Perturbations in The Arrow of Time:
Computational and Procedural Dissociations of
Timing and Non-Timing Processes

By

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ABSTRACT

Timing performance is sensitive to fluctuations in time and motivation, thus interval timing and motivation are either inseparable or conflated processes. A behavioral systems model (e.g., Timberlake, 2000) of timing performance (Chapter 1) suggests that timing performance in externally-initiated (EI) procedures conflates behavioral modes differentially sensitive to motivation, but that response-initiated (RI) procedures potentially dissociate these behavioral modes. That is, timing performance in RI procedures is expected to *not* conflate these behavioral modes. According to the discriminative RI hypothesis, as initiating-responses become progressively discriminable from target responses, initiating-responses increasingly dissociate interval timing and motivation. Rats were trained in timing procedures in which a switch from a Short to a Long interval indexes timing performance (a latency-to-switch, LTS), and were then challenged with pre-feeding and extinction probes. In experiments 1 (Chapter 2) and 2 (Chapter 3), discriminability of initiating-responses was varied as a function of time, location, and form for rats trained in a switch-timing procedure. In experiment 3 (Chapter 4), the generalizability of the discriminative RI hypothesis was evaluated in rats trained in a temporal bisection procedure. In experiment 3, but not 1 and 2, RI enhanced temporal control of LTSs relative to EI. In experiments 1 and 2, the robustness of LTS medians to pre-feeding but not extinction increased with the discriminability of initiating-responses from target responses. In experiment 3, the mean LTS was robust to pre-feeding in EI and RI. In all three experiments, pre-feeding increased LTS variability in EI and RI. These results provide moderate support for the discriminative RI hypothesis, indicating that initiating-responses selectively and partially dissociate interval timing and motivation processes. Implications for the study of cognition and motivation processes are discussed (Chapter 5).

DEDICATION

I dedicate this work to my late grandfather, Robert Lillion Carter. His presence, support, and advice throughout the first quarter of my life has always guided me. I'm sure he would be proud of what I've produced and glad to see that, although I have yet to carry on his legacy of wood working, I carry on his self-sufficiency and love of learning.

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and those in Arizona. To all of you, I thank you for the support but also the constant humor and insistence I not be too serious.

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Chapter 1: Introduction

Defining, Measuring, and Describing Interval Timing

"What then is time? If no one asks me, I know what it is. If I wish to explain it to him [or her] who asks, I do not know" ~ Saint Augustine

Interval timing is the entrainment of behavior to periodicities of biologically significant events in the timescale of seconds-to-minutes, signaled by some stimulus (i.e., a time-marker; Buhusi & Meck, 2005; Gibbon, 1977, Sanabria & Killeen, 2007). Such entrainment is not just a feature of behavior, it is a critical ability leveraged in many disparate contexts (Marshall & Kirkpatrick, 2015; McMillan, Spetch, Sturdy, & Roberts, 2017). Interval timing is critical for both learning (Gallistel & Gibbon, 2000; Holland, Hamlin, & Parsons, 1997) and decision making (Gruart, Meck, & Doyere, 2012; Wittmann & Paulus, 2008). For example, animals use the passage of time to infer the structural and causal links between different stimuli (Kirkpatrick & Balsam, 2016; Ward, Gallistel, & Balsam, 2013). Individuals with impaired timing, as in individuals diagnosed with schizophrenia, are unable to structure their daily routines and thus often engage in activities out of sequence (Bonnot, Montalembert, Kermarrec, Botbol, Walter, & Coulon, 2011; Elvevåg, Egan, & Goldberg, 2000; Ueda, Maruo, & Sumiyoshi, 2018). Interestingly, individual differences in decision making are related to individual differences in interval timing (Galtress, Garcia, & Kirkpatrick, 2012) and can be improved by training individuals to more accurately and precisely estimate the passage of time (Bailey, Peterson, Schnegelsiepen, Stuebing, & Kirkpatrick, 2018). Recently, researchers have argued that interval timing plays a critical role in forming our conscious experience (Yin, Terhune, Smythies, & Meck, 2016). Thus, interval timing is both an interesting

phenomenon *per se* and a useful diagnostic tool, a window into regulated and dysregulated cognition (Ward, Kellendonk, Kandel, & Balsam, 2012).

Interval timing procedures can be classified into at least two different categories: immediate and retrospective timing (Killeen, Fetterman, & Bizo, 1997; Killeen & Fetterman, 1988) [1]. In immediate timing, subjects are trained to continuously estimate whether reinforcement will occur now or later, and thus when to start responding. Examples of immediate timing include fixed-interval (FI) schedules of reinforcement, the peak procedure, and the switch-timing procedure. In retrospective timing, subjects are trained to indicate whether a just elapsed interval is longer or shorter than some standard(s). Examples of retrospective timing include but are not limited to the temporal bisection procedure.

Figure 1.1 shows schematics of these immediate and retrospective timing procedures. In FI (Figure 1.1A), reinforcement is delivered following the first response after some interval *t* has elapsed. Following time-marker presentation, FI responding typically starts at a relatively low-rate and then transitions abruptly to a high-rate (Guilhardi & Church, 2004; Schneider, 1969). The time of this transition—also known as the *break point*—serves as an index of timing performance. Another index is the time to the first response following time-marker presentation, which is referred to as either the post-reinforcement pause or latency (e.g., Daniels & Sanabria, 2017a; Shull, 1971). All three indices approximate two-thirds *t*.

[1] There is a third category: prospective timing. In prospective timing procedures, subjects are trained to choose between different times to reinforcement. However, performance in prospective timing procedures is outside the scope of the current dissertation.

