentivized performance phase we did not display cursor position to participants so

231 they could not simply target the necessary effort level. Instead they exerted effort in

232 accordance with what they remembered the target effort level to be, and since they

233 were not able to see the target, any extra exertion that they produced captured implicit

234 incentive motivational spill-over into motor performance. 2) We parametrically

235 modulated incentive to provide a finer grained assessment of how performance varies

236 with incentive, unlike previous investigations of motor cortical influences on instrumental

237 performance, which used appetitive and aversive conditioned stimuli (in extinction) and

238 were not designed to examine parametric effects of rewards (Chiu et al., 2014; Freeman

239 et al., 2014; Freeman and Aron, 2016). Furthermore, these studies did not examine how

240 reward subjectivity influenced motor excitably and performance, rewards were not

241 contingent on performance, and they did not present data that implicated a mechanistic

242 framework by which valuation could influence motivated performance through motor

243 excitability. Notably, the previous TMS studies that did parametrically vary incentive

244 were designed to study decision-making and not reward-contingent incentive motivated

245 performance (Klein-Flügge and Bestmann, 2012; Klein-Flügge et al., 2013). 3) To

246 evaluate the influence of subjective preferences on incentive motivation we had

247 participants perform a separate prospect theory task that provided a precise

248 measurement of subjective preferences for incentive (i.e. loss aversion, risk

249 aversion) (Sokol-Hessner et al., 2009; Chib et al., 2012, 2014). This task generated

250 measures of subjective preferences for reward that were independent of the incentive

12

251   motivation task, which allowed an unbiased means to examine relationships between

252   sensitivity to incentive, incentive motivated behavior, and motor cortical excitability.

253   **Subjective Reward Preference Task (Measurement of Loss Aversion and Risk**
254   **Aversion)**

255   Participants received an initial endowment of $25 in cash (this amount was

256   separate from their show-up fee and earnings/endowment from the motor task) and

257   were told that, at the end of the experiment, one trial would be selected randomly and a

258   payment made according to their actual decision during the experiment. Participants

259   were told that their $25 endowment was given to them so that they could pay any

260   eventual losses at the end of the experiment. Any amount from the endowment that

261   remained after subtracting a loss was theirs to keep, and similarly any eventual gain

262   earned in the experiment was added to the initial endowment. During the experiment,

263   participants made choices among 140 different pairs of monetary gambles. Each pair

264   contained a certain option involving a payout with 100% probability S and a risky option

265   involving gain G and loss L with equal probability (Figure 2). Participants had 4 s to

266   make a choice. The values for gain, loss, and sure options were the same as those

267   used in previous studies that estimated individuals' loss aversion (Sokol-Hessner et al.,

268   2009; Frydman et al., 2011). Specifically, gambles involving a potential gain or loss, and

269   an alternative sure amount of $0 were generated from the comprehensive combination

270   of $G \in \{2,4,5,6,8,9,10,12\}$ and $L \in [.25 * G, 2 * G]$ in multiplier increments of 0.125. For the

271   options involving a potential gain for an alternative sure amount, the set was $(G, S) \in$

272   {(2,1), (3,1), (4,2), (5,2), (7,3), (8,3), (12,6), (12,5), (12,4), (13,5), (13,6), (19,8),

273   (22,10), (23,10), (25,9), (25,10), (26,10), (26,12), (28,13), (30,12)}.

274   **Data Analysis**

275   *Behavioral performance analysis*

276   Our main behavioral measure of performance was the mean effort exerted on

277   each trial, defined as mean force exerted between the time the exertion threshold is met

278   (i.e., the first recording above 10% of MVC after the 'Go' cue) and the end of the trial.

279   We excluded trials if detected reaction time intersected with MEP onset, participants

280   were unable to reach the target within the allotted time, or participants failed to move.

281   We used a general linear model with the magnitude of potential gain and loss $x \in$

282    $\{0, 10, 20\}$ and valence $v \in \{1, -1\}$ as independent variables, and performance (log

283   transformed mean force to correct for skewness) as the dependent variable.

$$\log(\text{Mean Force}) = \begin{cases} \beta_{\text{Exertion}}^{\text{Gain}} x + C^{\text{Gain}} & \text{if } v = 1 \\ \beta_{\text{Exertion}}^{\text{Loss}} x + C^{\text{Loss}} & \text{if } v = -1. \end{cases}$$

284   The regression coefficients $\beta_{\text{Exertion}}^{\text{Gain}}$ and $\beta_{\text{Exertion}}^{\text{Loss}}$ represent a participant's

285   sensitivity in performance to increasing potential gains and losses — larger β

286   parameters correspond to a participant having greater increases in performance as a

287   function of increasing incentives. The parameters C^{Gain} and C^{Loss} capture the

14

288   performance off-set associated with each valence condition, equivalent to the behavior

289   at $0 incentivization.

290   *Motor cortical excitability analysis*

291   We assessed cortical excitability by measuring the peak-to-peak amplitudes (in

292   mV) of the motor evoke potential from the FDI muscle on all stimulation trials. This

293   measure was defined as the MEP. In a similar fashion to the behavioral analysis, we

294   used a general linear model to examine the sensitivity of motor cortical excitability to

295   reward, at 50ms and 150ms following the 'Go' cue. In this model the magnitude of

296   potential gain and loss x, valence v, and stimulation time t, were independent variables;

297   and MEP was the dependent variable. We z-scored within session and stimulation

298   condition to account for between session variability in MEP measurements resulting

299   from factors such as subject movement, repositioning of TMS coil, etc., during rest

300   periods.

$$\text{z-scored(MEP at 50ms)} = \begin{cases} \beta_{50}^{\text{Gain}} x + C_{50}^{\text{Gain}} & \text{if } v = 1 \\ \beta_{50}^{\text{Loss}} x + C_{50}^{\text{Loss}} & \text{if } v = -1. \end{cases}$$

$$\text{z-scored(MEP at 150ms)} = \begin{cases} \beta_{150}^{\text{Gain}} x + C_{150}^{\text{Gain}} & \text{if } v = 1 \\ \beta_{150}^{\text{Loss}} x + C_{150}^{\text{Loss}} & \text{if } v = -1. \end{cases}$$

301   The coefficient terms (β_{50}^{Gain}, β_{50}^{Loss}, $\beta_{150}^{\text{Gain}}$, and $\beta_{150}^{\text{Loss}}$) represent an individual's

302   motor cortical sensitivity to incentive at time points following incentive presentation at 50

303   ms or 150 ms after the 'Go' cue. The intercept terms (C_{50}^{Gain}, C_{50}^{Loss}, C_{150}^{Gain}, and C_{150}^{Loss})

304   capture the MEP offset associated with each valence condition.

