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

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Abstract

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

Significance Statement

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

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

Introduction

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

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

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

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

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

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

Materials and Methods

Participants

Ethics statement.

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

Young healthy participants

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

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

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

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

[INSERT TABLE 1 HERE]

Experimental design

Experimental set up

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

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

Effort-based decision-making task

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

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

Adaptive staircase algorithm

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

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

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

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

[INSERT FIGURE 2 HERE]

Data and statistical analysis

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

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

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

Computational modelling of choice

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

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

$$\text{Linear: } U(t) = A(t) - lE(t)$$

$$\text{Parabolic: } U(t) = A(t) - lE(t)^2$$

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

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

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

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

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

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

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

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

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

Results

Evidence for loss aversion in young healthy participants

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

[INSERT FIGURE 3 HERE]

Reduced loss aversion in PD patients compared to HC

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

[INSERT FIGURE 4 HERE]

Decision-making behaviour in our task was modelled using an effort-based discount model that quantifies how the utility of reward decreases as the physical effort associated with it becomes progressively more demanding. We fitted participant choices to three typical discounting functions: linear, parabolic and hyperbolic, which are often used to capture effort discounting (Białaszek et al., 2017; Hartmann et al., 2013; Klein-Flügge et al., 2015; McGuigan et al., 2019; Lockwood et al., 2017). We found that a parabolic effort discounting function with separate discounting parameters for the reward and punishment conditions provided the best fit for both the PD and HC groups (Table 2). Specifically, the summed Bayesian Information Criterion (BIC) was lowest for the parabolic function with separate discounting parameters (the lower the value, the better the model fit) (Table 2). To investigate this at a subject-level, a Friedman's test on individual BIC was performed (Rigoux et al., 2014; Stephan et al., 2009). In general, similar results were observed with the parabolic function consistently being associated with significantly lower BIC for both groups (Table 2). To reinforce these results, R_2 was found to be greater for the parabolic function for both groups (Table 2).

[INSERT TABLE 2 HERE]

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

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

[INSERT FIGURE 5 HERE]

Discussion

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

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

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

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

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

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

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

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

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

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Table 1: Demographics for PD and HC groups (means ± SD)

		PD	HC	Group difference
N		18	20	
Age (years)		66 ± 7.68	69 ± 4.54	t(36)= 1.30, p=0.20
Gender (M: F)		9:9	9:11	$\chi_2(1)$= 0.001, p= 0.97
MMSE[a]		28.9±1.5	29.5±0.85	t(36)=1.61, p=0.12
BIS/BAS[b]	BIS	20.22±2.75	20.18±2.38	t(36)=-0.05, p=0.96
	Reward responsiveness	9.11±2.91	8.95±1.58	t(36)=-0.21, p=0.83
	Drive	9.77±3.07	9.91±2.22	t(36)= 0.16, p=0.88
	Fun seeking	9.66±2.45	8.72±2.21	t(36)=-1.27, p=0.21
DASS21[c]	Depression	3.45±3.76	4.93±4.94	t(33)=-1.03, p=0.30
	Anxiety	1.81±2.75	6.13±4.03	t(33)=-3.87, **p<0.001**
	Stress	5.90±5.53	6.93±5.00	t(33)=-0.57, p=0.46
UPDRS[d]		23.61±18.88	N/A	
Hoehn and Yahr stage		1.85±0.60	N/A	
Disease duration (months)		39.22±30.1	N/A	
Duration since last dose (hours)		2.08±0.90	N/A	

a. MMSE=Mini-Mental Status Exam is a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment (Folstein et al., 1975).
b. BIS/BAS= the behavioural inhibition system (BIS) and the behavioural activation system (BAS) (Carver & White, 1994).
c. DASS-21=Depression (Normal: 0-9), Anxiety (Normal 0-7) and Stress (Normal: 0-14) Scales (Antony, Cox, Enns, Bieling, & Swinson, 1998). Three PD patients chose not to finish this questionnaire. d. UPDRS=Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn & Elton, 1987).

Table 2: Model comparison. The parabolic effort discounting with separate discount parameters ([l+,l-]) for the reward and punishment conditions provided the best fit for choices of both the PD and HC groups. Summed BIC, Friedman's test (Rigoux et al., 2014; Stephan et al., 2009) and R_2 (Median ± Median Absolute Deviation) are provided for each group (HC, PD). Specifically, for each model, the Bayesian Information Criterion (BIC) summed over all participants were compared (the lower the value, the better the model fit).

