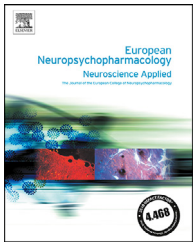
European Neuropsychopharmacology (2019) 000, 1–11



www.elsevier.com/locate/euroneuro

Modelling decision-making under uncertainty: A direct comparison study between human and mouse gambling data

Lidia Cabeza[a], Julie Giustiniani[a,b,c], Thibault Chabin[a], Bahrie Ramadan[a], Coralie Joucla[a], Magali Nicolier[a,b,c], Lionel Pazart[c], Emmanuel Haffen[a,b,c], Dominique Fellmann[a], Damien Gabriel[a,c], Yvan Peterschmitt[a,*]

[a] *EA-481 Laboratoire de Neurosciences Intégratives et Cliniques de Besançon, Université Bourgogne - Franche-Comté, France*
[b] *Department of Clinical Psychiatry, University Hospital, Besançon, France*
[c] *CIC-1431 Inserm, University Hospital, Besançon, France*

Received 11 March 2019; received in revised form 15 November 2019; accepted 20 November 2019
Available online xxx

KEYWORDS
Decision-making;
Iowa Gambling Task;
Mouse gambling task

Abstract
Decision-making is a conserved evolutionary process enabling us to choose one option among several alternatives, and relies on reward and cognitive control systems. The Iowa Gambling Task allows the assessment of human decision-making under uncertainty by presenting four card decks with various cost-benefit probabilities. Participants seek to maximise their monetary gain by developing long-term optimal-choice strategies. Animal versions have been adapted with nutritional rewards, but interspecies data comparisons are scarce. Our study directly compares the non-pathological decision-making performance between humans and wild-type C57BL/6 mice. Human participants completed an electronic Iowa Gambling Task version, while mice a maze-based adaptation with four arms baited in a probabilistic way. Our data shows closely matching performance between both species with similar patterns of choice behaviours. However, mice showed a faster learning rate than humans. Moreover, both populations were clustered into good, intermediate and poor decision-making categories with similar proportions. Remarkably, mice characterised as good decision-makers behaved the same as humans of the same category, but slight differences among species are evident for the other two

* Corresponding author.
E-mail address: yvan.peterschmitt@univ-fcomte.fr (Y. Peterschmitt).

https://doi.org/10.1016/j.euroneuro.2019.11.005

Please cite this article as: L. Cabeza, J. Giustiniani and T. Chabin et al., Modelling decision-making under uncertainty: A direct comparison study between human and mouse gambling data, European Neuropsychopharmacology, https://doi.org/10.1016/j.euroneuro.2019.11.005

subpopulations. Overall, our direct comparative study confirms the good face validity of the rodent gambling task. Extended behavioural characterisation and pathological animal models should help strengthen its construct validity and disentangle the determinants in animals and humans decision-making.

1. Introduction

Do animals gamble for food just like humans gamble for money? Most species, including human beings, have to make accurate assessments of the cost-benefit trade-off in reward-driven contexts. For example, the longer an animal is searching for food, the more likely it is to accumulate more and better rewards, however, the more likely it is to encounter a predator. Thus, decision-making (DM) is an essential mechanism for survival in partly predictable situations (de Froment et al., 2014). The underlying principles of how living beings achieve efficient DM are still not fully understood, and assessing human DM using animal models requires further validation. Laboratory tests simulating real-life DM, such as gambling tasks, have been developed. Particularly, the Iowa Gambling Task (IGT) is widely used to assess human DM under uncertainty. Participants are required to maximise the monetary gains by selecting cards from four decks with various cost-benefit probabilities (Bechara et al., 1994). Players face a choice-conflict between playing from long-term disadvantageous decks yielding higher gains but frequent losses, or from advantageous ones associated with smaller immediate rewards and less frequent penalties. Thus, optimal decisions involve the animal refraining from the preferred large immediate rewards whilst opting for lower but more frequent gains, leading to long-term benefits.

The IGT was originally created to study DM impairments in patients with ventromedial prefrontal cortex damage. Compared to healthy participants who progressively learn to select the advantageous decks, the impaired patients decisively underperform by being unable to set the optimal strategy from repeated negative outcomes. Besides this, many IGT studies with healthy populations have shown a high interindividual performance variability (Bechara and Damasio, 2002; Bechara et al., 2002; Steingroever et al., 2013). Indeed, several clinical reports indicated that, while a majority of healthy participants develop the optimal strategy (good DM individuals), others do not acquire a preference for one deck over the others, which is indicative of a lack of learning (poor DM individuals) (Bechara et al., 2001, 2002; Glicksohn et al., 2007a). The literature has shown that many factors may account for this variability in gambling performance. For example, Bechara et al. explain the poor IGT performance in terms of atypical sensitivity to the reward or punishment. Mechanisms underlying this atypical sensitivity are numerous and still not fully elucidated. Among the potential contributors to IGT failure, the presence of personality characteristics associated with risky behaviour (Buelow and Suhr, 2009), of weaknesses in executive functioning (Brand et al., 2007), a low motivation (Giustiniani et al., 2015), a negative affect at the time of task (Suhr and Tsanadis, 2007) as well as low educational (Davis et al., 2008) and low intellectual levels (Barry and Petry, 2008) have been reported. These data illustrate a behavioural continuum with an overlap in choice strategies between human non-pathological and pathological conditions.

Interestingly, animal versions of the IGT with species-appropriate adjustments to assess DM in a design comparable to humans (van den Bos et al., 2006; van Enkhuizen et al., 2013; Heilbronner, 2017; Pittaras et al., 2016; Rivalan et al., 2009, 2013; de Visser et al., 2011; Young et al., 2011; Zeeb et al., 2009) have been developed. For example, in rodent gambling tasks the decks of cards have been replaced by mazes or operant chambers equipped with different options of varying outcomes; monetary gains are replaced with nutritional rewards since money and food are thought to drive similar behaviours (Lehner et al., 2017).

Similar to human studies, rodents with lesions perform sub-optimally in adapted IGT versions and show a delay in adopting a consistent strategy compared to healthy individuals (Rivalan et al., 2011; Winstanley and Clark, 2015). For the majority of healthy rodents, as the task progresses a raise in advantageous choices is observed, which is commonly accompanied by individuals clustering in three subpopulations who reflect the variable choice strategies (van Enkhuizen et al., 2014; Pittaras et al., 2016; Rivalan et al., 2009). Good DM individuals quickly develop a strong preference for the advantageous options, while poor DM individuals display the worst performances, either not showing any preference for neither advantageous nor disadvantageous options or displaying a long-term preference for the disadvantageous ones. Intermediate DM individuals perform between the other two subgroups. Whether these interindividual variabilities observed in both healthy human and animal populations are similar has never been directly assessed to substantiate the face validity of the models.

Animal and human versions of gambling tasks usually evaluate performance with different analytical methods (Bechara et al., 2001; Zeeb and Winstanley, 2013) and are hence not compared in a direct manner even if animal gambling tasks have been specially created to simulate human DM processes. However, direct comparative research will be a valuable approach allowing clinicians and researchers to bridge their findings, rendering translational studies as a direct tool genuinely meaningful (van Enkhuizen et al., 2014).

Here, we bridge the clinical and preclinical findings on DM processes featuring uncertainty by directly comparing the performance of healthy humans and mice for the first time in the same study using IGT-adapted tasks and identical analytical methods.

