

# Dopamine-dependent loss aversion during effort-based decision-making

Chen, Xiuli; Voets, Sarah; Jenkinson, Ned ; Galea, Joseph

DOI:

<https://doi.org/10.1101/714840>  
[10.1523/JNEUROSCI.1760-19.2019](https://doi.org/10.1523/JNEUROSCI.1760-19.2019)

License:

Creative Commons: Attribution (CC BY)

*Document Version*

Peer reviewed version

*Citation for published version (Harvard):*

Chen, X, Voets, S, Jenkinson, N & Galea, J 2019, 'Dopamine-dependent loss aversion during effort-based decision-making', *The Journal of Neuroscience*, vol. 40, no. 3, pp. 661-670. <https://doi.org/10.1101/714840>, <https://doi.org/10.1523/JNEUROSCI.1760-19.2019>

[Link to publication on Research at Birmingham portal](#)

## General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

## Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact [UBIRA@lists.bham.ac.uk](mailto:UBIRA@lists.bham.ac.uk) providing details and we will remove access to the work immediately and investigate.



## 28 **Abstract**

29           From psychology to economics there has been substantial interest in how costs (e.g.,  
30 delay, risk) are represented asymmetrically during decision-making when attempting to gain  
31 reward or to avoid punishment. For example, in decision-making under risk, individuals show  
32 a tendency to prefer to avoid punishment than to acquire the equivalent reward (loss aversion).  
33 Although the cost of physical effort has recently received significant attention, it remains  
34 unclear whether loss aversion exists during effort-based decision-making. On the one hand,  
35 loss aversion may be hardwired due to asymmetric evolutionary pressure on losses and gains  
36 and therefore exists across decision-making contexts. On the other hand, distinct brain regions  
37 are involved with different decision costs, making it questionable whether similar asymmetries  
38 exist. Here, we demonstrate that young healthy human participants (Females:Males=16:6)  
39 exhibit loss aversion during effort-based decision-making by exerting more physical effort in  
40 order to avoid punishment than to gain a same-size reward. Next, we show that medicated  
41 Parkinson's disease (PD) patients (Females:Males=9:9) show a reduction in loss aversion  
42 compared to age-matched controls (Females:Males=11:9). Behavioural and computational  
43 analysis revealed that people with PD exerted similar physical effort in return for a reward, but  
44 were less willing to produce effort in order to avoid punishment. Therefore, loss aversion is  
45 present during effort-based decision-making and can be modulated by altered dopaminergic  
46 state. This finding could have important implications for our understanding of clinical disorders  
47 that show a reduced willingness to exert effort in the pursuit of reward.

## 48 **Significance Statement**

49           Loss aversion – preferring to avoid punishment than to acquire equivalent reward – is  
50 an important concept in decision-making under risk. However, little is known about whether  
51 loss aversion also exists during decisions where the cost is physical effort. This is surprising  
52 given that motor cost shapes human behaviour, and a reduced willingness to exert effort is a

53 characteristic of many clinical disorders. Here, we show that healthy human individuals exert  
54 more effort to minimise punishment than to maximise reward (loss aversion). We also  
55 demonstrate that medicated Parkinson’s disease patients exert similar effort to gain reward but  
56 less effort to avoid punishment when compared with healthy age-matched controls. This  
57 indicates that dopamine-dependent loss aversion is crucial for explaining effort-based decision-  
58 making.

## 59 **Introduction**

60         There has been substantial interest into how a cost, such as delay or reward uncertainty,  
61 discounts the utility, or ‘value’, an individual associates with the beneficial outcome of a  
62 decision (Bautista, Tinbergen, & Kacelnik, 2001; Daw & Doya, 2006; Fehr & Rangel, 2011;  
63 Green & Myerson, 2004; Kahneman & Tversky, 1979; Rachlin, 2006; Rachlin & Green, 1972;  
64 Stephens, 2001; Stephens & Krebs, 1986). One cost that has recently received significant  
65 attention is physical effort (effort-based decision-making, Chong et al., 2015; Klein-Flügge,  
66 Kennerley, Friston, & Bestmann, 2016; Le Bouc et al., 2016; Shadmehr, Huang, & Ahmed,  
67 2016). Previous work has investigated the computational, neural and neurochemical  
68 mechanisms involved when individuals evaluate rewards that are associated to physical effort  
69 (Burke, Brunger, Kahnt, Park, & Tobler, 2013; Hauser, Eldar, & Dolan, 2017; Kurniawan,  
70 Guitart-Masip, & Dolan, 2011; Prévost, Pessiglione, Météreau, Cléry-Melin, & Dreher, 2010),  
71 with a diminished willingness to exert effort being a prevalent characteristic of many clinical  
72 disorders such as Parkinson’s disease (Baraduc, Thobois, Gan, Broussolle, & Desmurget, 2013;  
73 Chong et al., 2015).

74         With other costs, such as delay and uncertainty, prior work has examined how they are  
75 represented differently when attempting to gain reward or avoid punishment. For example, in  
76 decision-making under risk, individuals show a tendency to prefer to avoid punishment than to  
77 acquire the equivalent reward, a phenomenon called loss aversion (Kahneman & Tversky, 1979;

78 Tversky & Kahneman, 1992). Surprisingly, it remains unclear whether people also exhibit loss  
79 aversion during effort-based decision-making. On the one hand, loss aversion may be  
80 hardwired due to asymmetric evolutionary pressure on losses and gains (Kahneman & Tversky,  
81 1979; Tom, Fox, Trepel, & Poldrack, 2007; Tversky & Kahneman, 1992b), and thus should be  
82 observed in any cost-benefit decision-making context. On the other hand, distinct brain regions  
83 are involved in decision-making with different costs (Bailey, Simpson, & Balsam, 2016;  
84 Galaro, Celnik, & Chib, 2019; Hauser et al., 2017; Prévost et al., 2010), making it questionable  
85 whether similar asymmetries should exist. For example, while the cingulate cortex is  
86 implicated in effort-based decision-making, other brain areas such as the ventromedial  
87 prefrontal cortex are thought to play a more important role for decision-making under risk  
88 (Klein-Flügge et al., 2016). Although several studies have attempted to address this question,  
89 these either do not directly examine loss aversion (Galaro et al., 2019), do not involve the  
90 execution of the effortful action (Nishiyama, 2016) or the cost of effort is confounded with the  
91 cost of temporal delay (Porat, Hassin-Baer, Cohen, Markus, & Tomer, 2014).

92         The neurotransmitter dopamine appears to be crucial for effort-based decision-making.  
93 For example, People with Parkinson's disease (PD) when off dopaminergic medication exhibit  
94 a reduced willingness to exert effort in the pursuit of reward, with medication restoring this  
95 imbalance (Chong et al., 2015; Le Bouc et al., 2016; Skvortsova, Degos, Welter, Vidailhet, &  
96 Pessiglione, 2017). Interestingly, during decision-making under risk and reinforcement  
97 learning, Parkinson's disease patients on dopaminergic medication display an enhanced  
98 response to reward but a reduced sensitivity to punishment (Collins & Frank, 2014; Frank,  
99 2005; Frank, Seeberger, & O'Reilly, 2004). Although this suggests that dopamine availability  
100 might shape loss aversion across contexts (Clark & Dagher, 2014; Timmer, Sescousse,  
101 Esselink, Piray, & Cools, 2017), and in particular that medicated PD patients should show

102 reduced loss aversion, the role of dopamine during effort-based decision-making within a  
103 reward or punishment context has not been directly investigated.

104 In this paper, we demonstrate that young healthy participants exhibit loss aversion  
105 during effort-based decision-making; individuals were willing to exert more physical effort in  
106 order to minimise punishment than maximise reward. In addition, behavioural and  
107 computational analysis revealed that medicated Parkinson's disease patients showed a  
108 reduction in loss aversion compared to age-matched controls. Specifically, although patients  
109 exerted similar physical effort in return for reward, they were less willing to produce effort to  
110 avoid punishment. Therefore, loss aversion is present during effort-based decision-making and  
111 this asymmetry is modulated by dopaminergic state.

## 112 **Materials and Methods**

### 113 *Participants*

#### 114 *Ethics statement.*

115 The study was approved by Ethical Review Committee of the University of  
116 Birmingham, UK, and was in accordance with the Declaration of Helsinki. Written informed  
117 consent was obtained from all participants.

#### 118 *Young healthy participants*

119 Twenty-two young healthy participants (age:  $23.1 \pm 4.56$ ; 16 females) were recruited  
120 via online advertising and received monetary compensation upon completion of the study.  
121 They were naïve to the task, had normal/corrected vision, and reported to have no history of  
122 any neurological condition.

#### 123 *Parkinson's disease patients (PD) and healthy age-matched controls (HC)*

124 Eighteen PD patients were recruited from a local participant pool through Parkinson's  
125 UK. They were on their normal schedule of medication during testing (levodopa-containing

126 compound: n=7, dopamine agonists (including pramipexole, ropinirole): n=6, or combination  
127 of both: n=5). Clinical severity was assessed with the Unified Parkinson's Disease Rating Scale  
128 (UPDRS, Table 1) (Fahn & Elton, 1987). Twenty HC were also recruited via a local participant  
129 pool. All patients/participants had a Mini-Mental Status Exam (Folstein, Folstein, & McHugh,  
130 1975) score greater than 25 (Table 1). Table 1 summarises the demographics of the patients  
131 and age-matched controls. Both groups received monetary compensation upon completion of  
132 the study.