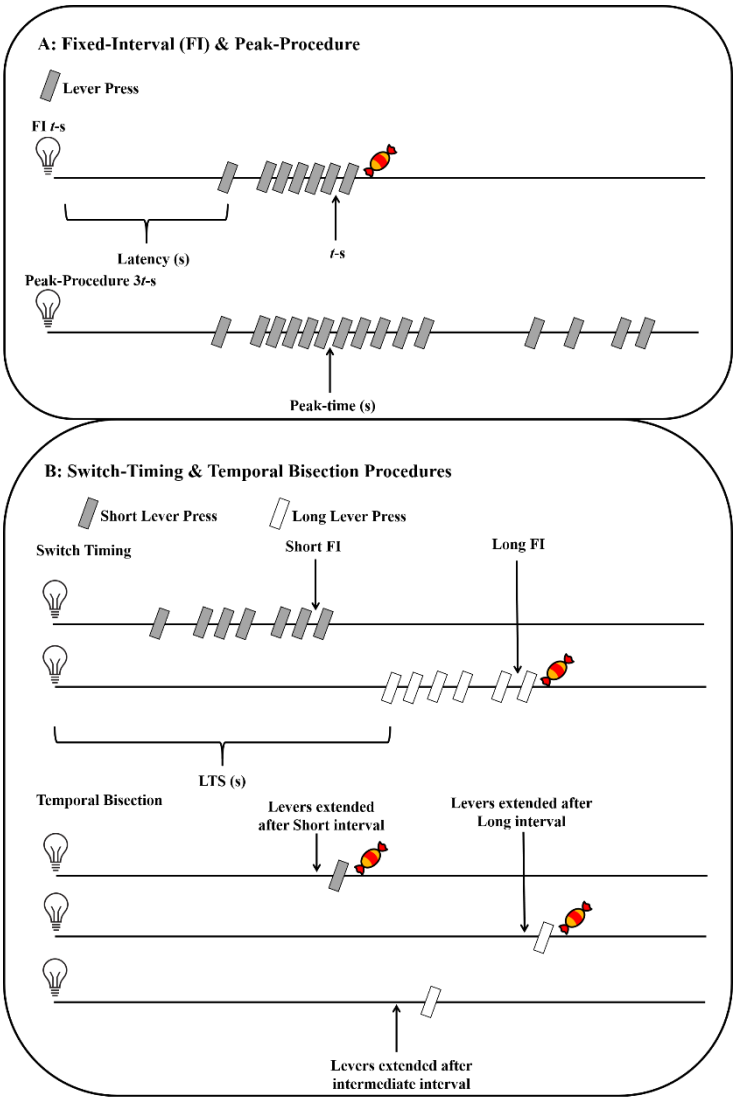

Figure 1.1. Schematic of typical immediate and retrospective interval timing procedures (Panel A = immediate timing: fixed-interval (FI) and peak procedure; Panel B = immediate timing: switch-timing procedure; and retrospective timing: temporal bisection procedure). Timing performance indices are indicated by a bracket and labeled (i.e., latency, peak-time, latency-to-switch [LTS]). Note that for the temporal bisection procedure, the index is the point-of-subjective equality (a.k.a, mean LTS) which is inferred by fitting a sigmoid-like function to the data relating choices 'long' to the Short, Long, and intermediate intervals.

A variant of FI, referred to as the peak procedure (Figure 1.1A; Roberts, 1981; Sanabria & Killeen, 2007), intermixes trials that are equal to 3*t* or 4*t* and terminate without reinforcement. In these peak-trials, responding initially accelerates and peaks

around the expected time of reinforcement (i.e., *t*) and then declines to some low level as the expected time of reinforcement recedes. Three timing performance indices can be calculated from this pattern of responding (Church, Meck, & Gibbon, 1994; Sanabria, & Killeen, 2007). The time at which responding transitions from a low- to a high-state is referred to as the start-time (similar to latencies in FI), which approximates two-thirds *t*. The time at which response rate is maximal is referred to as the peak-time, which approximates *t*. And the time at which responding transitions from a high-state to a low-state is referred to as the stop-time, which approximates 1.75-2*t*.

Recently, research has focused on two different, but complementary interval timing procedures: the switch-timing procedure and the temporal bisection procedure. In the switch-timing procedure (Figure 1.1B; e.g., Balci, Freestone, & Gallistel, 2009; Fox, Prue, & Kyonka, 2016; Stubbs & Pliskoff, 1969), reinforcement is delivered following the first response after either a Short FI or Long FI. Both the Short FI and Long FI are each associated with a unique manipulandum but nondifferentially signaled when active. Following time-marker presentation, well-trained subjects start responding on the Short FI and, if reinforcement is not forthcoming, switch over to the Long FI. In Long FI trials, the time to the first response on the Long FI indexes timing performance and is referred to as the latency-to-switch (LTS). LTSs approximate the geometric mean of the Short and Long FIs (Fox et al., 2016).

In the temporal bisection procedure (Figure 1.1B; e.g., Kopec & Brody, 2009; Church & Deluty, 1977; Raslear, 1985), subjects are trained to categorize a Short interval as ‘short’ by pressing, for example, the left lever, and a Long interval as ‘long’ by pressing, for example, the right lever. After sufficient training, subjects are tested with intermediate intervals to ascertain the degree to which subjects categorize these

nonreinforced, intermediate intervals as 'long'. A function is fit to the data relating choices 'long' to the Short, Long, and intermediate intervals. Typically, this function is sigmoidal, reflecting the fact that subjects choose 'long' more frequently as the interval increases. From this function, the interval at which subjects choose 'short' equally as often as 'long' indexes timing performance and is referred to as the point-of-subject-equality. Like LTSs, the point-of-subjective equality approximates the geometric mean of the Short and Long intervals (Church & Deluty, 1977).

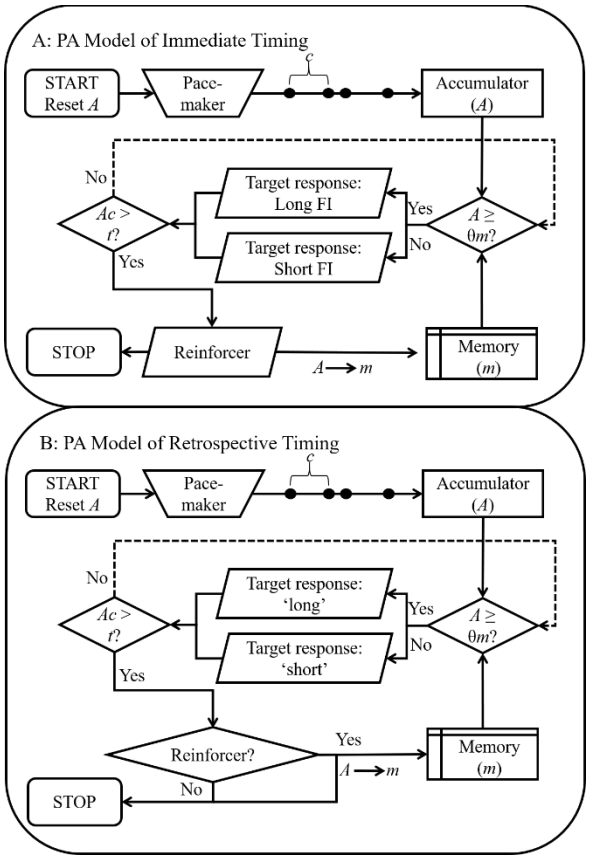

Figure 1.2. Schematic of the fundamental components of the pacemaker-accumulator (PA) family of interval timing models. Components of PA model in immediate (Panel A) and retrospective (Panel B) interval timing procedures adapted from the schematic proposed by Daniels, Fox, Konyka, & Sanabria (2015b). See text for details.

Interestingly, certain implementations of the temporal bisection procedure promote behavioral sequences akin to that observed in animals trained in the switch-timing procedure. When the 'short' and 'long' responses are in fixed locations, pigeons (Machado & Keen, 2003; Oliveira & Machado, 2009), rats (Gouvêa et al. 2014), and humans (Cambraia, Vasconcelos, & Machado, 2018) appear to make choices based on their relative position to the 'short' and 'long' responses at the end of the interval. At the beginning of an interval, subjects start in front of the 'short' response and then, as time elapses, switch over to the 'long' response; when the interval ends, subjects choose the closer of the two responses. This behavioral sequence is like the switching observed in Long FI trials in animals trained in the switch-timing procedure, suggesting that underlying choices 'long' are latent LTSs. To emphasize the similarity between performance in the switch-timing and temporal bisection procedures, the point-of-subjective equality will also be referred to as the mean LTS.

