Multi-dimensional reward evaluation in mice

Vladislav Nachev[1,*,†,§], Marion Rivalan[1,†,§], York Winter[1,§]

[1] Humboldt University, Berlin, Germany

[*]**For correspondence:** vladislav.nachev@charite.de
[†]These authors contributed equally to this work

Present Address: [§]Dept. of Biology, Humboldt University, Philippstr. 13, 10099 Berlin, Germany

Abstract

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Introduction

(Levy and Glimcher 2012)

Results

In order to test how (contradicting) information from two different dimensions is integrated and weighed, we performed a series of choice experiments (1-4, in chronological order) with mice in automated group cages (Rivalan, Winter, and Nachev 2017). The cages were outfitted with four computer-controlled liquid dispensers that delivered drinking water as a reward. During each of the 18h-long drinking sessions each mouse had access to all dispensers, but received rewards at only two of them. The two rewarding dispensers differed on one or both reward dimensions, probability and volume (Rivalan, Winter, and Nachev 2017). An overview of the differences between choice options in the different experimental conditions is given in Table 1. All experiments were conducted with three different cohorts of eight mice each. Cohort 2 was housed in a different automated group cage than cohorts 1 and 3 (See Animals, Materials, and Methods for differences between cages).

Experiment 1

In the baseline conditions rewards only differed on one dimension (the relevant dimension), but not on the other dimension (the background dimension). For example, in the BVP1 condition (read as baseline for volume at probability 1), both options had the same probability of 0.2, but one option had a volume of 4 μL and the other, a volume of 20 μL (Table 1). Based on previous experiments (Rivalan, Winter, and Nachev 2017), we expected a baseline difference between 4 μL and 20 μL volumes to result in a similar discrimination performance (relative preference for the superior option) compared to a baseline difference between probabilities 0.2 and 0.5. In the C (congruent) condition one option was superior to the other on both dimensions. Finally, in the I (incongruent) condition each of the two options was superior to the other on one of the two reward dimensions. Since the differences on both dimensions were chosen to be comparable, we expected the mean discrimination performance in the incongruent condition to be at chance level (0.5). In experiment 1 and in all subsequent experiments, each mouse had its own individual sequence of conditions, but each condition was followed by a reversal in the next drinking session, with a spatial inversion of the two rewarding dispensers. In order to investigate how the two reward dimensions contributed towards choice, we looked at the contrasts between the baselines (when only one dimension was relevant) to the conditions when the two dimensions were congruent or incongruent to each other. We used equivalence tests (Lakens 2017) with an *a priori* smallest effect size of interest (sesoi) of 0.1, i.e. we only considered absolute differences of at least 0.1 percentage points to be of biological relevance. Smaller differences, regardless of their statistical significance using other tests, were considered to be trivial.

Table 1: Overview of the experimental conditions in all four experiments.

		option A			option B			A/B
experiment[a]	condition	volume[b]	probability	return[c]	volume[b]	probability	return[c]	relative return
1	BPV1	4	0.2	0.8	4	0.5	2.0	0.40
1	BPV2	20	0.2	4.0	20	0.5	10.0	0.40
1	BVP1[c]	4	0.2	0.8	20	0.2	4.0	0.20
1	BVP2	4	0.5	2.0	20	0.5	10.0	0.20
1	C	4	0.2	0.8	20	0.5	10.0	0.08
1	I	4	0.5	2.0	20	0.2	4.0	0.50
2	BPV1	4	0.2	0.8	4	1.0	4.0	0.20
2	BPV2	20	0.2	4.0	20	1.0	20.0	0.20
2	BVP2	4	1.0	4.0	20	1.0	20.0	0.20
2	C	4	0.2	0.8	20	1.0	20.0	0.04
2	I	4	1.0	4.0	20	0.2	4.0	1.00
3	PV1	4	0.2	0.8	4	0.5	2.0	0.40
3	PV2	10	0.2	2.0	10	0.5	5.0	0.40
3	PV3	15	0.2	3.0	15	0.5	7.5	0.40
3	PV4	20	0.2	4.0	20	0.5	10.0	0.40
3	VP1	4	0.2	0.8	10	0.2	2.0	0.40
3	VP2	4	0.5	2.0	10	0.5	5.0	0.40
3	VP3	4	0.7	2.8	10	0.7	7.0	0.40
3	VP4	4	0.8	3.2	10	0.8	8.0	0.40

[a] conditions in experiment 1 and 4 were identical; only conditions for experiment 1 are shown here for brevity;
[b] the volumes (in microliters) shown are for cohorts 1 and 3. In cohort 2 the volumes were 4.8 instead of 4, 9.6 instead of 10, 14.4 instead of 15, and 20.8 instead of 20 microliters;
[c] condition BVP1 in experiment 1 was not repeated in experiment 2, but instead the results from experiment 1 were used in further analyses
[d] expected return rate

Compared to the baselines, mice showed an increase in discrimination performance in the congruent condition and a decrease in performance in the incongruent condition (Fig. 2). Contrary to our expectations, the trade-off between volume and probability did not abolish preference in the incongruent condition (Fig. 1). The mean discrimination performance in the incongruent condition was higher than the chance level of 0.5 (lower 95%CI $<$ mean $<$ upper 95%CI, $0.512 < 0.572 < 0.634$). Thus, the volume dimension exerted a stronger influence on choice, at least in absolute terms.

Experiment 2

In previous experiments (Rivalan, Winter, and Nachev 2017), we had shown that the relative stimulus intensity, i.e. the absolute difference between two options divided by their mean, was a good predictor of discrimination performance for both volume and probability differences. Another finding from these experiments was that, at least initially, mice responded less strongly to differences in volume than to differences in probability, despite equivalence in return rates (Rivalan, Winter, and Nachev 2017). We tried to correct for this in experiment 1 by selecting options with a higher relative intensity for volume (4 μL vs. 20 μL, rel.int. =