133

134 [INSERT TABLE 1 HERE]

135

### 136 *Experimental design*

#### 137 *Experimental set up*

138 Participants were seated in front of a computer (Figure 1A) running a task implemented  
139 in Psychtoolbox ([http:// Psychtoolbox.org](http://Psychtoolbox.org)) and Matlab (MathWorks, USA). Two custom-built  
140 vertical handles were positioned on a desk in front of the participants, each of which housed a  
141 force transducer with sample rate of 200 hertz (<https://www.ati-ia.com>). The force produced  
142 on each handle enabled participants to independently control two cursors on the computer  
143 screen (Figure 1A). During the main experiment, one handle was assigned as the decision-  
144 making handle; participants grasped this handle with their hand and produced a left or right  
145 directed force in order to move the decision cursor into the appropriate option box to indicate  
146 their choice. The other handle was designated as the force execution handle; participants rested  
147 their index finger next to the bottom of the handle and produced a force by pressing their index  
148 finger inward on the handle (i.e., push left for the right index finger, push right for the left index  
149 finger). As the lateral force recorded by the transducers was sensitive to the height at which the  
150 force was applied to the handle, participants were asked to maintain their index finger below a

151 protective ring placed 1.5cm above the bottom of the handle (Figure 1A). This ensured that the  
152 finger position on the handle did not change across the experiment. In addition, to maintain a  
153 consistent arm position and minimise the use of alternative proximal muscles the participants'  
154 forearm was firmly strapped to the table at the wrist and elbow.

155

156 [INSERT FIGURE 1 HERE]

157

### 158 *Procedure*

159 Before the main effort-based decision-making task, participants were asked to produce  
160 a maximal voluntary contraction (MVC) of their first dorsal interosseous (FDI) muscle  
161 (isometric contraction of the index finger against the handle) for 3 seconds. This was repeated  
162 3 times and the average maximum force was taken as their MVC. For the young healthy  
163 participants, the index finger of the dominant hand was chosen to produce the force. For people  
164 with PD, the index finger of the most affected side was chosen to produce the force (dominant  
165 hand: n=11, non-dominant hand: n=7). For the HC, we chose a similar ratio of dominant hand  
166 and non-dominant hand as their force producing hand (dominant hand: n=12, non-dominant  
167 hand: n=8). Following the MVC, participants had 12 trials to practise the 6 force levels that  
168 were used in the main decision-making task (see *Effort-based decision-making task* section for  
169 details). The force levels were shown to participants as a set of arcs (Figure 1A).

170 The effort-based decision-making task consisted of 2 conditions (reward and  
171 punishment), the order of which was counter-balanced across participants. For both PD and  
172 HC groups, each condition (reward or punishment) consisted of 10 epochs of 6 trials (60 trials).  
173 Each epoch included 1 trial of each of the 6 force levels in a randomised order, ensuring an  
174 even distribution of force levels. At the beginning of each condition (reward or punishment),  
175 the score started at 0. In the reward condition, the total score was positive and the participants



176 were asked to maximise the points they gained. In the punishment condition, the total score  
177 was negative and the participants were asked to minimize the points they lost. Following the  
178 effort-based decision-making task, participants were again asked to produce 3 consecutive 3-  
179 second MVCs. They were instructed that this had to be above 90% of the MVC they produced  
180 at the beginning of the experiment. Importantly, participants were made aware of this  
181 requirement at the beginning of the study (after the first MVC and before the main effort  
182 decision-making task). This protocol was intended to ensure that participants maintained an  
183 interest in not becoming overly fatigued by continually choosing the effortful (high reward,  
184 low punishment) choice throughout. In addition to the fixed monetary compensation for  
185 participating in the study (£15; ~90 mins), participants were told at the beginning of the  
186 experiment that they had the chance to be entered into a lottery to win an extra £100 if their  
187 performance (total score) was among the top 5 of participants (one lottery per group) and they  
188 were able to maintain 90% MVC at the end of the experiment. Therefore, all participants were  
189 encouraged to accumulate as many points as possible (and lose as few points as possible) whilst  
190 avoiding unnecessary effort.

#### 191 *Effort-based decision-making task*

192 The task was adapted from classic effort-based decision-making paradigms (Bonnelle,  
193 Manohar, Behrens, & Husain, 2016; Bonnelle et al., 2015; T. T.J. Chong, Bonnelle, & Husain,  
194 2016; Le Heron et al., 2018; Skvortsova et al., 2017). There were two trial types: reward and  
195 punishment (Figure 1B,C) and the task consisted of one block of each. On a reward trial (Figure  
196 1B), participants chose between executing a certain force level in return for reward (gaining  
197 points) and skipping the trial in return for 0 points. On a punishment trial (Figure 1C),  
198 participants chose between executing a certain force level in return for 0 points and skipping  
199 the trial in return for being punished (losing points).

200 On each trial, participants were presented with a combination of points and a force level,  
201 which was a percentage of their MVC (offer phase). For the young group, the force was 1 of 6  
202 levels: 11, 21, 32, 42 53, 67% of MVC. For both the older age groups (PD and HC), these six  
203 levels were: 9, 18, 27, 36, 45, 54% of MVC. The force levels used for the older age groups  
204 were lower because a pilot study revealed they fatigued significantly faster than younger  
205 participants. At the beginning of each condition (reward, punishment), these six force levels  
206 were paired with [5 10 15 20 25 30] points respectively. The initial pairings were selected based  
207 on pilot experiments. Unbeknown to participants, the points associated with each force level  
208 were then adjusted on a trial-by-trial basis using an adaptive staircase algorithm (see *Adaptive*  
209 *staircase algorithm* section for details). Following the offer phase, participants indicated their  
210 choice by exerting a force on the decision handle which moved the yellow decision cursor  
211 (Figure 1A) from the middle of the screen into one of the option boxes (execute force or skip  
212 force). As soon as participants indicated their choice, the unchosen option disappeared. If the  
213 force option was chosen, participants were required to execute the force on the handle with this  
214 being represented by the blue force cursor moving from the start position towards a target line,  
215 and staying above the target line for 4 seconds at which point they heard a cash register sound  
216 ‘ka-ching’ from the headphone. If they failed to exert the required force, the trial was repeated.  
217 The trial was always terminated 6.5 seconds after their choice. This meant that participants had  
218 to wait for 6 seconds if they chose to skip the force, or they had to produce the required force  
219 within 6 seconds. We carefully controlled the time for force execution and skip decisions to be  
220 identical so that there was no confound between delay and effort discounting as in previous  
221 studies (Doyle, 2010; Loewenstein, Frederick, & O’donoghue, 2002).

### 222 *Adaptive staircase algorithm*

223 A staircase procedure was performed independently for each of the six force levels  
224 (Figure 2A,D). Specifically, for each force level, the points offered were increased or decreased

225 using an initial step-size of 8, depending on whether participants rejected (skipped) or accepted  
226 the opportunity to execute the force in order to receive (or avoid losing) those points,  
227 respectively. The step-size was doubled if participants rejected or accepted a force level 3 times  
228 in a row, and the step-size was halved if participants reversed their decision on the force level,  
229 i.e., an acceptance followed by a rejection on a force level or vice-versa (Taylor & Creelman,  
230 2005). As the staircase procedure was performed independently for each of the six force levels,  
231 it allowed us to determine the point of subjective indifference at which participants assigned  
232 equal value to acceptance and rejection for each force level. Importantly, the points and force  
233 combinations offered in the reward and punishment conditions were under the same adaptive  
234 procedure as described above, the only difference being whether the points were framed as  
235 rewards or punishments (Figure 1 B,C; Tversky & Kahneman, 1981).

236 A possibility to be noted is that the adaptive staircase procedure might not stabilise due  
237 to fatigue (Massar, Csathó, & Van der Linden, 2018; Meyniel, Sergent, Rigoux, Daunizeau, &  
238 Pessiglione, 2013; Müller & Apps, 2019). A successful staircase procedure would lead to a  
239 situation where the points offered would fluctuate around a participant's indifference point (IP)  
240 (see *Data and statistical analysis*) by the end of each condition (Figure 2). For example, if the  
241 initial points offered were lower/higher than a participant's IP then the participant should  
242 initially reject/accept the offer until the points offered resembled their IP. The points offered  
243 should then remain stable around the IP. In this case, the variance of the points offered will  
244 decrease from early to late trials (Figure 2). However, if a participant experienced fatigue then  
245 it is likely that they would begin to reject offers that they had accepted in earlier trials; this  
246 would cause the variance of the points offered to remain high in later trials and lead to an  
247 unstable IP. To test for this possibility, we compared the variance in points offered (Figure 2A,  
248 D) for each force level between the first and second half of the trials within each condition. A  
249 four-way mixed ANOVA examined the effect of (1) Time (first vs second half), (2) Force

250 Level (six levels), (3) Condition (reward vs punishment) and (4) Group (HC vs PD) on the  
251 variance of points offered (Figure 2G-J).

252

253 [INSERT FIGURE 2 HERE]

254

### 255 *Data and statistical analysis*

256 Data were analysed with Matlab using custom scripts. The data and codes are available  
257 at <https://osf.io/hw4rk/>. Our first question was to ask if young healthy participants expressed  
258 loss aversion during effort-based decision-making, i.e., a preference to exert more physical  
259 effort in order to minimise punishment than maximise reward. For each of the six force levels,  
260 we estimated the points at which the probability of accepting the force option was 50% (effort  
261 IP). Specifically, for each force level, a logistic function ( $y = \frac{1}{1+e^{-\beta(x-\alpha)}}$ ) was fitted to the  
262 points offered and the binary choices made by participants (Figure 2). As shown in Figure 2B,  
263 the effort IP was then defined as the reward magnitude (x-axis) at which the sigmoid crossed  
264  $y = 0.5$ .

265 An average effort IP (across six force levels) was then calculated for each participant  
266 in the reward and punishment conditions (referred to as reward IP and punishment IP  
267 respectively), indicating an individual's tendency to produce force in each condition. Each  
268 participant's loss aversion index was then defined as a ratio between reward IP and punishment  
269 IP. A loss aversion index that was larger than 1 indicated loss aversion. Due to non-normalities  
270 in the data, a Wilcoxon Signed-ranks test (*signrank* function in Matlab) was used to test if the  
271 loss aversion index for young healthy participants was significantly greater than 1. To assess  
272 effort-based loss aversion in PD patients and HC, we compared their loss aversion index using  
273 non-parametric independent samples Mann-Whitney U-tests (*ranksum* function in Matlab). To  
274 examine the loss aversion differences in more detail, a two-way mixed ANOVA compared the

275 average effort indifference point across group (PD vs HC) and condition (reward vs.  
276 punishment). In order to address non-linearity and heteroscedasticity (unequal variance), the  
277 effort IP was log-transformed.