Based on the recent literature addressing the validity of mouse gambling tasks (mGT) (van den Bos et al., 2013; van Enkhuizen et al., 2014; Heilbronner, 2017; Pittaras et al., 2016; Winstanley and Clark, 2015), we

Please cite this article as: L. Cabeza, J. Giustiniani and T. Chabin et al., Modelling decision-making under uncertainty: A direct comparison study between human and mouse gambling data, European Neuropsychopharmacology, https://doi.org/10.1016/j.euroneuro.2019.11.005

forecasted a good face validity of our animal model with a similar overall performance regarding the human population (Giustiniani et al., 2015). To check for the existence of a similar variability in the choice strategies among the species, we then compared the stratification of both populations according to the endpoint performances. To evaluate the construct validity, we further studied the behavioural indexes of the cognitive processes sub-serving the optimal choices. Finally, we sought to find the correlations with an endpoint performance, focusing on the parameters of rigidity (Pittaras, 2013), flexibility (van Enkhuizen et al., 2014) and win-stay and lose-shift choices (de Visser et al., 2011). We also analysed the psychometric scores from human participants and reward sensitivity data in mice, to relate the performance or choice strategies to additional behavioural traits.

2. Experimental procedures

2.1. Participants

To reduce conceptual and methodological differences between the tasks, we controlled factors known to interfere with the results such as sex differences and the presence of instructions, especially in humans. In that respect, we recruited only male subjects because they have been described as less risky than females, choosing the advantageous options more frequently in the IGT (Singh, 2016) and its rodent adaptations (van den Bos et al., 2006). Further characterisations will include both genders, allowing us to take into account the variability we accepted to overlook in the present study (Prendergast et al., 2014).

2.2. Humans

Forty healthy right-handed participants (mean age ± SEM = 24.7 ± 5.1; range 19-38) were involved in the study. None reported a previous medical history of psychiatric disorders, substance or alcohol abuse, neurological diseases, traumatic brain injury or stroke, and none reported taking any medication.

Participants received information regarding the aim of the task and gave their written informed consent to take part in the study. Given the influence of real money playing a significant role on motivation, subjects were informed that the monetary payment would be proportional to the global gain obtained in the task (Meyer, 2004; Meyer et al., 2000; Miedl et al., 2010). Due to the ethical considerations and independent of individual performance, all participants received the maximum amount of €85 at the end of the experiment. The protocol was approved by the Committee of Protection of Persons (CPP-Est-11; authorisation given by the General Health Administration (ANSM 2016-A00870-51 and NCT 02862821)).

2.3. Mice

Forty C57BL/6JRj mice (Ets Janvier Labs, Saint-Berthevin, France) were used for this study. Inbred animals such as C57BL/6J are known to behave uniformly and display low interindividual variability (Festing, 2014) (but see recent work by Tuttle et al., 2018). All animals were 3-5 months old at the time of testing, group-housed and maintained under a 12 h-circadian cycle with a constant temperature (22 ± 2 °C). Water was available ad libitum and all mice were food-restricted at 80-90% of their free-feeding weight (mean weight (g) ± SEM = 22.2 ± 0.2) in order to motivate exploration and completion of the nutritionally rewarding task (Rivalan et al., 2009). Experiments were performed in behavioural rooms with tight luminous intensity. All procedures met the NIH guidelines for the care and use of laboratory animals and were approved by the University of Franche-Comte Animal Care and Use Committee (CEBEA-58). All efforts were taken to minimise animal suffering during the testing according to the Directive from the European Council on the 22nd of September 2010 (2010/63/EU).

2.4. Human gambling task

The task was an adapted electronic version of the IGT (Giustiniani et al., 2015), whose aim was to maximise monetary gain through successive selections between four decks. The decks' composition, values and scheduled reward-penalty were predetermined identically to match the original IGT (Bechara, 1997; Bechara and Damasio, 2005; Bechara et al., 1994). The decks looked identical, but differed in composition. Decks A and B were disadvantageous, yielding immediate rewards but involved major economic losses on the long run. Decks C and D were advantageous, yielding frequent small wins and smaller long-term penalties, resulting in long-term gain. The decks also varied in their schedule of losses, with decks B and D featuring infrequent, decks A and C frequent losses, respectively. All decks contained an infinite number of cards in this computerised version of the IGT. The monetary reward was converted from US Dollars to Euros in order to match the currency of the test subjects. At the beginning of the task, participants had a loan of €2000.

Contrary to most IGT experiments, participants were not provided with information regarding the presence of advantageous or disadvantageous decks and the number of trials. This ensured that a somewhat partial advantage compared to the animals was avoided (Macphail, 1996) (but see Rivalan et al., 2011 work). In the absence of such information the final performance usually worsen; therefore, the exploration phase typically lenghtens and the optimal strategy is hardly found in 100 trials (Balodis et al., 2006; Fernie and Tunney, 2006; Glicksohn et al., 2007). However, when more trials are allowed, many individuals performing poorly in the first 100 trials are able to achieve good final performance (Balodis et al., 2006; Buelow et al., 2013; Bull et al., 2015). To that purpose, the number of trials was increased from 100 to 200. A full description of the electronic version of the IGT is given in Giustiniani et al. (2015).

2.5. Mouse gambling task

DM was evaluated using an mGT adapted from published protocols (Pittaras et al., 2016; de Visser et al., 2011). The experiment took place in a completely opaque four-arm radial maze (identical and equidistant arms, 37 cm long and 5.7 cm wide), with the common central zone used as a start-point. Mice were rewarded with grain-based pellets (20 mg Dustless Precision Pellets® Grain-Based Diet, PHYMEP s.a.r.L., Paris, France) or punished with grain-based pellets previously treated with quinine (180 mM quinine hydrochloride, Sigma-Aldrich, Schnelldorf, Germany). Quinine pellets were poorly palatable but edible.

Prior to every experimental session, the animals were acclimatised to the behavioural room for 30 min. The experimental design was composed of 5 blocks of 20 trials over five days (a total of 100 trials per animal). The first ten trials of each block took place during the morning, the second ten trials during the afternoon. Before the first trial of the first block, mice had 3 min to explore and eat inside the maze (*first habituation period*). From the second block, mice had 2 min to explore the maze before the first trial, but no food was available (*general habituation period*). These habituation periods aimed to reduce the stressing effect of the

Please cite this article as: L. Cabeza, J. Giustiniani and T. Chabin et al., Modelling decision-making under uncertainty: A direct comparison study between human and mouse gambling data, European Neuropsychopharmacology, https://doi.org/10.1016/j.euroneuro.2019.11.005

animals' first exposure to the dispositive. After this habituation, mice were placed at the start-point inside an opaque cylindrical structure to avoid early orientation. The cylinder was removed after 5 s and animals were allowed to choose an arm. Mice had one minute to choose an arm, explore it and eat the reward. An extra-minute was given if the choice was not made in time.

Our mGT was adapted in order to minimise the effect of satiety during the task. For that, two arms gave access to a small reward (1 pellet) in the first trial of each half block (trials 1, 11, 21, 31, 41, 51, 61, 71, 81 and 91) and bigger rewards (3–4 pellets) in the other 18 choices of each block with a small probability of presenting a punishment (3–4 quinine pellets, twice in 18 possible choices) (*advantageous arms C'* and *D'*). Arm C' and D' provided a maximal amount of 50 and 66 rewards per block, respectively.

The other two arms (*disadvantageous arms A'* and *B'*) gave access to a bigger reward (2 pellets) during the first trials of each half block, but bigger punishments (4–5 quinine pellets) and a smaller reward-possibility (4–5 pellets, once in 18 possible choices) in the block's remaining 18 choices. Arm A' gave access to a maximal amount of 10 rewards per block, arm B' until 14. Between consecutive trials, the animals were placed in their home cages for 90 s. The localisation of advantageous and disadvantageous arms was randomised with different award and punishment sequences for each animal.

