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Sequential Temporal Discrimination in Humans and Mice

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Previous studies showed that humans and mice can maximize their rewards in two alternative temporal discrimination tasks by incorporating exogenous probabilities and endogenous timing uncertainty into their decisions. The current study investigated whether the probabilistic relations modulated the temporal discrimination performance in scenarios with more than two temporal options. In order to address this question, we tested humans (Experiment 1) and mice (Experiment 2) in the dual-switch task, which required subjects to discriminate three time intervals (short, medium, and long durations) in a sequential fashion. The latencies of switches from short to medium and from medium to long option were the main units of analysis. The results revealed that the timing of switches between the first two options (short-to-medium) were sensitive to probabilistic information in both humans and mice. Mice but not humans adapted the timing of their subsequent switches between the last two options (medium-to-long) based on the probabilistic information associated with these latter options. These results point at a suboptimal tendency in the temporal decisions of humans with multiple options.

Many studies of temporal decision-making have utilized temporal discrimination procedures (Balcı, Freestone, & Gallistel, 2009; Çoşkun, Sayalı, Gürbüz, & Balcı, 2015; Kheifets & Gallistel, 2012). These procedures often contain two reference durations presented with equal probability and subjects are required to indicate which of these two reference durations is best represented by a given experienced test duration. Several studies that used variants of temporal discrimination procedures have manipulated the probability of different reference durations and demonstrated that humans and mice can adaptively incorporate stimulus probabilities into their time-based decisions. Furthermore, these decisions nearly maximized the reward attained, which entailed the integration of probabilistic contingencies and the level of decision-makers' endogenous (representational) timing uncertainty into the decision outputs in a normative fashion. In order to test the generalizability of the effect of probabilistic information on temporal decision-making and evaluate the resultant decision outputs with respect to optimality in more complex temporal decision-making scenarios, the current study investigated the temporal discrimination performance of humans and mice with more than two temporal options.

Previous studies on temporal decision-making have emphasized the importance of stimulus probabilities and endogenous timing uncertainty in defining the reward maximizing temporal decision strategies (e.g., Balcı et al., 2011; Brunner, Kacelnik, & Gibbon, 1992; Kacelnik, Brunner, & Gibbon, 1990). Based on the well-established

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findings of interval timing literature, these studies assumed that the timing behavior exhibits trial-to-trial variation and that the standard deviation of response times is proportional to the target time intervals (i.e., constant coefficient of variation: CV; Buhusi & Meck, 2005; Gibbon, 1977; Gibbon, Church, & Meck, 1984; Simen, Rivest, Ludvig, Balcı, & Killeen, 2013). Balcı et al. (2009) designed a probabilistic temporal discrimination task (i.e., switch task, Balcı et al., 2008) and formulated the optimal temporal choice behavior based on this well-established statistical property of interval timing coupled with stimulus probabilities. In this task, the reinforcement is delivered either after a short delay at one location (short location) or after a long delay at a second location (long location). The reward delivery is contingent on the first response emitted at the active location on that particular trial at or after the associated fixed delay (e.g., reinforcing the first response at the short location after the short delay in the short delay trials). Subjects typically start the trial by anticipating the reinforcement at the short location. If and when their response at the short location is not reinforced after the short delay, they switch to the long location presumably due to judging that the long delay is in effect in that trial.

Balcı et al. (2009) manipulated the probabilities of different trial types in the temporal discrimination task described above, and found that the switch latencies of humans and mice were shorter when the short-latency trial probability was lower and longer when the short-latency trial probability was higher. Importantly, they also found that the observed adjustments in switch latencies were nearly optimal; subjects nearly maximized the reward earned for their level of timing uncertainty (see also Kheifets & Gallistel, 2012). Recent studies with humans and mice (Akdoğan & Balcı, 2015; Çoşkun et al., 2015) have also pointed at the same results in the temporal bisection task, where the categorization response is emitted after, rather than during the timed interval. These findings, along with others, point at the optimal temporal risk assessment performance of humans and other animals in scenarios with one or two probabilistic options associated with supra-second delays (for review see Balcı et al., 2011).

The optimal temporal decision-making performance has also been demonstrated in the domain of motor planning in tasks that required a simple isolated timed movement (Battaglia & Schrater, 2007; Dean, Wu, & Maloney, 2007; Hudson, Maloney, & Landy, 2008). For instance, in Hudson et al. (2008) participants were asked to respond within a particular time window to earn reward. Other time windows were associated either with penalty or no payoff. Hudson and his colleagues found that participants could integrate their timing uncertainty into the timing of their motor endpoints in a normative fashion. However, the number of targets in these studies appeared to be a limiting factor for the adoption of reward-maximizing decision strategies (optimality) in the motor planning domain. For instance, in a study by Wu, Dal Martello, and Maloney (2009), participants were presented with two targets on a touch screen and were required to touch both in a specific order within 400 ms to receive reward. The amount of reward assigned to hitting each target was varied across conditions. As the results indicated, participants exhibited a sub-optimal tendency by spending more time than optimal on the first target even in conditions where the payoff associated with the second target was much larger. Note that the timing of motor endpoints was a determinant of the overall gain in all of these experimental scenarios, the latter of which required a sequence of movements.