Performance in both immediate and retrospective timing procedures is typically studied within the same predominant theoretical framework: the pacemaker-accumulator (PA) family of computational timing models (Gibbon 1977, Treisman, 1963; Simen, Rivest, Ludvig, Balci, & Killeen, 2013; for some limitations see Dragoi, Staddon, Palmer & Buhusi, 2003; Machado, Malheiro, & Erlhagen, 2009; Staddon & Higga, 1999). Figure 1.2 shows a schematic of the fundamental components of PA models for immediate and retrospective timing in the context of switch-timing and temporal bisection procedures, respectively[2]. Briefly, PA models generally assume that following

[2] The model described in Figure 1.2 is not unique to the switch-timing and temporal bisection procedures. These models can be reorganized to account for performance in almost any interval timing procedure. To account for performance in FI and peak procedures, it can be assumed that subjects switch from engaging in other, non-timing behaviors to responding on the FI (Sanabria, Thrailkill, & Killeen, 2009). Such an

onset of a time-marker, a pacemaker emits pulses at some rate ($1/c$, where c = average inter-pulse interval), which are counted by an accumulator (A). In switch-timing procedures (Figure 1.2A), it is assumed that the pulse count in A is continuously compared to a pulse count sampled from memory (m) such that when the pulse count in A becomes sufficiently like the pulse count sampled from m, target responses switch from the Short FI to the Long FI (e.g., lever presses). Likewise, in temporal bisection procedures (e.g., location variant of temporal bisection; Figure 1.2B), it is assumed that subjects continuously compare whether A is similar to m and thus transition from the 'short' response to the 'long' response in the form of a latent LTS, with choice expressed at the end of the interval[3].

Performance indices of both immediate and retrospective timing procedures are derived from target responses. Depending on how PA models are instantiated, PA models predict that performance indices are best described by either a gamma (Killeen & Fetterman, 1988; Machado 1997), normal (Gibbon, 1977; Machado, Malheiro, & Erlhagen, 2009), or Wald distribution (Simen, Rivest, Ludvig, Balci, & Killeen, 2013). For example, according to the behavioral theory of timing (Killeen & Fetterman, 1988), pulses are behavioral states differentially associated with target responses. The rate at which subjects transit behavioral states proceeds according to an endogenous Poisson clock at some rate ($1/c$). As such inter-pulse intervals are exponentially distributed and

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assumption is consistent with the notion that responding, even in single schedules of reinforcement, reflects a choice between two alternatives (Herrnstein, 1974)

[3] Other decision rules have been suggested. For example, Gibbon (1981) suggested a ratio similarity decision rule in which subjects compare the similarity of A to samples of m associated with the Short interval and samples of m associated with the Long interval, with subjects choosing 'short' or 'long' based on whether A was most similar to the Short or Long interval (Allan & Gibbon, 1991; Meck & Church, 1983). However, this ratio similarity rule is less parsimonious than the decision rule depicted in Figure 1.2 (it requires two rather than one memory store), and previous research indicates that this decision rule is limited in applicability (see Siegel, 1986).

the sums of inter-pulse intervals preceding target response emission are gamma distributed. Thus, performance indices are gamma distributed[4]. This timing process is assumed to take a minimal amount of time to complete, requiring performance index distributions be shifted by the minimum performance index (δ). This variant of the PA model may be formally expressed as,

$$
\begin{aligned}
&p(\text{performance index} = \tau \mid \tau < \delta) = 0 \\
&p(\text{performance index } = \tau \mid \tau \geq \delta) = \frac{1}{\Gamma(\theta M) c^{\theta M}} (\tau - \delta)^{\theta M - 1} e^{-\frac{\tau - \delta}{c}} \\
&\theta M \geq 1; \theta, M, c, \delta > 0
\end{aligned}
\tag{1.1}
$$

where parameters are as described above and Γ is the gamma function.

Scalar and Motivated Timing Performance

Of critical interest is whether performance index distributions are selectively sensitive to the passage of time. Performance indices (i.e., latencies, peak-times, LTSs, mean LTS) adhere to the *scalar property* (Gibbon, 1977). The scalar property states that the mean and standard deviation of indices linearly scale with programmed intervals (i.e., *t* or the geometric mean of Short and Long FIs in the switch-timing procedure and Short and Long intervals in the temporal bisection procedure) such that if the standard deviation is normalized by the mean, the resulting quotient (i.e., the coefficient of

[4] Technically, such a process gives rise to an Erlang distribution, which is a special case of the gamma distribution in which the shape parameter $\theta M \in \mathbb{N}_{\geq 1}$ rather than $\theta M \in \mathbb{R}_{\geq 1}$ and thus states that the requisite number of accumulated pulses for a target response denoting a performance index must be an integer. Fractional pulse counts gives the gamma distribution greater flexibility in describing performance indices than the Erlang distribution.

variation) is constant over a wide range of intervals. Adherence to the scalar property can also be assessed by determining if performance index distributions superimpose across a range of *t*. This scaling is consistent with Weber's law, which generally states that the discrimination threshold of two stimuli is a linear function of stimulus intensity (Dehaene, 2003). This indicates that time perception follows regularities evident in other modalities, such as vision and audition (Howard & Shankar, 2018). Evidence for the scalar property is relatively ubiquitous across species (Lejeune & Wearden, 1991; cf. Bizo, Chu, Sanabria, & Killeen, 2006) suggesting that scalar timing performance is highly conserved across evolution. This also indicates that regulated and dysregulated interval timing can be studied in model species (e.g., laboratory rats) to directly probe both behavioral and neurological mechanisms.

Surprisingly, performance indices are also sensitive to fluctuations in motivation (for reviews see Balci, 2014 and Galtress, Marshall, & Kirkpatrick, 2013). According to Bailey, Simpson, & Balsam (2016), motivation may be conceptualized as the set of processes governing the intensity and direction of goal-directed action. Whereas intensity may describe the vigor, that is the rate, at which some action is emitted, direction refers to whether subjects work for food over milk, water over milk, etc. (also see Niv, Joel, & Dayan, 2006). For example, a satiated subject may work for the same goal as when it is hungry but will do so at a slower pace (e.g., Corbit & Balleine, 2005; Dickinson, 1985). Similarly, augmenting dopaminergic signaling via administration of dopaminergic drugs or modulating genes related to dopaminergic signaling appears to alter the rate at which subjects work for goals (e.g., Beeler, Daw, Frazier, Zhuang, 2010; Balci 2014; Niv, Daw, Noel, & Dayan, 2007; Niv, Joel, & Dayan, 2006). In contrast, if the number of lever presses to obtain a goal is increased or if a goal is devalued due to pairing the goal with illness, then subjects will work at a similar pace but opt for the less

effortful and more valuable alternative (e.g., Corbit & Balleine, 2005; Dickinson, 1985; Johnson, Gallagher, & Holland, 2009).

Interestingly, performance indices are sensitive to changes in food deprivation (e.g., Daniels & Sanabria, 2017a; Plowright, Church, Behnke, & Silverman, 2000) and goal costs (e.g., Bickel, Higgins, Kirby, & Johnson, 1988; Zeiler & Buchman, 1979), contingencies (e.g., Buriticá & dos Santos, 2017; Machado & Cevik, 1998; Ward & Odum, 2006), and relative value. The relative value of goals may be altered by changes in magnitude (e.g., Balci, Wiener, Çavdaroğlu, & Coslett, 2013; Daniels, Garcia, Watterson, Mazur, Brackney, & Sanabria, 2015; Daniels, Fox, Kyonka, & Sanabria, 2015; Ludvig, Balci, & Spetch, 2011; Ludvig, Conover, & Shizgal, 2007), presence of alternative sources of reinforcement (e.g., Sanabria, Thrailkill, & Killeen, 2009), inducing illness by pairing goals with lithium chloride (e.g. Galtress & Kirkpatrick, 2009; cf. Delamater, Desouza, Rivkin, & Derman, 2014; Delamater, Chen, Nasser, & Elayouby, 2018), administration of psychostimulants thought to modulate dopaminergic output (e.g., Balci, Papachristos, Gallistel, Brunner, Gibson, & Shumyatsky, 2008; Buhusi & Meck, 2002; Daniels et al., 2015a; Drew, Fairhurst, Malapani, Horvitz, & Balsam, 2003; for a reviews see Meck, 1996 and Balci et al., 2014), and genetic differences in dopamine release (e.g., Balci, Wiener, Çavdaroğlu, & Coslett, 2013; Meck, Cheng, MacDonald, Gainetdinov, Caron, & Çevik, 2012; Wiener, Lohoff, & Coslett, 2011). Thus, timing performance appears to be sensitive to fluctuations in both the vigor and direction of goal-directed action.