### 278 *Computational modelling of choice*

279 Decision-making behaviour was modelled using an effort-based discount model that  
280 quantifies how the utility of obtaining reward or avoiding punishment decreases as the physical  
281 effort associated with it becomes progressively more demanding. Such models have been  
282 extensively used to examine the behavioural and neural basis of effort-based decision-making  
283 (Białaszek, Marcowski, & Ostaszewski, 2017; Botvinick, Huffstetler, & McGuire, 2009;  
284 Hartmann, Hager, Tobler, & Kaiser, 2013; Klein-Flügge, Kennerley, Saraiva, Penny, &  
285 Bestmann, 2015; Lockwood et al., 2017; Prévost et al., 2010). The key aim of the modelling  
286 analysis was to quantify each participant's willingness to invest effort for a beneficial outcome  
287 within a single parameter (i.e., the effort discounting parameter). This enabled us to compare  
288 decision-making behaviour between the HC and PD groups in the reward and punishment  
289 conditions in a relatively simple manner (Chong et al., 2017; Hartmann et al., 2013; Lockwood  
290 et al., 2017).

291 We fitted participant responses using linear, parabolic and hyperbolic effort discounting  
292 functions, which are often used to capture effort discounting (Białaszek et al., 2017; Hartmann  
293 et al., 2013; Klein-Flügge et al., 2015; McGuigan et al., 2019; Lockwood et al., 2017). The  
294 shape of these functions reflects how increasing costs (i.e., effort) discounts or 'devalues' the  
295 associated benefits (i.e., the number of points gained or avoided losing):

296 Linear:  $U(t) = A(t) - lE(t)$

297 Parabolic:  $U(t) = A(t) - lE(t)^2$

298 Hyperbolic:  $U(t) = \frac{A(t)}{1+lE(t)}$

299 The total utility,  $U(t)$ , of the offer on trial  $t$  is a function of: (1)  $E(t)$ , the physical effort required  
300 (scaled to the proportion of the MVC) in order to gain a reward or to avoid a punishment, (2)  
301  $A(t)$ , the reward/punishment amplitude (i.e., the number of points offered) and (3)  $l$ , the  
302 discounting parameter. The parameter,  $l$ , reflects the steepness of the effort discounting  
303 parameter, with a higher value indicating that the participant required a greater reward in order  
304 to perform the same level of effort.

305 The probability of choosing the effort option at trial  $t$  is given by the softmax function:

$$306 \quad P(t) = \frac{1}{1 + \exp(-\beta \times U(t))}$$

307 where  $U(t)$  is the total utility of the offer on trial  $t$ , and  $\beta$  accounts for stochasticity in participant  
308 choices. Let  $y(t)$  be the participant choice on trial  $t$  (skip=0; accept effort=1). The parameters  
309 ( $l$  and  $\beta$ ) that maximises the likelihood function over  $N$  trials was found for each participant:

$$310 \quad L = \sum_{t=1}^N y(t) \log(p(t)) + (1 - y(t)) \log(1 - p(t))$$

311 where  $N$  is the number of trials for each participant (reward and punishment conditions  
312 combined;  $N=120$ ). The parameters that maximised this likelihood was found for each  
313 participant by using the search function *fmincon* in Matlab (minimizing the negative of the log  
314 likelihood). In addition, to avoid local minima, the function *MultiStart* in Matlab was used with  
315 a 1000 start positions.

316 For each type of discount function (linear, hyperbolic and parabolic), we explored both  
317 the possibility of one joint discounting parameter for reward and punishment and separate  
318 discounting parameters for reward and punishment. A total of 6 models were compared. To  
319 compare the models, we utilised Bayesian Information Criterion (BIC) (Schwarz, 1978).  
320 Specifically, for each model, the BIC summed over all participants were compared (the lower

321 the value, the better the model fit) (Rigoux, Stephan, Friston, & Daunizeau, 2014; Stephan,  
322 Penny, Daunizeau, Moran, & Friston, 2009). Such aggregation of BIC across participants  
323 corresponds to fixed-effect analyses (Stephan et al., 2009). To account for the random-effect  
324 analysis in which models are treated as a random variable that can differ between participants  
325 (Stephan et al., 2009), we also conducted Friedman's test on individual BIC to compare the  
326 model fits. To examine the effect of Group (HC vs PD) and Condition (Reward vs Punishment)  
327 on the discount parameter, a two-way mixed ANOVA was used. The normality assumption in  
328 the data (the discount parameter in each cell) was not violated, as assessed by Shapiro-Wilk's  
329 test of normality ( $p > .05$ ). In addition, there was homogeneity of variances ( $p > .05$ ) and  
330 covariances ( $p > .001$ ) as assessed by Levene's test of homogeneity of variances and Box's M  
331 test, respectively.

## 332 **Results**

### 333 *Evidence for loss aversion in young healthy participants*

334 Our first question was to ask if young healthy participants expressed loss aversion  
335 during effort-based decision-making. To examine this, we first assessed how the effort IP  
336 (Figure 2) was affected by the force level in the reward and punishment conditions. As expected,  
337 the effort IP became progressively larger as the force level became more demanding, indicating  
338 a sensitivity to effort across reward and punishment conditions (Figure 3A). For each  
339 participant, an average effort IP was obtained across force levels for the reward (reward IP)  
340 and punishment (punishment IP) conditions, with the loss aversion index being defined as a  
341 ratio between these values ( $>1$  = loss aversion; Figure 3B). As the loss aversion index was  
342 significantly greater than 1 ( $z=3.65$ ,  $p<0.001$ , median=1.369, Figure 3B), it suggests that loss  
343 aversion was clearly evident in young healthy participants during effort-based decision-making.

344 [INSERT FIGURE 3 HERE]

345

346 *Reduced loss aversion in PD patients compared to HC*

347         Similar to the young healthy participants, the effort IP for both the HC (Figure 4A) and  
348 PD (Figure 4B) groups increased progressively as the force level became more demanding,  
349 suggesting sensitivity to effort across reward and punishment conditions. In addition, as the  
350 loss aversion index was significantly greater than 1 for both HC ( $z=3.823$ ,  $p<0.001$ ,  
351 median=2.09, Figure 4C) and PD ( $z=2.983$ ,  $p=0.003$ , median=1.260, Figure 4D), it indicates  
352 that loss aversion was present in both groups. Importantly, PD patients displayed significantly  
353 less loss aversion than HC ( $z=2.441$ ,  $p=0.015$ , Figure 4E), with this being a result of medicated  
354 PD patients appearing less sensitive to punishment (Figure 4F). This was confirmed by a two-  
355 way mixed ANOVA which revealed a significant interaction between Group (HC vs PD) and  
356 Condition (reward vs punishment) ( $F(1,36)=6.412$ ,  $p=0.016$ ) for the average indifference point.  
357 Specifically, Bonferroni-corrected independent t-tests revealed the PD and HC groups had a  
358 similar reward IP ( $p=0.591$ , Figure 4F), but the PD group displayed a higher punishment IP  
359 ( $p=0.011$ , Figure 4F). As the adaptive staircase procedure (i.e. the process of determining the  
360 IP for each participant) showed similar variability across conditions (reward, punishment) and  
361 groups (HC, PD), it suggests the results were unlikely due to differences in fatigue (Figure 2).  
362 Specifically, while there was a decrease in variance in the points offered from early to late trials  
363 ( $F(1,36)=12.744$ ;  $p=0.001$ ), there was no significant effects of Condition or Group (reward vs  
364 punishment:  $F(1,36)=0.230$ ,  $p=0.634$ ; HC vs PD:  $F(1,36)=3.780$ ;  $p=0.062$ ). In addition, there  
365 was no significant differences between participant's MVC before and after the main effort-  
366 based decision-making task (HC:  $z=0.635$ ,  $p=0.526$ , pre-MVC:  $16.08\pm 14.04$ N (Newton,  
367 Median  $\pm$  Median Absolute Deviation), post-MVC  $12.00\pm 8.26$ N; PD:  $z=0.500$ ,  $p=0.617$ , pre-  
368 MVC:  $12.66 \pm 11.40$  N, post-MVC  $12.70 \pm 6.18$ ). Therefore, it is unlikely that PD patients  
369 reduced loss aversion was due to fatigue.



370

371

[INSERT FIGURE 4 HERE]

372

373           Decision-making behaviour in our task was modelled using an effort-based discount  
374 model that quantifies how the utility of reward decreases as the physical effort associated with  
375 it becomes progressively more demanding. We fitted participant choices to three typical  
376 discounting functions: linear, parabolic and hyperbolic, which are often used to capture effort  
377 discounting (Białaszek et al., 2017; Hartmann et al., 2013; Klein-Flügge et al., 2015;  
378 McGuigan et al., 2019; Lockwood et al., 2017). We found that a parabolic effort discounting  
379 function with separate discounting parameters for the reward and punishment conditions  
380 provided the best fit for both the PD and HC groups (Table 2). Specifically, the summed  
381 Bayesian Information Criterion (BIC) was lowest for the parabolic function with separate  
382 discounting parameters (the lower the value, the better the model fit) (Table 2). To investigate  
383 this at a subject-level, a Friedman’s test on individual BIC was performed (Rigoux et al., 2014;  
384 Stephan et al., 2009). In general, similar results were observed with the parabolic function  
385 consistently being associated with significantly lower BIC for both groups (Table 2). To  
386 reinforce these results,  $R^2$  was found to be greater for the parabolic function for both groups  
387 (Table 2).