305   *Subjective reward preference analysis*

306   We fit prospect theory-inspired models of the non-linear processes underlying

307   subjective valuation of reward to participant's choice data from the subjective reward

308   preference task, using a hierarchical Bayesian approach. This model was identical to

309   that used previously (Sokol-Hessner et al., 2009; Chib et al., 2012, 2014), implemented

310   using Monte-Carlo Markov Chain sampling methods provided by rStan (v2.2.0; (Stan

311   Development Team, 2017)) in R (v3.0.2; (RDevelopment CORE TEAM, 2008)), using

312   the methodology described by the hBayesDM package (Ahn et al., 2017). We

313   expressed participants' utility function $u(x)$ for monetary values x as follows:

$$u(x|\lambda,\rho) = \begin{cases} x^\rho & \text{if } x \geq 0 \\ -\lambda(-x)^\rho & \text{if } x < 0. \end{cases}$$

314   This formulation is used to compute the utilities of the risky and certain

315   alternative. The model's parameters quantify loss aversion (λ, the relative multiplicative

316   weight placed on losses compared with gains), risk attitudes (ρ, feelings about chance,

317   or diminishing marginal sensitivity to value). Assuming participants combine

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318   probabilities and utilities linearly, the expected utility of a mixed gamble can be written

319   as $U(\mathrm{G}, \mathrm{L}, \mathrm{S}|\lambda, \rho) = .5(\mathrm{G}^\rho - \lambda \mathrm{L}^\rho) - \mathrm{S}^\rho$ where G and L are the respective gain and loss of

320   a presented risky option and S is a fixed alternative choice. The probability that a

321   participant chooses to make a gamble is given by the softmax function:

$$P(\mathrm{G}, \mathrm{L}, \mathrm{S}|\lambda, \rho, \tau) = \frac{1}{1 + e^{-\tau * U(\mathrm{G}, \mathrm{L}, \mathrm{S}|\lambda, \rho)}}$$

322   where τ is a temperature parameter representing the stochasticity of a participant's

323   choice ($\tau = 0$ means choices are random). This model was fit to the choice data using

324   standard hierarchical Bayesian methods, and applied constraints on the fit parameters

325   such that: $\lambda \in (0,5)$, $\rho \in (0,2)$, and $\tau \in (0,10)$. Weakly informative priors were used on

326   the constrained domain, and a non-centered parametrization was used to facilitate

327   model convergence (Betancourt and Girolami, 2013). All analyses of loss aversion used

328      $\log(\lambda)$; the logarithm is commonly used because lambda is positively skewed.

329   _Mediation analysis_

330   Mediation analysis is a specific case of structural equation modeling that refers to

331   a situation that includes three or more variables, such that there is a causal process

332   between all three variables (Judd and Kenny, 1981). In a mediation relationship, there is

333   a direct effect between an independent variable and a dependent variable. There are

334   also indirect effects between an independent variable and a mediator variable and

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335   between a mediator variable and a dependent variable. This formulation allows for a

336   test of the strength of the direct effect between the independent and dependent

337   variables, accounting for connections via a mediating variable. A measure of the direct

338   effect (after controlling for the mediator) can be obtained using a series of regressions

339   for all of the causal pathways and estimating a change in the direct effect.

340   We performed a mediation analysis of our data using standardized linear

341   regression to test the possibility that the relationships between subjective preferences

342   for reward (instantiated by loss aversion), and task performance (performance

343   sensitivity to increasing potential gain) were mediated through motor cortical excitability.

344   For these analyses, we performed between-participant standardized regressions with

345   variables for participants' behavioral loss aversion, the difference in motor cortical

346   sensitivity to prospective gain between stimulation at 50ms and 150ms ($\beta_{150}^{\text{Gain}} - \beta_{50}^{\text{Gain}}$),

347   and the performance sensitivity to increasing potential gain ($\beta_{\text{Exertion}}^{\text{Gain}}$). Our main

348   mediation hypothesis was that $\beta_{150}^{\text{Gain}} - \beta_{50}^{\text{Gain}}$ mediates the relationship between $\log(\lambda)$

349   and performance. To rule out model misspecification, we also tested control models in

350   which the causal structure of our experiment was preserved (i.e., motor excitability

351   preceded performance), and alternative relationships were modeled. This included a

352   model in which $\log(\lambda)$ mediated the relationship between $\beta_{150}^{\text{Gain}} - \beta_{50}^{\text{Gain}}$ and $\beta_{\text{Exertion}}^{\text{Gain}}$, and

353   another model in which $\beta_{\text{Exertion}}^{\text{Gain}}$ mediates the relationship between $\beta_{150}^{\text{Gain}} - \beta_{50}^{\text{Gain}}$ and

354    $\log(\lambda)$. We used bootstrapping (a nonparametric sampling procedure) to test whether

355 the specified mediator significantly mediated the relation between the independent and

356 dependent variables (Preacher and Hayes, 2004).

357 **RESULTS**

358 　　To test our hypothesis, we developed a task in which participants were instructed

359 to exert pinch grip beyond a predetermined threshold in order to win or avoid losing

360 monetary incentives ranging from $0 to $20. We stimulated participants' motor cortex

361 with TMS at two time points, between the presentation of incentive and movement

362 onset, in order to examine how motor cortical sensitivity to incentive was related to

363 incentive motivation. Participants also performed a separate decision-making task after

364 performing the motor task, in which they made choices over prospective monetary gains

365 and losses. This task allowed us to obtain computational parameters that described

366 each participants' subjective preferences for incentive (i.e., loss aversion and risk

367 aversion).

368 　　To foreshadow the results, we found that participants exhibited increasing

369 behavioral performance for increasing incentives, and that these increases in

370 performance were related to motor cortical sensitivity to incentive in the time period

371 between incentive presentation and movement. Both performance and motor cortical

372 sensitivity to incentive were related to measures of participants' loss aversion, such that

373 those individuals that were more loss averse (i.e., had a greater sensitivity to incentive)

374 exhibited larger behavioral and motor cortical sensitivity to incentive. A formal mediation

375   analysis revealed that motor cortical sensitivity to incentive mediated the relationship

376   between subjective preferences for incentive and performance.

377   **Behavioral Performance**

378   As expected, prospective gains and losses led to increases in participants'

379   percent success when comparing $0 trials to $10 and $20 trials (Figure 3A; Wilcoxon

380   signed rank paired test to account for skewed distribution at $10 and $20 and including

381   otherwise excluded trials, Gain: $z = 2.6; p = 0.011$; Loss: $z = 2.8; p = 0.0048$). We also

382   observed robust relationships between participants' mean exertion as a function of

383   incentive. We found that participants also exhibited increasing mean exertion, with

384   increasing incentives, in both the gain and loss conditions (Figure 3B; hierarchical linear

385   model, Gain; $\beta = 0.018, t(104) = 3.8, p = 2.6 * 10^{-4}$; Loss; $\beta = 0.025, t(104) = 7.0, p =$

386    $2.9 * 10^{-10}$). Together, these results illustrate that increasing incentives serve to

387   increase behavioral performance in both the gain and loss domain.

388   We next examined the relationship between participants' behavioral sensitivity to

389   increasing prospective gains and losses in the incentive motivation task (encoded as

390   the slope between mean force exertion and incentive value), and an independent

391   measure of participants' sensitivity to incentive obtained from a separate decision-

392   making task. We reasoned that those individuals that found incentives to be more

393   subjectively valuable (i.e., have a higher loss aversion) would have increased

394   behavioral sensitivity to incentive. We found a significant relationship between

20

395   participant-specific loss aversion and behavioral sensitivity in the gain domain

396   (Figure 3C; Pearson correlation, $r = 0.58, 95\%$ CI $[0.10, 0.87], p = 0.011$), however we

397   failed to find a significant relationship between these measures in the loss domain

398   (Figure 3D; Pearson correlation, $r = 0.16, 95\%$ CI $[-0.17, 0.50], p = 0.52$). This suggests

399   that, for prospective gains, processing of the subjective value of incentive serves to

400   motivate behavioral performance in the incentive motivation task. These results align

401   with our previous work which found that loss aversion was predictive of increases in

402   performance for incentives in the range tested in this experiment. In those previous

403   studies, we found that worries about loss (instantiated by loss aversion) served to

404   motivate performance for both prospective gains (Chib et al., 2012, 2014) and

405   losses (Chib et al., 2014). Specifically, measures of loss aversion not only predicted

406   performance decrements for large incentives, but also the incentive leading to peak

407   performance for small levels of incentive.