Pre-feeding Affects Timing Performance

The present dissertation is concerned with pre-feeding-induced reductions in motivation, which reduces the vigor but not the direction of goal-directed action. In most published studies, pre-feeding promotes longer and more varied performance indices

relative to baseline (Daniels & Sanabria, 2017a; Eskin & Bitterman, 1960; Galtress & Kirkpatrick, 2009; Galtress, Marshall, & Kirkpatrick, 2012; Grace & Nevin, 2000; Plowright, et al. 2000; Shull & Brownstein, 1968). This effect has been predominantly observed in immediate timing procedures such as FI and the peak procedure across a wide range of intervals (10 s to 100 s) in a variety of animals with a variety of feeding regimens. Interestingly, the effect of pre-feeding on performance indices appears permanent so long as the reduced motivational state is maintained.

In some cases, however, the effect of pre-feeding on timing performance appears transient. In rats trained on the peak procedure, Roberts (1981) observed that pre-feeding results in later peak times at the beginning but not at the end of the session. Such transience could reflect learning under a new motivational state. Recently, however, Daniels, Overby, and Sanabria (2018) showed that within-session elongation of latencies in rats trained in FI is present regardless of motivational state and is not modulated by motivational state or the programmed FI. A similar process has also been observed on peak times in mice trained in the peak procedure (Balci, Ludvig, & Brunner, 2010). Although whether the within-session elongation of peak times is sensitive to fluctuations in motivation or to the programmed FI has not been tested, the data of Daniels et al. (2018) suggests that the transiency of the effect reported by Roberts (1981) could be due to the within-session elongation of peak times swamping the pre-feeding-induced later peak times. This interpretation indicates that the effect of pre-feeding on peak times is permanent but potentially obscured by processes prevalent in the latter part of sessions, giving the appearance of transience.

Longer and more varied performance indices are not always observed simultaneously following pre-feeding. This appears particularly true in retrospective

timing procedures such as the temporal bisection procedure, where data on pre-feeding effects are scant and equivocal. For example, whereas Ward & Odum (2006) reported that pre-feeding resulted in a flatter psychophysical function and no shift in the mean LTS, McClure, Saulsgiver, & Wynne (2009) reported that pre-feeding resulted in a later mean LTS but not a flatter psychophysical function. McClure et al. (2009) suggest that this discrepancy could be due to differences in implementation of the temporal bisection procedure. Whereas Ward & Odum (2006) trained pigeons to associate different key colors with choices 'short' and 'long', with key colors counterbalanced between locations across trials, McClure et al. (2009) trained pigeons in the location variant of the temporal bisection procedure, in which choices 'short' and 'long' are in fixed locations. Thus, pre-feeding-induced shifts in the mean LTS might only be observed when temporal bisection procedures facilitate behavioral sequences akin to the behavioral sequences observed in animals trained in the switch-timing procedure. Surprisingly, even though there is some evidence indicating that overt LTSs in subjects trained in the switch-timing procedure are sensitive to fluctuations in motivation (e.g., Daniels et al., 2015 a, b; Balci, Papchristos, Gallistel, Brunner, Gibson, & Shumyatsky, 2008), no study to-date has investigated whether such LTSs are sensitive to pre-feeding.

There have also been a few cases in which the effects of pre-feeding have not been observed on performance indices. For example, McClure et al. (2009) only observed pre-feeding effects when pigeons were pre-fed 40 g rather than 20 g of food. Studies in which subjects were pre-fed 20 g or less of food may therefore represent weak manipulations. Interestingly, the studies that used relatively weak pre-feeding manipulations are the same studies that used relatively long FIs, where 60 s < t < 180 s (e.g., Powell, 1972; Weiss & Moore, 1956; cf. Daniels & Sanabria, 2017a; Eskin & Bitterman, 1960; Shull & Brownstein, 1968). This suggests that whether pre-feeding yields longer, and more

varied performance indices depends on the degree to which subjects are pre-fed and the programmed intervals. It may be that the amount of pre-feeding required for effects on performance indices to emerge scales with the length of the programmed interval.

Methods for Dissociating Interval Timing and Motivation Processes

The sensitivity of timing performance to fluctuations in time and motivation—specifically pre-feeding-induced reductions in motivation—suggests that most performance indices are not selectively sensitive to the passage of time. That is, most performance indices do not provide a "pure" characterization of interval timing (Plowright et al., 2009). Some researchers have interpreted this relationship as indicating that "cognition [interval timing] and motivation are inseparable mental operations" (Avlar et al., 2015, p. 586). However, it is unclear whether interval timing and motivation are "inseparable". It is possible that interval timing and motivation are conflated, resulting in the appearance that interval timing and motivation are linked.

Conflation of interval timing and motivation is evident in the assumptions of PA models. PA models do not allow for the possibility that interval timing and motivation are dissociable. The tacit assumption of all PA models is that *all* target responses are the output of a timing process and thus *all* performance indices characterize that timing process. Therefore, changes in performance indices induced by changes in motivation indicate, according to PA models, that motivation processes are inherent to timing processes. Such a relationship has influenced theory development, procedure design, and analyses of performance indices. For example, many theories explain the sensitivity of performance indices to motivation by drawing a direct link between parameters of PA models and motivation, such as the response threshold (θ; e.g., Balci, 2014) and the speed of the clock ($1/c$; *e.g.*, Killeen & Fetterman, 1988; Killeen, 1995). In turn, such

assumptions result in procedures designed to facilitate detection of only target responses and analyses that assume that all performance indices characterize the output of PA models (i.e., all performance indices are well described by a single distribution, Equation 1.1). The purpose of the present dissertation is to test the assumption that interval timing and motivation processes are inseparable.

A Computational Approach to Dissociating Interval Timing and Motivation

Interval timing procedures are relatively complex, making it unlikely that target responses are always under temporal control. To quote Stubbs, Dreyfus, Fetterman, Boynton, Locklin, & Smith (1994), "with complex stimulus arrangements, like those used in much current nonhuman animal research [on interval timing], multiple aspects of complex stimuli affect behavior and complex stimuli exert multiple effects on behavior" (p. 31). Such complexity suggests that the assumption that all target responses are the output of a timing process is untenable. Indeed, recent research suggests that although temporal information is always available and may even be learned within the first few trials (e.g., Balsam & Gallistel, 2009; Balsam, Dew, & Yang, 2002; Ward, Gallistel, Jensen, Richards, Fairhurst, & Balsam, 2012), target responses are not always under temporal control (e.g., Daniels & Sanabria, 2017a; Daniels, Fox, Kyonka, & Sanabria, 2015; Freestone, Balci, Simen, & Church, 2015; Sanabria & Killeen, 2008). Interestingly, target responses may flexibly alternate between temporal and non-temporal control based on whether temporally-controlled target responses maximize reinforcement (e.g., MacDonald & Roberts, 2018; Rayburn-Reevees, Qadri, Brooks, Keller, & Cook 2017). Thus, performance indices should be analyzed assuming that some target responses are the output of a non-timing process.