388

389

[INSERT TABLE 2 HERE]

390

391           Using the winning model (parabolic function with separate discounting parameters),  
392 we compared parameters across the PD and HC groups. In the reward condition, the effort  
393 discounting parameter was found to be similar between the HC and PD groups, suggesting  
394 medicated PD patients were equally as motivated to exert effort in return for reward (Figure

395 5A,B). However, in the punishment condition, the PD group had an increased effort  
396 discounting parameter suggesting they were less willing to exert effort in order to avoid  
397 punishment (Figure 5A,C). This was confirmed by a two-way mixed ANOVA that showed a  
398 significant interaction between group (HC vs PD) and condition (reward vs punishment)  
399 ( $F(2,36)=5.22$ ,  $p=0.042$ ). Bonferroni-corrected independent t-tests revealed that while the  
400 discounting parameter ( $\beta$ ) was similar between PD and HC ( $p=0.548$ ) for reward, it was  
401 significantly higher for the PD group in the punishment condition ( $p=0.018$ , Figure 5A).

402

403 [INSERT FIGURE 5 HERE]

404

## 405 Discussion

406 In summary, we have shown that loss aversion is consistently present during effort-  
407 based decision-making in young healthy participants and both people with Parkinson's disease  
408 (PD) and healthy older adults (HC). Although loss aversion is widely regarded as one of the  
409 most robust and ubiquitous findings in economic decision-making (Kahneman & Tversky,  
410 1979; Tversky & Kahneman, 1992), the surprisingly few studies that have directly examined  
411 loss aversion during physical effort-based decision-making have found it to not exist. For  
412 instance, Porat et al., (2014) showed that while half of young healthy participants were willing  
413 to expend greater effort to avoid punishment than to gain an equivalent reward, the other half  
414 showed the opposite preference. In addition, Nishiyama, (2016) found a similarly large degree  
415 of variability across participants in preference for maximising gains or minimising losses  
416 during an effort-based decision-making task. Therefore, while both studies found differences  
417 between gain and loss at an individual level, they did not find loss aversion during effort-based  
418 decision-making at a group level. However, we believe that there are several issues with the  
419 previous studies which may restrict their capacity to directly examine loss aversion during

420 effort-based decision making. First, in Porat et al., (2014), gaining reward or avoiding  
421 punishment required the participant to execute additional key presses. As a result, to obtain  
422 more reward (or avoid more punishment) the participants had to produce more effort and also  
423 had to wait longer. Therefore, the additional effort cost was confounded with a delay cost. It is  
424 worth noting that the temporal discount for losses is generally less steep than that for gains  
425 (Estle, Green, Myerson, & Holt, 2006). Importantly, this confound was carefully eliminated in  
426 our paradigm as all trials, including the skip option trials, had identical durations. Second, in  
427 Nishiyama, (2016), participants were tasked with making a series of choices of whether to  
428 engage in an effortful task (to obtain reward or to avoid punishment) via a questionnaire. That  
429 is, participants did not actually have to perform an effortful task. The absence of loss aversion  
430 could be a result of participants being less sensitive to the imaginary effort involved in a  
431 questionnaire. This possibility is supported by our results in which loss aversion is more clearly  
432 expressed at higher effort levels.

433         The second key finding of the present study was that medicated PD patients showed a  
434 reduction in loss aversion compared to HC. This reduction in loss aversion was due to people  
435 with PD investing similar physical effort in return for a reward but being less willing to produce  
436 effort to avoid punishment. Although previous studies have already demonstrated that  
437 medicated PD patients are equally as motivated to exert effort in return for reward as aged-  
438 matched controls (Chong et al., 2015; Le Heron et al., 2018; McGuigan et al., 2019), this is the  
439 first study to show that medicated PD patients exhibit a reduction in their willingness to  
440 produce effort to avoid punishment.

441         To understand this reduced loss aversion in medicated PD patients, one key question is  
442 whether it is due to an altered sensitivity to the cost of effort, an altered sensitivity to the action  
443 outcomes (i.e., the reward or punishment that is associated with the action) or a combination  
444 of both. In effort-based decision making, it has been repeatedly shown that PD patients exhibit

445 reduced willingness to expend effort in return for reward and dopaminergic medication is able  
446 to ameliorate this deficit (Chong et al., 2015, Le Heron et al., 2016, Skvortsova et al., 2017).  
447 Many earlier studies have also shown that manipulating dopamine can shift the effort/reward  
448 trade-off in healthy participants and animals (Bardgett, Depenbrock, Downs, Points, & Green,  
449 2009; Chong et al., 2015; Floresco, Tse, & Ghods-Sharifi, 2008; J. D. Salamone, Correa, Farrar,  
450 & Mingote, 2007). However, despite dopamine being clearly central to effort-based decision-  
451 making, its precise role is unclear. This uncertainty is because an increased sensitivity to reward  
452 or a decreased sensitivity to effort could both explain a similar shift in preference. On the one  
453 hand, previous work has highlighted the effect of dopamine on effort expenditure.  
454 Hyperdopaminergic rats, for example, have been shown to be more willing to expend physical  
455 effort to obtain reward (Beeler, Daw, Frazier, & Zhuang, 2010). While in humans, Le Heron  
456 et al., (2018) showed that medicated PD patients exert more effort to obtain a similar level of  
457 reward compared to when in an off-medication state (Le Heron et al., 2018). However, other  
458 work has claimed that even if dopamine seems to promote energy expenditure, it only does so  
459 as a function of the upcoming action outcome (reward) and not as a function of the upcoming  
460 energy cost itself (Le Bouc et al., 2016; Skvortsova et al., 2017; Walton & Bouret, 2019).  
461 Unfortunately, as the current study did not isolate effort from action outcomes it is unable to  
462 provide any further insight into this argument. In future, it would be interesting to test people  
463 with PD on and off medication during our task in addition to a task that selectively measures a  
464 participant's sensitivity to effort (Salimpour, Mari, & Shadmehr, 2015). This experiment  
465 should help determine whether the current results are linked to dopamine medication altering  
466 sensitivity to effort or due to it altering sensitivity to the action outcome associated with  
467 producing that effort.

468         Interestingly, similar differences in sensitivity to reward and punishment have  
469 previously been observed in medicated PD patients during reinforcement learning. Specifically,

470 Frank et al., (2004) showed that medicated PD patients expressed normal learning from reward-  
471 based tasks (positive outcomes) but impaired learning from punishment-based tasks (negative  
472 outcomes). Conversely, unmedicated PD patients showed the opposite bias where they were  
473 better at learning from punishment than reward. The authors used biologically-based  
474 computational modelling to explain these results where medicated PD patients, with sufficient  
475 dopamine, learn from positive feedback through the direct, pro-kinetic ('GO') pathway of the  
476 Basal Ganglia (Frank, 2005). In contrast, learning from negative feedback is impaired because  
477 the medication blocks/reduces the dips in dopamine associated with punishment that would  
478 lead to learning via the indirect, anti-kinetic ('NoGo') pathway. Such a dual opponent actor  
479 system represented by distinct striatal (D1/D2) populations can differentially specialize in  
480 discriminating positive and negative action values. As such, this model can explain the effects  
481 of dopamine on both learning and decision making across a variety of tasks including  
482 probabilistic reinforcement learning and effort-based choice (Collins & Frank, 2014; Shiner et  
483 al., 2012; Smittenaar et al., 2012). Therefore, although highly speculative, our current results  
484 could be explained by dopaminergic medication having a differential effect on the direct and  
485 indirect pathway of the Basal Ganglia which have been associated with the processing of  
486 reward and punishment-based action outcomes, respectively (Argyelan et al., 2018; Kravitz,  
487 Tye, & Kreitzer, 2012). At the very least, it would be interesting to interrogate whether  
488 unmedicated PD patients showed a reduced sensitivity to reward but normal sensitivity to  
489 punishment (reflecting enhanced loss aversion) as suggested by this previous work (Collins &  
490 Frank, 2014; Frank, 2005).

491 In conclusion, loss aversion is clearly present during effort-based decision-making and  
492 is modulated by dopaminergic state. This presents interesting future questions surrounding  
493 clinical disorders that have shown a reduced willingness to exert effort such as depression and  
494 stroke. For example, it is possible that disorders that have shown a reduced willingness to exert

495 effort in the pursuit of reward could show a normal, or even enhanced, willingness to exert  
496 effort in order to avoid punishment.

## 497 **References**

- 498 Antony, M. M., Cox, B. J., Enns, M. W., Bieling, P. J., & Swinson, R. P. (1998).  
499 Psychometric properties of the 42-item and 21-item versions of the Depression Anxiety  
500 Stress Scales in clinical groups and a community sample. *Psychological Assessment*.  
501 <https://doi.org/10.1037/1040-3590.10.2.176>
- 502 Argyelan, M., Herzallah, M., Sako, W., DeLucia, I., Sarpal, D., Vo, A., ... Gluck, M. (2018).  
503 Dopamine modulates striatal response to reward and punishment in patients with  
504 Parkinson's disease: A pharmacological challenge fMRI study. *NeuroReport*.  
505 <https://doi.org/10.1097/WNR.0000000000000970>
- 506 Bailey, M. R., Simpson, E. H., & Balsam, P. D. (2016). Neural substrates underlying effort,  
507 time, and risk-based decision making in motivated behavior. *Neurobiology of Learning  
508 and Memory*. <https://doi.org/10.1016/j.nlm.2016.07.015>
- 509 Baraduc, P., Thobois, S., Gan, J., Broussolle, E., & Desmurget, M. (2013). A Common  
510 Optimization Principle for Motor Execution in Healthy Subjects and Parkinsonian  
511 Patients. *Journal of Neuroscience*. <https://doi.org/10.1523/jneurosci.1482-12.2013>
- 512 Bardgett, M. E., Depenbrock, M., Downs, N., Points, M., & Green, L. (2009). Dopamine  
513 Modulates Effort-Based Decision Making in Rats. *Behavioral Neuroscience*.  
514 <https://doi.org/10.1037/a0014625>
- 515 Bautista, L. M., Tinbergen, J., & Kacelnik, A. (2001). To walk or to fly? How birds choose  
516 among foraging modes. *Proceedings of the National Academy of Sciences*.  
517 <https://doi.org/10.1073/pnas.98.3.1089>
- 518 Beeler, J. A., Daw, N., Frazier, C. R. M., & Zhuang, X. (2010). Tonic dopamine modulates  
519 exploitation of reward learning. *Frontiers in Behavioral Neuroscience*.