In the current study we investigated whether the number of temporal options resulted in deviations from reward maximization in the temporal discrimination performance of humans and mice with supra-second target intervals. To this end, we adapted a temporal switch task previously developed for pigeons (Fetterman & Killeen, 1995) to mice (see also Balcı et al, 2008). In this task, we tested subjects with three mutually exclusive probabilistic temporal options. Furthermore, our design allowed us to investigate if the probabilistic information was taken into account globally across all three options or computed and treated locally comparing the relative frequency of each two consecutive pairs of options. For instance, if the probabilities were calculated and treated locally, then the switch time between the short and the medium options should not differ between $p(T_S) = 0.33$: $p(T_M) = 0.33$: $p(T_L) = 0.33$ and $p(T_S) = 0.17$: $p(T_M) = 0.17$: $p(T_L) = 0.66$ conditions. If, on the other hand, the probabilities were taken into account across all three options (if decisions were not treated as isolated), then the switch time between the short and the medium options should be different between these two conditions. Consequently, the current study broadened the scope of the previous temporal decision-making studies (Balcı et al., 2009; Kheifets & Gallistel, 2012) and tested the generalizability of their key results to more complex scenarios in a comparative fashion.

Method

Subjects

Humans. Ten adult participants (5 females and 5 males; $M_{age} = 21.10$, $SD_{age} = 0.55$) took part in this study after providing informed consent. Participants were recruited through a publically available daily newsletter (KUDaily) published on Koç University website. Monetary compensation was provided based on each participant's performance. Total payments ranged between 55-86 TL (~20-32 USD). All procedures were approved by the Koç University Ethical Committee on Human Research.

Mice. Twenty experimentally naive male C57BL/6J mice were used in the study. One mouse was discarded from the experiment due to health problems. Mice were approximately 10 weeks old upon arrival. They were kept in individually ventilated cages lit on a 12:12 hr photoperiod. The experimental sessions were conducted during the light period. During the experimentation, mice were kept at about 85% of their baseline weight through caloric restriction. Each mouse was weighed daily and fed 30 min after the completion of the test session. Mice had ad-lib access to water in their home cages. Water was removed from the cage one hour prior to the session. All procedures were approved by the Koç University Animal Research Local Ethics Committee.

Apparatus

Humans. The temporal stimuli displays were generated and the responses were recorded in MATLAB on a Macintosh computer, using the Psychophysics Toolbox extensions (Kleiner, Brainard, & Pelli, 2007).

Mice. Experiments were conducted in eight operant chambers (Med Associates, ENV-307W: 21.6 cm x 17.8 cm x 12.7 cm) located inside ventilated and sound-attenuated boxes. All operant chambers were equipped with three illuminable feeding hoppers with liquid dippers (ENV-302RW), and each dipper cup was able to deliver 0.1 cc liquid reinforcement (Isosource Standard Nutrition Product) to the associated hopper. These three illuminable hoppers were located along one of the sidewalls of the chamber and each was equipped with a head entry detector (ENV-302HD). Another hopper located at the middle panel of the

opposing wall was used for mice to initiate the trials. White-noise generator (ENV-230) signaled the auditory stimuli. Before each session started, a cooling fan was turned on for ventilation and eliminating any other sound effects. Med-PC IV Software (Med Associates) was used to control the experimental protocol. The event times were recorded in time-event format with a resolution of 10 ms.

Procedure

General Procedure. Three types of trials were used: short trials, medium trials, and long trials. In each trial type, a temporal stimulus (visual stimulus for humans and visual/auditory stimuli for mice) was presented until the target duration elapsed. There were three response locations each of which was associated with a different target duration. In each trial, subjects had to respond at the correct location for the corresponding trial type at the end of the target interval (or after the target interval, for mice) in order to receive reward. As the trial type was not signaled by a discriminative stimulus, the expected response pattern was (1) waiting at the short location until the short interval was judged to have elapsed, (2) switching to the second location associated with the medium delay-to-reward if the reward was not received at the current location, and (3) switching to the third location associated with the long delay if no reward was presented at the second location by the time the medium interval was judged to have elapsed.

In the short trials, subjects could only make an error if they switched earlier than the duration of the short interval. Subjects could make two types of errors in medium trials: one by either failing to have switched to the hopper associated with this trial type by the end of the target interval, and second by making a switch from the medium to the long interval location before the medium duration elapsed. Lastly, in the long trials, the subjects could miss the reward if they had not switched to the long location by the end of the long interval. Correct responses were reinforced for both humans and mice. For incorrect responses, mice only missed the reward whereas humans received point penalty. In the study, the probability of different trial types was manipulated across sessions (for humans) or phases (for mice) in order to investigate its possible modulatory effect on switch latencies.

Humans. The target durations were 2, 3, and 4.5 s for short, medium, and long trials, respectively. Three neighboring gray squares were presented on the computer screen. Each square was associated with a different delay-to-reward availability: the left-most square was associated with the short duration, the middle square was associated with the medium duration, and the right-most square was associated with the long duration. Each trial started with the presentation of the three gray squares and a red frame around the left-most square, which subjects moved in order to indicate their decisions. Participants were asked to catch the reward by moving the red frame between the squares. They could move the frame from the left-most square to the middle square and from the middle square to the right-most square by pressing the keys ‘B’, and ‘N’, respectively. The participants gained reward if the frame was at the correct location by the end of the active trial duration. Otherwise, they lost a point in that trial. Correct responses resulted in a brief beep sound while incorrect responses resulted in a brief buzzer sound. Subjects could see the total score they had accrued and take a break every 20 trials.

The experiment was comprised of five daily sessions, each consisting of 420 trials. In each session, the participants were tested in a different probability condition. In the first session, each participant was tested in the equal reference duration probability condition ($p(T_S)$ = 0.33: $p(T_M)$ = 0.33: $p(T_L)$ = 0.33). This was the practice session in which the baseline performance was established. There were four unequal probability conditions: (1) the lowest probability for the short duration ($p(T_S)$ = 0.17: $p(T_M)$ = 0.415: $p(T_L)$ = 0.415), (2) the lowest probability for the long duration ($p(T_S)$ = 0.415: $p(T_M)$ = 0.415: $p(T_L)$ = 0.17), (3) the highest probability for the short duration ($p(T_S)$ = 0.66: $p(T_M)$ = 0.17: $p(T_L)$ = 0.17), (4) the highest probability for the long duration ($p(T_S)$ = 0.17, $p(T_M)$ = 0.17, $p(T_L)$ = 0.66). The order of the unequal probability conditions was counterbalanced across participants. As the first session was treated as the practice session, all participants, except for one, were tested in the equal probability condition in one more (final) session.