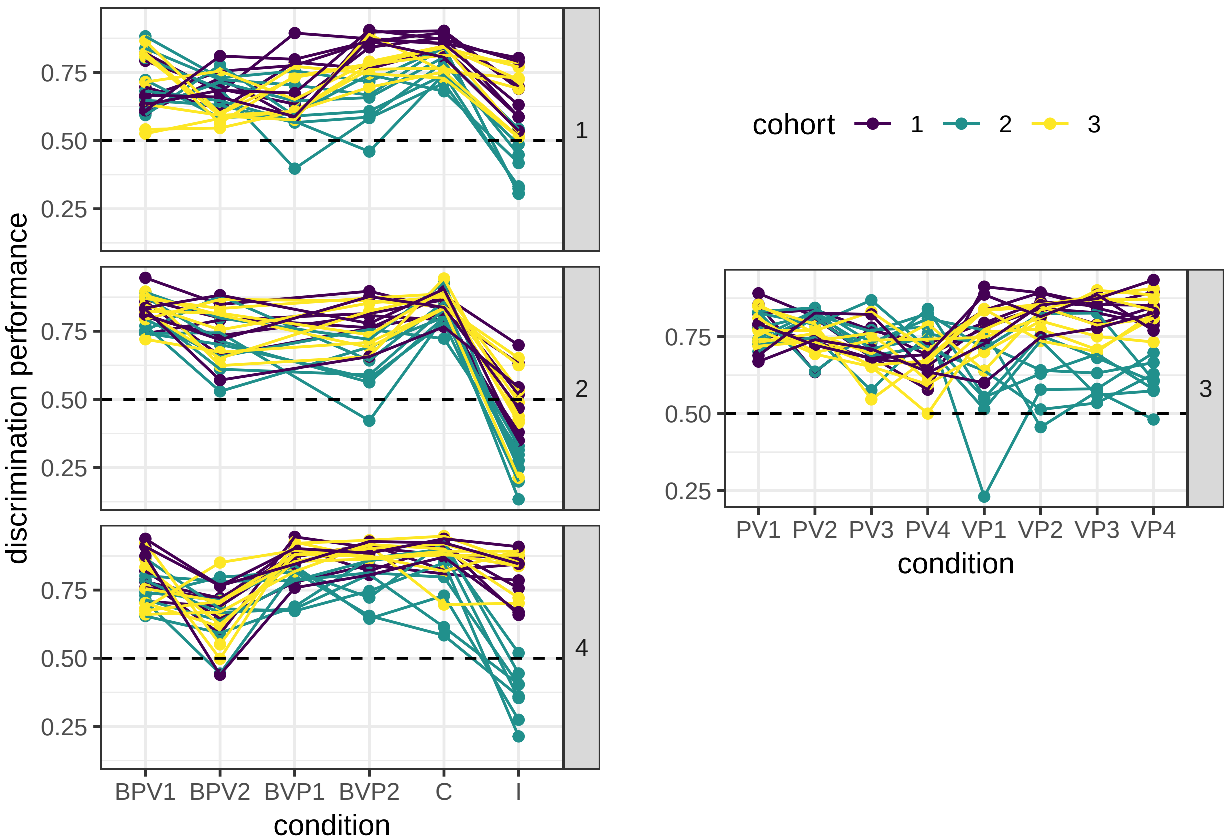

Figure 1: **Overview of discrimination performance for all mice in all experiments.** Experiments 1 through 4 are shown in different panels (1-4). Each symbol is the mean discrimination performance of an individual mouse over two presentations of the same condition (original and reversal). The experimental conditions are described in detail in Table 1. The discrimination performance gives the relative visitation rate of the more profitable option, or, in the incongruent condition, the option with the higher volume. Dashed line gives the chance level of 0.5. Data are shown in different colors for three different cohorts of eight mice each (total $N = 24$). Data from the same individuals are connected with lines. Cohort 2 (green symbols and lines) was tested in a different cage set-up than cohorts 1 and 2 (see Animals, Materials, and Methods for details).

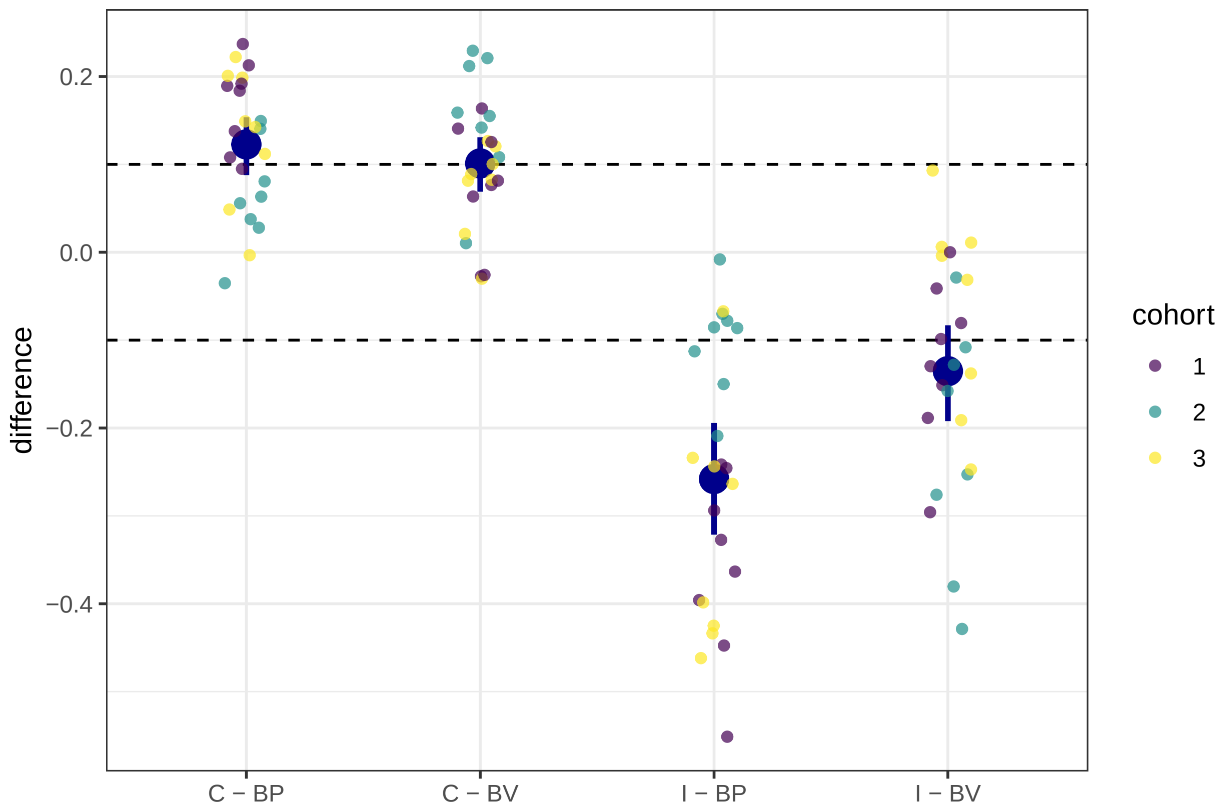

Figure 2: **Difference between discrimination performance in the baseline conditions and in the congruent and incongruent conditions in experiment 1**. Symbols show the individual differences in discrimination performance for the given conditions of each individual mouse ($N = 24$). Mice from different cohorts are shown in different colors. Large blue symbols give the means and the blue vertical lines the 90%-confidence intervals from bootstraps, corrected for multiple comparisons. When the confidence intervals lie completely within the smallest effect size of interest (sesoi) interval bounded by the dashed lines, there is statistical support for equivalence (Lakens 2017). When the confidence intervals do not cross the zero line, there is statistical support for difference. If the confidence intervals cross the zero line, but are not completely bounded by the sesoi, the results are inconclusive. The discrimination performances in the baseline conditions were calculated from the mean values from the two different baseline conditions for each reward dimension (volume and probability), i.e. BP was the mean of BPV1 and BPV2, and BV was the mean of BVP1 and BVP2 (Table 1). The discrimination performance in the incongruent condition was calculated as the relative preference for the higher probability dispenser when contrasted with the probability baseline (I - BP) and for the higher volume dispenser when contrasted with the volume baseline (I - BV).