		HC			**PD**		
		BIC	Mean Rank	R_2	BIC	Mean Rank	R_2
Linear	(l)	3045	4.17	0.64±0.21	2973	4.33	0.58±0.22
	(l+, l-)	3072	4.70	0.72±0.18	2964	4.28	0.61±0.22
Parabolic	(l)	2991	2.77	0.74±0.24	2867	2.89	0.72±0.25
	(l+, l-)	**2870**	**2.05**	**0.81±0.22**	**2785**	**2.11**	**0.85±0.26**
Hyperbolic	(l)	3065	3.55	0.60±0.18	2962	3.83	0.64±0.22
	(l+, l-)	3005	3.75	0.70±0.21	2924	3.56	0.69±0.25
Friedman test			$\chi2$=26.26 p<0.001			$\chi2$=19.11 p=0.002	

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

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

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

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

Figure 5: Parabolic (winning model) discounting parameter (l) for the HC and PD groups. (A) Effort discounting parameter (*l*) for the HC and PD groups in the reward and punishment conditions. **(B, C)** Parabolic model predictions for the effort IP across force options in the 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
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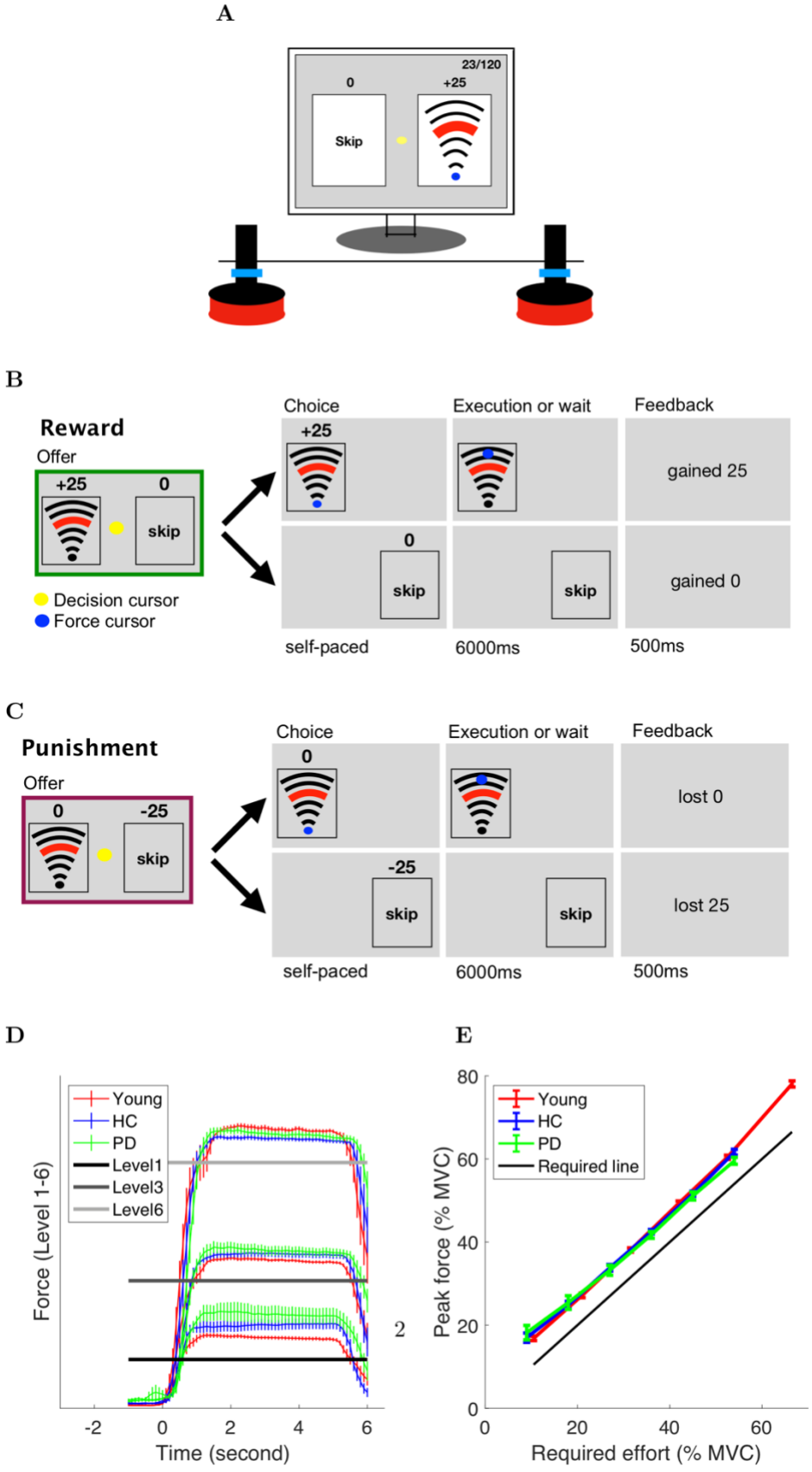
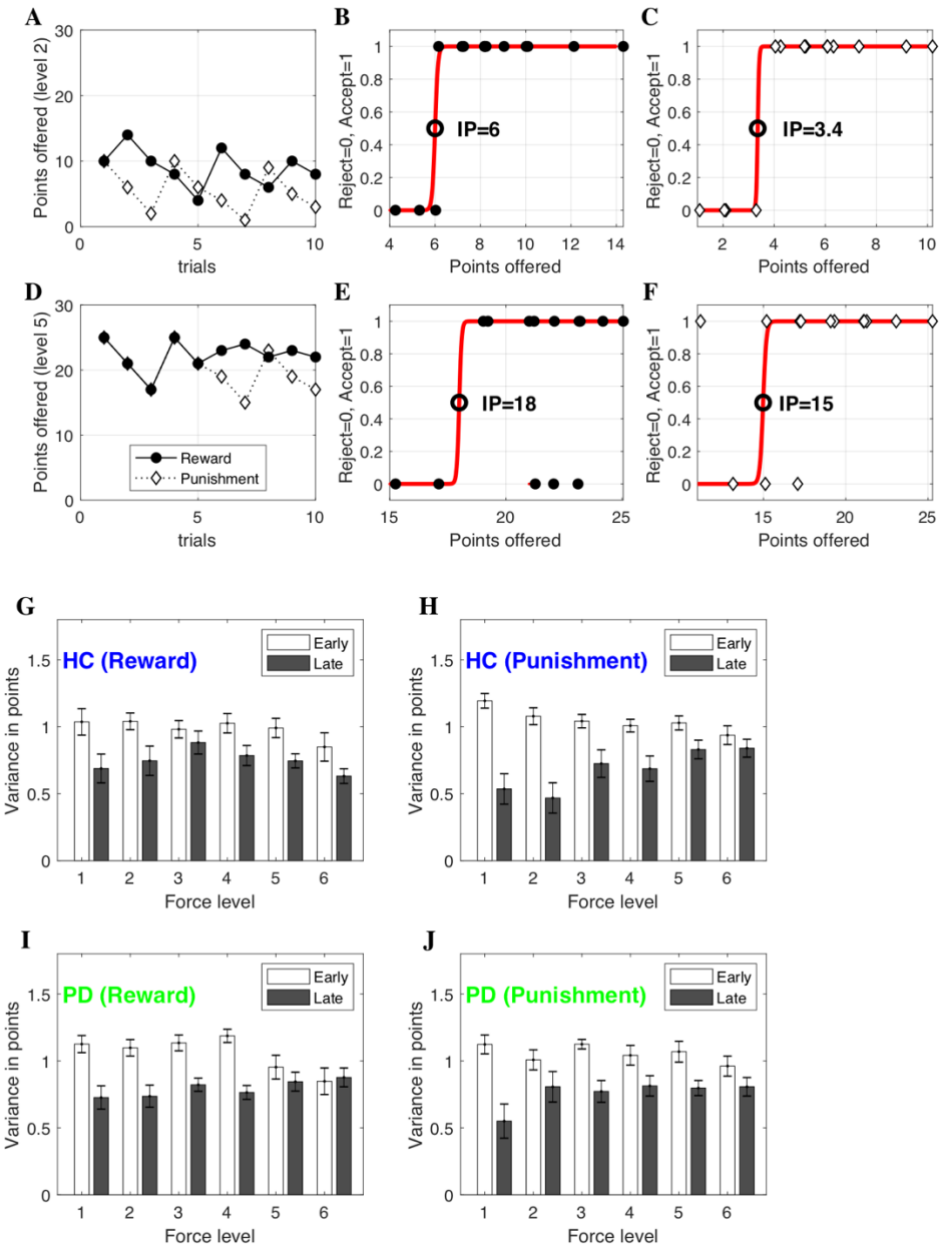
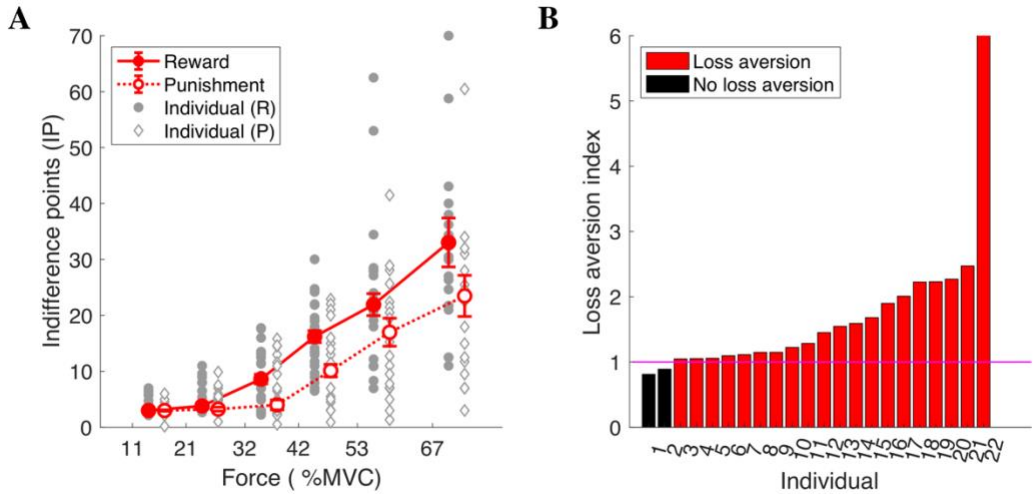
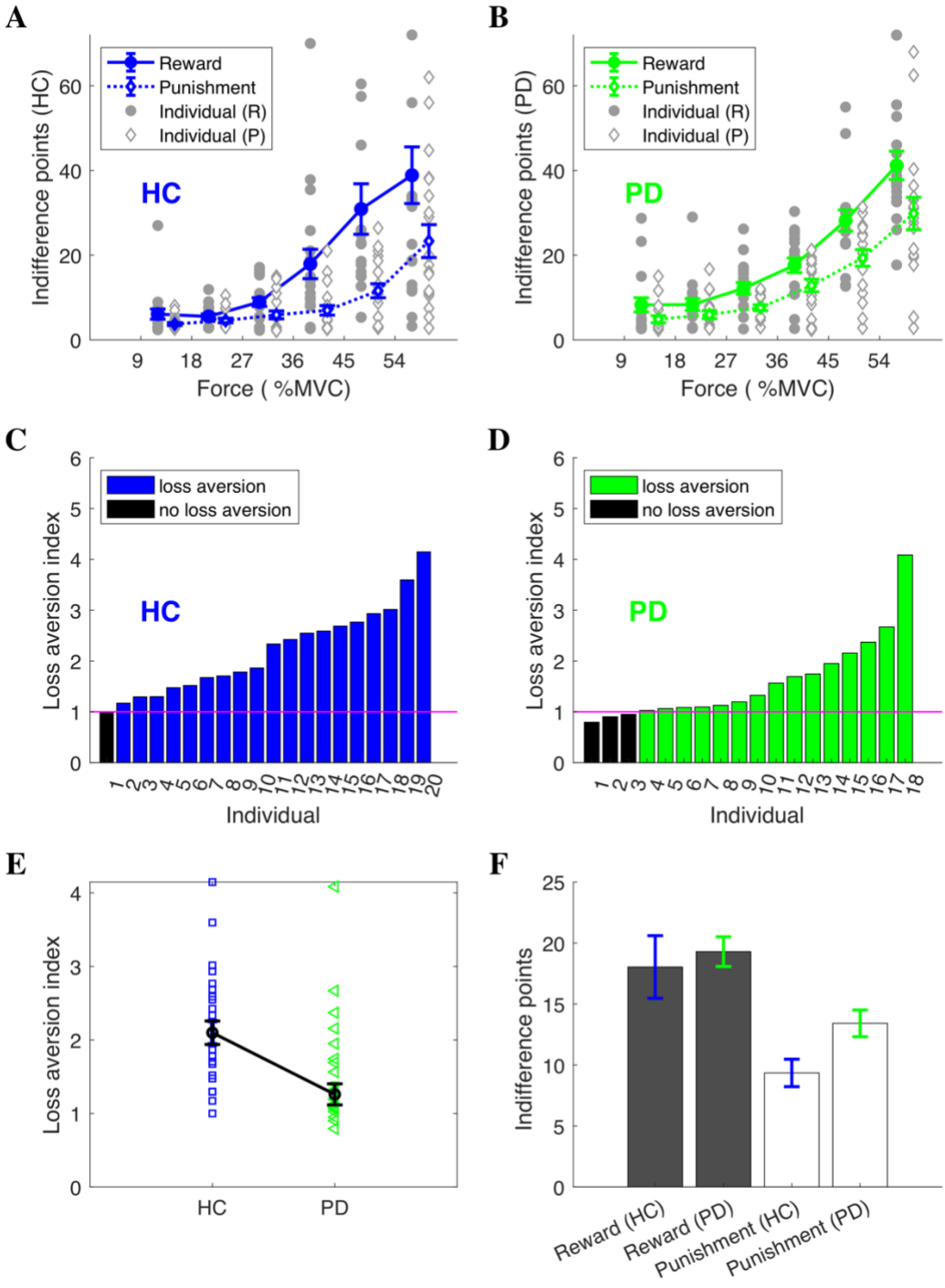