2.6. Determination of interindividual differences

A k-mean clustering method, already used in mouse gambling tasks (Pittaras, 2016; Pittaras et al., 2016), was applied to identify interindividual differences in both, human and mice populations. This enabled the automatic identification of the objects' optimum partition into a specific number of clusters, minimising and maximising the intra and inter-cluster variance, respectively (Timmerman et al., 2013). In accordance with the literature (Pittaras et al., 2016), the mean percentage of advantageous choices was calculated for the tasks' final 30% when performance was highly stable (*W:* $p < 0.01$ in mice and humans). The individual performances were then divided into three groups: *good*, *intermediate* and *poor decision-makers (DMs)*.

2.7. Choice behaviours: rigidity, flexibility, lose-shift and win-stay scores

Maximisation of benefits and the reduction of costs, which characterise optimal performances, require flexibly adapting contingencies in order to favourably orient future choices. To compare different DM strategies, behavioural measures of cognitive processes at the beginning and the end of the task have been calculated. We measured our populations' rigidity score by calculating the highest percentage of choice of a deck or arm. The flexibility score is then the proportion of switches from one deck or arm to another. The lose-shift score, as a measure of negative outcome aversion, was assessed by calculating the proportion of switches after a penalty outcome. Win-stay scores likewise reflect the choice of the same option after receiving a reward. Each behavioural measure was calculated at the beginning (first 40% of the task) and at the end of the experiment (last 40% of the task), according to previous studies (Pittaras et al., 2016).

2.8. Reward sensitivity

In humans, the Behavioural Inhibition and Activation System scales (BIS/BAS) allowed us to approach behavioural motivation (Rizvi et al., 2016). In mice, reward sensitivity was evaluated at the end of the mGT using the sucrose preference test (adapted from Lutz et al., 2013). For details, see Supplementary data.

3. Data analysis

3.1. Whole group analyses

A population's overall performance in terms of the advantageous choices for the gambling tasks was analysed with Bayesian and frequentist approaches. To consider learning rates, the relative risk (the ratio of the 'risk' of success in both populations (humans/mice) – RR) was measured. The resulting proportions were compared by Beta laws, whose parameters are interpreted in terms of the number of successes and failures, establishing the probability law of success rates' ratio. A credibility interval, inside which a parameter has a given probability (CI), was then calculated.

Hereafter, in order to address the behavioural kinetics the performance was divided into five blocks, each representing 20% of the task. The performance of each block was compared to the chance level using Student's tests (*t*-tests). The evolution of the performance was assessed by the analysis of variance (ANOVA), with the factor being 20%-blocks. Differences between populations were analysed using a partially repeated ANOVA with species as the between-subject variable and 20%-blocks as the within-subject variable.

The evolution of choice behaviours scores was first compared for each group using a *t*-test, followed by a comparison of the overall population's scores by two-way repeated-measures ANOVA with factors species and time course (first and last 40% of the task).

BIS/BAS data in humans and sucrose preference in mice were analysed using the Kruskal–Wallis (KW) test (see Supplementary data). Correlations between the endpoint performance (percentage of advantageous choices in the last 30% of the task) and choice behaviours were also carried out. Comparisons were Bonferroni corrected when necessary to account for the multiple comparisons.

3.2. Interindividual data analysis

For each group, the evolution of the gambling performance was assessed by repeated-measures ANOVAs, with the factors being 20%-Blocks and clusters (*good, intermediate* and *poor DMs*), followed by Mann Whitney U (MW) tests to show subgroup differences two by two. Each interindividual distribution was also compared between mice and humans using an MW test.

We used Wilcoxon (W) tests to compare, for each subgroup, the evolution of the gambling performance relative to the chance level. The subgroup's proportions of each population were compared using the Chi-square test. Differences in the choice behaviour scores between the subgroups in mice and humans were assessed by KW tests for the beginning and the end of the task. These measures were also compared between the species using MW tests. All MW and W tests were Bonferroni corrected.

The statistical significance threshold of all the tests was set at $p < 0.05$.

Please cite this article as: L. Cabeza, J. Giustiniani and T. Chabin et al., Modelling decision-making under uncertainty: A direct comparison study between human and mouse gambling data, European Neuropsychopharmacology, https://doi.org/10.1016/j.euroneuro.2019.11.005

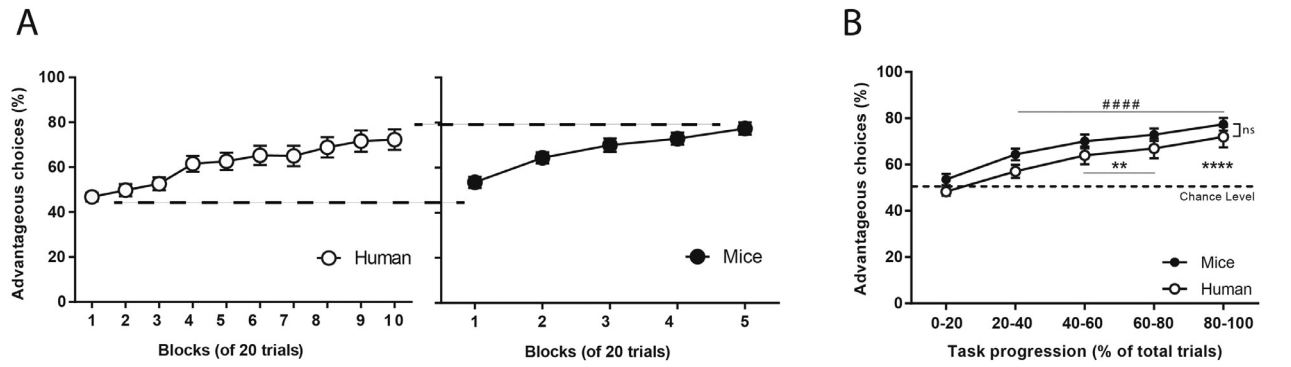


Fig. 1 Gambling performance in human and mice populations.
(A) Performances expressed as percentage of advantageous choices (mean ± SEM) during task progression (blocks of 20 trials). After 100 trials, mice performed better than humans did (CI 95% = 1191 to 1.277), but final performances were similar (CI 95% = 0.956 to 1.016). (B) No significant (ns) differences between species when comparing performance in 20% trial-blocks (repeated measures ANOVA). Human performance differed from chance level from the 3rd 20%-block onwards, while mice performance was already different from the 2nd block (*t*-test: mice: ####, $p < 0.0001$; human: **, $p < 0.01$: ****, $p < 0.0001$).

4. Results

4.1. Overall gambling performance: mice learn faster than humans (Fig. 1 and Supplementary Analysis 1)

The Bayesian analysis revealed a difference in the learning rate between the species (Fig. 1(A)), showing that mice learned faster than humans did: after 100 trials, mice had better overall gambling performance (CI 95% = 1.191 to 1.277). However, comparing the last 100 mice and human trials shows similar performances (CI 95% = 0.956 to 1.016).

In order to circumvent variations in the gambling tasks' designs and to allow for the direct comparison of data, we analysed performance as a function of task progression, expressed as percentages. Splitting all trials into five 20% trial-blocks (Fig. 1(B)) clearly shows that humans acquired the task contingencies after completion of 40% of the task, performing above the chance level from the third 20%-block onwards (*t*-test, $p < 0.01$). A learning effect has been evidenced as the performance gradually improved over time (F (4,156) = 15.4; $p < 0.0001$) after 20% of the task was completed and till the end ($p < 0.0001$, above the behavioural output of the 1st 20%-block).

Mice, however, performed above the chance level already after the first 20% of the task, thus, orientating towards the favourable choices earlier than humans (*t*-test, $p < 0.0001$). The performance progressively improved over time (F (4,195) = 11.9; $p < 0.0001$) from the second 20%-block (2nd block: $p < 0.05$, 3rd block: $p < 0.001$, 4th and 5th blocks: $p < 0.0001$) and compared to the beginning of the task.