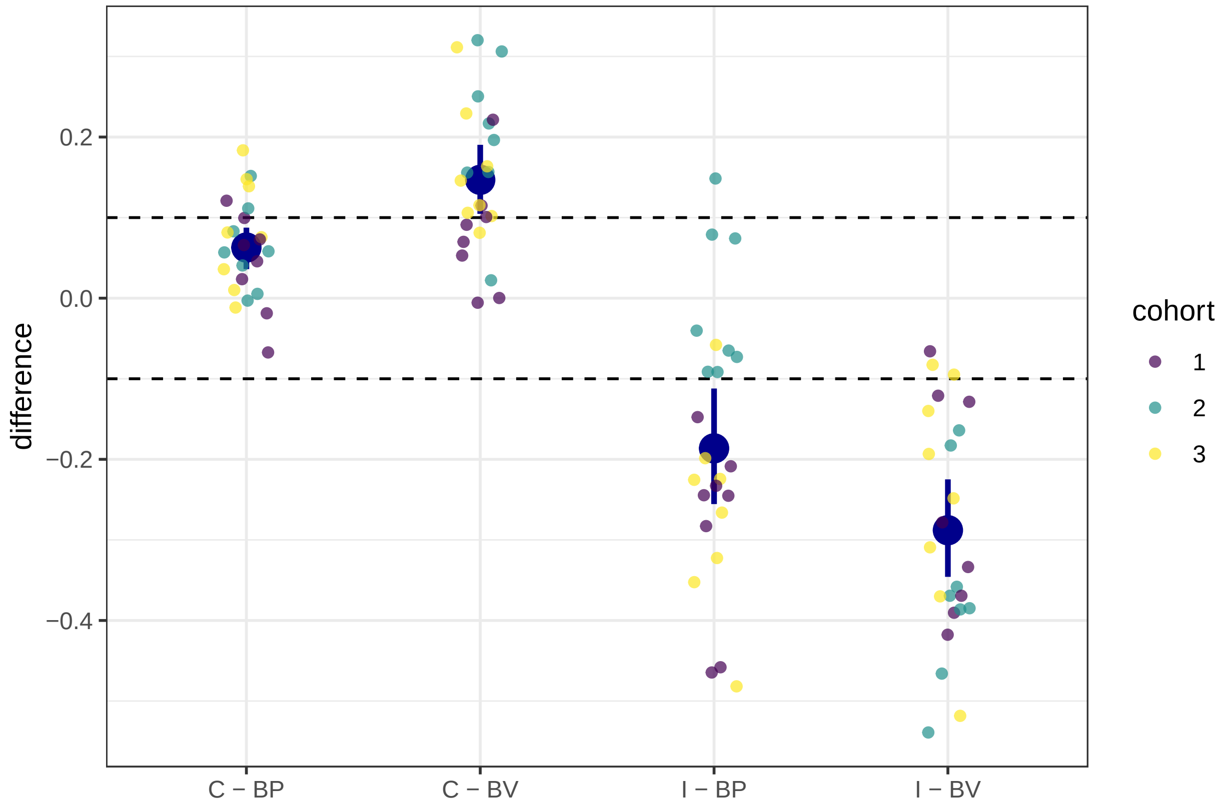

Figure 3: **Difference between discrimination performance in the baseline conditions and in the congruent and incongruent conditions in experiment 2**. Same notation as in Fig. 2. The discrimination performances in the baseline conditions were calculated from the mean values from the two different baseline conditions for each reward dimension (volume and probability), i.e. BP was the mean of BPV1 and BPV2, and BV was the mean of BVP1 and BVP2, where the values for condition BVP1 were taken from experiment 1 (Table 1). The discrimination performance in the incongruent condition was calculated as the relative preference for the higher probability dispenser when contrasted with the probability baseline (I - BP) and for the higher volume dispenser when contrasted with the volume baseline (I - BV).

1.33) than for probability (0.2 vs. 0.5, rel.int. = 0.857). In order to test whether we had over-corrected for decreased sensitivity to volume in experiment 1, we performed a slightly modified version, experiment 2, which was the same, but with probability of 1 instead of 0.5 in every choice option (Table 1). Thus, with the two choice options having the same relative intensities (rel.int. = 1.33) and being equivalent in return rates, we expected the discrimination performance in the incongruent condition to be at chance level if both dimensions were equally weighed and equally perceived. On the other hand, if mice were less sensitive for volume than for probability differences as in our previous experiments, then the discrimination performance in the incongruent condition should be skewed towards probability (< 0.5).

In contrast to experiment 1, in experiment 2 mice showed an increase in discrimination performance in the congruent condition only when compared to the volume baseline, but not when compared to the probability baseline (Fig. 3). As in experiment 1, the discrimination performance in the incongruent condition was lower than in either of the two baselines (Fig. 3). Although the discrimination performance in the incongruent condition was again different from 0.5 ($0.349 < 0.407 < 0.472$), it was lower than chance, thus skewed towards probability (Fig. 1).

Experiment 3

In the previous experiments we used two different baseline conditions for each dimension (BPV1, BPV2, BVP1, and BVP2, Table 1), in order to exhaust all combinations of reward stimuli and balance the experimental design. But could it be that the level of the background dimension despite being the same across choice options nevertheless affects the discrimination performance on the relevant dimension? Researches have proposed that in multidimensional choice the decision process can be considerably simplified if differences that are (nearly) equal are are not evaluated but ignored (Tversky 1969; Shafir 1994; Shafir and Yehonatan 2014). Thus we can predict that regardless of the level of the background dimension, the discrimination performance on the relevant dimension should remain constant. Alternatively, animals could use all information from every reward dimensions for the estimation of a single value (utility) (Tversky 1969; Shafir 1994; Shafir and Yehonatan 2014). Since the utility curve is generally assumed to progressively increase with the increase in any given good, but with a decreasing slope (Kahneman and Tversky 1979; Kenrick et al. 2009; but see also Kacelnik and Brito e Abreu 1998), we may expect that as the background dimension increases the subjective difference between the options will decrease and the discrimination performance will also decrease as a result. An alternative hypothesis is that as the probability of reward increases, In order to test whether the two reward dimensions (volume and probability) interact with each other even when one of them is irrelevant (being the same across choice options), we performed experiment 3.

