

Mice tune out not in: Violation of prediction drives auditory saliency

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1 Abstract

2 Successful navigation in complex acoustic scenes requires focusing on relevant
3 sounds while ignoring irrelevant distractors. It has been argued that the ability to
4 track stimulus statistics and generate predictions supports the choice what to
5 attend and what to ignore. However, the role of these predictions about future
6 auditory events in drafting decisions remains elusive. While most psychophysical
7 studies in humans indicate that expected stimuli serve as implicit cues attracting
8 attention, most work studying physiological auditory processing in animals
9 highlights the detection of unexpected, surprising stimuli. Here, we tested whether
10 in the mouse, target probability is used as an implicit cue attracting attention or
11 whether detection is biased towards low-probability deviants using an auditory
12 detection task. We implemented a probabilistic choice model to investigate
13 whether a possible dependence on stimulus statistics arises from short term serial
14 correlations or from integration over longer periods. Our results demonstrate that

15 target detectability in mice decreases with increasing probability, contrary to
16 humans. We suggest that mice indeed track probability over a time scale of at least
17 several minutes but do not use this information in the same way as humans do:
18 instead of maximizing reward by focusing on high-probability targets, the saliency
19 of a target is determined by surprise.

20 Introduction

21 An individual that uses acoustical information for behavioral choices is confronted
22 nearly continuously with numerous sounds from different sources. To
23 differentiate between non-associated sounds that are present simultaneously,
24 relevant stimuli need to be detected while irrelevant ones should be ignored.
25 During this process of differentiation, the ability of tracking stimulus statistics (if
26 a stimulus occurs with high or low probability) is essential, sets expectations, and
27 creates predictions about future auditory events (Malmierca et al., 2015; Skerritt-
28 Davis and Elhilali, 2018). While there is general agreement on the principal
29 importance of expectation in auditory perception, there are different ways in
30 which these predictions may be used to guide decisions.

31 On the one hand, high-probability, expected and relevant signals may attract
32 selective listening, thus the ability to group and separate sounds from different
33 sources and selectively pick and monitor one in the presence of others. This ability
34 forms an important part of selective attention and supports the analysis of complex
35 auditory scenes (Bregman, 1994; Sussman et al., 2007; Woods and McDermott,
36 2015). It has already been demonstrated that adult humans listen selectively for an
37 expected auditory stimulus in reward-based auditory listening tasks (Scharf et al.,
38 1987). More generally, humans internally monitor the probability of a stimulus and

39 adapt their behavior according to the stimulus statistics (Bargones and Werner,
40 1994a; Gordon Z. Greenberg and Larkin, 1968). This form of selective auditory
41 attention does not require awareness of the subject and is driven by unconscious
42 expectations (Wolmetz and Elhilali, 2016). Within this framework, the
43 improvement of detectability is based on the expectation as an implicit cue and
44 serves as an internal reward-maximizing strategy that drives the attention towards
45 the expectation (Girshick et al., 2011).

46 While most psychophysical studies indicate that expected stimuli serve as implicit
47 cues attracting attention, most work studying the physiology of auditory
48 processing highlights the detection of unexpected, surprising stimuli. Stimuli are
49 more salient when presented rarely to the auditory system and thus might be
50 easier to detect due to pre-attentive mechanisms (Malmierca et al., 2015; Pérez-
51 González et al., 2005; Tiitinen et al., 1994). Within this framework, the evaluation
52 of stimulus statistics serves to detect novelty, emphasizing changes in the auditory
53 scene rather than enabling tracking of task relevant information.

54 Thus, tracking of stimulus probability influences auditory processing in two
55 contrary ways: on the physiological level, low-probability sounds elicit maximal
56 responses, but during listening tasks, relevant high-probability sounds appear to
57 attract attention, improving their detectability. While physiological evidence for
58 deviant detection spans all the way from animal models to humans (Heilbron and
59 Chait, 2017; Khouri and Nelken, 2015), behavioral assessment of the effects of
60 target probability is largely restricted to humans. In order to understand the neural
61 mechanisms underlying predictive coding, animal models such as rodents in
62 which both physiology and behavior can be studied are needed.

63 Although rodents serve as widely used animal models to study auditory
64 phenomena, little is known about their ability to monitor stimulus probability and
65 its involvement in selective auditory attention. One study using chinchillas could
66 not reproduce human results for auditory selective attention (Yost and Shofner,
67 2009). However, it remains unclear whether this generalizes to other rodents. Also,
68 it is unknown if the animals simply do not adapt their behavior according to
69 stimulus statistics, or if they rather respond towards unexpected, surprising
70 stimuli instead of high-probability stimuli, as suggest by physiological data.

71 Here, we asked how target probability influences auditory perception in mice, as
72 revealed in detection paradigms. More specifically, we tested whether target
73 probability is used as an implicit cue attracting attention or whether detection is
74 biased towards low-probability deviants. To this end, we employed three different
75 tasks. First, we used faint tones in noise of different frequencies and varied the
76 probability of a given tone frequency between different sessions. This paradigm
77 resembles those used to test for the 'listening band phenomenon', the most
78 prominent example of probability-guided attention in the human literature (Scharf
79 et al., 1987). Subsequently, we tested whether the probability-dependence
80 generalizes to other detection tasks, namely streaming paradigms, in which a
81 target has to be detected in one out of multiple streams. Here we separately tested
82 for effects on the detection of both spectral and temporal stimulus dimensions.
83 Finally, we present a probabilistic choice model to investigate whether the
84 dependence on stimulus statistics arises from short term serial correlations or from
85 integration over longer periods.