520 <https://doi.org/10.3389/fnbeh.2010.00170>

521 Białaszek, W., Marcowski, P., & Ostaszewski, P. (2017). Physical and cognitive effort  
522 discounting across different reward magnitudes: Tests of discounting models. *PLoS*  
523 *ONE*. <https://doi.org/10.1371/journal.pone.0182353>

524 Bonnelle, V., Manohar, S., Behrens, T., & Husain, M. (2016). Individual Differences in  
525 Premotor Brain Systems Underlie Behavioral Apathy. *Cerebral Cortex*.  
526 <https://doi.org/10.1093/cercor/bhv247>

527 Bonnelle, V., Veromann, K. R., Burnett Heyes, S., Lo Sterzo, E., Manohar, S., & Husain, M.  
528 (2015). Characterization of reward and effort mechanisms in apathy. *Journal of*  
529 *Physiology Paris*. <https://doi.org/10.1016/j.jphysparis.2014.04.002>

530 Botvinick, M. M., Huffstetler, S., & McGuire, J. T. (2009). Effort discounting in human  
531 nucleus accumbens. *Cognitive, Affective and Behavioral Neuroscience*.  
532 <https://doi.org/10.3758/CABN.9.1.16>

533 Burke, C. J., Brunger, C., Kahnt, T., Park, S. Q., & Tobler, P. N. (2013). Neural Integration  
534 of Risk and Effort Costs by the Frontal Pole: Only upon Request. *Journal of*  
535 *Neuroscience*. <https://doi.org/10.1523/jneurosci.3662-12.2013>

536 Carver, C. S., & White, T. L. (1994). Behavioral Inhibition, Behavioral Activation, and  
537 Affective Responses to Impending Reward and Punishment: The BIS/BAS Scales.  
538 *Journal of Personality and Social Psychology*. [https://doi.org/10.1037/0022-](https://doi.org/10.1037/0022-3514.67.2.319)  
539 [3514.67.2.319](https://doi.org/10.1037/0022-3514.67.2.319)

540 Chong, T. T.J., Bonnelle, V., & Husain, M. (2016). Quantifying motivation with effort-based  
541 decision-making paradigms in health and disease. In *Progress in Brain Research*.  
542 <https://doi.org/10.1016/bs.pbr.2016.05.002>

543 Chong, Trevor T.J., Apps, M., Giehl, K., Sillence, A., Grima, L. L., & Husain, M. (2017).  
544 Neurocomputational mechanisms underlying subjective valuation of effort costs. *PLoS*

545 *Biology*. <https://doi.org/10.1371/journal.pbio.1002598>

546 Chong, Trevor T.J., Bonnelle, V., Manohar, S., Veromann, K. R., Muhammed, K., Tofaris,  
547 G. K., ... Husain, M. (2015). Dopamine enhances willingness to exert effort for reward  
548 in Parkinson's disease. *Cortex*. <https://doi.org/10.1016/j.cortex.2015.04.003>

549 Clark, C. A., & Dagher, A. (2014). The role of dopamine in risk taking: a specific look at  
550 Parkinson's disease and gambling. *Frontiers in Behavioral Neuroscience*.  
551 <https://doi.org/10.3389/fnbeh.2014.00196>

552 Collins, A. G. E., & Frank, M. J. (2014). Opponent actor learning (OpAL): Modeling  
553 interactive effects of striatal dopamine on reinforcement learning and choice incentive.  
554 *Psychological Review*. <https://doi.org/10.1037/a0037015>

555 Daw, N. D., & Doya, K. (2006). The computational neurobiology of learning and reward.  
556 *Current Opinion in Neurobiology*. <https://doi.org/10.1016/j.conb.2006.03.006>

557 Doyle, J. R. (2010). Survey of Time Preference, Delay Discounting Models. In *SSRN*.  
558 <https://doi.org/10.2139/ssrn.1685861>

559 Estle, S. J., Green, L., Myerson, J., & Holt, D. D. (2006). Differential effects of amount on  
560 temporal and probability discounting of gains and losses. *Memory and Cognition*.  
561 <https://doi.org/10.3758/BF03193437>

562 Fahn, S., & Elton, R. L. (1987). The Unified Parkinson's Disease Rating Scale. In *Recent*  
563 *Developments in Parkinson's Disease, Vol. 2., Florham Park, NJ: Macmillan*  
564 *Healthcare Information*,.

565 Fehr, E., & Rangel, A. (2011). Neuroeconomic Foundations of Economic Choice—Recent  
566 Advances. *Journal of Economic Perspectives*. <https://doi.org/10.1257/jep.25.4.3>

567 Floresco, S. B., Tse, M. T. L., & Ghods-Sharifi, S. (2008). Dopaminergic and glutamatergic  
568 regulation of effort- and delay-based decision making. *Neuropsychopharmacology*.  
569 <https://doi.org/10.1038/sj.npp.1301565>



570 Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). “Mini-mental state”. A practical  
571 method for grading the cognitive state of patients for the clinician. *Journal of*  
572 *Psychiatric Research*. [https://doi.org/10.1016/0022-3956\(75\)90026-6](https://doi.org/10.1016/0022-3956(75)90026-6)

573 Frank, M. J. (2005). Dynamic dopamine modulation in the basal ganglia: A  
574 neurocomputational account of cognitive deficits in medicated and nonmedicated  
575 Parkinsonism. *Journal of Cognitive Neuroscience*.  
576 <https://doi.org/10.1162/0898929052880093>

577 Frank, M. J., Seeberger, L. C., & O’Reilly, R. C. (2004). By carrot or by stick: cognitive  
578 reinforcement learning in parkinsonism. *Science*, 306, 1940–1943.  
579 <https://doi.org/10.1126/science.1102941>

580 Galaro, J. K., Celnik, P., & Chib, V. S. (2019). Motor Cortex Excitability Reflects the  
581 Subjective Value of Reward and Mediates Its Effects on Incentive-Motivated  
582 Performance. *The Journal of Neuroscience : The Official Journal of the Society for*  
583 *Neuroscience*. <https://doi.org/10.1523/JNEUROSCI.1254-18.2018>

584 Green, L., & Myerson, J. (2004). A discounting framework for choice with delayed and  
585 probabilistic rewards. *Psychological Bulletin*. [https://doi.org/10.1037/0033-](https://doi.org/10.1037/0033-2909.130.5.769)  
586 [2909.130.5.769](https://doi.org/10.1037/0033-2909.130.5.769)

587 Hartmann, M. N., Hager, O. M., Tobler, P. N., & Kaiser, S. (2013). Parabolic discounting of  
588 monetary rewards by physical effort. *Behavioural Processes*.  
589 <https://doi.org/10.1016/j.beproc.2013.09.014>

590 Hauser, T. U., Eldar, E., & Dolan, R. J. (2017). Separate mesocortical and mesolimbic  
591 pathways encode effort and reward learning signals. *Proceedings of the National*  
592 *Academy of Sciences*. <https://doi.org/10.1073/pnas.1705643114>

593 Kahneman, D., & Tversky, A. (1979). Prospect Theory: An Analysis of Decision under Risk  
594 Daniel. *Econometrica*, 47(2), 263–291. <https://doi.org/10.2307/1914185>

595 Klein-Flügge, M. C., Kennerley, S. W., Friston, K., & Bestmann, S. (2016). Neural  
596 Signatures of Value Comparison in Human Cingulate Cortex during Decisions  
597 Requiring an Effort-Reward Trade-off. *The Journal of Neuroscience : The Official*  
598 *Journal of the Society for Neuroscience*. [https://doi.org/10.1523/JNEUROSCI.0292-](https://doi.org/10.1523/JNEUROSCI.0292-16.2016)  
599 16.2016

600 Klein-Flügge, M. C., Kennerley, S. W., Saraiva, A. C., Penny, W. D., & Bestmann, S.  
601 (2015). Behavioral Modeling of Human Choices Reveals Dissociable Effects of Physical  
602 Effort and Temporal Delay on Reward Devaluation. *PLoS Computational Biology*.  
603 <https://doi.org/10.1371/journal.pcbi.1004116>

604 Kravitz, A. V., Tye, L. D., & Kreitzer, A. C. (2012). Distinct roles for direct and indirect  
605 pathway striatal neurons in reinforcement. *Nature Neuroscience*.  
606 <https://doi.org/10.1038/nn.3100>

607 Kurniawan, I. T., Guitart-Masip, M., & Dolan, R. J. (2011). Dopamine and effort-based  
608 decision making. *Frontiers in Neuroscience*. <https://doi.org/10.3389/fnins.2011.00081>

609 Le Bouc, R., Rigoux, L., Schmidt, L., Degos, B., Welter, M.-L., Vidailhet, M., ...  
610 Pessiglione, M. (2016). Computational Dissection of Dopamine Motor and Motivational  
611 Functions in Humans. *The Journal of Neuroscience*.  
612 <https://doi.org/10.1523/jneurosci.3078-15.2016>

613 Le Heron, C., Manohar, S., Plant, O., Muhammed, K., Griffanti, L., Nemeth, A., ... Husain,  
614 M. (2018). Dysfunctional effort-based decision-making underlies apathy in genetic  
615 cerebral small vessel disease. *Brain*. <https://doi.org/10.1093/brain/awy257>

616 Lockwood, P. L., Hamonet, M., Zhang, S. H., Ratnavel, A., Salmony, F. U., Husain, M., &  
617 Apps, M. A. J. (2017). Prosocial apathy for helping others when effort is required.  
618 *Nature Human Behaviour*. <https://doi.org/10.1038/s41562-017-0131>