408   Loss aversion represents a tendency to value losses greater than equal

409   magnitude gains. Risk aversion, on the other hand, is a more general aversion to

410   increased variance in potential gains or losses. To ensure a loss aversion-based

411   hypothesis better accounted for our behavioral data than a general aversion to risk, we

412   also examined the relationship between risk aversion and behavioral sensitivity in the

413   gain and loss domains. We did not find a significant correlation between behavioral

414   sensitivity to incentive and risk preferences (Pearson correlation, Gain:

415    $r = 0.12, 95\%$ CI $[-0.39, 0.60], p = 0.63$; Loss: $r = 0.19, 95\%$ CI $[-0.26, 0.56], p = 0.46$),

416   nor choice stochasticity (Pearson correlation, Gain: $r = 0.22, 95\%$ CI $[-0.27, 0.73], p =$

417 0.39; Loss: $r = -0.19, 95\%$ CI $[-0.53, 0.25], p = 0.45$). Furthermore, we failed to find a

418 significant correlation between maximum likelihood estimated loss aversion and either

419 risk aversion or choice stochasticity parameters, suggesting that distinct processes

420 underlie these parameters (correlations with $\log(\lambda)$, $-\log(\rho) : r = 0.32, p =$

421 $0.19; \log(\tau): r = -0.41, p = 0.09$). We also ran a model comparison of the separately

422 estimated choice parameters and found that $\log(\lambda)$ provided the best description of the

423 behavioral sensitivity to incentive in the gain domain ($BIC_{\log(\lambda)}$ = -150.72; $BIC_{-\log(\rho)}$ = -

424 143.46; $BIC_{\log(\tau)}$ = -144.06). This provides converging evidence that behavioral

425 sensitivity to prospective gains is best described by an independent measure of reward

426 subjectivity characterized by a measure of loss aversion. These results are in keeping

427 with our previous results showing the loss aversion was predictive of behavioral

428 performance during a skilled-motor task for incentive (Chib et al., 2012, 2014).

429 **Motor Cortical Excitability in Response to Incentive**

430 We sought to identify how motor cortical sensitivity to incentive, in the context of

431 the incentive motivation task, was related to subjective preferences for incentive. To this

432 end we explored parameter estimates from our general linear model of motor cortical

433 sensitivity to incentive, separated by participants' behavioral loss aversion (participant

434 specific medial split) (Figure 4A, 4B). These parameter estimates capture the slope of

435 the relationship between motor cortical excitability and incentive level. Larger parameter

436 estimates correspond to a more pronounced change in motor cortical excitability in

437 response to increasing incentive.

438   In the gain domain, we found a significant interaction between stimulation time

439   and loss aversion, indicating that individuals with higher loss aversion had an increased

440   motor cortical sensitivity to incentive, closer to movement onset (Figure 4A; mixed

441   effects ANOVA, $F(1,32) = 8.0, p = 0.0078$). Moreover, we found that this effect was

442   driven by individuals with higher loss aversion having an increased motor cortical

443   sensitivity at the 150ms stimulation time point (Figure 4A, *post hoc* one-tailed Welch's t-

444   test, $t(10.48) = 3.0, p = 0.0059$). In the loss domain, we failed to find a significant

445   interaction between changes in MEP sensitivity between the 50 and 150 stimulation

446   time points and behavioral loss aversion (Figure 4B; mixed effects ANOVA, $F(1,32) = $

447    $.0093, p = 0.92$).

448   Our paradigm did not elicit correlations between behavioral and motor cortical

449   sensitivity to value in the loss domain. It should be noted that this null result is

450   consistent with a previous study of motor cortical responses to aversive stimuli which

451   failed to find a significant change in motor evoked potentials, relative to baseline, when

452   individuals were presented an aversive conditioned stimulus paired with an instrumental

453   response (Chiu et al., 2014). With this null result in the loss domain in mind, we focused

454   the remainder of our motor cortical analyses on trials for prospective gain.

455   To further examine the temporal dynamics of motor cortical sensitivity to

456   incentive over the continuum of loss aversion, we performed a between participant

457   regression of loss aversion and difference in sensitivity to incentive between the 50ms

458 and 150ms time points $\beta_{150}^{\text{Gain}} - \beta_{50}^{\text{Gain}}$. The difference between these metrics is an

459 indication of the stability of motor cortical excitably to incentive over time. The greater

460 the difference between these parameter estimates, the more positively correlated to

461 incentive an individual's motor cortical excitably is closer to movement onset. We found

462 that those individuals that were more sensitive to incentive when comparing 50ms and

463 150ms time points, exhibited increased incentive motivated performance (Figure 4C;

464 Pearson correlation, $r = 0.70, 95\% \, CI \, [0.32, 0.89], p = 0.0013$). We also performed a

465 regression between participant-specific loss aversion and sensitivity to incentive

466 between the 50ms and 150ms time points and found that individuals with higher loss

467 aversion exhibited increased changes in motor cortical sensitivity closer to movement

468 onset (Figure 4D; Pearson correlation, $r = 0.68, 95\% \, CI \, [0.29, 0.88], p = 0.0017$).

469   In keeping with our incentive motivation hypotheses of motor cortical activity,

470 these relationships suggest that in the gain domain, subjective preferences for incentive

471 (instantiated by an individuals' loss aversion) could serve to amplify motor cortical

472 sensitivity to incentive and energize motor performance.

473   We performed a series of analyses to ensure that the TMS incentive effects that

474 we observed were not simply the byproduct of confounds between stimulation timing

475 and movement execution. Pre-movement motor cortical stimulation is known to elicit

476 movement quickening, in which stimulations delivered closer to movement onset

477 decrease reaction time. To ensure that our TMS incentive effects were not simply the

478   byproduct of a quickening response, we examined the relationship between log reaction

479   time sensitivity to incentive (i.e., the regression coefficient between log reaction time

480   and incentive) and motor cortical sensitivity to incentive, at each stimulation time point,

481   using the measure $\beta_{150}^{\text{Gain}} - \beta_{50}^{\text{Gain}}$. We failed to find a significant correlation between

482   these measures, suggesting that our effects were not simply the results of TMS

483   quickening movements as a function of incentive (Figure 5A; Pearson correlation,

484    $r = -0.065, 95\% \ CI \ [-0.67, 0.41], p = 0.80$).

485   Another possible confounding factor in our motor cortical data could be that

486   participants initiate their movements based on the auditory cue of TMS pulses, rather

487   than the 'Go' cue. This would result in no segregation between motor cortical activity

488   between the 50ms and 150ms stimulation conditions, making it difficult to distinguish the

489   temporal features of motor cortical sensitivity to incentive. To determine if our data was

490   confounded in this way, we evaluated motor cortical excitability using a model in which

491   trials were separated based on the eventual time of movement onset (as identified from

492   participants EMG data using AGLRStep (Staude et al., 2001)), rather than presentation

493   of the 'Go' cue (as in our main experimental results). We found that, although there was

494   some quickening as a result of TMS (i.e., MEPs were not separated by a full 100ms),

495   motor evoked potentials occurred at significantly different time points relative to

496   movement onset (Figure 5B; paired t-test, $t(17) = 15.4, p = 2.0 * 10^{-11}$). Moreover, we

497   found that motor evoked potentials were larger in the 150ms stimulation condition

498   compared to the 50ms condition (Figure 5B; paired t-test, $t(17) = 4.7, p = 2.3 * 10^{-4}$),

499   consistent with previous studies that have shown increasing motor cortical excitability

500   approaching movement onset (Chen and Hallett, 1999).

501   To rule out the possibility that our behavioral effects were simply the byproduct of

502   motor cortical stimulation, we first examined the interaction between incentive and

503   stimulation time by partitioning trials between the 50 and 150 ms stimulation conditions.