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87

88 Results

89 Experiment 1: Tone in noise detection

90 When humans are asked to detect faint tones in a noise background, performance
91 for high-probability targets is better than for those played with low probability,
92 even if listeners are not consciously aware of the probabilities (Greenberg and
93 Larkin, 1968). This is usually explained by focused attention on specific auditory
94 filters, thereby listening selectively to a certain frequency range (Bargones and
95 Werner, 1994). In our first experiment, we aimed to test whether mice are able to
96 track target probabilities from session to session and display a preference for either
97 high- or low-probability targets. We devised a behavioral paradigm (Fig. 1), in
98 which mice were trained to indicate the detection of faint tones embedded in a
99 noise background by leaving a small pedestal after the presentation of a target (Fig.
100 1A). A typical single session contained 60 targets and lasted ~30 minutes. In order
101 to test the animals near their individual thresholds, we first tested a single
102 frequency in each session, varying the level of the tones to determine the threshold
103 (Fig. 1C, upper panel). In the next step, we presented tones with varying
104 probability as targets in mixed sessions (lower panel in (Fig. 1C). We hypothesized
105 that if mice displayed selective listening to high-probability tones they should (1)
106 be better at tone detection in the single frequency session compared to the mixed
107 session and (2) show better performance for the high-probability compared to the
108 low probability stimulus within the mixed session.

109 Contrary to our hypothesis, all animals tested showed higher sensitivity in the
110 mixed than in the single frequency session tested before (example data in Fig. 2A;
111 repeated measures ANOVA, $F(1;20)=32.2$, $p<0.001$). Within the mixed session, the
112 impact of stimulus probability on the preference of the mice for low-probability
113 tones was confirmed. Sensitivity was positively influenced by surprise, quantified

114 as the prediction error (log of the stimulus probability, Fig. 2B). This relation was
115 highly significant, both when taking the single frequency sessions into account and
116 for mixed sessions only, and independent of the frequency that was played.
117 We concluded that mice are able to track target probabilities over a time frame of
118 minutes to hours, but instead of the high-probability sound the low-probability
119 sounds were detected more reliably.

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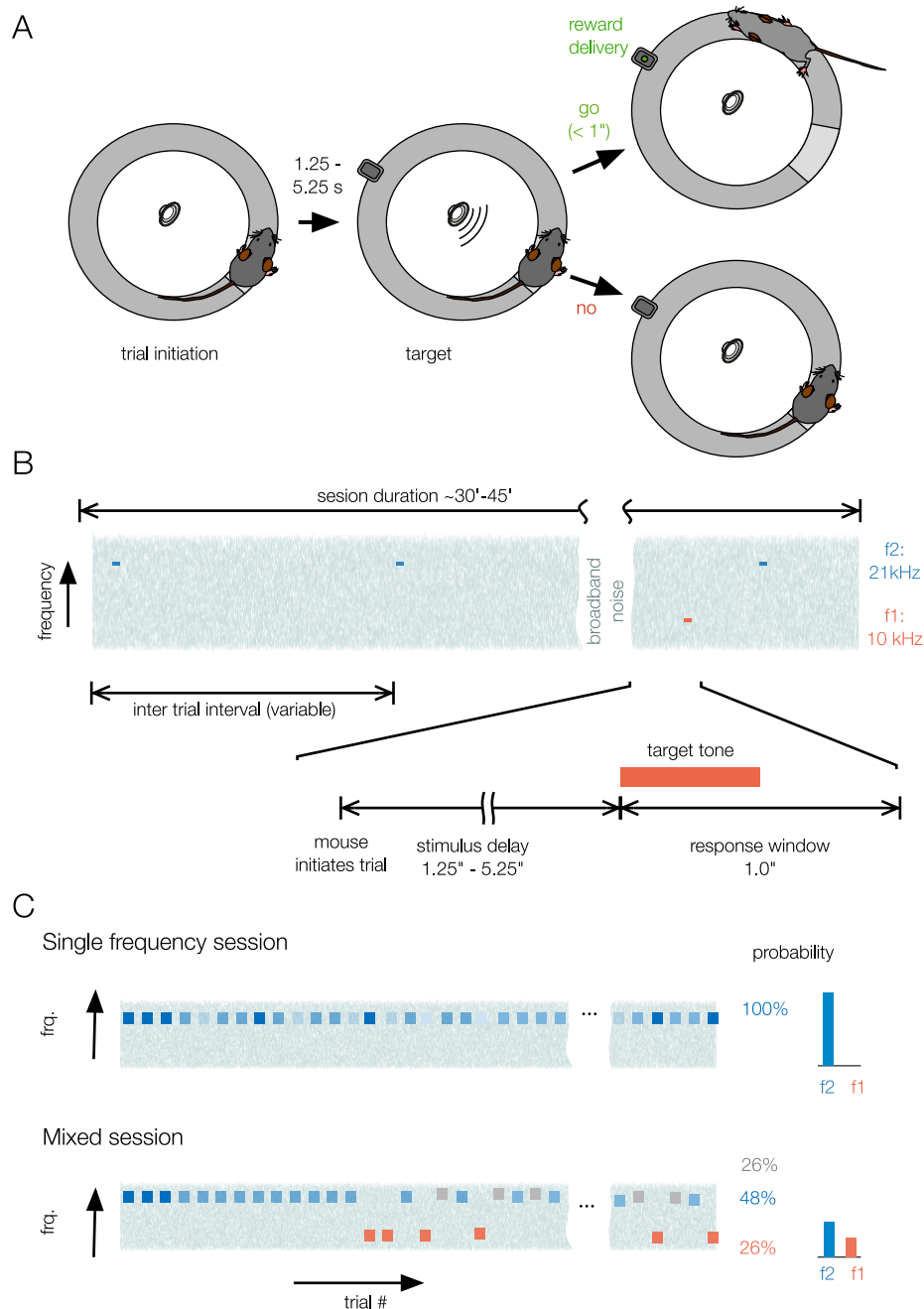


Fig. 1 - Behavioral paradigm and stimulus protocol used in Experiment 1

(A) Go/No Go paradigm used in this study. Mice initiated a trial by climbing on a small pedestal on the circular platform. After a variable waiting interval, a target was presented. Animals received a reward if they left the platform within 1s after target presentation. The next trial could be initiated immediately.