619 Loewenstein, G., Frederick, S., & O'donoghue, T. (2002). Time Discounting and Time

620 Preference: A Critical Review. *Journal of Economic Literature*.  
621 <https://doi.org/10.1257/002205102320161311>

622 Massar, S. A. A., Csathó, Á., & Van der Linden, D. (2018). Quantifying the motivational  
623 effects of cognitive fatigue through effort-based decision making. *Frontiers in*  
624 *Psychology*. <https://doi.org/10.3389/fpsyg.2018.00843>

625 McGuigan, S., Zhou, S. H., Brosnan, M. B., Thyagarajan, D., Bellgrove, M. A., & Chong, T.  
626 T. J. (2019). Dopamine restores cognitive motivation in Parkinson's disease. *Brain*.  
627 <https://doi.org/10.1093/brain/awy341>

628 Meyniel, F., Sergent, C., Rigoux, L., Daunizeau, J., & Pessiglione, M. (2013).  
629 Neurocomputational account of how the human brain decides when to have a break.  
630 *Proceedings of the National Academy of Sciences of the United States of America*.  
631 <https://doi.org/10.1073/pnas.1211925110>

632 Müller, T., & Apps, M. A. J. (2019). Motivational fatigue: A neurocognitive framework for  
633 the impact of effortful exertion on subsequent motivation. *Neuropsychologia*.  
634 <https://doi.org/10.1016/j.neuropsychologia.2018.04.030>

635 Nishiyama, R. (2016). Physical, emotional, and cognitive effort discounting in gain and loss  
636 situations. *Behavioural Processes*. <https://doi.org/10.1016/j.beproc.2016.02.004>

637 Porat, O., Hassin-Baer, S., Cohen, O. S., Markus, A., & Tomer, R. (2014). Asymmetric  
638 dopamine loss differentially affects effort to maximize gain or minimize loss. *Cortex*.  
639 <https://doi.org/10.1016/j.cortex.2013.10.004>

640 Prévost, C., Pessiglione, M., Météreau, E., Cléry-Melin, M.-L., & Dreher, J.-C. (2010).  
641 Separate valuation subsystems for delay and effort decision costs. *The Journal of*  
642 *Neuroscience : The Official Journal of the Society for Neuroscience*.  
643 <https://doi.org/10.1523/JNEUROSCI.2752-10.2010>

644 Rachlin, H. (2006). NOTES ON DISCOUNTING. *Journal of the Experimental Analysis of*

645 *Behavior*. <https://doi.org/10.1901/jeab.2006.85-05>

646 Rachlin, H., & Green, L. (1972). COMMITMENT, CHOICE AND SELF-CONTROL 1 .  
647 *Journal of the Experimental Analysis of Behavior*. <https://doi.org/10.1901/jeab.1972.17->  
648 15

649 Rigoux, L., Stephan, K. E., Friston, K. J., & Daunizeau, J. (2014). Bayesian model selection  
650 for group studies - revisited. *NeuroImage*.  
651 <https://doi.org/10.1016/j.neuroimage.2013.08.065>

652 Rudebeck, P. H., Walton, M. E., Smyth, A. N., Bannerman, D. M., & Rushworth, M. F. S.  
653 (2006). Separate neural pathways process different decision costs. *Nature Neuroscience*.  
654 <https://doi.org/10.1038/nn1756>

655 Salamone, J. D., Correa, M., Farrar, A., & Mingote, S. M. (2007). Effort-related functions of  
656 nucleus accumbens dopamine and associated forebrain circuits. *Psychopharmacology*.  
657 <https://doi.org/10.1007/s00213-006-0668-9>

658 Salamone, John D., Correa, M., Yang, J.-H., Rotolo, R., & Presby, R. (2018). Dopamine,  
659 Effort-Based Choice, and Behavioral Economics: Basic and Translational Research.  
660 *Frontiers in Behavioral Neuroscience*. <https://doi.org/10.3389/fnbeh.2018.00052>

661 Salimpour, Y., Mari, Z. K., & Shadmehr, R. (2015). Altering effort costs in Parkinson's  
662 disease with noninvasive cortical stimulation. *Journal of Neuroscience*.  
663 <https://doi.org/10.1523/JNEUROSCI.1827-15.2015>

664 Schwarz, G. (1978). Estimating the Dimension of a Model. *The Annals of Statistics*.  
665 <https://doi.org/10.1214/aos/1176344136>

666 Shadmehr, R., Huang, H. J., & Ahmed, A. A. (2016). A Representation of Effort in Decision-  
667 Making and Motor Control. *Current Biology*. <https://doi.org/10.1016/j.cub.2016.05.065>

668 Shiner, T., Seymour, B., Wunderlich, K., Hill, C., Bhatia, K. P., Dayan, P., & Dolan, R. J.  
669 (2012). Dopamine and performance in a reinforcement learning task: Evidence from

670 Parkinson's disease. *Brain*. <https://doi.org/10.1093/brain/aws083>

671 Skvortsova, V., Degos, B., Welter, M.-L., Vidailhet, M., & Pessiglione, M. (2017). A  
672 Selective Role for Dopamine in Learning to Maximize Reward But Not to Minimize  
673 Effort: Evidence from Patients with Parkinson's Disease. *The Journal of Neuroscience*.  
674 <https://doi.org/10.1523/JNEUROSCI.2081-16.2017>

675 Smittenaar, P., Chase, H. W., Aarts, E., Nusslein, B., Bloem, B. R., & Cools, R. (2012).  
676 Decomposing effects of dopaminergic medication in Parkinson's disease on  
677 probabilistic action selection - learning or performance? *European Journal of*  
678 *Neuroscience*. <https://doi.org/10.1111/j.1460-9568.2012.08043.x>

679 Stephan, K. E., Penny, W. D., Daunizeau, J., Moran, R. J., & Friston, K. J. (2009). Bayesian  
680 model selection for group studies. *Drug and Alcohol Dependence*.

681 Stephens, D. W. (2001). The adaptive value of preference for immediacy: when shortsighted  
682 rules have farsighted consequences. *Behavioral Ecology*.  
683 <https://doi.org/10.1093/beheco/12.3.330>

684 Stephens, D. W., & Krebs, J. R. (1986). *Foraging theory*. Princeton Univ Press.

685 Stevens, J. R., Rosati, A. G., Ross, K. R., & Hauser, M. D. (2005). Will travel for food:  
686 Spatial discounting in two New World monkeys. *Current Biology*.  
687 <https://doi.org/10.1016/j.cub.2005.09.016>

688 Taylor, M. M., & Creelman, C. D. (2005). PEST: Efficient Estimates on Probability  
689 Functions. *The Journal of the Acoustical Society of America*.  
690 <https://doi.org/10.1121/1.1910407>

691 Timmer, M. H. M., Sescousse, G., Esselink, R. A. J., Piray, P., & Cools, R. (2017).  
692 Mechanisms Underlying Dopamine-Induced Risky Choice in Parkinson's Disease With  
693 and Without Depression (History). *Computational Psychiatry*.  
694 [https://doi.org/10.1162/cpsy\\_a\\_00011](https://doi.org/10.1162/cpsy_a_00011)

695 Tom, S. M., Fox, C. R., Trepel, C., & Poldrack, R. A. (2007). The neural basis of loss  
696 aversion in decision-making under risk. *Science*.  
697 <https://doi.org/10.1126/science.1134239>

698 Tversky, A., & Kahneman, D. (1981). The framing of decisions and the psychology of  
699 choice. *Science*. <https://doi.org/10.1126/science.7455683>

700 Tversky, A., & Kahneman, D. (1992a). Advances in Prospect-Theory - Cumulative  
701 Representation of Uncertainty. *Journal of Risk and Uncertainty*, 5(4), 297–323.  
702 [https://doi.org/Doi 10.1007/Bf00122574](https://doi.org/Doi%2010.1007/Bf00122574)

703 Tversky, A., & Kahneman, D. (1992b). Advances in prospect theory: Cumulative  
704 representation of uncertainty. *Journal of Risk and Uncertainty*, 5(4), 297–323.  
705 <https://doi.org/10.1007/BF00122574>

706 Walton, M. E., & Bouret, S. (2019). What Is the Relationship between Dopamine and Effort?  
707 *Trends in Neurosciences*. <https://doi.org/10.1016/j.tins.2018.10.001>  
708

709 **Table 1: Demographics for PD and HC groups (means  $\pm$  SD)**

710

		PD	HC	Group difference
<b>N</b>		18	20	
<b>Age (years)</b>		66 $\pm$ 7.68	69 $\pm$ 4.54	t(36)= 1.30, p=0.20
<b>Gender (M: F)</b>		9:9	9:11	$\chi^2(1)= 0.001$ , p= 0.97
<b>MMSE<sub>a</sub></b>		28.9 $\pm$ 1.5	29.5 $\pm$ 0.85	t(36)=1.61, p=0.12
<b>BIS/BAS<sub>b</sub></b>	<b>BIS</b>	20.22 $\pm$ 2.75	20.18 $\pm$ 2.38	t(36)=-0.05, p=0.96
	Reward responsiveness	9.11 $\pm$ 2.91	8.95 $\pm$ 1.58	t(36)=-0.21, p=0.83
	Drive	9.77 $\pm$ 3.07	9.91 $\pm$ 2.22	t(36)= 0.16, p=0.88
	Fun seeking	9.66 $\pm$ 2.45	8.72 $\pm$ 2.21	t(36)=-1.27, p=0.21
<b>DASS21<sub>c</sub></b>	<b>Depression</b>	3.45 $\pm$ 3.76	4.93 $\pm$ 4.94	t(33)=-1.03, p=0.30
	<b>Anxiety</b>	1.81 $\pm$ 2.75	6.13 $\pm$ 4.03	t(33)=-3.87, <b>p&lt;0.001</b>
	<b>Stress</b>	5.90 $\pm$ 5.53	6.93 $\pm$ 5.00	t(33)=-0.57, p=0.46
<b>UPDRS<sub>a</sub></b>		23.61 $\pm$ 18.88	N/A	
<b>Hoehn and Yahr stage</b>		1.85 $\pm$ 0.60	N/A	
<b>Disease duration (months)</b>		39.22 $\pm$ 30.1	N/A	
<b>Duration since last dose (hours)</b>		2.08 $\pm$ 0.90	N/A	

711 **a.** MMSE=Mini-Mental Status Exam is a 30-point questionnaire that is used extensively in clinical and research  
712 settings to measure cognitive impairment (Folstein et al., 1975).