A
23/120
0
+25
Skip
B
Reward
Offer
+25
0
skip
Decision cursor
Force cursor
Choice
Execution or wait
Feedback
+25
gained 25
0
skip
skip
gained 0
self-paced
6000ms
500ms
C
Punishment
Offer
0
-25
skip
Choice
Execution or wait
Feedback
0
lost 0
-25
skip
skip
lost 25
self-paced
6000ms
500ms
D
Young
HC
PD
Level1
Level3
Level6
Force (Level 1-6)
Time (second)
E
Young
HC
PD
Required line
Peak force (% MVC)
Required effort (% MVC)

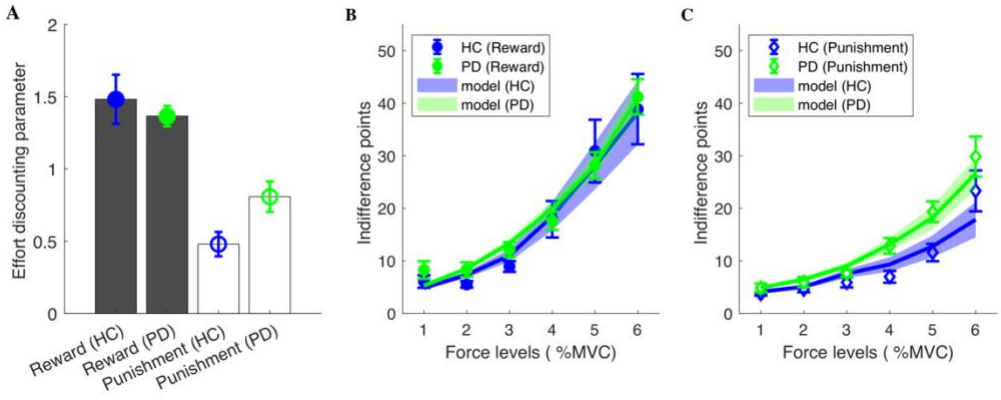
783


A
B
C
D
E
F
G
H
I
J
Points offered (level 2)
Points offered (level 5)
trials
Reject=0, Accept=1
Points offered
IP=6
IP=3.4
IP=18
IP=15
Reward
Punishment
HC (Reward)
HC (Punishment)
PD (Reward)
PD (Punishment)
Early
Late
Variance in points
Force level


A
B
Reward
Punishment
Individual (R)
Individual (P)
Indifference points (IP)
Force (%MVC)
Loss aversion
No loss aversion
Loss aversion index
Individual


A
Reward
Punishment
Individual (R)
Individual (P)
HC
Indifference points (HC)
Force (%MVC)
B
PD
Indifference points (PD)
C
loss aversion
no loss aversion
Loss aversion index
Individual
D
E
HC
PD
F
Indifference points
Reward (HC)
Reward (PD)
Punishment (HC)
Punishment (PD)

786


A
Effort discounting parameter
2
1.5
1
0.5
0
Reward (HC)
Reward (PD)
Punishment (HC)
Punishment (PD)
B
HC (Reward)
PD (Reward)
model (HC)
model (PD)
Indifference points
50
40
30
20
10
0
1
2
3
4
5
6
Force levels (%MVC)
C
HC (Punishment)
PD (Punishment)
model (HC)
model (PD)
Indifference points
Force levels (%MVC)

787