(B) Timeline of one experimental session. Throughout the entire session, a broad band noise stimulus was presented. Once a trial was initiated, a 500ms pure tone was presented after a random stimulus delay. In a single session, an animal had to complete 73 or 78 trials, which typically lasted 30-45 minutes.

(C) Different probabilities of single frequency pure tone targets in different sessions. In single frequency sessions, the level of the tones was varied, but only pure tones of either frequency f1 (10kHz) or f2 (21kHz) were presented. In mixed session, level was held constant near the behavioral threshold, but three different frequencies were presented. In any one session, either f1 or f2 was presented with 48% probability and the respective other with only 26%. In addition, a tone of the frequency close to the high-probability targets was presented in 26% of the trials.

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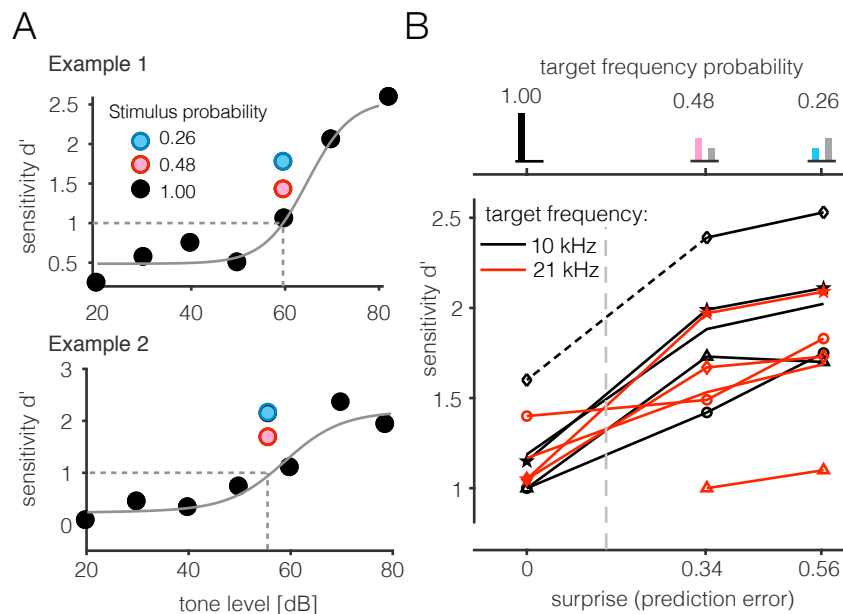


Figure 2 - Results for Experiment 1 - tone in noise detection

(A) Example performance of two different animals for the tone-in-noise stimuli at a single tone frequency, presented with different probabilities. Before the mixed-frequency experiments, animals were tested individually for their thresholds at each tone frequency by presenting tones of a single frequency (probability 100%) at different levels to construct psychometric functions (black circles, grey line). In the mixed experiments, tones with a level corresponding to a d' of 1 (dashed line) were presented with probabilities of 48% (red circle) or 26% (blue circle).

(B) Population data for all four animals at the two different frequencies used (red: 21kHz, black: 10kHz). The values for a probability of 100% were taken from the psychometric function obtained after the mixed experiments. Histograms above the graph visualize the probability of the tone in the respective sessions, the x-axis shows the surprise quantified as the prediction error. Note that larger numbers indicate more surprising stimuli. Total number of sessions included: 208 (152 for the mixed session, 56 for the psychometric functions).

122 Experiment 2: Frequency change detection in streams

123 Contrary to the behavior displayed in experiment 1, a strategy to focus on high-
124 probability sounds would have maximized rewards. A possible explanation for
125 mice not taking advantage of tracking probabilities is that they are not able to focus
126 on a single frequency band in a continuous noise background with very sparse
127 tones appearing at random times. We reasoned that a more natural situation could
128 be the presence of multiple streams of tones that allow to attach selective attention
129 to one of these streams (Lakatos et al., 2013; Schwartz and David, 2018). We
130 therefore designed an experiment in which the animals had to detect a frequency
131 change in either one of two continuous streams of tone pips (Fig. 3A). The
132 repetition rate was rapid (5 Hz for either stream) and the tone streams were more
133 than an octave apart in frequency, a parameter range that results in a clear two-
134 stream percept in most animals, including rodents (Itatani and Klump, 2017; Noda
135 et al., 2013). Again, we varied the probability that a target could appear in either
136 of the two streams. In one set of sessions, frequency changes would be inserted in
137 either one of the two streams only. In a second set, targets appeared in both streams
138 with equal probability. Sessions were randomized in order to avoid sequence
139 effects.

140 When we compared the mean sensitivity for the two different probability levels,
141 we observed a higher mean sensitivity for the mixed sessions for all tested
142 frequency changes (Fig. 3C). As in Experiment 1 (Fig. 2), targets were more salient
143 to the mice if they were distributed between the two streams than if they were
144 played in one of the two streams only. This was confirmed when we compared all
145 animals for both streams (Fig. 3E; rmANOVA, $F(1;88) = 6.0$, $p=0.0171$). Experiment
146 2 confirmed that the animals are able to track probabilities from session to session,
147 but saliency is determined by surprise, or prediction violation rather than by
148 expectation, despite the latter being the better strategy to maximize rewards in a
149 given session.