The comparison of the IGT and mGT performances shows no significant effect of the species in the percentage of advantageous choices (F (1,78) = 3.1; p = 0.80). Both populations performed similarly along the task progression, as shown by the absence of a statistical difference in the interaction between factors (species and 20%-Blocks) (F (4,312) = 0.06; p = 0.99).

These results show that both species learn the task contingencies, however demonstrating that mice are faster learners than humans are. When compared as function of task progression, both populations display a similar improvement in performance and reach equivalent final performance despite the design differences.

4.2. Comparable categories of good, intermediate and poor DMs with similar proportions among the species (Fig. 2 and Supplementary Fig. 1 and Analyses 2 and 3)

In Figs. 2, A1 and B1 we plot individual data showing larger dispersion in humans than in mice. Intraspecies variability was investigated using k-mean clustering stratification according to the endpoint performance, discriminating three subpopulations: good, intermediate and poor DMs. Individuals majoratively displaying the optimal strategy were referred to as good DMs and represent 42.5% of the human population (mean percentage of advantageous choices ± SEM: 97.4 ± 0.8) and 40% of the mice population (91.3 ± 1.5). Poor DMs remained at around 50% of advantageous choices, hence showing no significant preference for advantageous nor for disadvantageous options, represent 25% of humans (34.3 ± 5.2) and 22.5% of mice (54.1 ± 2.5). The third subpopulation corresponds to individuals that developed a preference towards some options -although they did not find the optimal strategy. These intermediate DMs represent 32.5% of humans (64.5 ± 2.4) and 37.5% of mice (73.8 ± 1.0). The proportions of each subpopulation in humans and mice were compared, and no significant differences were found (Chi-square test = 0.011, p = 0.99; confirmed by Bayesian analysis, see Supplementary Analysis 2) (Figs. 2, A2 and B2).

In humans, good DMs performed above the chance level after 40% of the task was completed (*W*, $p < 0.01$), while intermediate and poor DMs differed from the chance level only in the last 20%-block ($p < 0.05$). Furthermore, the ANOVA revealed a significant interaction between the clusters and 20%-blocks (F (8,148) = 16.2; $p < 0.0001$). Good DMs performed differently than poor DMs from the second

Please cite this article as: L. Cabeza, J. Giustiniani and T. Chabin et al., Modelling decision-making under uncertainty: A direct comparison study between human and mouse gambling data, European Neuropsychopharmacology, https://doi.org/10.1016/j.euroneuro.2019.11.005

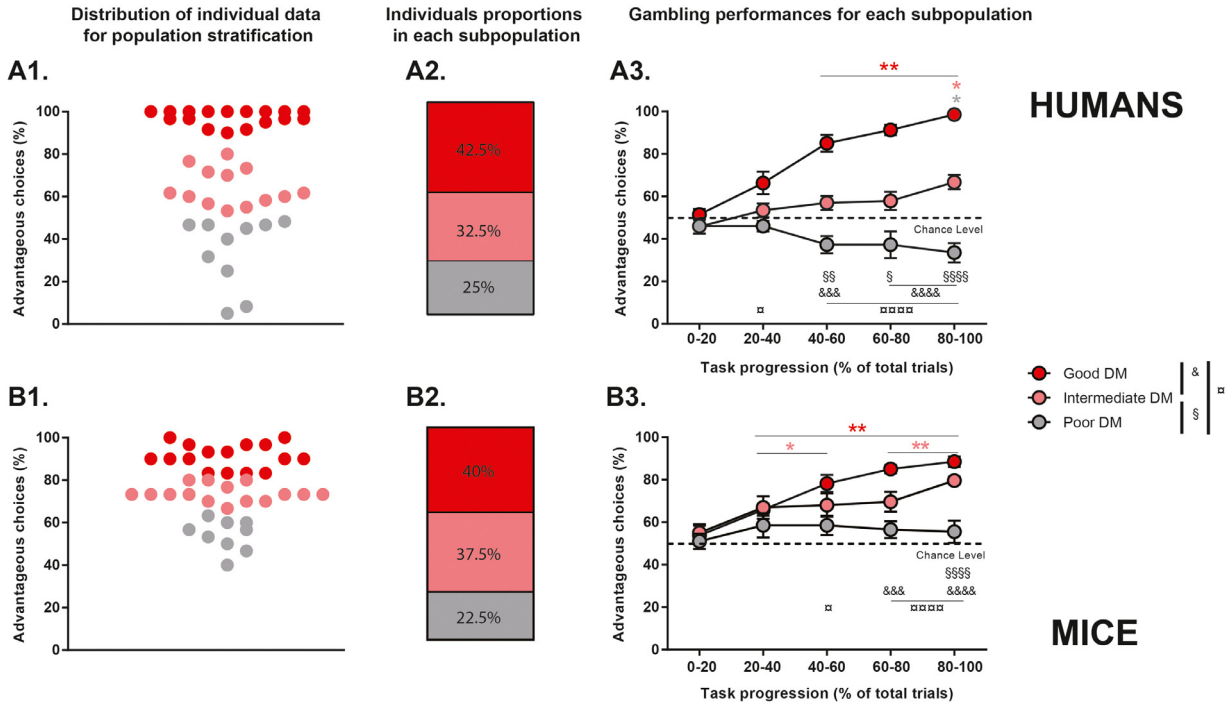


Fig. 2 Comparable categories of good, intermediate and poor DMs with similar proportions among species.
Distribution in humans (A1) and mice (B1) of individual performance at the end of the task used for k-mean clustering.
Proportions in humans (A2) and mice (B2) of individuals in good (red), intermediate (pink) and poor (grey) DM subpopulations (Chi^2, $p = 0.99$).
Gambling performance in human (A3) and mice (B3) during task progression (20% trial-blocks). *W* tests to show group performance different from chance level (50%) (*, $p < 0.05$; **, $p < 0.01$). MW tests to show group differences (good vs intermediate: &, $p < 0.05$; &&, $p < 0.01$; &&&, $p < 0.001$; &&&&, $p < 0.0001$; good vs poor: ¤; intermediate vs poor: §). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

20%-block onwards (MW, 2nd block: $p < 0.05$, 3rd to 5th blocks: $p < 0.0001$), and differently than intermediate DMs in the last 60% of the task (3rd block: $p < 0.001$, 4th and 5th blocks: $p < 0.0001$). Intermediate and poor DMs performed differently from the third block onwards (3rd block: $p < 0.01$, 4th block: $p < 0.05$, 5th block: $p < 0.0001$) (Figs. 2 and A3).

Regarding mouse data, intermediate and good DMs performed above the chance level soon after 20% of the task was completed (*W*, good 2nd to 5th blocks: $p < 0.01$; intermediate 2nd and 3rd blocks: $p < 0.05$, 4th and 5th blocks: $p < 0.01$), while poor DMs did not differ from the chance level ($p > 0.05$). The ANOVA also revealed a significant interaction between the factors ($F(8,185) = 5.3$; $p < 0.0001$). Mice from the good DM category performed differently than poor DMs after 40% of the task was completed (MW, 3rd block: $p < 0.05$, 4th and 5th blocks: $p < 0.0001$), and differently from the intermediate DMs later on (4th block: $p < 0.001$; 5th block; $p < 0.0001$). Mice from the intermediate and poor DM categories performed differently only during the last 20% of the task ($p < 0.0001$).

When comparing the gambling performance in mice and humans for each subpopulation, differences were found for intermediate DMs (MW, $p < 0.05$), with mice making more advantageous choices than humans. On the contrary, humans from the good DM category achieved more advantageous choices than mice of the same subgroup ($p < 0.01$). Furthermore, humans from the poor DM category made worse decisions than mice ($p < 0.01$). In addition, mice from the intermediate subgroup developed a weaker preference for the most advantageous option (D') than good DMs did, whilst humans from the same category chose the best deck (D) as good DMs did (see Supplementary Fig. 1 and Analysis 3).