504   Our behavioral finding of increased performance with increasing incentive was

505   preserved in both the gain and loss conditions (Figure 5C; hierarchical linear model

506   interaction term, Gain: $\beta = -0.001, t(208) = -0.20, p = 0.85$; Loss: $\beta = 0.009, t(208) =$

507    $1.5, p = 0.15$). This suggests that our behavioral effects were not simply the result of

508   stimulation timing. Second, while we found increasing behavioral performance in both

509   the loss and gain conditions (Figure 3A,B), we found prospective gains resulted in a

510   modulation of motor cortical excitability (Figure 4A) while prospective losses did not

511   (Figure 4B). Together these results suggest that our behavioral and stimulation effects

512   were specifically the result of the presentation of prospective gains, and not simply the

513   result of a general influence of brain stimulation on motor performance or motor cortical

514   excitability.

515   **Causal Influences of Loss Aversion and Motor Cortical Excitability on Incentive**
516   **Motivation**

517   Because loss aversion and behavioral sensitivity to incentive are correlated, and

518   both of these variables are correlated with the temporal evolution of motor cortical

519   sensitivity to incentive (Figure 6A), we investigated the hypothesis that motor cortical

520   sensitivity to incentive has a causal influence on loss aversion-related incentive

521   motivated exertion. To test this hypothesis, we used mediation analysis, a form of linear

522   modeling in which correlations observed in the data are explained by assuming that a

523   specific set of causal influences exist among the variables (Judd and Kenny, 1981).

524   This analysis alone does not establish causality but identifies if a causal hypothesis is

525   best fit for the data. We fit a model to the data that followed the logical progression of

526   our experimental paradigm. In this model we assumed that behavioral loss aversion

527   influenced incentive motivated exertion and that the temporal dynamics of motor cortical

528   sensitivity to incentive (the mediating variable) influenced incentive motivated exertion.

529   In our causal model (Figure 6B), behavioral loss aversion had a significant effect

530   on the difference in motor cortical sensitivity to incentive between the 50ms and 150ms

531   time points (standardized linear regression, $\beta = 0.68, t(16) = 3.8, p = 0.0017$). When

532   behavioral loss aversion and this measure of motor cortical sensitivity to incentive were

533   simultaneously modeled as predictors of performance, loss aversion no longer

534   significantly predicted performance (standardized linear regression, $\beta = 0.20, t(15) =$

535    $0.81, p = 0.43$), whereas motor cortical sensitivity to incentive remained significant in the

536   model (standardized linear regression, $\beta = 0.56, t(15) = 2.3, p = 0.040$). This reduction

537   in the direct relationship between loss aversion and incentive motivation was significant

538   (standardized indirect effect size, $ab = 0.38, 95\% \, CI \, [0.047, 0.80], p < 0.05$, as tested by

539   a bootstrapping procedure based on 10000 resamples). This model provides causal

540   support for the idea that manifestations of subjective preferences for incentive motivate

541   incentivized performance through the influence of the temporal dynamics of motor

542   cortical sensitivity on motor performance. Alternative models (Figure 6C, 6D) ruled out

543   model misspecification and did not find significant mediation effects by loss aversion

544   (95% confidence interval, $-0.28 \text{ to } 0.50; p \not< 0.05$) or performance (95% confidence

545   interval, $-0.23 \text{ to } 0.68; p \not< 0.05$).

546   We explored additional alternative models to test if the temporal dynamics of

547   motor cortical sensitivity to incentive partially mediated the relationship between either

548   risk aversion (Figure 7A) or choice stochasticity (Figure 7B) and incentive motivated

549   exertion. These alternative models did not contain the significant correlations required to

550   test if motor cortical sensitivity to incentive mediated the relationship between

551   performance and other subjective reward valuation parameters. These results lend

552   further support to the specificity of loss aversion to predict relationships between

553   behavioral performance and motor cortical activity.

554   **DISCUSSION**

555   In this study we show that incentive motivated performance emerges from the

556   temporal dynamics of motor cortical sensitivity to incentive, and that this signature of

557   motor cortical activity reflects an individual's subjective preferences for incentive and

558   eventual behavioral performance. Our neural findings are consistent with previous

559   results in humans showing that appetitive stimuli serve to increase motor cortical

560   excitability (Chiu et al., 2014; Freeman et al., 2014) and that the dynamics of motor

561   cortical excitability is sensitive to the value of options presented during simple

562   choice (Klein-Flügge and Bestmann, 2012). Furthermore, our results align with non-

563   human primate studies which found that motor cortical activity increased in response to

564   cues predicting receipt of reward (Marsh et al., 2015; Ramkumar et al., 2016;

565   Ramakrishnan et al., 2017; Tarigoppula et al., 2018). However, as previous studies

566   either investigated instrumental responding or value-based choice in separate

567   paradigms, they did not examine the relationship between the temporal dynamics of

568   motor cortical sensitivity to incentive, subjective preferences for incentive, and eventual

569   motor performance. Our results go beyond these studies by separately characterizing

570   the temporal dynamics of motor cortical sensitivity to incentive and subjective

571   preferences for incentive, and further, modeling the causal relationship between these

572   independent measures and behavioral performance. In so doing, we demonstrate a

573   mechanism by which motor cortical activity mediates the relationship between

574   subjective preferences for incentive and incentive motivated performance. These results

575   suggest that an individual's subjective preferences for incentive modulate the vigor of

576   the motor system to drive incentive motivated performance.

577   We previously used functional imaging to show that when performing an

578   instrumental motor task for incentive, prospective incentives are first encoded as a

579   potential gain and subsequently, during the task itself, individuals encode the potential

580   loss that would arise from failure (Chib et al., 2012, 2014). This reframed loss encoding

581   served to motivate behavioral performance — those individuals that were more loss

582   averse had a greater behavioral sensitivity to incentive, such that they reached peak

583   performance at lower incentive levels. Moreover, we found that activity in the ventral

584   striatum, a region of the brain thought to serve as the interface between motivation and

585   motor performance (Mogenson et al., 1980; Bray et al., 2008; Talmi et al., 2008), was

586   predictive of both performance and loss aversion. Notably, ventral striatal reward

587   circuitry is widely implicated in motivated performance (Adcock et al., 2006; Pessiglione

588   et al., 2006; Clithero et al., 2011; Liljeholm and O'Doherty, 2012; Schmidt et al., 2012).

589   Consistent with our previous results, here we found that behavioral sensitivity to

590   incentive in the gain domain was related to an individuals' loss aversion. Those

591   individuals that were more loss averse had increased behavioral sensitivity to incentive,

592   suggesting they were more motivated for increasing incentives. The temporal dynamics

593   of motor cortical sensitivity to incentive also reflected an individual's behavioral loss

594   aversion – those individuals that were more loss averse showed an increasing motor

595   cortical sensitivity to incentive closer to movement onset. These new TMS results take

596   our previous reframing interpretation further and show that motivational constructs (i.e.

597   loss aversion), known to be encoded by reward regions of the brain, transfer to motor

598   areas (as reflected by motor cortical excitability changes), giving rise to motivated

599   behavioral performance.

600   The present results provide important new insights into how incentive

601   motivational processing influences motor cortical activity to give rise to performance.