150 Experiment 3: Gap detection in streams

151 Since the two streams were separated by frequency and target changes were along
152 the same dimension, we aimed to test whether our results would generalize to
153 other stimulus dimensions. Therefore, we trained a new set of animals to detect
154 temporal irregularities in the form of short gaps introduced into one of the two
155 streams (Fig. 3B). Here, we used three probabilities for each condition: targets in
156 only one of the two streams (100%), or 66.7% and 33.3% probability in sessions
157 with targets in both streams. As already observed for the frequency changes,
158 sensitivity for detection of gaps strongly depended on target probability, with the
159 best detectability for low probability targets in the mixed sessions, and lowest
160 detection performance for targets in only one out of two streams (Fig. 3D). We
161 observed this effect for both possible target streams in all animals (Fig. 3F,
162 rmANOVA, $F(1,118) = 10.4$, $p=0.0016$). Experiment 3 confirmed our results from
163 the previous experiments and generalizes the saliency of surprising targets to
164 temporal features as well.

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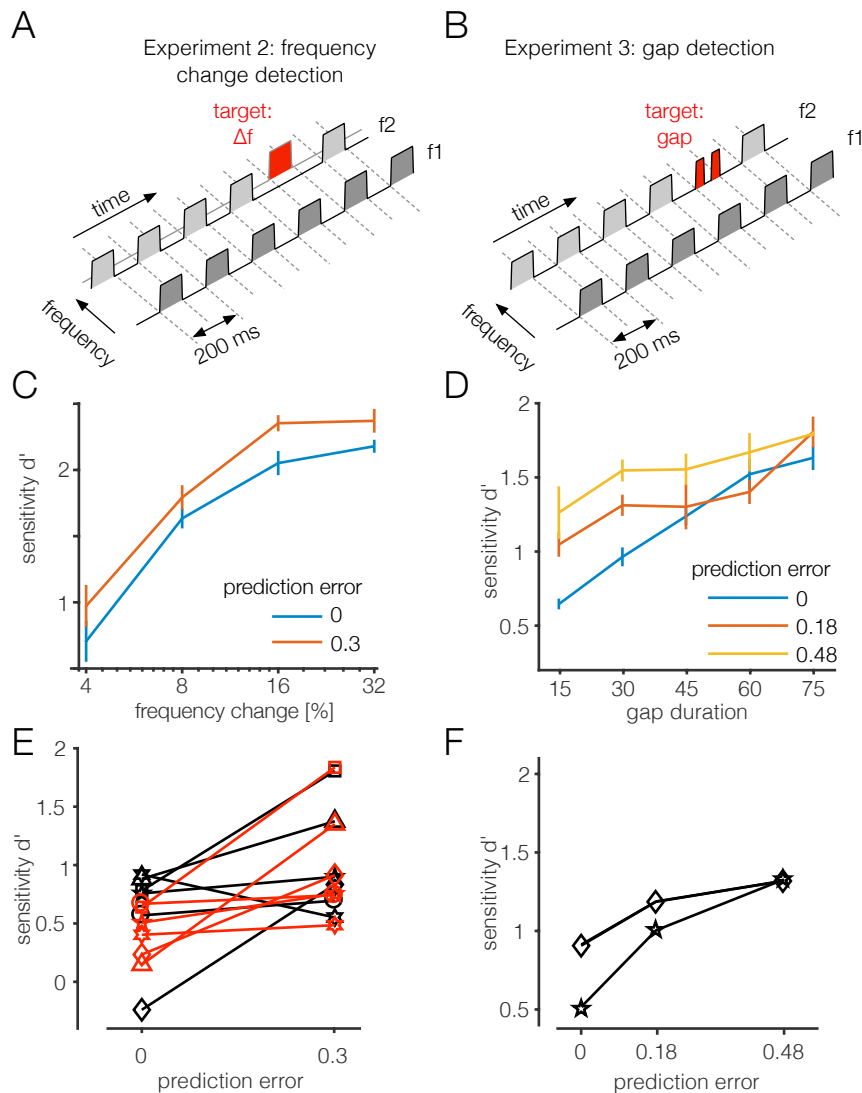


Figure 3 - Stimulus paradigms and results for Experiments 2 and 3

(A) Paradigm for Experiment 2: Two continuous, interleaved streams of tone pips with different frequencies were presented. $f1 = 10\text{kHz}$, $f2 = 21\text{kHz}$. Animals had to detect a change of the frequency in either of the two streams.

(B) Paradigm for Experiment 3: A short gap was inserted into one of the the two narrowband noise streams (center frequency same as $f1$ and $f2$ in A) as a target for detection.

(C) Mean performance of all animals (n=6) in Experiment 2 tested at different values of frequency change at either 50% (red) or 100% (blue) probability. Errorbars show standard error of the mean (SEM).

(D) Mean performance of all animals (n=4) in Experiment 3 tested at different gap durations at 33.3% (yellow), 66.7% (red) or 100% (blue) probability. Errorbars depict SEM.

(E) Sensitivity as a function of prediction error for Experiment 2 - tone change detection - for all animals tested in both frequency streams (black: 10 kHz, red: 21kHz). Each line joins data from an individual mouse for targets with a frequency change of 16%.

(F) Sensitivity as a function of prediction error for Experiment 3 -gap detection - for all animals tested in both frequency streams (black: 10kHz, red: 21kHz) fir targets with a gap duration of 30ms.