Mice. At the beginning of each trial, the light in the control hopper was turned on. Mice initiated the trials with a nose poke into this illuminated hopper. This requirement ensured that mice were at a fixed location at the trial onset. An inter-trial interval of a fixed 30 s plus a variable interval sampled from an exponential distribution with a mean of 30 s was used. All sessions lasted 60 min.

Training. In the training phase, the target durations for short, medium, and long trials were 3, 9, and 27 s, respectively. All trial types were presented with equal probability. When the mouse started a trial, three feeding hoppers were illuminated and the white noise was initiated. The white noise was terminated after the target interval elapsed and reward was presented in the correct location for that trial type irrespective of the subjects' response (autoshaping). The location-duration pairing for the shortest and longest durations was counterbalanced across subjects.

The expected response pattern was a sequential timed switching behavior: first switching from the short to the medium location when the short latency was judged to have elapsed without reward delivery (in the medium and long trials), and then switching from the medium to the long location when the medium duration was judged to have elapsed without reward delivery in the long trials. When a mouse exhibited this response pattern in 75% of the long trials in three consecutive sessions, the testing phase was completed.

Mice were tested in two batches. Subjects in the second batch (seven mice) were tested until this criterion was met. The total number of sessions ranged between 10-28. In the first batch (13 mice), the animals that had not met the criteria by the end of 15 sessions (eight mice) were assigned to a new five-session-long autoshaping procedure, where only the active hopper was illuminated in a given trial. In this way, mice were signaled the correct location for the corresponding trial type. After completing five sessions, these mice were again assigned to the previous training procedure (the learning criterion was held the same). Two mice met the criteria within four sessions and were moved to the next phase. The remaining six mice that failed to reach the criteria were assigned to the next phase after completing 14 sessions.

Testing Phase 1. During the testing phase, the reward was delivered only if the first response at or after the offset of the target interval was emitted at the correct hopper. The hopper lights remained on until a head entry was detected in any of the three hoppers. The testing phase lasted for at least 33 sessions. The criteria for completing this phase were exhibiting sequential timed switching behavior in at least 75% of the long trials and attaining at least 95 % of the maximum possible expected gain (see *Optimality Analysis*) in five successive sessions.

Three subjects failed to meet the criteria as they exhibited low switch ratios by the end of the 27th session. For these mice, the procedure was modified: the trials were terminated if the animals were not responding by the end of the target duration. This training aimed to induce the timed switching behavior. The criteria for proceeding to the next phase were held the same (exhibiting timed switching behavior in at least 75% of the long trials and attaining at least 95% of the maximum possible expected gain in five consecutive sessions). These mice met the criteria within at least 10 and at most 21 sessions.

After mice completed the testing phase, the durations were decreased to 3, 6, and 12 s, constituting a lower ratio. After 10 sessions, the durations were further decreased to 4, 6, and 9 s (constituting the same ratios with the human experiment). All subjects were tested with these durations for 13 sessions. Upon completion of this phase, one mouse was discarded from the study due to health problems.

Testing Phase 2. In Phase 2, subjects were divided into two groups each of which was assigned to an unequal probability condition. Group 1 was tested in $p(T_S) = 0.2$: $p(T_M) = 0.2$: $p(T_L) = 0.6$ condition and Group 2 was tested in $p(T_S) = 0.6$: $p(T_M) = 0.2$: $p(T_L) = 0.2$ condition. This phase lasted for 13 sessions.

Testing Phase 3. In Phase 3, the probability conditions were reversed for the two groups. Thus, Group 1 was tested in $p(T_S) = 0.6$: $p(T_M) = 0.2$: $p(T_L) = 0.2$ condition, whereas Group 2 was tested in $p(T_S) = 0.2$: $p(T_M) = 0.2$: $p(T_L) = 0.6$ condition. The mice were tested for 13 sessions in this phase.

Data Analysis

Human data for all five different probability conditions collected in different sessions were used in the analyses. Participants were tested with the equal probability condition in the first and last sessions. For this probability condition, the data from the last session was included in the analyses. For one subject who was not tested in the equal probability condition twice, the data from the first session was used. For mice,

different trial type probabilities were manipulated across phases. For each phase, data pooled across the last five sessions were used in the analyses.

The main units of analysis were the first and the second switch latencies observed in the long trials. Only the long trials were included in the analysis because they constitute the ideal/non-censored conditions for observing the sequence of temporal decisions. The latency at which the subjects shifted from the short location to the medium location was recorded as the first switch latency, whereas the latency at which the subjects shifted from the medium location to the long location was recorded as the second switch latency. In order to record a second switch latency, a first switch was required in the long trials. The trials with no switching behavior were eliminated from the analyses as they did not reflect task-representative behavior and/or task engagement.

Cumulative exponential Gaussian mixture distribution functions were fit to the switch latencies using the least squares method. The best fitting Gaussian parameters were treated as the timing indices of the task-representative timed responses; the mean was treated as the target switch latency and the coefficient of variation (CV = σ/μ) of the obtained distributions was treated as the index of primarily timing uncertainty.

Repeated-measures ANOVAs were run to compare the mean first and second switch latencies and CV values across different probability conditions. The Greenhouse-Geisser correction was used when the sphericity assumption was violated. The alpha level was set to .05 (two-tailed) for all of the statistical analyses. Where appropriate, pair-wise comparisons were conducted using paired-samples *t*-tests. The Holm-Bonferroni correction was applied to adjust the *p* values for multiple comparisons.