602   One possible mechanistic account of our findings relates to the role of the ventral

603   striatum as a limbic-motor interface, mediating interactions between systems for

604   Pavlovian valuation and motoric instrumental responding (Mogenson et al., 1980;

605   Alexander and Crutcher, 1990; Cardinal et al., 2002; Balleine and Ostlund, 2007).

30

606   Whereas previous literature has focused on the role of the ventral striatum in mediating

607   the effect of reward-predicting cues in increasing or enhancing instrumental

608   performance for reward, less is known about how such reward processing influences

609   activity in motor cortex to give rise to behavioral performance. An elegant set of studies

610   used a Pavlovian instrumental transfer paradigm to study such effects, and showed that

611   appetitive cues served to increase motor cortical excitability during instrumental

612   responding in extinction (Chiu et al., 2014; Freeman et al., 2014). In our experiment, it is

613   possible that during motor performance the prospect of reward (and loss-aversion

614   induced motivation) elicits participants' Pavlovian conditioned responses. These

615   responses could include motor approach and engagement of attentional or orienting

616   mechanisms towards task performance. Such ventral striatal encoding of Pavlovian

617   responses could energize the motor cortical commands necessary for successful

618   execution of instrumental responses, and this motor energization could manifest in the

619   motor cortical sensitivities to incentive that we observe in our data. Accordingly, there

620   are strong direct and indirect connections between ventral striatal regions known to

621   encode such Pavlovian and reward values and motor cortex (Mogenson et al., 1980;

622   Haber and Knutson, 2010).

623   Further supporting these ideas about the motor cortex, was a mediation analysis

624   showing that motor cortical sensitivity to incentive mediated the effects of behavioral

625   loss aversion on performance. This mediation suggests that the motor cortex is not

626   merely indirectly correlated with performance through its relationship with loss aversion,

627   but instead plays a critical role in moderating incentive motivated behavioral

628   performance itself. This provides a mechanistic account of how the motor cortex

629   influences motivated motor performance via its reflection of subjective preferences and

630   incentive value.

631   A number of studies have reported that performance-based incentives can lead

632   to paradoxical effects on behavior (i.e., decreasing motivation (Gneezy and Rustichini,

633   2000) or performance (Ariely et al., 2009)), yet here we examined the case in which

634   performance-based incentives lead to increases in motoric output. The effects of reward

635   undermining and other paradoxical effects on performance have implicated the same

636   ventral striatal reward circuitry that is responsible for the facilitatory effects of incentives

637   on performance (Murayama et al., 2010; Chib et al., 2012, 2014). Therefore, it is

638   plausible that similar motor cortical responses to those identified in this study could be

639   responsible for mediating other paradoxical responses to incentive. Investigating such a

640   role of motor cortical excitability on other effects of performance-based incentives will be

641   an important future direction in dissecting the general motor cortical signals that

642   influence both facilitatory and deleterious influences of incentives on performance.

643   Given the likely role of ventral striatal reward processing in the context of our

644   task, an alternative account of our results is that the motor cortical stimulation in our

645   experiment could remotely-induce responses in the striatum that cause the incentive

646   motivational effects we observed. Previous brain stimulation studies have shown that

647   repetitive TMS of prefrontal cortex (Strafella et al., 2001) and motor cortex (Strafella et

648   al., 2003), and transcranial direct current stimulation of prefrontal cortex (Chib et al.,

649   2013), can remotely induce changes in striatal and midbrain activity. However, such an

650   interpretation of our results seems unlikely given that these studies used montages that

651   required a sustained stimulation of cortex to alter its resting state, whereas we used a

652   single pulse paradigm in which pulses are less likely to result in prolonged changes in

653   motor cortical excitability.

654   It is important to note that although we found a significant modulation of

655   behavioral performance for increasing prospective loss, we failed to find such an effect

656   in motor cortical excitability responses. Notably, a previous study that examined how

657   aversive conditioned stimuli influenced motor cortical excitability, during instrumental

658   responding, also failed to find a modulation of motor cortical excitability by aversive

659   stimuli (Chiu et al., 2014). One interpretation of these null results is that distinct neural

660   circuits could process the effects of appetitive and aversive stimuli on motivated motor

661   performance (Pessiglione and Delgado, 2015). Indeed, distinct amygdala nuclei have

662   been shown to encode appetitive (basolateral amygdala) (Holland et al., 2002) and

663   aversive (central nuclei) (Petrovich et al., 2009) stimuli during motivated behavior.

664   These amygdala nuclei are essential components in the circuits that mediate Pavlovian

665   instrumental transfer and have different circuit pathways that connect to ventral striatum

666   to influence motivated performance (Cador et al., 1989; Corbit et al., 2001; Lingawi and

667   Balleine, 2012). However, it is not known if these pathways also have different

668   connections to the motor cortex. It is possible that such differential TMS effects could be

669   the result of such distinct pathways for appetitive and aversive stimuli. Resolving this

670   possibility is beyond the design of the current study and could be achieved using

671   functional neuroimaging techniques, combined with noninvasive brain stimulation, to

672   examine how motor cortical excitability is related to amygdala and ventral striatal

673   function in the context of motor performance for prospective gains and losses.

674   Integrating behavioral analysis of motivated performance, modeling of subjective

675   preferences for incentive, and motor cortical physiology; we provide evidence that the

676   motor cortex is sensitive to the subjective value of incentive. Our work outlines a

677   mechanism by which the subjective value of reward serves to invigorate motor cortical

678   excitability, leading to incentive motivated performance. Far from simply being a

679   reflection of motor output, it appears that motor cortical physiology integrates cognitive

680   mechanisms related to reward valuation. These results suggest that incentive motivated

681   performance is the reflection of an interaction between reward valuation and motor

682   cortical excitability.

683　**Figure 1. The incentive motivation motor task.　A**) Participants first performed an

684　unincentivized phase of the experiment to calibrate TMS parameters and familiarize

685　them with the requirements of behavioral paradigm. At the beginning of each trial,

686　participants were presented a blue cursor that moved across the screen in proportion to

687　the amount of pinch exertion. Squeezing the force transducer moved the cursor

688　horizontally to the left, while relaxing caused the cursor to move to the right. To initiate

689　the task, participants placed the cursor in the start position (×) for a random amount of

690　time (3–6 s). The start position corresponded to minimal exertion while still grasping the

691　transducer. During the task, a 'Go' cue and red target line appeared that was registered

692　to 45% of MVC. To successfully achieve the task, participants had to move their cursor

693　across the target line within 0.5 seconds. At the end of the trial they were shown a

694　message indicating the outcome of their performance. In the case that a participant

695　successfully moved the cursor across the target line, a positive message was displayed

696　("You Won"); otherwise, the participant was informed of the negative outcome ("You

697　Lost"). **B**) The timeline of unincentivized trials. Participants first performed 30 calibration

698　trials in which stimulation occurred 50ms after the onset of the 'Go' Cue/motor task

699　presentation (calibration). After these trials, familiarization trials were performed in

700　which stimulation was delivered for another 30 trials at either 50ms or 150ms after 'Go'

701　cue/motor task presentation (familiarization). **C**) Incentivized trials were identical to the

702　unincentivized trials, except participants were presented with the incentive they were

703　performing for prior to the motor task screen, and they were not given feedback of their

704　cursor or the target line. **D**) The timeline of incentivized trials. There were a total of 180

705 incentivized trials and stimulation was delivered at either 50ms or 150ms after 'Go'

706 cue/motor task presentation.

707 **Figure 2. Subjective Preferences Task.** After performing the motor task, participants

708 performed a separate task in which they made a series of forced monetary choices

709 between a risky option ("Flip" option; equal probability of gain and loss) and a

710 guaranteed amount ("Sure" option). A blank screen was shown during the intertrial

711 interval for a duration randomly selected from a uniform distribution ranging from 0.5 – 2

712 seconds.

713 **Figure 3. Behavioral results. A**) Participants exhibited increasing performance (%

714 success) for increasing prospective gains and losses. **B**) Participants exerted more

715 pinch force (mean effort exertion) for increasing prospective gains and losses. Mean

716 exertion was z-scored to control for inter-participant variability in performance. Plots of

717 the correlation between participants' behavioral sensitivity to prospective (**C**) gains and

718 (**D**) losses (i.e., slope of the relationship between un-normalized log mean exertion and

719 incentive) and loss aversion. Error bars denote SEM.