The conditions in experiment 3 were chosen to be similar to the background conditions in the previous experiments, by having one background and one relevant dimension (Table 1). The relevant dimension always differed between the two options. For the probability dimension, we took the same values of 0.2 and 0.5 (rel.int. = 0.86), as in the previous experiments. For the volume dimension we took the values of 4 μL (4.8 μL in cohort 2) and 10 μL (9.6 μL in cohort 2), because the combination of a higher volume with a probability of 0.8 was expected to result in an insufficient number of visits for analysis (Table 1). Cohort 2 had different reward volumes due to differences in the pumping process (Animals, Materials, and Methods), which also resulted in a lower relative intensity for volume (0.67 instead of 0.86). There were four different levels for each background dimension (volume and probability, Table 1). Each mouse had its own pseudo-random sequence of the eight possible conditions. As in all other experiments, each condition was followed by a reversal. In order to test whether the background dimension affected discrimination performance, we fitted linear mixed models for each dimension, with discrimination performance as the dependent variable, background level as the independent variable and mouse as a random variable, using lme4 in R (Bates et al. 2015). The background level was the proportion of the actual value to the maximum of the four values tested, e.g. the background levels for volumes 4, 10, 15, 20 were 0.2, 0.5, 0.75, 1, respectively. We defined *a priori* a smallest effect size of interest (sesoi), as 0.125, which is the slope that would result from a difference of 0.1 in discrimination performance between the smallest and the largest background levels (PV1 and PV4, 0.2 and 1, respectively). A slope (whether positive or negative) within the sesoi interval was considered equivalent to zero and demonstrating a lack of an effect of background dimension.

The results of experiment 3 show that the discrimination performance on the relevant dimension was independent from the level of the background dimension, because the slope was equivalent to zero for both probability and volume (Fig. 1, Fig. 4). These results support the hypothesis that reward dimensions may be ignored if options do not vary along them.

Experiment 4

In previous experiments (Rivalan, Winter, and Nachev 2017), mice showed an improved discrimination performance for volume over time. A potential explanation is that, with experience mice become more attuned to the relevant dimension [More references and explanation on selective attention in multi-attribute choice here. . .]

In order to test whether the discrimination performance for one or both dimensions improves over time, we performed experiment 4, which had the same conditions as experiment 1, but with a new pseudo-random order. The same mice participated in all experiments (1-4), with about seven weeks between experiment 1 and experiment 4. We tested the discrimination performance of all mice in each experimental condition

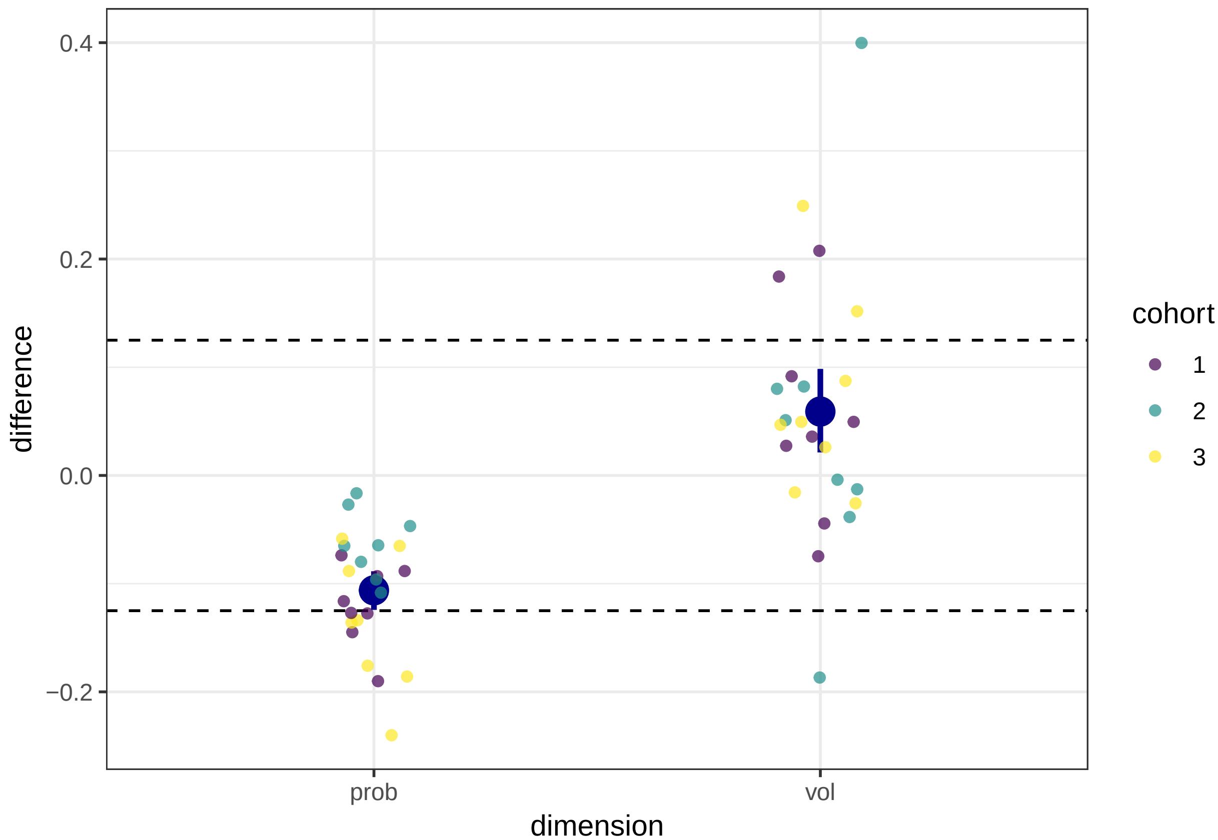

Figure 4: **Slope estimates for the effect of the background dimension on the discrimination performance in the relevant dimension**. The two choice options always differed along the relevant dimension (either probability or volume, given on the abscissa) at a fixed relative intensity. The discrimination performance for each mouse was measured at four different levels of the background dimension, which was set at the same values on both choice options during a single drinking session, but differed from condition to condition (Table 1). Each symbol is the average for an individual mouse over the two presentations of the same condition (original and reversal). The smallest effect size of interest was determined to be the slope that would have resulted in a difference in discrimination performance of 0.1, from the lowest to the highest level of the background dimension. The remaining notation is the same as in Fig. 2.