Optimality Analysis. The expected gain in this task was dependent on the level of endogenous uncertainty, the probability of different trial types, and the payoffs associated with correct/incorrect responses. In order to find the optimal target latencies separately for the first and second switches, we calculated the expected gain of each subject that would result from targeting different hypothetical switch latencies (given its CV), using the following formula:

$$EG(\hat{t}) = g(\hat{t}>T_1 \mid T_1)\, p(T_1)\, (1 - \Phi(T_1, \hat{t}, \hat{w}\hat{t})) + g(\hat{t}<T_2 \mid T_2)\, p(T_2)\, \Phi(T_2, \hat{t}, \hat{w}\hat{t}) +$$

$$g(\hat{t}<T_1 \mid T_1)\, p(T_1)\, (\Phi(T_1, \hat{t}, \hat{w}\hat{t})) + g(\hat{t}>T_2 \mid T_2)\, p(T_2)(1- \Phi(T_2, \hat{t}, \hat{w}\hat{t}))$$

Eq. 1

In Eq. 1, T_1 and T_2 are the shorter and the longer of the two scheduled latencies, $g(\hat{t}>T_1 \mid T_1)$ is the gain associated with not switching in the shorter of the two trials (i.e., not leaving the location associated with this trial type), $g(\hat{t}<T_2 \mid T_2)$ is the gain associated with switching before the longer latency in the longer of the two trials, $g(\hat{t}<T_1 \mid T_1)$ is the loss associated with switching before the shorter latency in the shorter of the two trials, $g(\hat{t}>T_2 \mid T_2)$ is the loss associated with not switching in the longer of the two trials, $p(T_1)$ and $p(T_2)$ are the probabilities of the corresponding trial types, $\hat{w}$ (CV) = $\hat{\sigma}/\hat{t}$, $\hat{\sigma}$ is the standard deviation, $\hat{t}$ is the mean target switch latency estimated from the Gaussian portion of the cumulative exponential Gaussian function fits, Φ is the cumulative Gaussian distribution function with mean $\hat{t}$ and standard deviation $\hat{w}\hat{t}$ evaluated at values corresponding to the latencies-to-reward for the associated trials. Note that $\hat{w}\hat{t}$, is used to capture the scalar property when evaluating hypothetical target switch points. The optimal switch latency for a given subject was defined as the target switch point that maximized the output of the above-mentioned function given $\hat{w}$.

Results

Human Data

Figure 1 shows average normalized first and second switch latencies for different probability conditions. A one-way repeated-measures ANOVA was conducted to investigate the effect of probability condition separately on the first and second switch latencies. The results revealed a significant difference in the first switch latencies across different probability conditions, $F(4, 36) = 9.78$, $p < 0.001$, $\eta_p^2 = 0.52$. The results of the pair-wise comparisons (Holm-Bonferroni corrected) are presented in Table 1. The difference between all pairs was in the expected direction; participants switched earlier when the probability of the short trial was low and later when this probability was high.

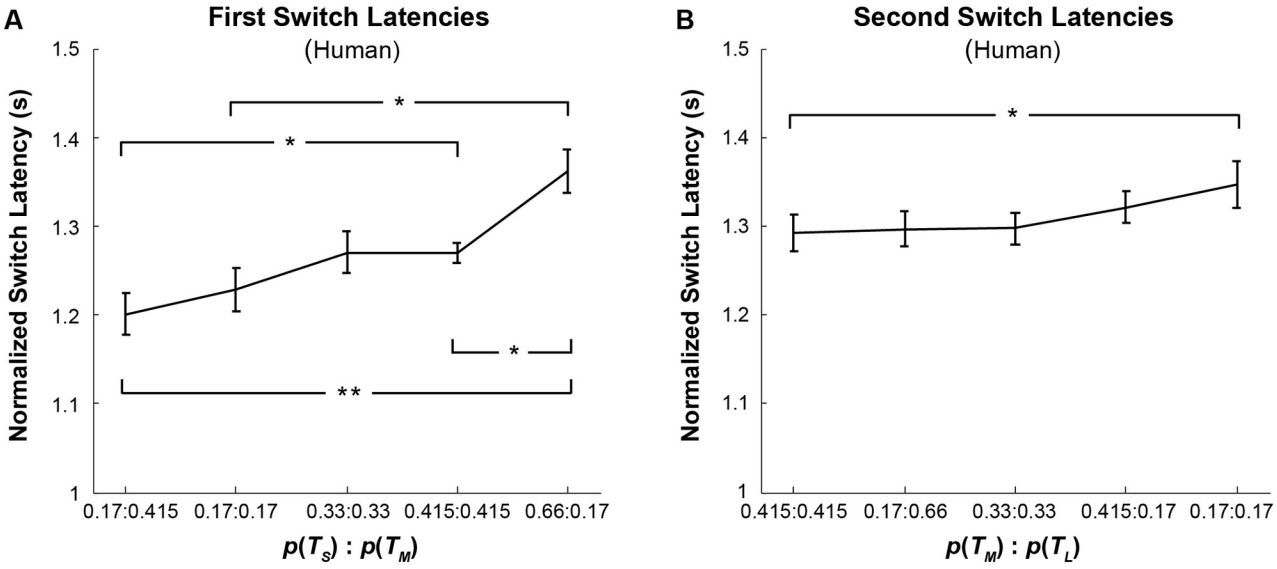

Figure 1. First (A) and second (B) mean switch latencies (normalized by 2 and 3 s, respectively) for different probability conditions (*$p < 0.05$, **$p < 0.01$).