The assumption that target responses fluctuate in and out of temporal control implies that not all performance indices characterize the timing process. Fluctuations in the generative process underlying target responses can be accounted for by analyzing performance indices under the assumption that performance indices are best described by a mixture of timed and non-timed performance indices. Such a mixture distribution assumes that, at the beginning of some trials, animals enter a timing state with probability *q* and emit *timed* target responses, and in other trials they enter a non-timing state with complementary probability 1-*q* and emit *non-timed* target responses.

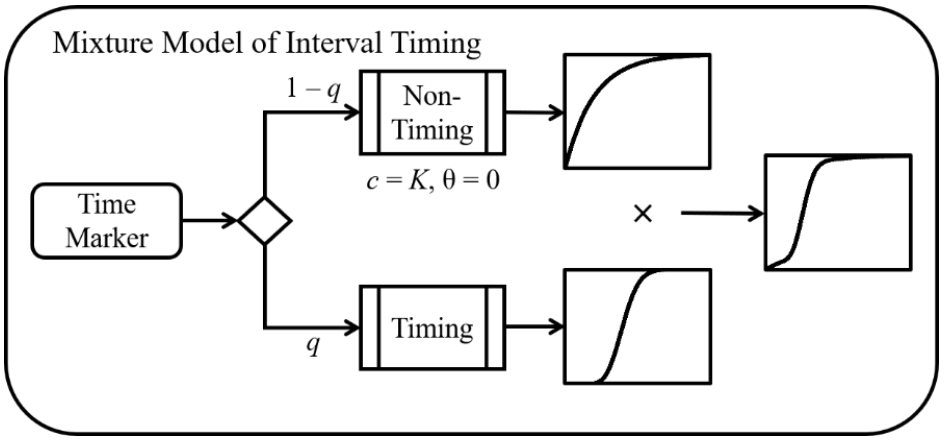

Figure 1.3. Schematic of the gamma-exponential mixture model. When target responses are the output of a timing process, performance indices are described by a gamma distribution; when target responses are the output of a non-timing process, performance indices are exponentially distributed. Distributions are represented as cumulative rather than probability density functions. See Figure 1.2 for description of the timing process.

Figure 1.3 shows a schematic of this mixture model of timing and non-timing processes. Timed target responses are assumed to be generated by a PA-like timing process and thus yield gamma distributed performance indices (Equation 1.1; Killeen & Fetterman, 1988). In contrast, non-timed target responses are assumed to be generated randomly such that non-timed target responses are emitted at any given time with some constant probability. This is equivalent to a timing process wherein a target response

occurs after a single inter-pulse interval, because θ = 1 and M = 1, with an average mean of K (Daniels et. al., 2015a, b). Thus, non-timed performance indices are expected to be exponentially distributed. This revised PA model is expressed formally as,

$$p(\text{performance index} = \tau \mid \tau < \delta) = 0$$
$$p(\text{performance index} = \tau \mid \tau \geq \delta) = q\frac{1}{\Gamma(\theta M)c^{\theta M}}(\tau-\delta)^{\theta M-1}e^{-\frac{\tau-\delta}{c}} + (1-q)\frac{1}{K}e^{-\frac{\tau-\delta}{K}}$$
$$\theta M \geq 1; \theta, M, c, K, \delta > 0; 0 \leq q \leq 1 \qquad (1.2)$$

where parameters are as described in Equation 1.1, the probability of a performance index of length τ is equal to the mixture weight of a shifted gamma distribution and the complementary mixture weight of a shifted exponential distribution described by mean parameter K.

Fits of Equation 1.2 to performance indices (e.g., latencies and LTSs) have revealed that there is indeed a small subset of non-timed target responses, and thus non-timed performance indices, in many interval timing procedures (Balci, Freestone, & Gallistel, 2009; Daniels et al., 2015a,b; Daniels & Sanabria, 2017a; Laude, Daniels, & Zentall, 2016; Sanabria & Killeen, 2008; Watterson et al., 2015). Non-timed performance indices even occur in animals trained in the switch-timing procedure and the temporal bisection procedure, suggesting that there are few interval timing procedures in which target responses are exclusively under temporal control (Laude et al., 2016). Whereas non-timed performance indices appear shorter than timed performance indices in immediate timing procedures (Berkay, Freestone, & Balci, 2016; Daniels et al., 2015b; Daniels & Sanabria, 2017a; Hill, Covarrubias, Terry, & Sanabria, 2012; Sanabria & Killeen, 2008), in retrospective timing procedures non-timed performance indices appear much longer than timed performance indices (unreported

data from Laude et al., 2016). For example, when subjects are not timing in the switch-timing procedure, subjects produce very short LTSs, engaging the long FI relatively quickly. In contrast, when subjects are not timing in the temporal bisection procedure, subjects tend to choose 'short' rather than 'long'. This suggests that the expression of non-timing depends on whether subjects were trained in immediate or retrospective timing procedures.

Importantly, the parameters of Equation 1.2 are differentially sensitive to timing and motivational manipulation. Whereas parameters of timed performance indices are selectively sensitive to time, parameters of non-timed performance indices are selectively sensitive to fluctuations in motivation, specifically pre-feeding (Berkay et al., 2016; Daniels & Sanabria, 2017a; Daniels, Overby, & Sanabria, 2018; Mazur, Wood-Isenberg, Watterson, & Sanabria, 2014; Watterson et al., 2015; Sanabria & Killeen, 2008). For example, Daniels & Sanabria (2017a) found that increasing the FI selectively slowed down the speed of the internal clock, resulting in a scalar increase in timed latencies. In contrast, they found that five consecutive days of pre-feeding resulted in an increase in the prevalence and mean of non-timed performance indices. These effects are robust to parameter estimation techniques, indicating that such effects are reliable and do not depend on arbitrary analytic choices (Daniels, et al. 2018).

However, there are instances in which fluctuations in motivation alter parameters of both timed and non-timed performance indices. For example, fits of Equation 1.2 revealed that increasing the reward magnitude following completion of the Long FI in the switch-timing procedure decreases the mean timed LTSs by reducing the response threshold, while also decreasing the prevalence of timed LTSs in both pigeons and rats (Daniels et al., 2015a, b). Increasing the reward magnitude also increased the

mean non-timed LTSs for rats (Daniels et al. 2015b). Likewise, nicotine—a psychostimulant known for, among other things, increasing relative reward value by enhancing dopamine release in the mesolimbic system (e.g., Barr, Pizzagalli, Culhaen, Goff, & Evins 2008; Olausson, Jentsch, & Taylor, 2004; Overby, Daniels, Del Franco, Goenaga, Powell, Gipson, & Sanabria, 2018)—reduces the mean timed LTSs by speeding up the clock, while increasing the prevalence and mean non-timed LTSs (Daniels et al., 2015a). Thus, whereas some motivation manipulations such as pre-feeding affect the prevalence and mean of non-timed performance indices, other motivation manipulations modulate both timed and non-timed performance indices. Importantly, when fluctuations in motivation do affect parameters of timed and non-timed performance indices, the effect on non-timed performance indices is often larger than or at least equivalent to the effect on timed performance indices.