Collectively these data reveal that both mice and human populations clustered into three comparable DM categories with closely matching proportions. However, the performance dispersion was more pronounced in the human population.

4.3. Relationship between the DM performance and choice behaviours in humans and mice (Fig. 3 and Supplementary Figs. 2 and 3)

4.3.1. Correlations between the endpoint performance and behavioural determinants of DM (Supplementary Fig. 2)

In humans, rigidity scores significantly correlated with the final performance at the beginning ($r = 0.428$, $p < 0.05$) and at the end of the task ($r = 0.489$, $p < 0.01$). Flexibility scores showed a negative correlation with the endpoint

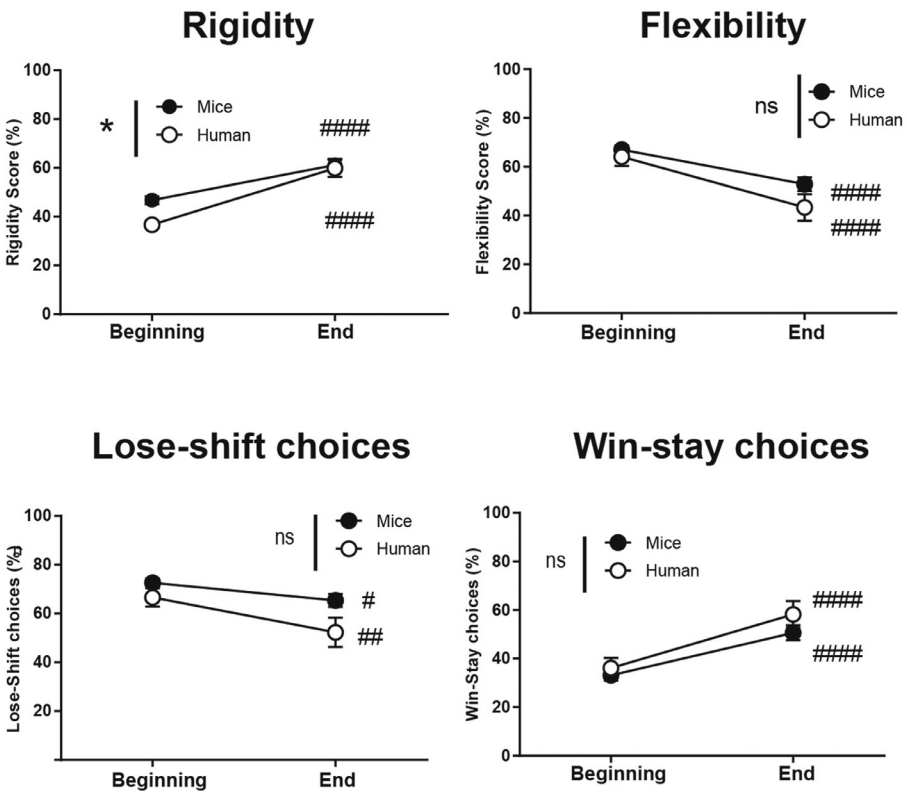


Fig. 3 Evolution of choice behaviors during task progression.
Significant progression of the rigidity, flexibility, lose-shift and win-stay choices for human and mice populations, between the beginning and the end of the task. Comparison of choice strategies at the population level by repeated measures ANOVA and post hoc *t*-tests (beginning vs end of the task: #, $p < 0.05$; ##, $p < 0.01$; ####, $p < 0.0001$; humans vs mice: *, $p < 0.05$).

performance at the beginning of the task ($r = -0.509$, $p < 0.01$), which disappeared at the end ($p > 0.05$). No significant correlation was found for the lose-shift choices and the endpoint performance, independently of the moment of the experiment. However, the win-stay choices at the beginning of the task significantly correlated with the endpoint performance ($r = 0.518$, $p < 0.01$).

In mice, like in humans, rigidity scores significantly correlated with the endpoint performance at the end of the task ($r = 0.669$, $p < 0.001$) but not at the beginning ($p > 0.05$). On the contrary, no correlation was found for flexibility and the endpoint performance at the beginning of the task ($p > 0.05$), but a negative correlation was found at the end ($r = -0.595$, $p < 0.001$). In the same way as humans, no correlation was found regarding the lose-shift choices ($p > 0.05$), but a significant correlation between the win-stay choices and endpoint performance at the end of the task ($r = 0.582$, $p < 0.001$).

In brief, DM strategies in humans and mice seem to rely on comparable adaptive choice behaviours that correlate with the endpoint performance.

4.3.2. Evolution of choice behaviours during task progression (Fig. 3 and Supplementary Fig. 3)

In both populations, a significant effect of the time course was found for flexibility (F (1,78) = 48.4, $p < 0.0001$), lose-shift (F (1,78) = 15.8; $p < 0.001$) and the win-stay scores (F (1,78) = 51.9, $p < 0.0001$) (Fig. 3).

Whereas no global difference among the species was found for any parameters, a significant interaction between the factors (species and time course) was found for rigidity (F (1,78) = 4.6, $p < 0.05$). Both populations became more rigid along the task (*t*-test, $p < 0.0001$), humans were significantly less rigid than mice at the beginning ($p < 0.05$) but not at the end of the experiment ($p = 1$) (Fig. 3).

The interspecies comparisons in all subpopulations revealed that, at the beginning of the task, humans from the intermediate and poor DM categories were significantly less rigid than the corresponding mice (MW, intermediate: $p < 0.0001$; poor: $p < 0.01$) but not good DMs ($p > 0.05$). At the end of the task, this property only remained preserved for humans from the intermediate DM subgroup ($p < 0.01$).

Flexibility scores were similar in both species for the intermediate and poor DMs at the beginning and the end of the experiment ($p > 0.05$). However, humans from the good DM category remained less flexible than mice of the same subgroup throughout the experiment (beginning: $p < 0.05$; end: $p < 0.001$). No subgroup differences in the lose-shift and win-stay choices were observed between the populations at the beginning of the task ($p > 0.05$). In the end, only mice from the good DM category were more prone to switch from an option after a penalty than humans ($p < 0.05$). However, humans from the good DM category continued choosing the same option after a positive outcome more frequently than mice ($p < 0.01$). No differences were found for the other subgroups ($p > 0.05$) (see Supplementary Fig. 3).

Overall, these data show that humans and mice do not differ in their choice strategies at the population level, but suggest there are slight differences in the intermediate and poor DMs subpopulations among the species. Remarkably, mice and humans from the good DM category behaved alike.

5. Discussion

The goal of this study was to directly compare DM under uncertainty between humans and mice using IGT adaptations according to the literature (van den Bos et al., 2006; Giustiniani et al., 2015; Pittaras et al., 2016). Our study shows closely related performance curves when comparing data as a function of task progression, suggesting that our animal model is a suitable candidate to bridge the findings between preclinical and clinical data. Therefore, our study offers a chance to get a better insight into the common conserved cognitive processes among mammals.

Humans rewarded with money and mice rewarded with food started the task with an explorative search, displaying an equal preference for either the advantageous or disadvantageous options. A preference for advantageous choices progressively emerged in both populations during what has been referred to as the exploitation phase (Daniel et al., 2017; Rivalan et al., 2013; de Visser et al., 2011). The overall performance was very similar, however, mice more promptly selected advantageous options than humans. The learning curves observed in our mice confirm previous animal results obtained in similar conditions (Pittaras, 2013; Pittaras et al., 2016) and in other variants of rodent gambling tasks (van Enkhuizen et al., 2014; de Visser et al., 2011).