Table 1
The paired-samples t-test comparisons of the mean first switch latencies between different probability conditions (human data)

	M	*SD*	*T*(9)	*p*
$p(T_S) = 0.66$: $p(T_M) = 0.17$	**2.72**	**0.15**		
$p(T_S) = 0.17$: $p(T_M) = 0.415$	2.40	0.15	5.29	0.01

$p(T_S) = 0.17$: $p(T_M) = 0.17$	2.46	0.16	3.72	0.04
$p(T_S) = 0.415$: $p(T_M) = 0.415$	2.54	0.07	3.70	0.04
$p(T_S) = 0.17$: $p(T_M) = 0.415$	**2.40**	**0.15**		
$p(T_S) = 0.415$: $p(T_M) = 0.415$	2.54	0.07	-3.64	0.04

Note: Bolded rows indicate the reference condition for the comparisons.

The same analyses were conducted to compare second switch latencies across different probability conditions. The results revealed a significant effect of trial type probability, $F(4, 36) = 4.69$, $p = 0.004$, $\eta_p^2 = 0.34$. Follow-up pair-wise comparisons indicated that there was a significant difference only between $p(T_M) = 0.415$: $p(T_L) = 0.415$ ($M = 3.88$, $SD = 0.20$) and $p(T_M) = 0.17$: $p(T_L) = 0.17$ ($M = 4.04$, $SD = 0.25$) conditions ($p = 0.03$, Holm-Bonferroni corrected).

In order to investigate particularly whether participants treated the probabilities within pairs locally or globally, one can evaluate the pair-wise comparisons of the conditions where the probability of two consecutive options were equal separately for the first switch latencies ($p(T_S) = 0.17$: $p(T_M) = 0.17$, $p(T_S) = 0.33$: $p(T_M) = 0.33$, and $p(T_S) = .415$: $p(T_M) = 0.415$) and the second switch latencies ($p(T_M) = 0.17$: $p(T_L) = 0.17$, $p(T_M) = 0.33$= 0.33: $p(T_L) = .33$, and $p(T_M) = 0.415$*:* $p(T_L) = 0.415$). If participants made local probabilistic judgments between consecutive pairs, we would not expect switch latencies to differ across these equal probability conditions; however, if participants made global probabilistic judgments we would observe a significant difference in switch latencies across these equal probability conditions. The pair-wise comparisons revealed that the first switch latencies did not differ across different equal-probability pairs, all ps > 0.30; whereas there was a significant difference in second switch latencies between $p(T_M) = 0.17$: $p(T_L) = 0.17$ and $p(T_M) = 0.415$: $p(T_L) = 0.415$ conditions (see results above).

Given the results of our first set of analyses of the switch latencies, it is possible that first switch latencies constrained the timing of the second switch latencies. To address this possibility, we investigated the relation between normalized first and second switch latencies of each participant using linear regression. Next, we compared the obtained slopes to the value of 0. Our one-sample t-tests revealed that the obtained coefficients were significantly higher than 0 in all experimental conditions, all ps < 0.001 (see Table 2).

The comparison of CV values for first switch latencies did not reveal any significant difference across conditions, $F(2, 18) = 0.79$, $p = 0.47$, $\eta_p^2 = 0.08$. Similarly, no significant difference emerged between CV values for the second switch latencies observed in different probability conditions, $F(2, 17) = 0.37$, $p = 0.69$, $\eta_p^2 = 0.04$. These results suggest that scalar property held for the timed responses of human participants.

Table 2
One-sample t-test comparisons of the linear regression slopes of second switch latencies on first switch latencies to the value of 0 separately for different probability conditions (human data)

Probability condition	M_{beta}	SD_{beta}	$t(9)$
0.17: 0.415: 0.415	0.55	0.10	18.39*
0.17: 0.17: 0.66	0.58	0.10	18.07*
0.33: 0.33: 0.33	0.61	0.08	22.79*
0.415: 0.415: 0.17	0.52	0.13	13.01*
0.66: 0.17: 0.17	0.57	0.10	17.10*

Note: $*p < 0.001$

In order to examine whether participants tracked optimal switch latencies, we regressed (Deming regression) each individual's mean empirical switch latencies observed in different probability conditions on the corresponding optimal switch latencies. The one-sample *t*-test comparison of obtained slopes ($M = 2.15$, $SD = 0.78$) to the value of 0 revealed a significant difference for first switch latencies, $t(9) = 8.68$, $p < 0.001$. However, the obtained regression slopes for second switch data ($M = -0.23$, $SD = 2.11$) were not significantly different from 0, $t(9) = -0.34$, $p = 0.74$. These results indicate that, human participants tracked the optimal strategies in their first switches whereas this was not the case for their second switches.

In order to further investigate the possible deviations from optimal switch latencies, we compared empirical and optimal switch latencies in each probability condition. Empirical first switch latencies in $p(T_S) = 0.66$: $p(T_M) = 0.17$ condition ($M = 2.72$, $SD = 0.15$) were significantly longer than optimal first switch latencies for this condition ($M = 2.59$, $SD = 0.08$), $t(9) = 4.22$, $p = 0.002$. There was also a significant difference between optimal ($M = 2.45$, $SD = 0.03$) and empirical ($M = 2.54$, $SD = 0.07$) first switch latencies in $p(T_S) = 0.415$: $p(T_M) = 0.415$ condition, $t(9) = 3.60$, $p = 0.006$ (Holm-Bonferroni corrected). There were no other significant differences. The analyses conducted for the second switch latencies revealed that the empirical switch latencies were significantly longer than the optimal switch latencies in all probability conditions, (all ps < 0.05, Holm-Bonferroni corrected).