720 **Figure 4. Motor cortical excitability in response to incentive.** Shown are parameter

721 estimates from our general linear model predicting motor cortical sensitivity to incentive

722 at the different TMS time points. Positive parameter estimates indicate increasing motor

723 excitability with increasing incentive, negative estimates indicate decreasing motor

724 excitability with increasing incentive, and zero estimates indicate no modulation of motor

725 cortical excitability with incentive. **A, B**) We separated trials based on prospective gain

726 and loss, and grouped participants by the extent of their loss aversion (median split). In

727 the gain domain, we found that those participants that were more loss averse had

728 greater increases in motor cortical excitability in response to incentive, closer to

729 movement onset (150ms). We failed to find significant modulation of motor cortical

730 excitably for prospective loss. The significance levels shown are for planned

731 comparisons between conditions (*$p < 0.05$). Error bars denote SEM. Plots of the

732 correlations between difference in motor cortical sensitivity to incentive between the

733 150ms and 50ms stimulation conditions, in the gain domain, and (**C**) behavioral

734 sensitivity to incentive (i.e., slope of the relationship between un-normalized log mean

735 exertion and incentive) and (**D**) behavioral loss aversion.

736 **Figure 5. Control TMS analyses.** **A**) We did not to find a significant relationship

737 between difference in motor cortical sensitivity to incentive between 50ms and 150ms

738 and reaction time sensitivity to incentive. **B**) Motor evoked potentials were segregated in

739 intensity and time when aligning them to EMG detected movement onset, rather than

740 the 'Go' cue. **C**) Participants' z-scored mean exertion was separated by stimulation

741 timing conditions. The behavioral finding of increased performance with increasing

742 incentive was preserved across stimulation conditions.

743　**Figure 6. Mediation analyses. A**) The three variables assessed using mediation

744　analysis: behavioral loss aversion $\log(\lambda)$ difference in motor cortical sensitivity to

745　incentive between the 50ms and 150ms TMS time points $\beta_{150}^{\text{Gain}} - \beta_{50}^{\text{Loss}}$, and behavioral

746　sensitivity to incentive $\beta_{Exertion}^{Gain}$. The numbers next to the double-headed arrows are

747　coefficients of correlations between the variables. Regression analyses (illustrated in

748　Figures 3C,4C,4D) established correlations between participants' behavioral loss

749　aversion, differences in motor cortical sensitivity to incentive, and behavioral sensitivity

750　to incentive. **B**) The causal model illustrates the mediation analysis, and the alternative

751　models (**C, D**) illustrate control models that were tested to rule out model

752　misspecification. Solid arrows represent significant relationships between variables,

753　dashed arrows are not significant.

754　**Figure 7. Alternative relationships between choice parameters motor excitability**

755　**and performance.** We also explored the possibility of mediation relationships between

756　choices parameters, obtained from the subjective reward preference task, related to **A**)

757　risk aversion $-\log(\rho)$, and **B**) choice stochasticity $\log(\tau)$. These alternative models did

758　not contain the significant correlations required to test if motor cortical sensitivity to

759　incentive mediated the relationship between performance and these other choice

760　parameters.

38

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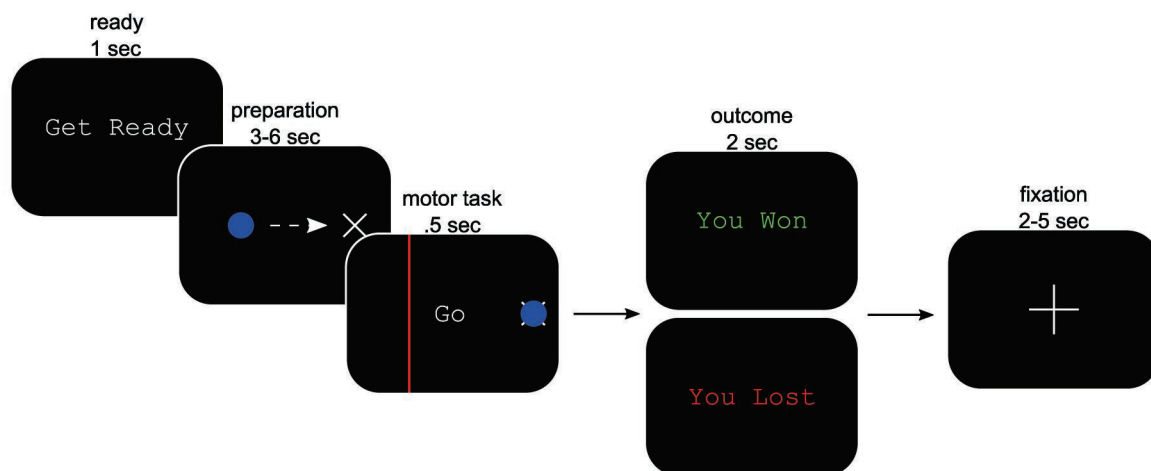862   between the limbic system and the motor system. Prog Neurobiol 14:69–97.

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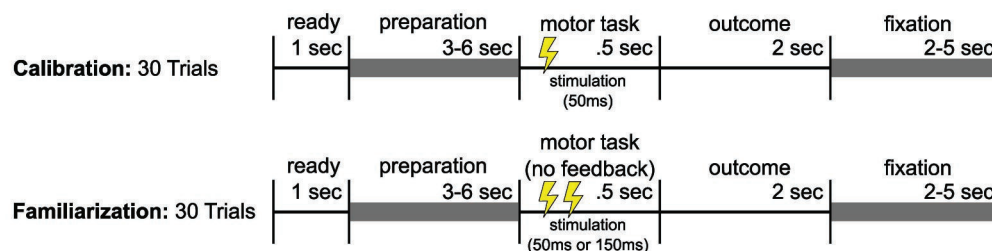929   healthy adults. Neurosci Lett 549:151–156.
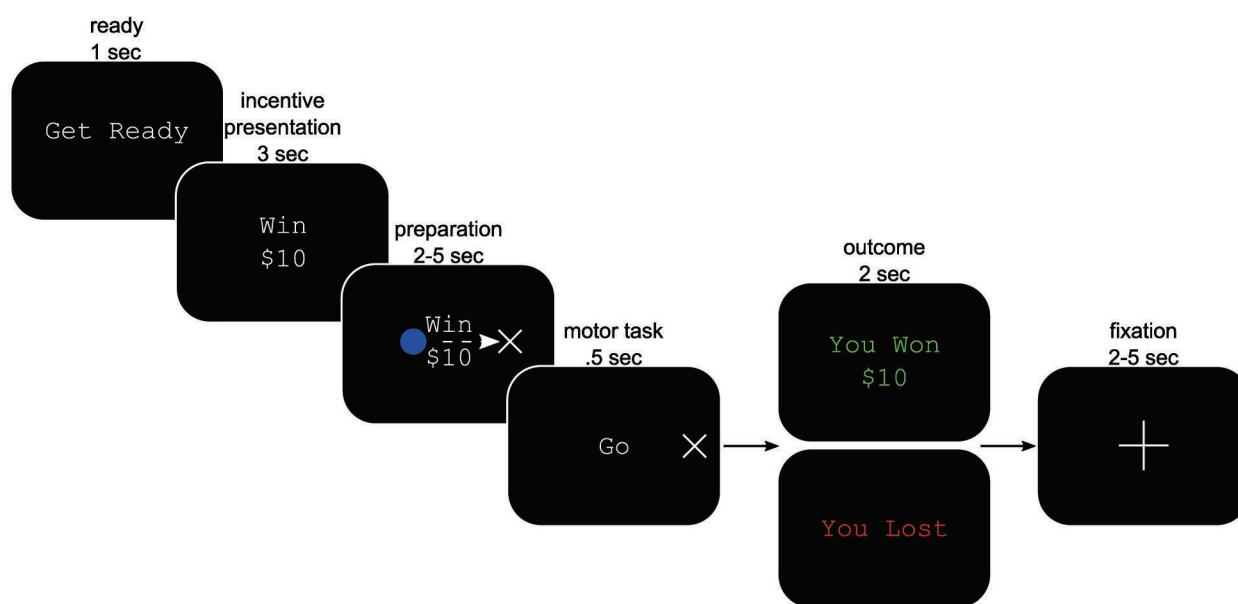
930