Mice being faster than humans in developing a favourable strategy could be explained in terms of the rewards' nature, which is considered a major limitation for animal versions of gambling tasks. Modelling loss of reward in animals in a similar manner as in humans is a challenge. Food aids in the survival of species: it is a primary reinforcer since it strengthens behaviour and satiates the basic biological drives. Money, however, is a secondary reinforcer: its value is relative to the primary reinforcer. Hunger and satiety are factors difficult to control, which patently influence animals motivational state (van den Bos et al., 2014; Brevers et al., 2013). However, due to its subjective nature, the interest in money is also difficult to control, which raises similar concerns and can lead to similar consequences. This is the reason why the performance alignment in our mice and human participants is relevant.

In addition to the challenge associated with the reward nature and processing, the internal state (see *the somatic marker theory,* Verdejo-García and Bechara, 2009) and context also generate differences in behaviour. Animal automated operant testing would also help deepen the analysis of motivational aspects for instance (Nithianantharajah et al., 2015).

A good validity of the model should also be substantiated by similar choice strategies, which can be investigated from additional cognitive proxies sub-serving behaviour (Winstanley and Clark, 2015). A closer look at the endpoint performance revealed that they correlated with the choice behaviours similarly but not identically in both populations. In fact, as advantageous choices increased along the task progression, preference for one option progressively emerged (increased rigidity), while fewer options were explored (decreased flexibility) with individuals becoming more sensitive to the reward (increased win-stay choices) and tending to more easily cope with penalties (decreased lose-shift choices).

Our results also highlighted close common interindividual variability in mice and humans when clustered into three subgroups of individuals, ranging from good over intermediate to poor DMs. Whether this clustering reflects the speed of acquiring a favourable strategy, or actually to different behavioural strategies could be further investigated (by a computational modelling analysis, for instance). However, the similar matched proportions of these subgroups for both species strengthen the face validity of our animal model.

Good DMs composed the largest subgroup in both species. Several human studies correlate a good performance predominantly with the development of an optimal strategy, accepting risky options (Barbalat et al., 2010; Charpentier et al., 2017). In mice studies a good performance is related to a secure strategy (Pittaras et al., 2016). Interestingly, mice from this category needed less time than humans to perform above chance level. Regarding the other subgroups, humans from the good DM category developed a stronger preference for one option over the intermediate and poor DMs, whereas mice of the same category differed only from the poor DMs. The evolution of the penalty aversion was also similar for both species, suggesting that the cognitive strategies underlying the DM performance might be similar in both species, at least for the good DM subgroup.

Individuals conforming to the intermediate DM category, while selecting advantageous choices more often, maintained a high level of exploration of all the options but did not achieve the best strategy to maximise their rewards. However, IGT studies have shown that the performance can be significantly enhanced with additional trials (Overman and Pierce, 2013). Furthermore, mice from this category became more sensitive to a reward along the task progression, whereas humans did not. This suggests that intermediate categories might not completely overlap between the species.

The subgroup with the worst performance, poor DMs, maintained the exploration of all the available options, exhibiting high behavioural flexibility. Nevertheless, they did not manage to find a favourable strategy along the task, suggesting an ineffective exploration of options. However, humans from this category ended the task performing significantly below the chance level in terms of the advantageous choices, which did not happen in the animal population. This kind of deleterious preference has also been described in mice following singled-session mGT protocols (van Enkhuizen et al., 2014) and other rodent IGT versions (Rivalan et al., 2009, 2013). Mice performing poorly in the gambling tasks have been proposed as models for the vulnerability of pathological gambling or addiction (van den Bos et al., 2013; Pittaras et al., 2016), in the same line of clinical studies seeking behavioural markers of pathological predisposition or endophenotypes (Cavedini et al., 2010; Zhang et al., 2015). Indeed, these animals seem less risk-averse, a trait that has been already

Please cite this article as: L. Cabeza, J. Giustiniani and T. Chabin et al., Modelling decision-making under uncertainty: A direct comparison study between human and mouse gambling data, European Neuropsychopharmacology, https://doi.org/10.1016/j.euroneuro.2019.11.005

interpreted as an indicator of weaker cognitive control over immediate loss (de Visser et al., 2011).

Concerning the endpoint performance, interindividual variabilities show a larger spread in the human population, accounting for better and worse decisions. The extreme upper scores in humans might be a consequence of a longer gambling design (Balodis et al., 2006; Buelow et al., 2013; Bull et al., 2015). Food restriction in our animals could also explain why they never preferred the disadvantageous options. Noticeably, very low performance more reminiscent of human data than ours (Rivalan et al., 2009, 2013), illustrates that performance output highly depends on task design.

A general common pattern between humans and mice subpopulations has not been fully revealed when the endpoint performance is correlated with choice behaviours. By themselves, rigidity, flexibility and sensitivity to positive and negative outcomes cannot explain the evolution of the performance, neither their emergence, in the three subgroups equally. The IGT alone, unfortunately, does not allow to distinguish reward maximisation from ambiguity aversion for instance; its output is insufficient to determine why a participant selected an option. In this perspective, further behavioural characterisation has been attempted. In humans, we evaluated the motivation to avoid aversive and to approach goal-oriented outcomes, respectively by the behavioural inhibition and activation system's scales (BIS/BAS). The endpoint performance did not correlate with the BIS/BAS scores in humans (data not shown). In parallel, the reward sensitivity assessed by the sucrose preference task in mice did not significantly differ between the subgroups (see Supplementary Fig. 4). These results contrast with those from Pittaras et al. (2016), who described a stronger sucrose preference for good decision-makers ("safe") compared to mice which perform poorly ("risky"). Moreover, reward sensitivity did not correlate with the endpoint performance either (data not shown), whereas poor performance was likely mediated by sensitivity to a high reward in a single session mGT (van Enkhuizen et al., 2014). These apparent discrepancies could be accounted for by protocol variations and suggest complex relationships between reward sensitivity and DM strategies (van Enkhuizen et al., 2014).

A similar overall performance and comparable gambling strategies observed between both species suggest that they share conserved cognitive processes essential for successful DM. A wide range of comparative approaches, in rodents and in humans, have been proposed to discern between these processes during cognitive tasks, both at the attentional and the mnemonic level (Steckler and Muir, 1996). The literature has also shown that there is a strikingly similar range of cognitive abilities between rodents and humans, as well as a remarkably high degree of anatomical overlap in their brain functions (Woolley et al., 2013). Rodents are even able to outperform humans in some learning tasks (Vermaercke et al., 2014), but we do believe that our slightly differing kinetics are mainly accounted for by the task design variability (including the rewards' nature, the number of trials and the tasks 'probabilistic schedule).

To conclude, our data thus far suggest that in DM, mice behave in a way similar to humans: they tend to choose the option with the best long-term payoff more often as the task progresses. Our results point to close patterns of choice behaviours present across species, but the parameters we evaluated are insufficient to draw a firm conclusion for the relationship between reward maximisation and risk aversion. Extensive behavioural characterisations and validated animal models will be crucial to study brain regions and circuits involved in DM, and the relationships between reward and cognitive control systems. Nonetheless, our results directly support good face validity of the mouse version of IGT. Future studies including pathological animal models, manipulations with pharmacological tools or brain stimulation techniques and computational modelling should help disentangle processes sub-serving choice strategies, clarifying DM in animals and humans.

Role of the funding source

This study was supported by grants from the Communauté d'Agglomération du Grand Besançon (LC), the French Eastern Interregional Group of Clinical Research and Innovation (GIRCI Est; appel à projet « jeunes chercheurs », APJ 2015; JG), which had no role in the study design; collection; analysis or interpretation of the data; writing of the report and in the decision to submit the paper for publication.

Contributors

LC, JG, DF, DG, YP conceived and designed the study. LC, JG, TC, BR, CJ, DG, MN, LP, EH performed the experiments. LC, DG, YP wrote the draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

All authors declare no conflicts of interest.