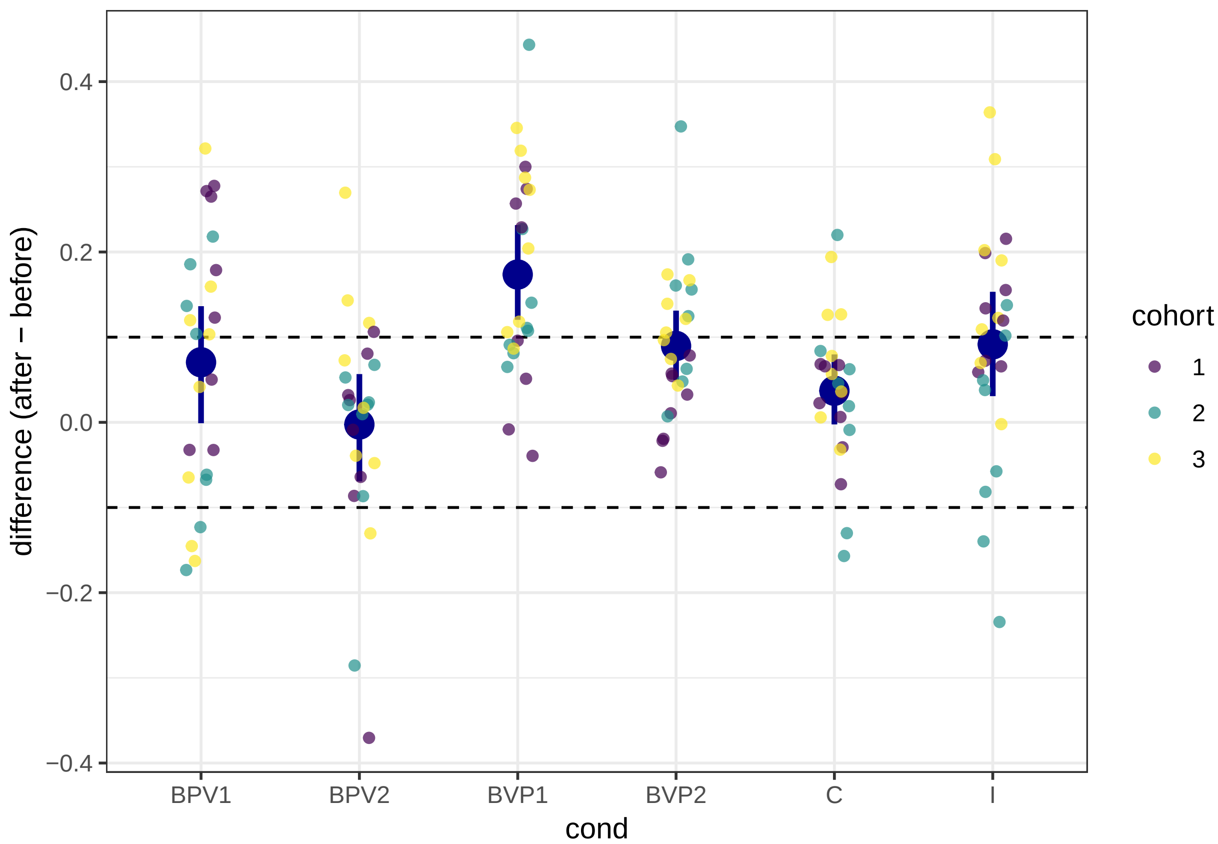

Figure 5: **Difference in discrimination performance between identical conditions in experiment 1 and experiment 4**. Same notation as in in Fig. 2. The sequence of conditions was pseudo-random in each experiment and different for each individual. Positive differences indicate an increase in discrimination performance with time. Mice were seven weeks old at the beginning of experiment 1 and 13-14 weeks old at the beginning of experiment 4. The discrimination performance in the incongruent condition was calculated as the relative preference for the higher volume dispenser.

for equivalence (Table 1). As in the previous experiments, we also used equivalence tests on the contrasts between the baselines and the congruent and incongruent conditions.

When comparing experiment 1 to experiment 4, mice showed an improved discrimination performance in both volume baselines and in the incongruent condition (Fig. 5). There was no change in the BVP2 and C conditions, and the results for BPV1 were inconclusive (confidence interval crosses zero line and not completely bounded by sesoi). Thus, consistent with our prior findings mice get better at discriminating volumes over time. Consequently, the discrimination performance in the congruent condition was better than in the probability baseline, but the same as in the volume baseline (Fig. 6). The discrimination in the incongruent condition was lower than in any of the two baselines, but the difference to the volume baseline was smaller (Fig. 6). Thus, as in our previous experiments, mice showed an improvement in volume discrimination over time. Furthermore, compared to experiment 1 the influence of the volume dimension on choice was even more pronounced.

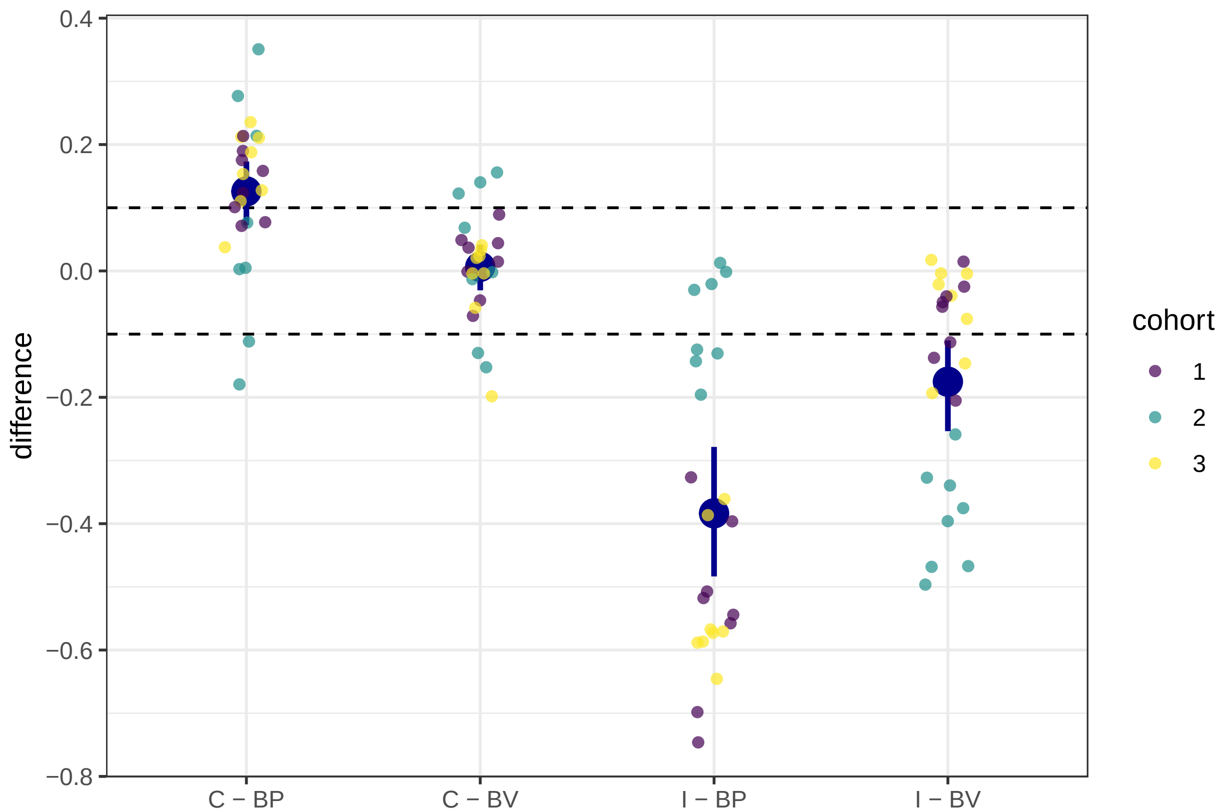

Figure 6: **Difference between discrimination performance in the baseline conditions and in the congruent and incongruent conditions in experiment 4**. Same notation as in Fig. 2. The discrimination performance in the incongruent condition was calculated as the relative preference for the higher probability dispenser when comparing to the probability baseline and for the higher volume dispenser when comparing to the volume baseline. Compare to Fig. 2.