The ability of Equation 1.2 to at least partially dissociate timing and motivation processes is reinforced by the success of a special case of Equation 1.2 (Brackney, Cheung, Neisewander, & Sanabria, 2011; Daniels & Sanabria, 2017b; Romero, Daniels, Gipson, & Sanabria, 2018; Shull, 2004, 2011; Shull, Grimes, & Bennet, 2004). When trained in variable interval (VI) schedules of reinforcement, animals tend to respond in a bout-like structure wherein clusters of responses are separated by relatively long pauses. The special case of Equation 1.2 (where $\theta = 1$ and $M = 1$, reducing the gamma to an exponential distribution) is a biexponential mixture distribution that suggests a relatively simple generative process that controls VI performance: bouts are initiated at some constant but low probability and within-bout responses are emitted at some constant but high probability. Whereas bout-initiation rate appears uniquely sensitive to motivation, within-bout responding is relatively robust and only changes when response topography or reinforcer contingencies are altered (for a review see Brackney &

Sanabria, 2015; Brackney, Cheung, & Sanabria, 2017; Daniels & Sanabria, 2017b; or Shull 2011). Likewise, the length and duration of a bout is relatively insensitive to fluctuations in motivation. Such effects have also been observed on the bout-structure of schedule-induced polydipsia following administration of psychostimulants (Íbias, Daniels, Miguéns, Pellón, 2017; Íbias, Pellón, & Sanabria, 2015) and the bout-structure of post-latency FI performance following pre-feeding (Daniels & Sanabria, 2017a). It thus appears that, in general, motivation and schedule-controlled performance can be computationally dissociated.

Despite the utility of mixture models, there has been very little systematic research investigating the sensitivity of timing and non-timing processes to independent and selective manipulation. More problematic is that mixture models inherently conflate structural and parameter uncertainty (Daniels & Sanabria, 2017b). Whereas structural uncertainty refers to whether the correct underlying generative process and thus distribution (model of interval timing) has been identified, parameter uncertainty refers to whether the probability of entering a timing state, the response threshold, etc. are accurately estimated. For example, consider that some models of timing predict that timed performance indices are normally distributed (Gibbon, 1977), others predict that timed performance indices are gamma distributed (Equation 1.1; Killeen & Fetterman, 1988), and yet others predict that timed performance indices are Wald distributed (Simen et al., 2013). If performance indices are better described by a normal than a gamma distribution, then parameter estimates of Equation 1.2 will be partly based on misidentifying some performance indices as timed when they are in fact non-timed, and vice versa. Misidentification could, and in some cases does, result in misleading inferences (e.g., Daniels & Sanabria, 2017b). Although such uncertainty may be

ameliorated by parametrically varying the distributions that comprise Equation 1.2 (e.g., Tanno, 2016) and selecting the version of Equation 1.2 that yields the best overall fit, the conflation of structural and parameter uncertainty can never be fully reduced. Thus, such models should be accompanied by experimental validation (e.g., Daniels & Sanabria, 2017b).

A Procedural Approach to Dissociating Interval Timing and Motivation Process

Behavioral Systems Activated in Interval Timing.

The success of mixture models in dissociating interval timing and motivation processes suggests that interval timing and motivation may also be procedurally dissociable. Importantly, procedural dissociations allow for validation of assumptions underlying computational models (i.e., Equation 1.2) while simultaneously avoiding the limitations inherent in computational models (e.g., Daniels & Sanabria, 2017b). Procedural dissociations may be developed by considering the ecology and ethology of subjects in appetitive experimental contexts (Barnett, 1975; Collier, 1981; Timberlake, 1984, 1993, 1994, 2000; Timberlake & Lucas, 1989; Timberlake & Washburne, 1989; Tinbergen, 1951). When foraging, unique behavioral and sensory systems are activated. For example, in rats, stimuli predicting imminent food activate the predatory subsystem, consisting of, but not limited to, general locomotion, sniffing, and orienting towards relevant stimuli (e.g., Barnett, 1975; Timberlake, 2000). These systems are activated in both natural and experimental contexts, suggesting that interval timing procedures (Figure 1.1; and indeed, any procedure designed for assessing animal cognition) entrain and modify the expression of these systems.

For example, the length of FIs determines which behavioral mode is predominantly expressed: relatively Short FIs condition lever pressing and relatively Long FIs condition locomotion and sniffing (for a review see Timberlake, 2000). Likewise, whether subjects are working for solid or liquid reinforcers modulates how subjects search for reinforcement and interact with stimuli predicting imminent reinforcement (e.g., Cleland & Davey, 1983; Davey & Cleland, 1982; Goeders, Murnane, Banks, & Fantegrossi, 2009). Whereas solids facilitate lever pressing, liquids promote lever licking and head-entries into the reinforcement receptacle. This indicates that the structure and sensitivity of activated behavioral and sensory systems to time and motivation can guide the development of procedures that dissociate interval timing and motivation.