Figure 1

A **Unincentivized Phase**

ready
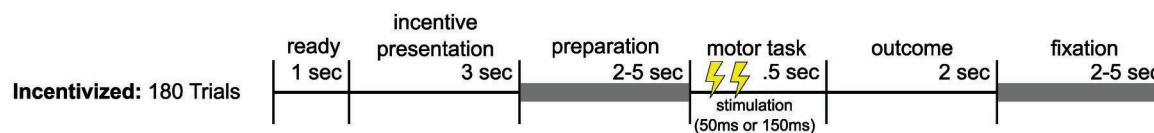1 sec

Get Ready

preparation
3-6 sec

motor task
.5 sec

Go

outcome
2 sec

You Won

You Lost

fixation
2-5 sec

B

Calibration: 30 Trials

| ready 1 sec | preparation 3-6 sec | motor task .5 sec | outcome 2 sec | fixation 2-5 sec |

stimulation
(50ms)

Familiarization: 30 Trials

| ready 1 sec | preparation 3-6 sec | motor task (no feedback) .5 sec | outcome 2 sec | fixation 2-5 sec |

stimulation
(50ms or 150ms)

C **Incentivized Phase**

ready
1 sec

Get Ready

incentive
presentation
3 sec

Win
$10

preparation
2-5 sec

Win
$10

motor task
.5 sec

Go

outcome
2 sec

You Won
$10

You Lost

fixation
2-5 sec

D

Incentivized: 180 Trials

| ready 1 sec | incentive presentation 3 sec | preparation 2-5 sec | motor task .5 sec | outcome 2 sec | fixation 2-5 sec |

stimulation
(50ms or 150ms)

Figure 2

A

B

Figure 3

A

B

C

D

Figure 4

A

Gain

B

Loss

C

D

Figure 5

A

B

C

Figure 6

A   Correlations

B   Causal Model

C   Alternative Model 1

D   Alternative Model 2
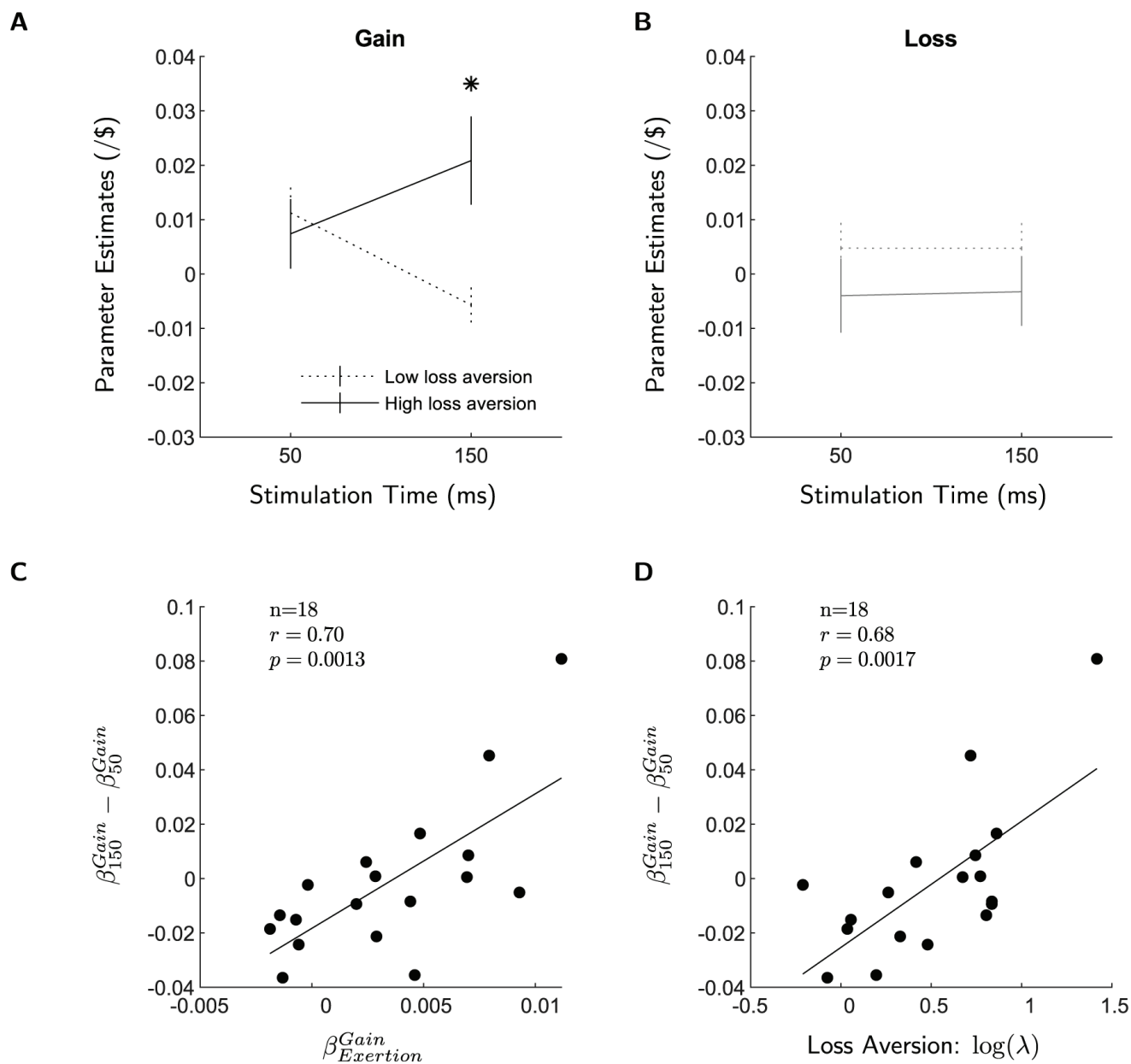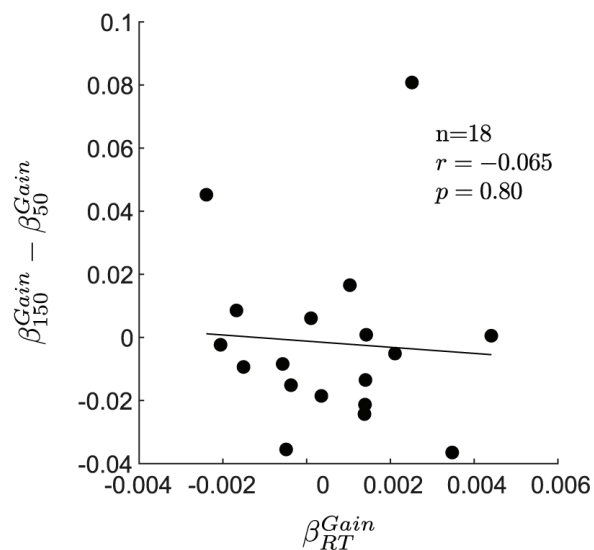
Figure 7