Mouse Data

In the long trials, the correct response pattern was first going to the short location, then switching from the short location to the medium location, and lastly switching from the medium location to the long location. In order to evaluate whether subjects consistently displayed this specific sequence, we calculated the proportion of the long trials in which mice exhibited switching behavior in an incorrect order (i.e., short-long, mid-short, long-mid, long-short). First we calculated this proportion for all long trials and observed that the subjects followed an incorrect sequence in 21, 11, and 16% of the long trials in the $p(T_S) = 0.2$, $p(T_S) = 0.33$, and $p(T_S) = 0.6$ conditions, respectively. However, in order to investigate this proportion observed in the trials where the subjects exhibited task-engagement and task-representative performance,

we repeated our analysis using the trials where there was at least a first switch from the short to the medium location. This calculation revealed that the subjects followed an incorrect sequence in 4, 7, and 9% of the trials for increasing short trial probability conditions, respectively. These trials were not included in the analyses.

Next, in order to investigate whether mice could time three durations accurately, response rates (in 200 ms bins) of each response type (short, medium, long) were calculated separately for each subject. The normalized average response curves for each probability condition are shown in Figure 2. Visual inspection of this figure suggests that mice could accurately time the short interval but *underestimated* the medium interval as manifested in the longer peak location of the response curves compared to the target duration. This shift from the medium duration can be explained by the travel time (i.e., the time spent switching from the short to the medium location). Since we did not test mice in probe trials for the long target intervals, it is not possible to evaluate the accuracy for time judgments of the long target time.

The first and second target switch latencies were estimated from the Gaussian portion of the exponential Gaussian mixture distribution function fits to individual subjects' data. Figure 3 depicts the average first and second switch latencies for different probability conditions. There was a significant increase in first switch latencies with increasing short trial probability, $F(2, 36) = 9.60$, $p < 0.001$, $\eta_p^2 = 0.35$. Follow-up pair-wise comparisons revealed a significant difference only between $p(T_S) = 0.2$ ($M = 4.97$, $SD = 0.04$) and $p(T_S) = 0.6$ ($M = 5.23$, $SD = 0.03$) conditions, $p = 0.003$ (Holm-Bonferroni corrected). There was a significant effect of probability condition on the second switch latencies as well, $F(1, 24) = 4.43$, $p = 0.03$, $\eta_p^2 = 0.21$. As pair-wise comparisons indicated, there was a significant difference in switch latencies between $p(T_L) = 0.6$ ($M = 7.18$, $SD = 0.33$) and $p(T_L) = 0.2$ ($M = 7.44$, $SD = 0.21$) conditions, $p = 0.001$ (Holm-Bonferroni corrected).

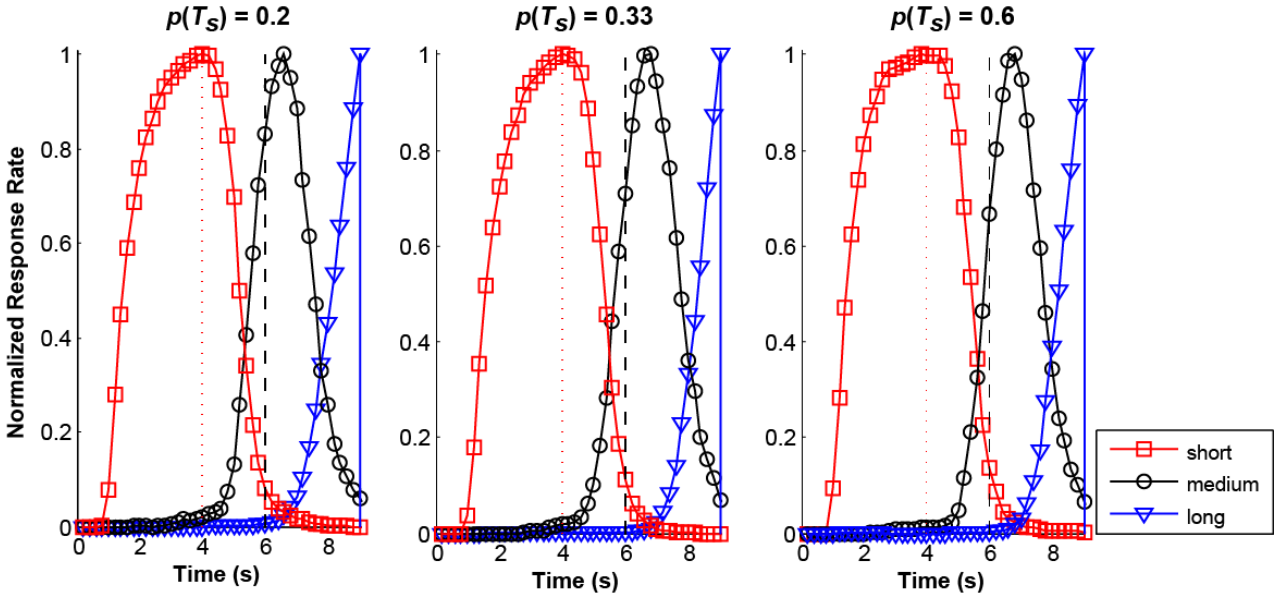

Figure 2. Average response curves (normalized by the maximum response rate for each response type) for short, medium, and long response types obtained from long trials in different probability conditions. Vertical lines correspond to the target latencies (dotted line: short latency, dashed line: medium latency, solid line: long latency).