166 Probabilistic choice model

167 We observed higher detection performance for low-probability stimuli in three
168 different behavioral experiments. However, this does not necessarily mean that
169 the animals were tracking long-term probability. When manipulating probability,
170 the structure of the randomized trial sequences is changed as well: In sessions in
171 which one type of target is presented with low probability, stimuli are more often
172 preceded by a different target than if presented in high-probability sessions. A
173 simple attentional switch after each trial could explain our results just as well as
174 tracking probability over a time course of minutes to hours. In order to test
175 whether the animals were tracking probability over longer time-scales or simply
176 displaying short-term trial-history effects, we devised a probabilistic choice model
177 (Fig. 4A). The model included the factors stimulus intensity, stimulus probability
178 within the session, and recent history of stimuli presented in the immediately
179 preceding trials. The model was fit separately for each mouse and experiment, in
180 versions including or excluding probability and history terms. If the probability-
181 dependence was due to recent history effects, a model including only the
182 respective term should perform equally well as one including both probability and
183 history, and better than one that takes only probability into account. Inclusion of
184 the probability term significantly improved model performance (Fig. 4B). In
185 contrast, inclusion of the recent-history term (up to four preceding trials) improved
186 the model only marginally (Fig. 4B).

187 The average interval between two trials was 30.2 ± 10.3 s (mean \pm standard
188 deviation, $n=528$ sessions from all three experiments). Since there was little effect
189 of recent trial history up to at least 4 trials, perception in the mice was apparently
190 shaped by long term probability on the time-scale of several minutes at least. In
191 line with this, we could not find a difference between hit rates after a switch of the
192 stimulus class between two trials or a repetition of stimuli from the same class (Fig.
193 4D). We also did not find a change of overall strategy between mixed and pure

194 sessions - false alarm rates did not differ between those session (Fig. 4C).

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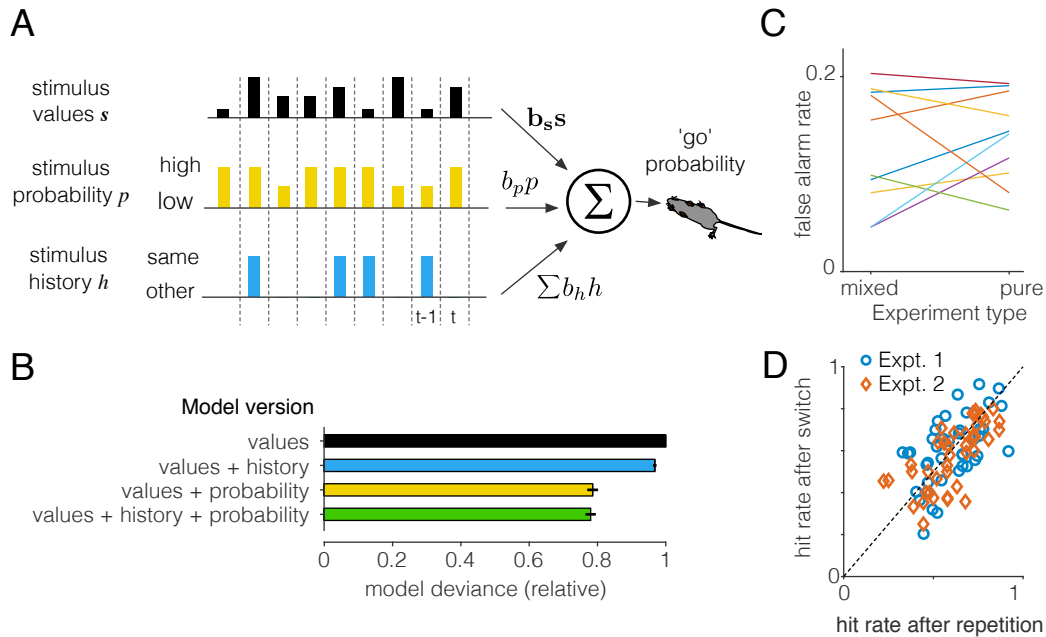


Figure 4 - Probabilistic choice model

(A) Schematic illustration of the probabilistic choice model. The full model includes stimulus intensity, stimulus probability within the session for each stimulus, and recent history of stimuli presented in the immediately preceding trial steps $t-i$. Stimulus values were different in each experiment: signal-to-noise ratio in Experiment 1, frequency shift in Experiment 2 and gap duration in Experiment 3. The model was fit for each mouse and experiment, in four different versions, including either all three factors, stimulus values only, values + history, or values + probability.

(B) Performance of the four model versions, plotted as deviance of model output to the data, relative to the model including stimulus values only. Note that smaller numbers mean better model performance. Bars represent mean deviances from all animals in the three experiments \pm SEM

(C) False alarm rate depending on whether stimuli of one class were presented as the only stimuli in the session ('pure') or whether they were combined with other stimuli ('mixed'). Each line represents mean false alarm rates from a single animal.

(D) Influence of immediate trial history on hit rate. x-axis: hit rate when the stimulus in the trial before was drawn from the same class as the current stimulus ('repetition'), y-axis: hit rate to stimuli that were preceded by a stimulus from another class ('switch').

196 Discussion

197 Stimulus statistics in auditory scenes have been suggested to shape auditory
198 perception in two contrary ways: (1) A focus on novelty detection, favouring low-
199 probability sounds (Khouri and Nelken, 2015) and (2) focusing attention on
200 expected, high-probability sounds, thereby maximizing overall detection rate
201 (Scharf et al., 1987; Wolmetz and Elhilali, 2016). Here we tested whether attention
202 in mice is drawn rather towards low- or high-probability target sounds. To this
203 end we conducted three different experiments varying the probability of targets.
204 While humans direct their attention to the most probable target out of several
205 acoustic channels or streams, target detectability in mice decreased with increasing
206 probability. Thus, the more surprising a stimulus was, the more reliably it was
207 detected. This was confirmed in three independent experiments, one with
208 changing probability of target frequency in noise (Fig. 2) and two using a
209 streaming paradigm (Fig. 3) with either a spectral or temporal variation to be
210 detected. Finally, our probabilistic choice model best predicted animal behavior
211 for all three tasks if it took overall probability into account, but not if we considered
212 recent trial history (Fig. 4B). These results suggest that mice indeed track
213 probability over a time scale of at least several minutes, but do not use this
214 information in the same way as humans do: instead of maximizing reward by
215 focusing on high-probability targets, the saliency of a target is determined by
216 surprise. Such a strategy obviously fails to maximize reward, since successful
217 detection of higher-probability targets directly results in a higher reward rate.