Recursive Bayesian learning models (or simplify considerably without trial-by-trial analysis)

Rather than fitting models to the observed data we took a “learning by building” approach by generating data from different decision models and comparing the resulting posterior distributions of discrimination performances to the observed distribitions of the mice in our experiments. For quantifying the differences between the distributions, we calculated the root-mean-square-deviations (RMSD) from the medians to the individual discrimination performances of each mouse in each condition of each experiment. We could then rank model performance by the RMSD scores.

The models we considered were different implementations of the same recursive Bayesian learning model (Foley and Marjoram 2017). We first fitted the models to two baseline conditions in experiment 1 (BPV2 and BVP2), in order to select values for the free parameters. We then used these values for the remaining conditions in all experiments. The models that we implemented differed in the memory of events that were tracked and the decision mechanism. These models were:

1. Hurdle model

2. Random dimension model

3. Winner-takes-it-all model

4. Probability first model

5. Volume first model

6. Volume only model

7. Logproduct rule model

Compared to the empirical data, models 2 and 7 performed best (Tables 2, 3, see also Appendix 1 Figures A1, A2, A3, and A4).

Table 2: Decision-making models

model	description
1	hurdle
2	random dimension
3	winner takes it all
4	probability first
5	volume first
6	only volume

Discussion

Difference between cohorts

Animals, Methods, and Materials

The different experimental conditions for all animals and cohorts are listed in Table 1.

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Table 3: Best performing models ranked by root-mean-square-deviations (RMSD).

	experiment			
rank	1	2	3	4
1	1	2	1	5
2	2	1	2	1
3	6	6	5	3
4	5	5	4	2
5	3	4	3	6
6	4	3	6	4

Note:
The deviations for the RMSD were calculated from the median of the model to the observed discrimination performances of the experimental mice.

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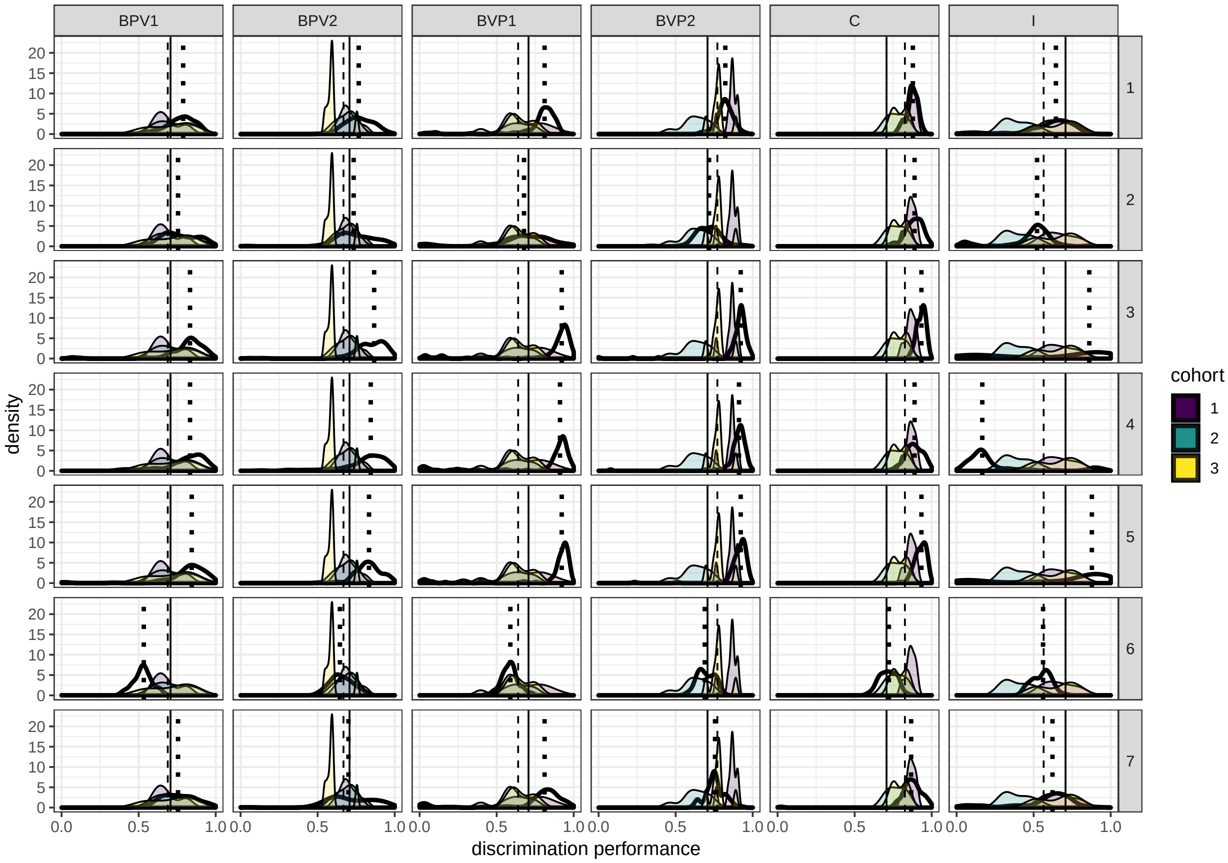

Figure A1: **Comparison of discrimination performances in all seven simulation models and in the three mouse cohorts in Experiment 1**. Columns give the condition names (Table 1) and rows, the model number (Table 2). Empirical data from the three cohorts are represented by differently color-filled density curves from the observed discrimination performances. Simulation data are represented by an empty thick-lined density curve. The dashed line gives the median of the empirical data and the dotted line - the median of the simulated data. The discrimination performance gives the relative visitation rate of the more profitable option, or, in the incongruent condition, the option with the higher volume.

Appendix

Acknowledgments

Individuals who have contributed materially to the work, but do not satisfy the authorship criteria should be listed in the acknowledgements section. Authors should seek permission to include any individuals mentioned in the acknowledgements.