Authors' disclosures

None.

Acknowledgements

The authors thank Dr Ruud van den Bos and Dr Sylvie Granon for their valuable advice in setting up the mGT. We are also grateful to Mr Hervé Reyssie from the *Animal Facilities, Besançon,* for his technical support, and Chrystelle Vidal for statistical support with Bayesian analysis.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.euroneuro.2019.11.005.

References

Balodis, I.M., MacDonald, T.K., Olmstead, M.C., 2006. Instructional cues modify performance on the Iowa Gambling Task. Brain Cognit. 60, 109–117.

Barbalat, G., Domenech, P., Vernet, M., Fourneret, P., 2010. [Risk-taking in adolescence: a neuroeconomics approach]. L'Encephale 36, 147–154.

Barry, D., Petry, N.M., 2008. Predictors of decision-making on the Iowa Gambling Task: independent effects of lifetime history of substance use disorders and performance on the Trail Making Test. Brain Cognit. 66, 243–252.

Bechara, A., 1997. Deciding advantageously before knowing the advantageous strategy. Science 275, 1293–1295.

Bechara, A., Damasio, A.R., 2005. The somatic marker hypothesis: a neural theory of economic decision. Games Econ. Behav. 52, 336–372.

Bechara, A., Damasio, H., 2002. Decision-making and addiction (part I): impaired activation of somatic states in substance dependent individuals when pondering decisions with negative future consequences. Neuropsychologia 40, 1675–1689.

Bechara, A., Damasio, A.R., Damasio, H., Anderson, S.W., 1994. Insensitivity to future consequences following damage to human prefrontal cortex. Cognition 50, 7–15.

Bechara, A., Dolan, S., Denburg, N., Hindes, A., Anderson, S.W., Nathan, P.E., 2001. Decision-making deficits, linked to a dysfunctional ventromedial prefrontal cortex, revealed in alcohol and stimulant abusers.. Neuropsychologia 39, 376–389.

Bechara, A., Dolan, S., Hindes, A., 2002. Decision-making and addiction (part II): myopia for the future or hypersensitivity to reward? Neuropsychologia 40, 1690–1705.

Bechara, A., Tranel, D., Damasio, H., 2000. Characterization of the decision-making deficit of patients with ventromedial prefrontal cortex lesions. Brain 123 (Pt 11), 2189–2202.

van den Bos, R., Koot, S., de Visser, L., 2014. A rodent version of the Iowa Gambling Task: 7 years of progress. Front. Psychol. 5, 203. doi:10.3389/fpsyg.2014.00203.

van den Bos, R., Lasthuis, W., den Heijer, E., van der Harst, J., Spruijt, B., 2006. Toward a rodent model of the Iowa gambling task. Behav. Res. Methods 38, 470–478.

van den Bos, R., Davies, W., Dellu-Hagedorn, F., Goudriaan, A.E., Granon, S., Homberg, J., Rivalan, M., Swendsen, J., Adriani, W., 2013. Cross-species approaches to pathological gambling: a review targeting sex differences, adolescent vulnerability and ecological validity of research tools. Neurosci. Biobehav. Rev. 37, 2454–2471.

Brand, M., Recknor, E.C., Grabenhorst, F., Bechara, A., 2007. Decisions under ambiguity and decisions under risk: correlations with executive functions and comparisons of two different gambling tasks with implicit and explicit rules. J. Clin. Exp. Neuropsychol. 29, 86–99.

Buelow, M.T., Okdie, B.M., Blaine, A.L., 2013. Seeing the forest through the trees: improving decision making on the Iowa gambling task by shifting focus from short- to long-term outcomes. Front. Psychol. 4, 1–10. doi:10.3389/fpsyg.2013.00773.

Buelow, M.T., Suhr, J.A., 2009. Construct validity of the Iowa Gambling Task. Neuropsychol. Rev. 19, 102–114.

Brevers, D., Bechara, A., Cleeremans, A., Noël, X., 2013. Iowa Gambling Task (IGT): twenty years after – gambling disorder and IGT. Front. Psychol. 4, 665. doi:10.3389/fpsyg.2013.00665.

Bull, P.N., Tippett, L.J., Addis, D.R., 2015. Decision making in healthy participants on the Iowa Gambling Task: new insights from an operant approach. Front. Psychol. 6, 1–17. doi:10.3389/fpsyg.2015.00391.

Cavedini, P., Zorzi, C., Piccinni, M., Cavallini, M.C., Bellodi, L., 2010. Executive dysfunctions in obsessive-compulsive patients and unaffected relatives: searching for a new intermediate phenotype. Biol. Psychiatry 67, 1178–1184.

Charpentier, C.J., Aylward, J., Roiser, J.P., Robinson, O.J., 2017. Enhanced risk aversion, but not loss aversion, in unmedicated pathological anxiety. Biol. Psychiatry 81, 1014–1022.

Daniel, M.L., Cocker, P.J., Lacoste, J., Mar, A.C., Houeto, J.L., Belin-Rauscent, A., Belin, D., 2017. The anterior insula bidirectionally modulates cost-benefit decision-making on a rodent gambling task. Eur. J. Neurosci. 46, 2620–2628.

Davis, C., Fox, J., Patte, K., Curtis, C., Strimas, R., Reid, C., McCOOL, C., 2008. Education level moderates learning on two versions of the Iowa Gambling Task. J. Int. Neuropsychol. Soc. 14, 1063–1068.

van Enkhuizen, J., Geyer, M.A., Young, J.W., 2013. Differential effects of dopamine transporter inhibitors in the rodent Iowa gambling task: relevance to mania. Psychopharmacology 225, 661–674.

van Enkhuizen, J., Henry, B.L., Minassian, A., Perry, W., Milienne-Petiot, M., Higa, K.K., Geyer, M.A., Young, J.W., 2014. Reduced dopamine transporter functioning induces high-reward risk-preference consistent with bipolar disorder. Neuropsychopharmacology 39, 3112–3122.

de Visser, L., Homberg, J., Mitsogiannis, M., Zeeb, F.D., Rivalan, M., Fitoussi, A., Galhardo, V., van den Bos, R., Winstanley, C.A., Dellu-Hagedorn, F., 2011. Rodent versions of the Iowa gambling task: opportunities and challenges for the understanding of decision-making. Front. Neurosci. 5, 1–21. doi:10.3389/fnins.2011.00109.

Fernie, G., Tunney, R.J., 2006. Some decks are better than others: the effect of reinforcer type and task instructions on learning in the Iowa gambling task. Brain Cognit. 60, 94–102.

Festing, M.F.W., 2014. Evidence should trump intuition by preferring inbred strains to outbred stocks in preclinical research. ILAR J. 55, 399–404.

de Froment, A.J., Rubenstein, D.I., Levin, S.A., 2014. An extra dimension to decision-making in animals: the three-way trade-off between speed, effort per-Unit-Time and accuracy. PLoS Comput. Biol. 10, e1003937.

Giustiniani, J., Gabriel, D., Nicolier, M., Monnin, J., Haffen, E., 2015. Neural correlates of successful and unsuccessful strategical mechanisms involved in uncertain decision-making. PLoS One 10, e0130871.

Glicksohn, J., Naor-Ziv, R., Leshem, R., 2007. Impulsive decision-making: learning to gamble wisely? Cognition 105, 195–205. doi:10.1016/j.cognition.2006.08.003.

Heilbronner, S.R., 2017. Modeling risky decision-making in nonhuman animals: shared core features. Curr. Opin. Behav. Sci. 16, 23–29.