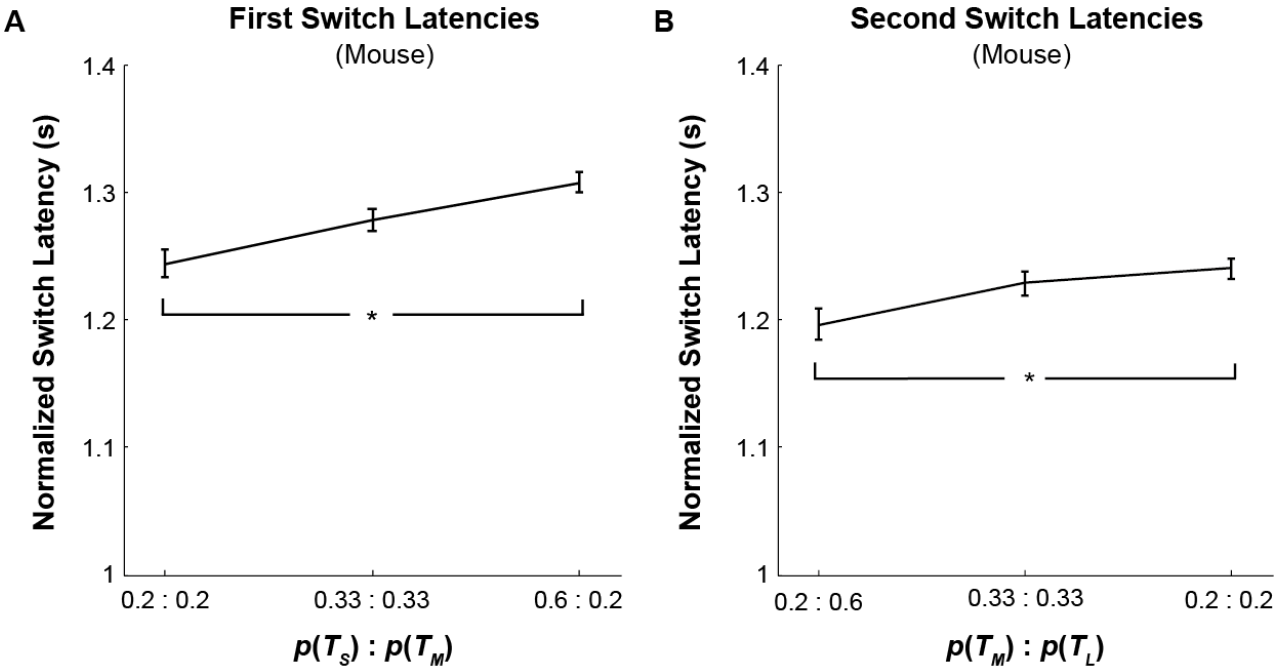

Figure 3. First (A) and second (B) mean switch latencies (normalized by 4 and 6 s, respectively) of mice for different probability conditions (*$p < 0.05$).

In order to investigate whether subjects made local or global judgments between neighboring options, we evaluated the pair-wise comparisons between those conditions where the probability of two consecutive options was equal separately for first switch latencies ($p(T_S) = 0.2$: $p(T_M) = 0.2$ and $p(T_S) = 0.33$: $p(T_M) = 0.33$) and second switch latencies ($p(T_M) = 0.2$: $p(T_L) = 0.2$ and $p(T_M) = 0.33$: $p(T_L) = 0.33$). For the first switch latencies, we observed a marginally significant increase from $p(T_S) = 0.2$: $p(T_M) = 0.2$ ($M = 4.97$, $SD = 0.04$) to $p(T_S) = 0.33$: $p(T_M) = 0.33$ ($M = 5.11$, $SD = 0.03$) condition, $p = 0.052$ (Holm-Bonferroni corrected). For the second switch latencies, the difference between equal-probability pairs did not approach significance, $p = 0.45$ (Holm-Bonferroni corrected).

The CV values for both first and second switch latencies were compared across different probability conditions. The results revealed no significant effect of stimulus probability condition on CV values obtained from the first switch latencies, $F(2, 36) = 1.02$, $p = 0.37$, $\eta_p^2 = 0.05$. Similarly, CV values obtained from the second switch latencies did not exhibit a significant change between different stimulus probability conditions, $F(2, 36) = 0.94$, $p = 0.40$, $\eta_p^2 = 0.05$. These results suggest that scalar property also held for the timed responses of mice.

In order to investigate the possible relation between first and second switch latencies of mice, we conducted linear regression on an individual subject basis. The mean slopes were 0.56, 0.62, and 0.70 for increasing short trial probability conditions, respectively. The one-sample *t*-test comparisons of the obtained regression slopes to

the value of 0 revealed a significant difference for all probability conditions ($p(T_S) = 0.2$: $t(18) = 9.17$; $p(T_S) = 0.33$: $t(18) = 26.96$; $p(T_S) = 0.6$: $t(18) = 16.10$; all ps < 0.001).

We also investigated the mean differences between optimal and empirical switch latencies separately for different probability conditions. Our results indicated that subjects' empirical first switch latencies were significantly longer than the optimal in $p(T_S) = 0.33$ ($M_{emp} = 5.11$, $M_{opt} = 4.95$, $t(18) = 4.81$) and $p(Ts) = 0.6$ ($M_{emp} = 5.23$, $M_{opt} = 5.08$, $t(18) = 4.81$) conditions, ps < 0.001 (Holm-Bonferroni corrected). There was no significant difference between the optimal and empirical second switch latencies in any probability condition (all ps > 0.05).

Discussion

The current study investigated whether and how stimulus probabilities are incorporated into time-based decisions of humans and mice in scenarios that required them to make subsequent decisions within a given trial. In order to study this question, we tested humans and mice in a three alternative timed switch task. In this task, each of the three different delays-to-reward was associated with a different reward location. In a given trial, only one of the trial types and thus reward locations was armed without marking it with a discriminative stimulus. The probability of different trial types was manipulated across different experimental conditions. In trials where the long-latency-related location was active (i.e., long-latency trial was in effect), subjects were expected to switch first from the short location to the medium location if the reward was not delivered after the short-latency, and they would switch to the long-latency-related location if the reward was not delivered after the medium-latency either. Consequently, they would make two subsequent time-based decisions in the long trials. The primary question was whether the switch latencies of humans and mice between short-medium options and medium-long options were sensitive to probabilistic manipulations. Furthermore, the specific design of this study aimed to investigate if the subjects were treating the probabilities within a pair locally or if the probabilities were treated globally.