Competing interests

At this stage we request that the corresponding author provides a statement of financial and non-financial competing interests on behalf of all authors. Examples include paid employment or consultancy, stock ownership, patent applications, personal relationships with relevant individuals, and membership of an

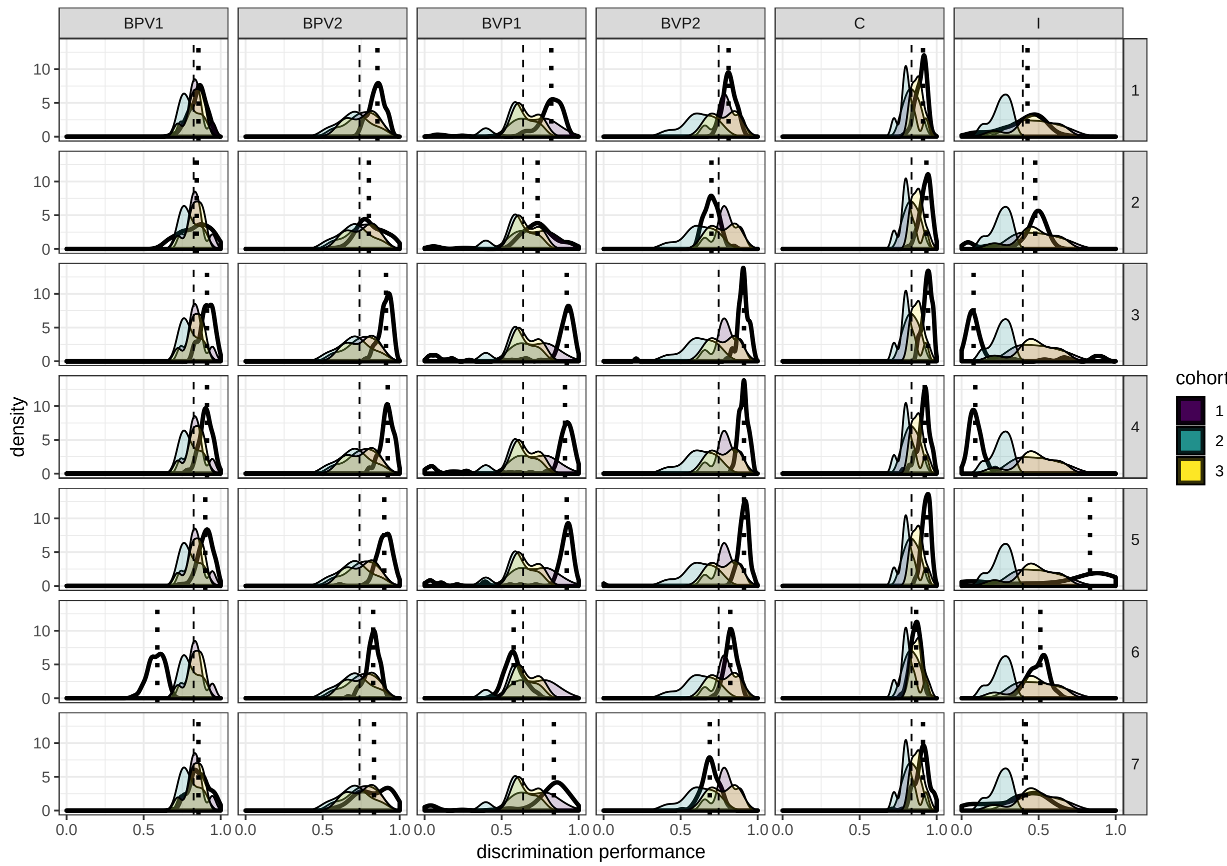

Figure A2: **Comparison of discrimination performances in all seven simulation models and in the three mouse cohorts in Experiment 2**. Same notation as in Fig. A1.

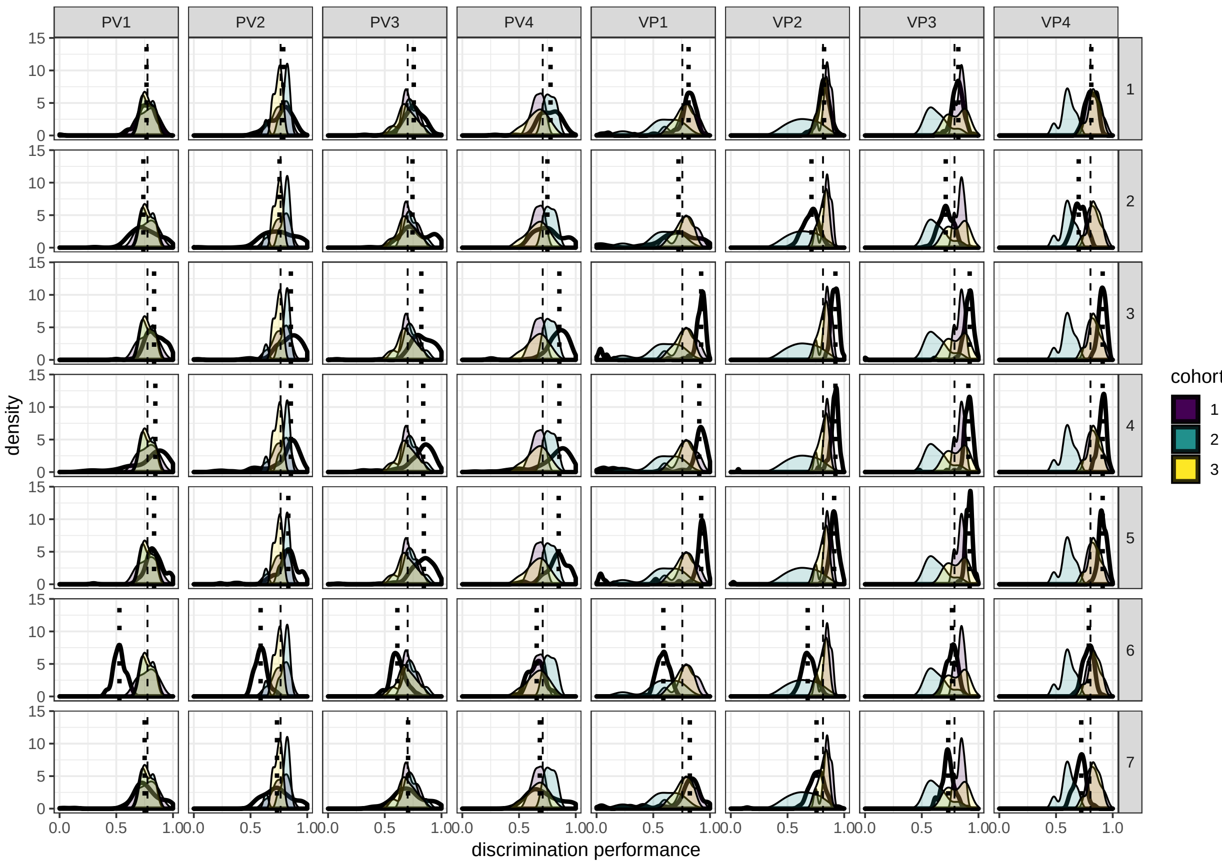

Figure A3: **Comparison of discrimination performances in all seven simulation models and in the three mouse cohorts in Experiment 3**. Same notation as in Fig. A1.