218 Different strategy or mouse-specific auditory processing?

219 It seems that mice are very good at something that humans find hard and vice
220 versa. Are our results in mice really caused by a different strategy with respect to
221 target probability or can it be explained by more basic differences in their auditory
222 system? Mice have much wider auditory filters (Lina and Lauer, 2013), so our
223 stimuli could have been merged into one perceptual category, such that no
224 separate streams would have built up. However, in all three experiments, we used
225 targets that were more than an octave apart, far above the frequency
226 discrimination threshold of mice (de Hoz and Nelken, 2014). It was not assessed
227 whether the two sequences used in experiments 2 and 3 resulted in a streaming
228 percept, as this was not the focus of our study and our results do not critically
229 depend on the sequences being perceived as streams. However, all animal species
230 that have been tested so far showed evidence for streaming for stimuli separated
231 by one octave and upwards (Itatani and Klump, 2017), including rats (Noda et al.,
232 2013), which have similar auditory filters to mice. Furthermore, our positive results
233 on the effect of target probability and its generalization across paradigms provide
234 evidence for perceptual separation rather than merging.

235 Deviance detection in the auditory system

236 We found clear evidence for mice to favor unexpected stimuli. This finding
237 suggests that saliency of a target is determined by it deviating from previous
238 acquired prior probabilities. One explanation for such a behavior is the dominance
239 of deviance detection over expectancy-attracted attention. There is a large body of
240 work on enhanced neural representation of deviant stimuli in the auditory system
241 in both animal models and humans. At the single cell level, stimulus specific
242 adaptation (SSA) describes the enhancement of the neural representation of low-

243 probability sounds (Khouri and Nelken, 2015; Malmierca et al., 2015). A typical
244 paradigm is the presentation of a sequence of tones of two different frequencies,
245 with varying relative probability (Ulanovsky et al., 2003). Experiment 1 of this
246 study is such a paradigm, but the ratio of stimulus duration (0.5s) and the very
247 long inter-stimulus interval (mean of all sessions: 30.2s) has not been reported
248 before. However, time scales up to several minutes are reasonable based on the
249 measurement of adaptation time constants in cat auditory cortex (Ulanovsky et al.,
250 2004).

251 The stimuli in our Experiments 2 and 3 extended this to two synchronously
252 presented sequences of standard and deviants - experiment 2 with frequency shifts
253 and experiment 2 with temporal deviants. SSA is likely to shape responses to the
254 deviant targets in both of the streams in either experiment. Deviants are very rare
255 with respect to each background stream: ~30s inter-trial intervals with a
256 background pulse repetition rate results in a deviant probability of ~1% in session
257 with target in one stream and ~0.5% in sessions with equal distribution between
258 the two streams. Different performance for these sessions would imply that SSA
259 has to reflect differences in probability as small as $\Delta 0.5\%$. Neural sensitivity for
260 such small changes has not been reported yet, but there is no principle reason why
261 they cannot exist. Alternatively, SSA could work on a higher structural level,
262 reflecting the task and the auditory scene as a whole. SSA has been shown to
263 extend beyond simple pure tone patterns (Nelken et al., 2013) and to more complex
264 statistical structure of the sensory context (Yaron et al., 2012). Similar to the
265 findings presented here (Fig. 4), SSA is sensitive to average statistics rather than
266 recent history (Rubin et al., 2016).

267 Not only in animal models, but also in humans, deviant detection represents one
268 of the main principles of auditory processing. It is reflected by the mismatch
269 negativity (MMN) component of the EEG and is present for a large range of stimuli
270 and time scales (Näätänen et al., 2007, 1978). Both SSA and MMN are discussed as
271 a response to the violation of expectation (Heilbron and Chait, 2017; Khouri and
272 Nelken, 2015; Malmierca et al., 2015) within the framework of predictive coding
273 (Friston, 2005).

274 Despite the pervasive presence of neural signatures of deviance detection in
275 auditory systems, it is very difficult to directly observe a correlate at the behavioral
276 level. This is probably due to its pre-attentive nature - deviance detection is
277 observable in passively listening subjects (Tiitinen et al., 1994) as well as in
278 anaesthetized animals (Antunes et al., 2010). In active listening tasks, implicit
279 cueing could then use the predictive signal to channel selective attention to high-
280 probability sounds (Wolmetz and Elhilali, 2016) by inverting the sign. The
281 interplay of MMN and top-down attention is still an open and debated topic
282 (Bendixen, 2014; Sussman, 2007).