The results of this study showed that both humans and mice exhibited the expected sequential timed switching behavior in the dual-switch task. Additionally, their first switches were sensitive to the probabilistic task contingencies such that subjects switched earlier if the medium trial had a higher probability whereas they switched later if the short trial probability was higher. Thus, subjects incorporated the stimulus probabilities into their decisions about when to leave the first option for the next one. On the other hand, the second switch latencies of humans did not show the same level of sensitivity to the probabilistic information as their first switch latencies. Our analyses suggested a constraining effect of the first switch latencies on the second switch latencies; as the time spent waiting on the first option increased, so did the time spent waiting on the second option irrespective of the probability condition. In all conditions, the empirical second switch latencies of humans were significantly longer than the optimal latencies (note also the occasional deviations from optimality for the first switch latencies). Consequently, our findings suggested that the human participants failed to adopt a (at least local) probability-adaptive strategy in their second timed decisions.

Similar findings in humans were obtained in a previous study (Wu et al., 2009), which investigated optimality in a sequential motor task. In that study, participants were required to allocate a fixed time between two sequential movements each of which entailed touching a target on the screen. In this task, the optimal stay duration at the first target before moving to the second changed depending on the ratio of their associated gains. Wu et al. (2009) found that human participants spent more time than optimal on the first target, even when the gain associated with the second target was five times larger. Consistent with these findings, in the current study, the number of options emerged as a significant limiting factor regarding the optimality of timed decisions of humans (especially in comparison to prior work that pointed at optimal temporal risk assessment performance). Despite that there were significant relations between the first and second switch latencies of mice, in contrast to the human data, this relation did not preclude probability-dependent adaptive timed response patterns in subsequent choice behavior. Consistently, the empirical and optimal target second switch latencies of mice did not show any significant difference (note deviations from optimality for the first switch latencies).

Overall, our findings point at a suboptimal tendency in the temporal discrimination performance of humans in decision-scenarios that contain multiple temporal options. These tendencies were not present or as apparent in the mouse data. This inter-species difference in adaptive timed behavior can be partially due to the decision biases in the case of human participants (e.g., Trommershäuser, Gepshtein, Maloney, Landy, & Banks, 2005). Alternatively, the fact that the probability conditions in the mouse experiment were not as varied as they were for the human experiment might have led to such differential findings between mice and humans. The differential level of training for humans and mice is another potential factor that might have contributed to these inter-species differences. Finally, it is possible that the significant differences between different probability conditions in second switch latencies of mice are simply due to the residual effects of the modulation of the first switch latencies based on initial probabilities. To this end, note the parallelism between the lines representing first and second switch latencies in Figure 3 coupled with the lack of differences compared to $p(T_S) = p(T_M) = p(T_L) = 0.33$ condition. Thus, future studies are needed to conduct a more comprehensive cross-species comparison of performance in this task.

Finally, our results suggest that humans compute and treat probabilities locally between each two consecutive option in their initial temporal decisions (i.e., first switches), as there were no significant differences in the first latencies between conditions that constituted equal probabilities of neighboring options. Despite the fact that these equal-probability conditions did not differ significantly, the visual inspection of the mean switch latencies revealed a trend to switch later as the total probability of these two options increased and the probability of the third option decreased (see Figure 2). Even though this trend could possibly suggest a global probability judgment across three options during temporal decision-making between the first two options, the fact that the differences were not significant prevents us from reaching such a definite conclusion. Unlike the first switches, the second switch latencies of humans differed significantly between one out of three comparisons of conditions where the neighboring options had equal probabilities. Together with the suboptimal tendency to wait longer at

the medium option, this result reveals the constraining effect of the first switch latency and/or the probability of the first two temporal options on the subsequent timed switching behavior of human participants. This was not the case for the mouse data; there were no significant differences in either first or second switch latencies of mice between conditions that contained equal probability of neighboring options. These results suggest that unlike humans, mice treated probabilities locally both for their initial and subsequent timed decisions. However, again note that even though the difference between conditions where the neighboring options had equal probabilities did not reach significance, there was a trend for a delay in switch latencies from the short to the medium option as their probabilities increased (see Figure 3). Similar to what is observed in the human data, this trend could suggest a global judgment across three options instead of a local judgment between each two consecutive pair of options for the first switch latencies. Again, it is not possible to reach such a definite conclusion as our analyses failed to reveal a significant difference between these conditions.

Consistent with previous studies that have demonstrated the modulatory effect of probabilistic information on perceptual two-alternative forced choice tasks (e.g., Carpenter & Williams, 1995; Leite & Ratcliff, 2011; Mulder, Wagenmakers, Ratcliff, Boekel, & Forstmann, 2012), our results indicated both humans and mice can modulate their time-based responses (at least the initial decisions) based on experienced probabilities (see also Akdoğan & Balcı, 2015; Çoşkun et al., 2015). Thus, both human and nonhuman animals have been shown to process and integrate probabilistic information into their decisions pertaining to different domains, which suggests possibly a common evolutionary basis for this ability. With the current study, we have expanded the scope of these previous findings by including more than two options in a temporal decision-making task. Our results showed that the presence of more than two options constitutes a limiting factor for the sensitivity of humans' temporal decisions to probabilistic manipulations. As the endogenous uncertainty necessitates and guides the integration of probabilistic contingencies for reward maximization, understanding how animals treat probabilities becomes an important topic of investigation. The current study has addressed how probabilities are treated (i.e., globally across all options or locally between each pair) when the task necessitates to make sequential timed decisions. Future studies can investigate this topic including a wider range of probabilistic conditions to establish a better understanding of the processes that underlie probabilistic sequential temporal judgments.

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