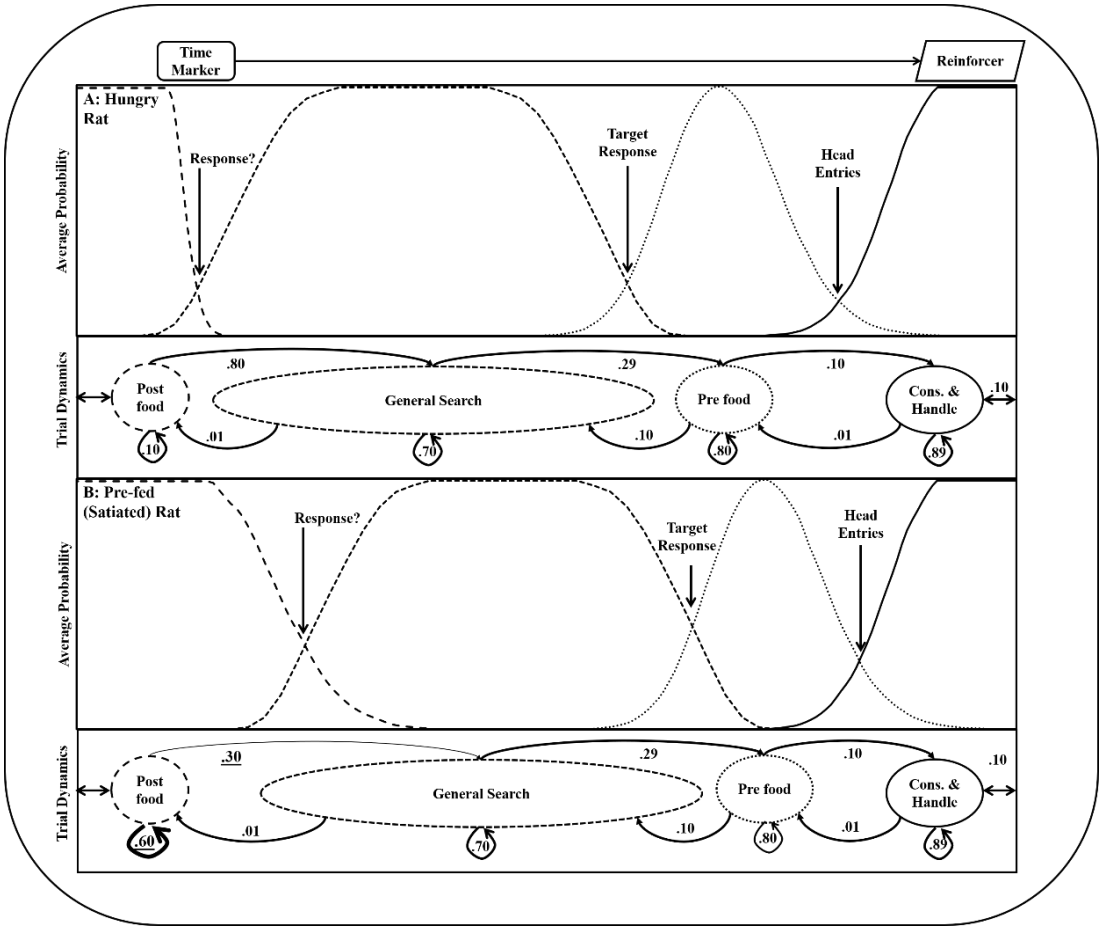

Figure 1.4. Schematic of the predatory subsystem of rats in interval timing procedures. Dynamics of behavioral systems are depicted for when rats are hungry (Panel A) and when rats are pre-fed (satiated; Panel B) based on schematics suggested by Timberlake (2000) and Staddon & Simmelhag (1971). See text for details. Note that the static transition probabilities are for illustrative purposes only, some probabilities are likely dynamic and may shift to 1 given certain experimental events, such as the probability of transitioning into the consumption\handling mode upon reinforcer delivery. Underlined transition probabilities illustrate the predicted effect of pre-feeding, with thicker and thinner arrows further indicating whether pre-feeding increased or decreased a specific probability.

Figure 1.4A shows a schematic of both the trial-by-trial and average dynamics of the predatory subsystem of a hungry rat activated by the presentation of a time-marker signaling imminent food delivery (Silva, Timberlake, & Cevik, 1998; Timberlake & Lucas,

1989; Staddon & Ayres, 1975)[5]. This subsystem is composed of four modes of behavior: general search, pre-food focal search, handle/consumption, and post-food focal search. In individual trials, each mode appears to be independently controlled by its own dynamics and characterized by modules of behavior related to specific actions (Lucas, Timberlake, & Gawley, 1988; Timberlake, 1994). For example, whereas general search is characterized by locomoting, crawling, scanning, and sniffing, pre-food focal search is characterized by pawing, tracking, and interacting with stimuli or manipulanda, which may be the same as or different from the time-marker (Timberlake & Lucas, 1989). Likewise, whereas consumption/handling is characterized by capturing, manipulating, and ingesting food, post-food focal search is characterized by digestion, grooming, and sometimes interacting with stimuli or manipulanda if still available (Silva & Timberlake, 1998; Staddon & Ayres, 1975). Transitions between these modes is bidirectional and probabilistic rather than unidirectional and deterministic (Innis, Simmelhag-Grant, & Staddon, 1983; Staddon & Simmelhag, 1971). When averaged over trials, the states and transitions may be jointly expressed in the form of probability distributions as a function of time.

Interestingly, general search and pre-food focal search appear to be the most readily conditioned to various stimuli, including the intervals signaled by time-markers. For example, Timberlake and colleagues (Lucas, Timberlake, Gawley, 1988; Silva & Timberlake, 1998a, b, 1999, 2005; Timberlake, 1994) have shown that the amount of time spent in general search and pre-food focal search scales with intervals; general

[5] The behavioral systems approach is largely described using laboratory rats as examples because most of the behavioral systems research has been conducted with rats (Timberlake, 2000) and some analogous work in pigeons (Staddon & Simmelhag, 1971). However, it is assumed that the behavioral systems approach transcends species and thus can be appropriated for the study of cognition in any species of interest.

search becomes more prevalent with relatively long intervals. Additionally, Timberlake and colleagues have argued forcefully that what animals learn in interval timing procedures is to time general-search-to-pre-food-focal-search transitions (Silva & Timberlake, 1998a, b, 1999, 2005). In contrast, the timing and duration of consumption/handling and post-food focal search are less malleable and appear insensitive to intervals signaled by time-markers (Staddon & Ayres, 1975; Staddon & Simmelhag, 1971; Timberlake, 2000; cf. Silva, Timberlake, & Cevik 1998). However, post-food focal search appears to be directly related to reward magnitude (Timberlake, 2000; Staddon, 1974), suggesting that it may be sensitive to motivation.

Because time-marker presentation (and thus interval onset) is typically controlled by the experimenter rather than by subjects, subjects may not always be in a behavioral mode receptive to time-marker presentation. Receptive behavioral modes are those in which rats are engaged in behaviors that allow for detection and subsequent attending of time-markers. The receptiveness of behavioral modes is assumed to be related to the degree to which behavioral modes are readily conditioned. Thus, general search and pre-food focal search are receptive behavioral modes, but handling/consumption and post-food focal search are not receptive behavioral modes.

The potential asynchronization between time-markers and general search provides an intuitive explanation for why mixture models have been useful in describing operant performance in general (e.g., Brackney et al., 2017), and in interval timing specifically (e.g., Daniels & Sanabria, 2017a). For example, hungry rats are typically in general search, and thus search for and attend the extension of a lever predicting food in 30 s. As the time to food approaches, rats transition to pre-food focal search via a timed target response denoting timed performance indices. In pre-food focal search, rats

investigate and capture food by approaching and interacting with the extended lever. Alternatively, extension of the lever may occur while rats are in post-food focal search. In this mode, the time-marker may not be attended and thus rats transition to general search and then pre-food focal search randomly. Thus, as the time to food approaches, rats transition to pre-food focal search via non-timed target response denoting non-timed performance indices. Once the reinforcer is delivered, rats transition into handle\consumption. Following food consumption, rats transition into post-food focal-search and then return to general-search. Whereas synchronization of time-markers and general search enhances attention and thus promotes generation of timed performance indices, asynchronization diminishes attention and thus promotes generation of non-timed performance indices.

Figure 1.4B shows how the behavioral systems approach may accommodate fluctuations in motivation, specifically the effect of pre-feeding on performance indices. Given that the time spent in post-food focal search appears to be sensitive to reward magnitude (Timberlake, 2000), the present dissertation posits that fluctuations in motivation are reflected in the time spent in post-food focal search. Specifically, the present dissertation hypothesizes that pre-feeding increases the time spent in post-food focal search, which (a) delays onset of general search which subsequently (b) reduces synchronization of time-markers and general search and (c) increases the frequency with which subjects switch between general search and pre-food focal search. Therefore, pre-feeding reduces the prevalence of and delays emission of timed target responses, resulting in longer and more variable non-timed performance indices. Obviously, when performance indices are analyzed as arising from just a timing process pre-feeding generally results in longer and more variable performance indices. Because post-food focal search is relatively insensitive to conditioning the pre-feeding-induced increase in

time spent in post-food focal search is not expected to recalibrate with feedback. That is, the effect of pre-feeding is expected to be permanent so long as the reduced motivational state is maintained.