283 Sensory ecology

284 From the perspective of reward maximization, selective attention to low-
285 probability targets in an auditory scene is undesirable. This raises the question
286 whether the strategy employed by mice is rather the result of the animals lacking
287 an appropriate mechanism for selective attention or whether it provides an
288 ecological benefit for the animals. Evidence for an ability to selectively attend one
289 out of several concurrently present objects or processes is surprisingly sparse for
290 rodents. Recent work suggests that mice are able to attend to explicitly cued visual
291 patterns (Wang and Krauzlis, 2018) or auditory streams (Chapuis and

292 Chadderton, 2018), indicating that mice may not lack a mechanism for top-down
293 attentional control. Both humans and carnivores (Schwartz and David, 2018) can
294 be cued implicitly using target probability - providing further evidence that the
295 effect of stimulus probability on perception may be due to sensory ecology rather
296 than taxonomy. While both primates and carnivores might use their auditory
297 senses to tune in and follow potential prey or conspecific communication signals,
298 tracking of the statistics in mice – a prey species - may predominantly serve to
299 detect sudden, potentially dangerous changes in the environment. Interestingly
300 and consistent with that hypothesis, while implicit cueing in humans usually
301 enhances perception of high-probability signals (Girshick et al., 2011; Scharf et al.,
302 1987; Wolmetz and Elhilali, 2016), threatening stimuli are best perceived if they
303 occur with relative low-probability (McFadyen et al., 2019). If mice use contextual
304 auditory information mainly for the detection of threats, this rule may be hard-
305 wired and not under the control of top-down signals. In this case, expectation is
306 computed along the sensory pathway, but mostly used to suppress ongoing input,
307 similar to sensory adaptation on shorter time scales. The development of
308 predictive coding and expectation-driven perception in mammals may have
309 tapped into this first step of probabilistic analysis of sensory scenes. Since the
310 representation was already available, this required merely a sign switch.

311 Perspective

312 In summary, our study provides the first evidence for animal detection behavior
313 being shaped directly by prediction error. This finding could be very helpful for
314 future work on prediction-guided attention, since we may be able to study the
315 neural mechanisms underlying extraction of complex contextual sensory
316 information without the confounding of the interplay with (top-down) reward
317 maximization. The mouse model offers unrivaled possibilities to record and

318 manipulate neural activity in the behaving animal. In future studies this may not
319 only enable measurements of neural deviance detection during relevant behavior.
320 It also offers the perspective of direct manipulation of potential mechanisms, with
321 the observed behavior as readout to infer causal relationships

322

323 Methods

324 Animals

325 In total 14 adult male mice bred at the University of Oldenburg animal facilities
326 were used in the experiments. All mice had a C57BL/6.CAST-*Cdh23*^{Ahl+} background
327 (the Jackson laboratory, #002756) and were between 3 and 9 month old. We used
328 this line because it does not display the age-dependent hearing loss which is
329 present in other C57BL/6 lines (Johnson et al., 1997; Kane et al., 2012). Animals
330 were kept at a reversed 12/12 hour dark-light cycle, all experiments were
331 performed during the dark period. Animals had unlimited access to water but
332 were food-deprived to a moderate extent (85-90% of their *ad libitum* weight) and
333 single-housed in standardized cages but with visual and olfactory contact to
334 neighboring animals. Cages were equipped with cage enrichment. All experiments
335 were approved by the responsible authorities (Lower Saxony State Office for
336 Consumer Protection and Food Safety, license number 33.9-42502-04-13/1271).

337

338 Behavioral paradigm

339 All three experiments were performed using the following reward-based go/no-go
340 paradigm. Animals were placed on an annular platform made from wire mesh
341 (Fig. 1A). The raised platform was placed in a custom sound-proof chamber that
342 was lined with pyramid foam. On one side of the platform, a small pedestal was
343 installed. Once the animals ascended the pedestal, a random, variable waiting time
344 started, ranging from 1.25 to 5.25s. After this random interval, a target was
345 presented.

346 The onset of the target triggered a 1s response window. If the animals descended

347 within the window (,go'), a food pellet (0.02g, Dustless precision pellets rodent,
348 grain based, Bio-Serv, #F0163) was delivered at the opposite side of the annular
349 platform. If the animals stayed on the pedestal, a new trial was presented after a
350 newly drawn waiting time. In order to estimate how many of hits were awarded
351 by chance, about one third of trials (depending on experiment) were unrewarded
352 sham trials, with the same distribution of waiting times as the target trails. Neither
353 false alarms nor misses were punished or rewarded. A typical session contained
354 60 targeted trials and 25 sham trials and lasted 30-40 minutes. Animals were tested
355 once per day. All experiments were controlled by custom Software (Github
356 Repository, <https://github.com/Spunc/PsychDetect>) written in MATLAB (The
357 Mathworks). Pellet dispenser and light barriers were custom build (University of
358 Oldenburg workshop) and controlled by a microcontroller (Arduino UNO,
359 Arduino AG, Italy) connected to a Windows PC.

360 Stimuli

361 For sound presentation a speaker (Vifa XT 300/K4, Denmark) was mounted in the
362 sound-proof chamber approximately 0.5m above the pedestal. Sound was
363 generated using a high-fidelity sound card (Fireface UC, RME, Germany)
364 connected to the PC. Sound was played back at either 192kHz (experiment 1) or
365 96kHz (experiments 2 & 3) sampling rate. The speaker was calibrated at the
366 approximate position of the head of the animals using a measurement microphone
367 (model 40BF, G.R.A.S, Denmark).

368

369 *Experiment 1 - Tone in noise detection*

370 Tones in noise served as a target in Experiment 1. Once a session started, broad-
371 band noise (4-64kHz, 60dB) was constantly played until the end of the session.
372 Pure tone of either 10 or 21kHz served as targets (2ms cosine ramps, 500ms
373 duration). In the sessions containing only one target frequency, the level for that

374 frequency was varied between 20 and 80dB in steps of 10dB in order to obtain a
375 psychometric function. Psychometric functions were fit with a logistic function
376 and an individual signal-to noise ratio (SNR) threshold was estimated. In the
377 mixed sessions, we used the level corresponding to the individual SNR thresholds,
378 estimated as the point on the psychometric curve with a d' value of 1. During the
379 mixed session, the first 10 trials were taken from either of the two frequencies
380 (priming frequency). For the rest of the sessions, both frequencies were played
381 back with equal probability. In addition, target tones of a third frequency close to
382 the priming frequency were played with equal probability. These stimuli were not
383 used for further analysis. Only the later part of the session was used for analysis
384 of the animal's performance. Each animal performed at least 10 session for both
385 priming frequencies. Measurement of psychometric function was repeated after
386 the mixed sessions in order to rule out effects of perceptual learning when
387 comparing single-frequency with mixed sessions.