713 **b.** BIS/BAS= the behavioural inhibition system (BIS) and the behavioural activation system (BAS) (Carver &  
714 White, 1994).

715 **c.** DASS-21=Depression (Normal: 0-9), Anxiety (Normal 0-7) and Stress (Normal: 0-14) Scales (Antony, Cox,  
716 Enns, Bieling, & Swinson, 1998). Three PD patients chose not to finish this questionnaire. **d.** UPDRS=Unified  
717 Parkinson's Disease Rating Scale (UPDRS) (Fahn & Elton, 1987).

718

719

720

721 **Table 2: Model comparison.** The parabolic effort discounting with separate discount  
722 parameters ([1+,1-]) for the reward and punishment conditions provided the best fit for choices  
723 of both the PD and HC groups. Summed BIC, Friedman's test (Rigoux et al., 2014; Stephan et  
724 al., 2009) and R<sub>2</sub> (Median  $\pm$  Median Absolute Deviation) are provided for each group (HC,  
725 PD). Specifically, for each model, the Bayesian Information Criterion (BIC) summed over all  
726 participants were compared (the lower the value, the better the model fit).

727

		HC			PD		
		BIC	Mean Rank	R <sub>2</sub>	BIC	Mean Rank	R <sub>2</sub>
<b>Linear</b>	(l)	3045	4.17	0.64 $\pm$ 0.21	2973	4.33	0.58 $\pm$ 0.22
	(1+, 1-)	3072	4.70	0.72 $\pm$ 0.18	2964	4.28	0.61 $\pm$ 0.22
<b>Parabolic</b>	(l)	2991	2.77	0.74 $\pm$ 0.24	2867	2.89	0.72 $\pm$ 0.25
	(1+, 1-)	<b>2870</b>	<b>2.05</b>	<b>0.81<math>\pm</math>0.22</b>	<b>2785</b>	<b>2.11</b>	<b>0.85<math>\pm</math>0.26</b>
<b>Hyperbolic</b>	(l)	3065	3.55	0.60 $\pm$ 0.18	2962	3.83	0.64 $\pm$ 0.22
	(1+, 1-)	3005	3.75	0.70 $\pm$ 0.21	2924	3.56	0.69 $\pm$ 0.25
<b>Friedman test</b>			$\chi^2=26.26$ p<0.001			$\chi^2=19.11$ p=0.002	

728

729 **Figure 1: Experimental setup.** (A) Experimental equipment. (B-C) Typical reward (B) and  
730 punishment (C) trials. (D) Average force trace across participants on levels 1, 3 and 6. 0 second  
731 (x-axis) is the moment at which the participants indicated their choice and they were allowed  
732 to start exerting the force. Error-bars represent SEM across participants. (E) Young participants  
733 (red), PD patients (green) and healthy age-matched controls (blue) all modulated their force  
734 appropriately. The solid black line indicates the minimum force required. Error-bars represent  
735 SEM across participants.

736  
737 **Figure 2: Procedure for determining the effort indifference point.** Exemplary choices and  
738 fits are shown for one participant and two effort levels. (A, D): The points offered for each  
739 force level (A: Level 2; D: Level 5). Unbeknown to participants, the points associated with  
740 each force level were adjusted on a trial-by-trial basis using an adaptive staircase algorithm.  
741 Specifically, the points offered were increased or decreased using an initial step size of 8,  
742 depending on whether participants rejected (skipped) or accepted the opportunity to execute  
743 the force in order to receive (or avoid losing) those points. (B,C, E, F): A sigmoid function  
744 (red line) was fitted separately to the choices (arrow) generated at each effort level (y axis: 0 =  
745 reject force, 1 = accept force), given the points (reward or punishment) offered for this force  
746 level (x-axis). The point of subjective indifference point (IP, circle) was defined as the  
747 magnitude at which the sigmoid crossed  $y = 0.5$ . (G-J): The variance of the points offered for  
748 each force level within the first and second half of each condition for the HC group (G= reward,  
749 H=punishment) and PD group (I-reward, J=punishment). Error-bars represent SEM across  
750 participants.

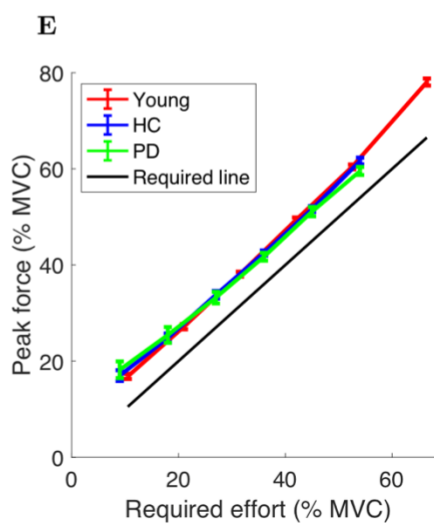
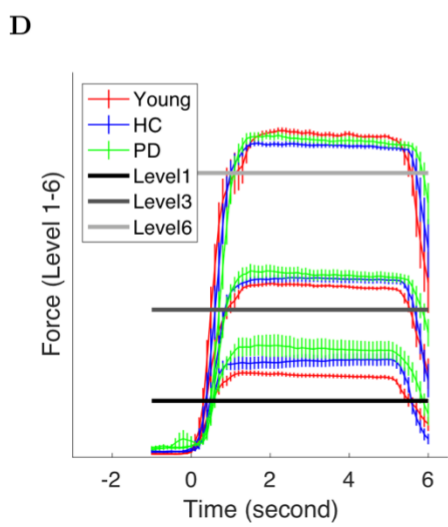
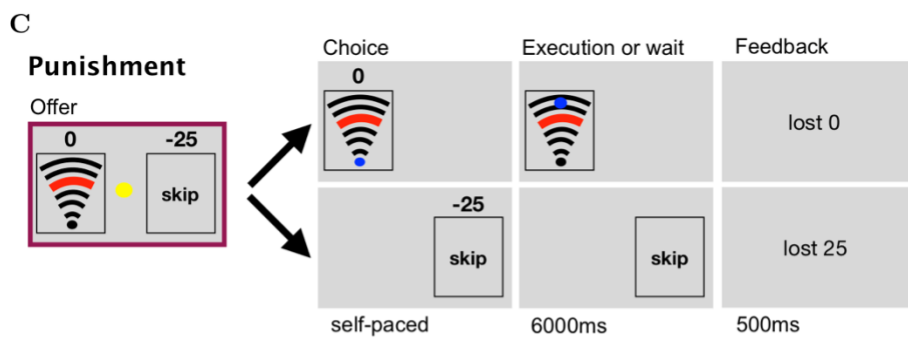
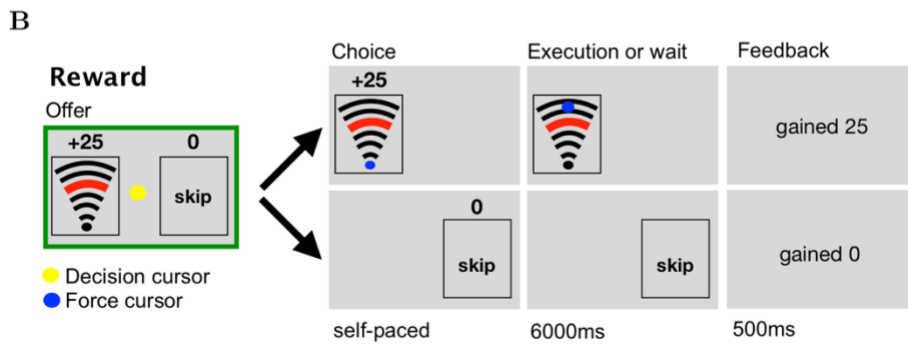
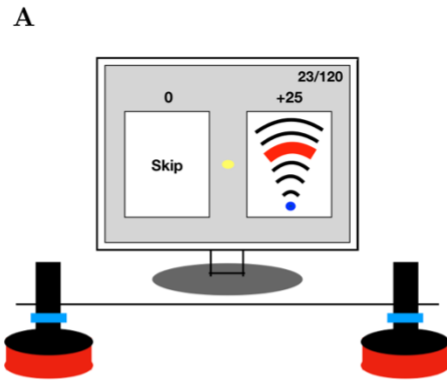
751  
752 **Figure 3: Loss aversion in young healthy participants.** (A) Effort IP in reward (solid circles)  
753 and punishment (open diamonds). For each force level (x-axis), we estimated a score at which  
754 the probability of choosing to produce the force was 50% (effort IP, y-axis). Given a particular  
755 force level, a higher IP indicated less willingness to produce the force. Error-bars represent  
756 SEM across participants. Grey circles/diamonds indicate individual data points. (B) Loss  
757 aversion index for each individual. Loss aversion is reflected by participants being more willing  
758 to produce a force to avoid losses than receive same-sized gains (higher reward IP than  
759 punishment IP given a force level). Loss aversion was therefore quantified as a ratio between  
760 the reward IP and the punishment IP (loss aversion index; y-axis). A value greater than 1  
761 indicates loss aversion.