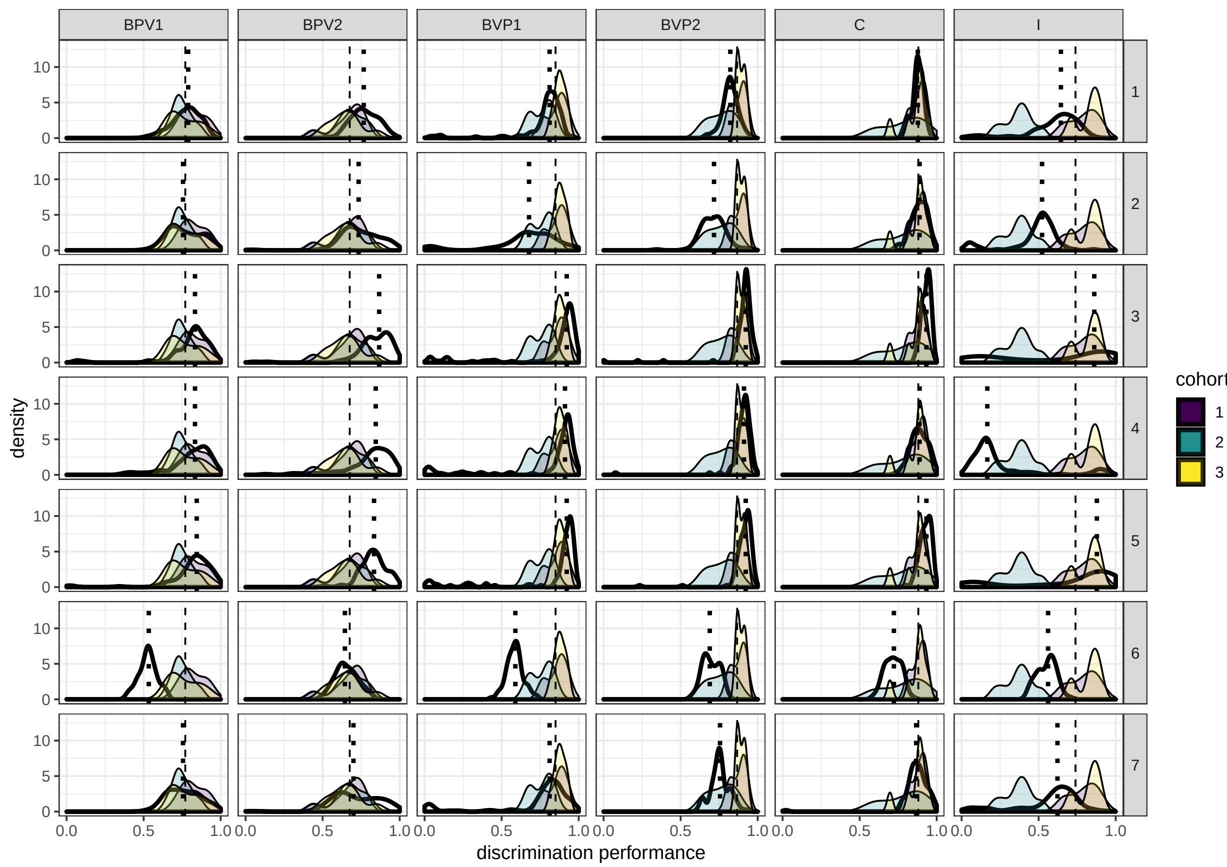

Figure A4: **Comparison of discrimination performances in all seven simulation models and in the three mouse cohorts in Experiment 4**. Same notation as in Fig. A1.

advisory board.

References

Bates, Douglas, Martin Mächler, Ben Bolker, and Steve Walker. 2015. “Fitting Linear Mixed-Effects Models Using Lme4.” *Journal of Statistical Software* 67 (1):1–48. https://doi.org/10.18637/jss.v067.i01.

Foley, Brad R., and Paul Marjoram. 2017. “Sure Enough: Efficient Bayesian Learning and Choice.” *Animal Cognition* 20 (5):867–80. https://doi.org/10.1007/s10071-017-1107-5.

Kacelnik, Alex, and Fausto Brito e Abreu. 1998. “Risky Choice and Weber’s Law.” *Journal of Theoretical Biology* 194 (2):289–98. https://doi.org/10.1006/jtbi.1998.0763.

Kahneman, Daniel, and Amos Tversky. 1979. “Prospect Theory: An Analysis of Decision Under Risk.” *Econometrica* 47 (2):263–91. https://doi.org/10.2307/1914185.

Kenrick, Douglas T., Vladas Griskevicius, Jill M. Sundie, Norman P. Li, Yexin Jessica Li, and Steven L. Neuberg. 2009. “Deep Rationality: The Evolutionary Economics of Decision Making.” *Social Cognition* 27 (5):764–85. https://doi.org/10.1521/soco.2009.27.5.764.

Lakens, Daniël. 2017. “Equivalence Tests: A Practical Primer for T Tests, Correlations, and Meta-Analyses.” *Social Psychological and Personality Science*, May. https://doi.org/10.1177/1948550617697177.

Levy, Dino J, and Paul W Glimcher. 2012. “The Root of All Value: A Neural Common Currency for Choice.” *Current Opinion in Neurobiology*, Decision making, 22 (6):1027–38. https://doi.org/10.1016/j.conb.2012.06.001.

Rivalan, Marion, York Winter, and Vladislav Nachev. 2017. “Principles of Economic Rationality in Mice.” *Scientific Reports* 7 (1):17441. https://doi.org/10.1038/s41598-017-17747-7.

Shafir, Sharoni. 1994. “Intransitivity of Preferences in Honey Bees: Support for ’Comparative’ Evaluation of Foraging Options.” *Animal Behaviour* 48 (1):55–67. https://doi.org/10.1006/anbe.1994.1211.

Shafir, Sharoni, and Lia Yehonatan. 2014. “Comparative Evaluations of Reward Dimensions in Honey Bees: Evidence from Two-Alternative Forced Choice Proboscis-Extension Conditioning.” *Animal Cognition* 17 (3):633–44. https://doi.org/10.1007/s10071-013-0694-z.

Tversky, Amos. 1969. “Intransitivity of Preferences.” *Psychological Review* 76 (1):31–48. https://doi.org/10.1037/h0026750.