Lehner, R., Balsters, J.H., Herger, A., Hare, T.A., Wenderoth, N., 2017. Monetary, food, and social rewards induce similar Pavlovian-to-instrumental transfer effects. Front. Behav. Neurosci. 10, 1–12. doi:10.3389/fnbeh.2016.00247.

Lutz, P.E., Reiss, D., Ouagazzal, A.M., Kieffer, B.L., 2013. A history of chronic morphine exposure during adolescence increases despair-like behaviour and strain-dependently promotes sociability in abstinent adult mice. Behav. Brain Res. 243, 44–52.

Macphail, E.M., 1996. Cognitive function in mammals: the evolutionary perspective. Brain Res. Cognit. Brain Res. 3, 279–290.

Meyer, G., 2004. Neuroendocrine response to casino gambling in problem gamblers. Psychoneuroendocrinology 29, 1272–1280.

Meyer, G., Hauffa, B.P., Schedlowski, M., Pawlak, C., Stadler, M.A., Exton, M.S., 2000. Casino gambling increases heart rate and salivary cortisol in regular gamblers. Biol. Psychiatry 48, 948–953.

Miedl, S.F., Fehr, T., Meyer, G., Herrmann, M., 2010. Neurobiological correlates of problem gambling in a quasi-realistic blackjack scenario as revealed by fMRI. Psychiatry Res. Neuroimaging 181, 165–173.

Please cite this article as: L. Cabeza, J. Giustiniani and T. Chabin et al., Modelling decision-making under uncertainty: A direct comparison study between human and mouse gambling data, European Neuropsychopharmacology, https://doi.org/10.1016/j.euroneuro.2019.11.005

Nithianantharajah, J., McKechanie, A.G., Stewart, T.J., Johnstone, M., Blackwood, D.H., St Clair, D., Grant, S.G.N., Bussey, T.J., Saksida, L.M., 2015. Bridging the translational divide: identical cognitive touchscreen testing in mice and humans carrying mutations in a disease-relevant homologous gene. Sci. Rep. 5, 14613.

Overman, W.H., Pierce, A., 2013. Iowa gambling task with non-clinical participants: effects of using real + virtual cards and additional trials. Front. Psychol. 4, 1–15. doi:10.3389/fpsyg.2013.00935.

Pittaras, E., 2013. Mice gamble for food: individual differences in risky choices and prefrontal cortex serotonin. J. Addict. Res. Ther. 1 (S4:011), 1–9. doi:10.4172/2155-6105.S4-011.

Pittaras, E., 2016. Marqueurs Comportementaux Et Neurochimiques Individuels De La Prise De Décision Chez La Souris Et Effets D'une Dette De Sommeil. Université Paris-Saclay.

Pittaras, E., Callebert, J., Chennaoui, M., Rabat, A., Granon, S., 2016. Individual behavioral and neurochemical markers of unadapted decision-making processes in healthy inbred mice. Brain Struct. Funct. 221, 4615–4629.

Prendergast, B.J., Onishi, K.G., Zucker, I., 2014. Female mice liberated for inclusion in neuroscience and biomedical research. Neurosci. Biobehav. Rev. 40, 1–5.

Rivalan, M., Ahmed, S.H., Dellu-Hagedorn, F., 2009. Risk-prone individuals prefer the wrong options on a rat version of the Iowa Gambling Task. Biol. Psychiatry 66, 743–749.

Rivalan, M., Coutureau, E., Fitoussi, A., Dellu-Hagedorn, F., 2011. Inter-Individual decision-making differences in the effects of cingulate, orbitofrontal, and prelimbic cortex lesions in a rat gambling task. Front. Behav. Neurosci 5, 1–10. doi:10.3389/fnbeh.2011.00022.

Rivalan, M., Valton, V., Seriès, P., Marchand, A.R., Dellu-Hagedorn, F., 2013. Elucidating poor decision-making in a rat gambling task. PLoS One 8, e82052.

Rizvi, S.J., Pizzagalli, D.A., Sproule, B.A., Kennedy, S.H., 2016. Assessing anhedonia in depression: potentials and pitfalls. Neurosci. Biobehav. Rev. 65, 21–35.

Singh, V., 2016. Sex-Differences, handedness, and lateralization in the Iowa Gambling Task. Front. Psychol. 7, 1–15. doi:10.3389/fpsyg.2016.00708.

Steckler, T., Muir, J.L., 1996. Measurement of cognitive function: relating rodent performance with human minds. Brain Res. Cognit. Brain Res. 3, 299–308.

Steingroever, H., Wetzels, R., Horstmann, A., Neumann, J., Wagenmakers, E.-J., 2013. Performance of healthy participants on the Iowa Gambling Task. Psychol. Assess. 25, 180–193.

Suhr, J.A., Tsanadis, J., 2007. Affect and personality correlates of the Iowa Gambling Task. Personal. Individ. Differ. 43, 27–36.

Timmerman, M.E., Ceulemans, E., De Roover, K., Van Leeuwen, K., 2013. Subspace K-means clustering. Behav. Res. Methods 45, 1011–1023.

Tuttle, A.H., Philip, V.M., Chesler, E.J., Mogil, J.S., 2018. Comparing phenotypic variation between inbred and outbred mice. Nat. Methods 15, 994–996.

Verdejo-García, A., Bechara, A., 2009. A somatic marker theory of addiction. Neuropharmacology 56, 48–62.

Vermaercke, B., Cop, E., Willems, S., D'Hooge, R., Op de Beeck, H.P., 2014. More complex brains are not always better: rats outperform humans in implicit category-based generalization by implementing a similarity-based strategy. Psychon. Bull. Rev. 21, 1080–1086.

de Visser, L., Baars, A.M., Lavrijsen, M., van der Weerd, C.M.M., van den Bos, R., 2011. Decision-making performance is related to levels of anxiety and differential recruitment of frontostriatal areas in male rats. Neuroscience 184, 97–106.

Winstanley, C.A., Clark, L., 2015. Translational models of gambling-related decision-making. In: Robbins, T.W., Sahakian, B.J. (Eds.), Translational Neuropsychopharmacology. Springer International Publishing, Cham, pp. 93–120.

Woolley, D.G., Laeremans, A., Gantois, I., Mantini, D., Vermaercke, B., Op de Beeck, H.P., Swinnen, S.P., Wenderoth, N., Arckens, L., D'Hooge, R., 2013. Homologous involvement of striatum and prefrontal cortex in rodent and human water maze learning. Proc. Natl. Acad. Sci. 110, 3131–3136.

Young, J.W., van Enkhuizen, J., Winstanley, C.A., Geyer, M.A., 2011. Increased risk-taking behavior in dopamine transporter knockdown mice: further support for a mouse model of mania. J. Psychopharmacol. 25, 934–943.

Zeeb, F.D., Winstanley, C.A., 2013. Functional disconnection of the orbitofrontal cortex and basolateral amygdala impairs acquisition of a rat gambling task and disrupts animals' ability to alter decision-making behavior after reinforcer devaluation. J. Neurosci. 33, 6434–6443.

Zeeb, F.D., Robbins, T.W., Winstanley, C.A., 2009. Serotonergic and dopaminergic modulation of gambling behavior as assessed using a novel rat gambling task. Neuropsychopharmacology 34, 2329–2343.

Zhang, L., Dong, Y., Ji, Y., Zhu, C., Yu, F., Ma, H., Chen, X., Wang, K., 2015. Dissociation of decision making under ambiguity and decision making under risk: a neurocognitive endophenotype candidate for obsessive-compulsive disorder. Prog. Neuropsychopharmacol. Biol. Psychiatry 57, 60–68.

Please cite this article as: L. Cabeza, J. Giustiniani and T. Chabin et al., Modelling decision-making under uncertainty: A direct comparison study between human and mouse gambling data, European Neuropsychopharmacology, https://doi.org/10.1016/j.euroneuro.2019.11.005