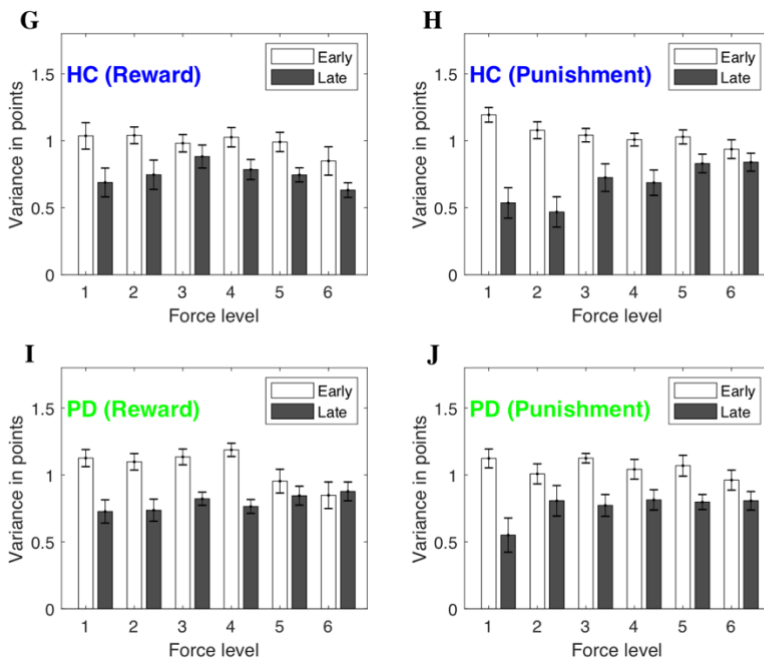
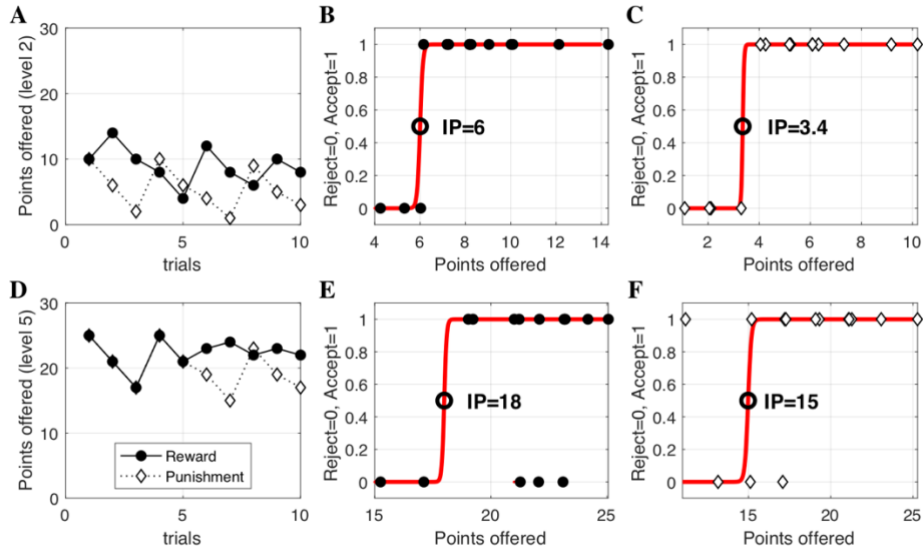
762  
763 **Figure 4: Loss aversion in HC and PD groups.** (A-B) Effort IP in reward (solid circle) and  
764 punishment (open diamond) conditions for the HC (A) and PD (B) groups. For each force level  
765 (x-axis), we estimated a score at which the probability of choosing to produce the force was  
766 50% (effort IP, y-axis). Given a particular force level, a higher IP indicated less willingness to  
767 produce the force. Error-bars represent SEM across participants. Grey indicates individual data  
768 points. (C-D) Loss aversion across participants for the HC (C) and PD (D) groups. Loss  
769 aversion is reflected by participants being more willing to produce a force to avoid losses than  
770 receive similar gains. Therefore, the loss aversion index was measured as a ratio between the  
771 reward IP and the punishment IP (y-axis). A value greater than 1 indicates loss aversion. (E)  
772 Loss aversion index. Error-bars represent SEM across participants. (F) Reward IP and  
773 punishment IP across groups.

774  
775 **Figure 5: Parabolic (winning model) discounting parameter ( $l$ ) for the HC and PD groups.**  
776 (A) Effort discounting parameter ( $l$ ) for the HC and PD groups in the reward and punishment  
777 conditions. (B, C) Parabolic model predictions for the effort IP across force options in the  
778 reward (B) and punishment (C) conditions. The model predictions were calculated by

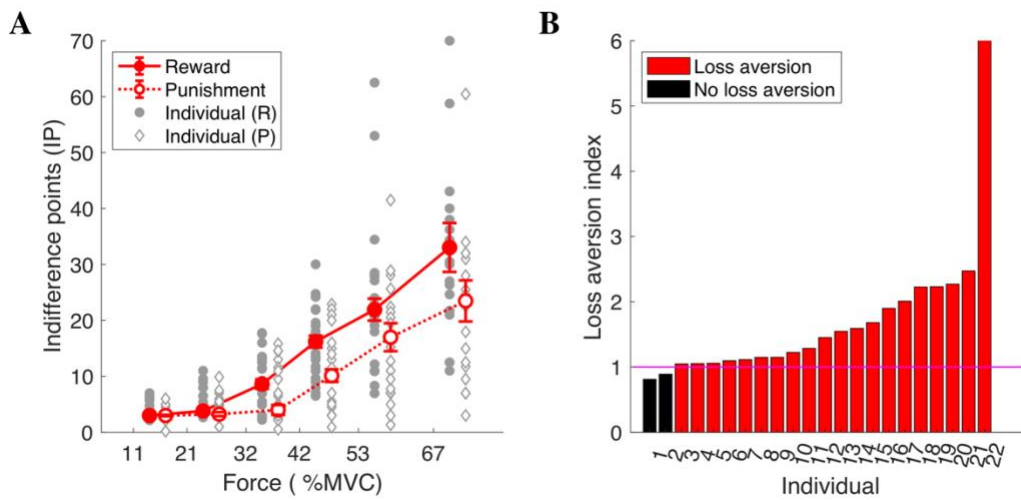


779 estimating a score for which the probability of the model choosing the force option was 50%.  
780 Error-bars represent SEM across participants.  
781  
782

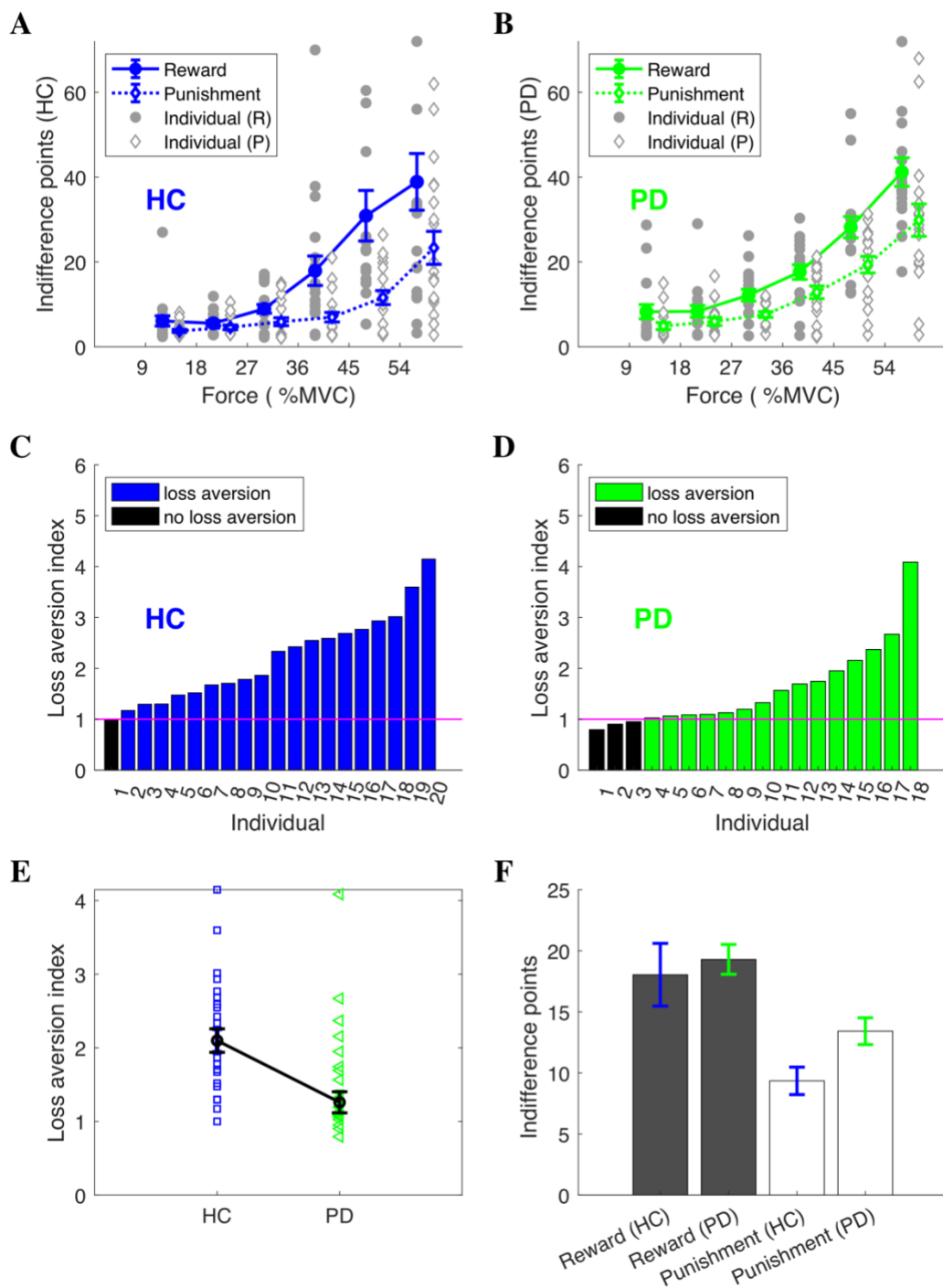




784



785



786

787