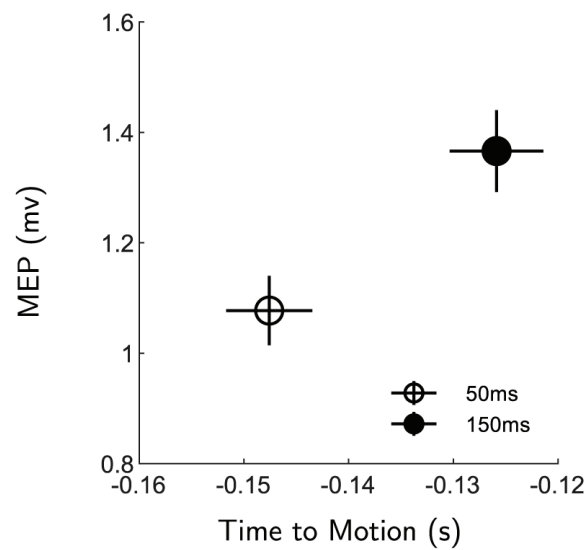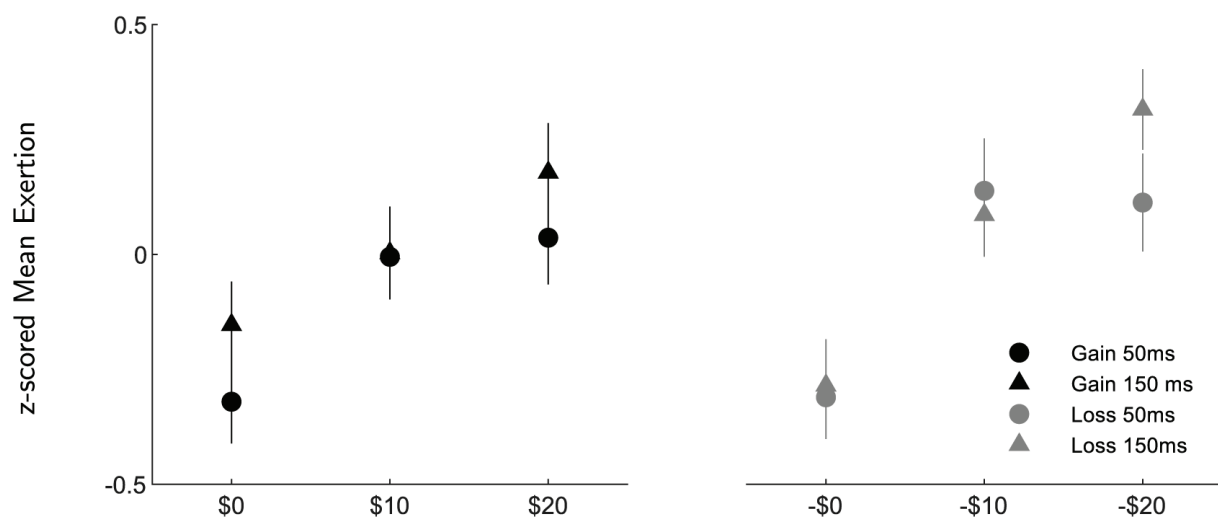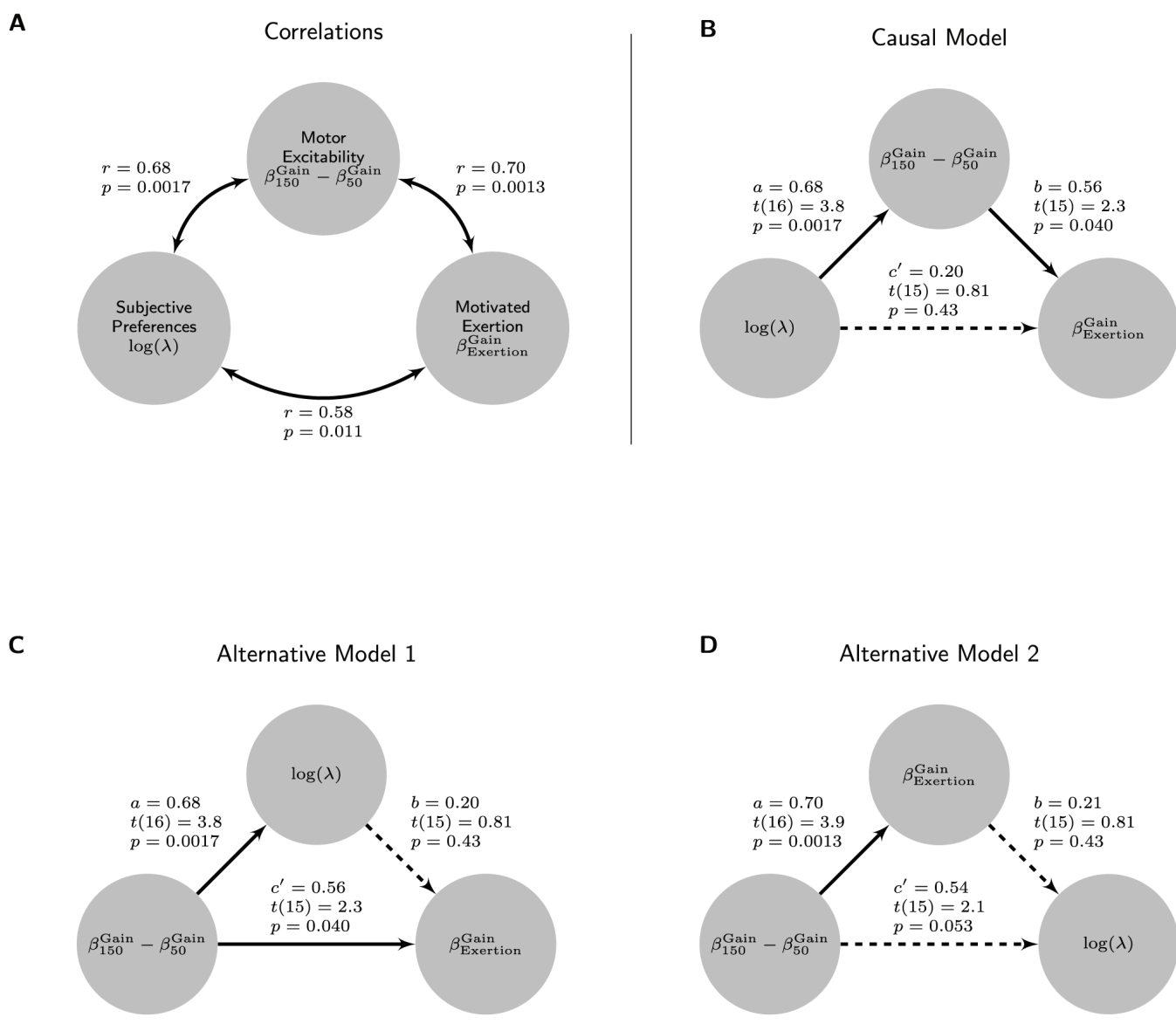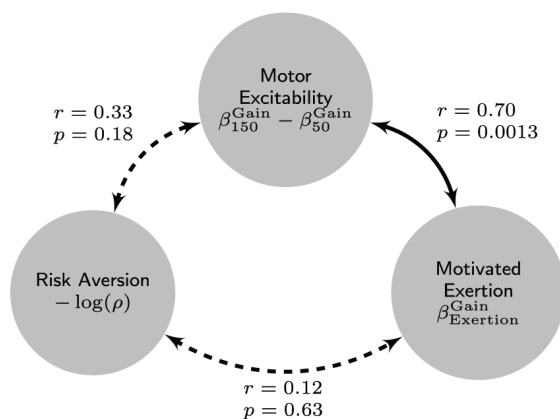**A**   Risk Aversion Correlations

B   Stochasticity Correlations