388

389 *Experiment 2 - Frequency change detection in streams*

390 For Experiment 2, two alternating tones with frequencies of 10 and 21kHz (1.07
391 octaves) were played at rate of 5 tones/s throughout the experimental session. Tone
392 duration was 100ms including 2ms cosine ramps. The level of each individual tone
393 was roved between 60 and 66dB SPL (randomly) in order to avoid the detection of
394 a differences in loudness when the shift in frequency occurred. The frequency of a
395 tone from either tone sequence was shifted upwards by 4%,8%,16% or 32%. Mice
396 had to report the appearance of the frequency shift within 700ms after onset of the
397 shifted tone. Within a session, targets appeared either in only one of the two tone
398 sequences (,single') or with 0.5 probability in either of the two sequences (,mixed').
399 Each animal completed at least 8 sessions for each of the mixed session types.

400

401 *Experiment 3 - Gap detection in streams*

402 The temporal structure of the sequences in Experiment 3 was the same as in

403 Experiment 2, but instead of pure tones, narrowband noise with a bandwidth of
404 0.25 octaves around 10 or 21kHz was used. We introduced this adjustment,
405 because mice were not able to detect temporal gaps in the tone streams used in
406 Experiment 2. The level of narrow band pulses was fixed at 60dB SPL. In the target
407 pulses, gaps with duration of 15, 30, 45, 60 and 75ms were introduced (including
408 2ms cosine pulses). The response window was 1 s. For Experiment 3, we used three
409 different probabilities: 1 (target only in one sequence), 0.66 or 0.33. Each animal
410 completed at least 8 sessions for each session type.

411 Data analysis and statistics

412 In all three experiments, for each session i and stimulus class s , the sensitivity d'
413 was calculated as:

$$414 \quad d'_{i,s} = z(H_{i,s}) - z(FA_i)$$

415
416
417 where $z()$ is the inverse of normal cumulative function, $H_{i,s}$ is the hit rate for the
418 stimuli with parameters s in the i th session $P(\text{response} | \text{stimulus } s)$ and FA_i is the
419 false alarm rate $P(\text{response} | \text{sham})$.

420 In order to check for significant effects of stimulus probability on the sensitivity,
421 we fit a generalized mixed effects model (MATLAB *fitglm*), with the d' values as
422 response variable and probability and stimulus parameters as factors. In
423 Experiment 1, the stimulus parameter factor was target tone frequency. For
424 Experiment 2, relative frequency shifts were entered as factor. For Experiment 3,
425 the stimulus factor was gap duration. For each experiment, we performed repeated
426 measures ANOVA (rmANOVA, MATLAB) and report both F-values and exact p-
427 values up to the fourth decimal.

428 Probabilistic choice model

429 To account for different factors affecting animal choice behavior we devised a
430 probabilistic choice model, similar to what has been used before in order to include
431 history in psychophysics (Busse et al., 2011).

432 The probability p_{go} to jump at a given trial t in a behavioral session is given by:

$$433 \quad p_{go}(t) = \frac{1}{1 - e^{L(t)}}$$

434
435 with the response variable $L(t)$, that is a weighted sum of three main terms: (1) the
436 stimulus parameters $s(t)$, (2) the overall probability of the stimulus to appear in the
437 given channel $p(t)$, and the stimulus history $h(t)$:

$$L(t) = \mathbf{b}_s \cdot \mathbf{s}(t) + b_p p(t) + \mathbf{b}_h \cdot \mathbf{h}(t)$$

440 The stimulus parameters depend on the paradigm. For Experiment 1, this was
441 absolute stimulus frequency and the signal to noise ratio. For Experiment 2, this
442 was the absolute frequency of the stream the target appeared in and the frequency
443 shift of the target. For Experiment 3, we entered absolute frequency of the target
444 stream and the gap duration in the target pulse.

445 The probability term is constant across a given session and only depends on the
446 target channel. The history term is described by:

$$\mathbf{b}_h \cdot \mathbf{h}(t) = \sum_{i=1}^n b_h^j h(t-i)$$

449 where $h(t-i)$ is 1 if the target in the $(t-i)$ th trial before the current was in the same
450 channel and 0 if it was presented in the respective other.

451 The weights were fit using the Matlab function *glmfit* with a logit link and no
452 constant term. For each animal, sessions were combined into sets that each
453 contained all probability distributions (four single sessions in Experiments 1 and
454 3, three sessions in Experiment 2). For each experiment and animal, at least five

455 such sets were combined randomly and corresponding models were fitted,
456 resulting in a total of 86 sets. For each such set four versions of the model were
457 fitted, the full model above and the following reduced versions:

458 Stimulus parameters only: $L(t) = \mathbf{b}_s \cdot \mathbf{s}(t)$

459

460 Stimulus parameters + probability: $L(t) = \mathbf{b}_s \cdot \mathbf{s}(t) + b_p p(t)$

461

462 Stimulus parameters + history: $L(t) = \mathbf{b}_s \cdot \mathbf{s}(t) + \sum_{i=1}^n b_h^j h(t - i)$

463

464 For each set and model version, the deviance between the animal's response and
465 the probability p_{go} was collected and normalized to the model deviance for the
466 model version including stimulus parameters only.

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