The ability of the behavioral systems approach to account for the effects of pre-feeding on performance indices suggests a route by which to dissociate interval timing and motivation processes. In interval timing procedures, there is no overt response that demarcates when subjects transition from post-food focal search to general search. Without an overt response demarcating post-food focal search and general search, performance indices reflect the sensitivities of both behavioral modes. To avoid performance indices conflating post-food focal search and general search and thus fluctuations in motivation with interval timing, subjects may be trained to emit a post-food-focal-search-to-general-search transiting response that also produces the time-marker. Thus, training rats to self-pace trials in interval timing procedures would circumscribe the effects of pre-feeding, and, in general, fluctuations in motivation, to post-food focal search, protecting general search and pre-food focal search.

Response-Initiated Interval Timing

The behavioral systems model implies that training subjects to self-pace interval timing procedures may dissociate post-food focal search and general search, thus protecting general search and pre-food focal search from fluctuations in motivation. Protection of general search and pre-food focal search would result in performance indices robust to motivational fluctuations. Such training procedures already exist in the form of response-initiated (RI) schedules of reinforcement. Interval timing procedures are typically externally-initiated (EI) and are thus programmed such that time-markers are activated by the experimenter or, in yoked designs, by another subject. In contrast,

RI procedures are programmed such that subjects produce the time-markers. For example, whereas in EIFI an experimenter programs a light to turn on, signaling activation of an FI 30-s in a lever, in RIFI an experimenter programs a response to turn on a light, signaling activation of an FI 30-s in a lever.

If RI effectively demarcates post-food focal search and general search then, compared to EI, RI is hypothesized to (a) reduce the degree to which pre-feeding effects on post-food focal search delay onset of general search and subsequently (b) ensure synchronization of time-markers and general search and (c) reduce switching between general search and pre-food focal search. Collectively, these hypotheses are called the *RI hypothesis*. The RI hypothesis predicts that RI interval-timing procedures should facilitate attention to time-makers and, thus, temporal control of target responses. RI interval timing procedures should also dissociate interval timing and motivation such that target responses are robust to pre-feeding. RI procedures are thus expected to circumscribe the effect of pre-feeding to the time it takes to emit an initiating-response—the latency-to-initiate (LTI)—while leaving performance indices robust to pre-feeding.

Although performance in RI interval-timing procedures has been studied (Chung & Neuringer, 1967; Cherek, Thompson, & Heistad, 1973; Innis, Mitchell, & Staddon, 1993; Kim, Jung, Byun, & Jung, 2009; Lowe, Davey, & Harzem, 1974; Mechner, Guevrekian, & Mechner, 1963; Shull, 1970; Todorov, Couto, & Carvalho, 2013), few studies have explicitly compared performance indices in RI and EI, let alone tested whether performance indices in RI and EI are differentially sensitive to fluctuations in motivation. To-date, there are only a few published studies in which RI and EI interval timing are compared. Caetano & Church (2009) compared performance of rats trained in a differential-reinforcement-of-low rates (DRL) 20-s schedule of reinforcement (RI) to

performance of rats trained in a yoked fixed-time (FT) 20-s (EI). Whereas in DRL subjects are trained to wait interval *t* between two consecutive responses (e.g., lever presses), in FT subjects are trained that response-independent reinforcement arrives every interval *t*. They found no systematic differences in performance indices between DRL or yoked FT performance. Caetano (2009) replicated this null effect in performance indices produced in RI and EI DRL, FT, and FI. Unfortunately, sensitivity of performance indices to motivation was not compared between RI and EI.

Fox and Kyonka (2013, 2015, 2016) trained pigeons in both RIFI and EIFI procedures with and without peak trials. They found that in RIFI, pigeons responded at a higher rate than in EIFI, but that performance indices were largely similar between RIFI and EIFI. When they introduced peak trials, they found that pigeons started responding much sooner and stopped responding much later in RI compared to EI. Correspondingly, peak times had similar means but were more variable in RI than EI. Interestingly, reduced temporal control of peak times was observed even when discriminative stimuli signaled an effective FI initiating-response and, thus, activation of the FI. LTIs were sensitive to the FI (Fox & Kyonka, 2013, 2015, 2016) and to pre-feeding (Fox & Kyonka, 2014). Unfortunately, the sensitivity of performance indices to motivation were not compared between RIFI and EIFI procedures.

It is important to highlight that in the studies reported by Fox and Kyonka (2013, 2015, 201), Caetano and Church (2009), and Caetano (2009), initiating-responses were not identifiably different from target responses. The only difference between initiating-responses and target responses was the passage of time, except in Fox & Kyonka (2016), where an initiating-response changed the color of the pecking key to signal activation of the FI. This suggests that, even when paired with discriminative stimuli, individual

responses differing as a function of only time are not easily discriminated from target responses. Poor discrimination of initiating and target responses may have resulted in encoding initiating-responses as target responses, and vice versa. Fluctuations in encoding leads to fluctuation in whether initiating and target responses are differentially controlled by their respective associations: trial activation and time, respectively.

Revealed operants and the discriminative RI hypothesis

The dearth of support for the RI hypothesis appears attributable to poor discriminability of initiating-responses from target responses. This conclusion is reinforced by an independent line of research conducted by Mechner and colleagues (e.g., Jones & Mechner, 2013; Mechner, Hyten, Field, & Madden, 1997; Mechner & Guevrekian, 1962; Mechner, & Guevrekian, & Mechner, 1963). In concurrence with the behavioral systems approach, Mechner (1994) argues that the traditional approach to measuring operant responses—i.e., measuring the occurrence of single responses as instantaneous discrete events—is limiting, because it conflates many measures of performance (e.g., latency, response-duration, IRT, etc.) that are differentially sensitive to underlying psychological processes. For example, it is well documented that the rate at which subjects respond decreases within-session (Killeen, 1995; McSweeney & Murphy, 2009), implying that response rate is sensitive to some within-session process such as satiation or reinforcer habituation. However, Daniels, Overby, & Sanabria (2018) showed that within-session response rate reductions are driven by within-session latency lengthening rather than within-session run rate reductions. Further, they showed that within-session latency lengthening is insensitive to both motivation and time, concluding that within-session latency lengthening likely reflects recovery from between-session

forgetting. Thus, decomposing response rate into its constituents revealed dissociable aspects of performance that were otherwise missed.

To overcome these limitations, Mechner suggests using a *revealed operant* technique. In this technique, an operant is initiated at some manipulandum (R_a) and terminated at another (R_c). In the interim, the operant (R_b) is expressed on the same manipulandum as R_a, R_c, or some other manipulandum. Alternatively, R_b may be unspecified so long as it does not contaminate expression of R_a or R_c. In most revealed operants, R_a emission also activates the schedule of reinforcement (cf. Daniels & Sanabria, 2017b). Thus, most RI schedules inherently involve revealed operants.

Figure 1.5 shows schematics of two different RI procedures: fixed-minimum interval (FMI) and DRL. In both schedules, a waiting interval *t* between two consecutive responses is reinforced, with *t* activated by the first of the two responses. Although both FMI and DRL are RI, only FMI reveals operants. In the original implementation of FMI (Mechner & Guevrekian, 1962), a lever press at one location initiates an operant and an interval *t* (R_a), a lever press at another location terminates the operant and the interval (R_c), and the operant (R_b) is unspecified. The duration of the operant is measured as an IRT (the time between R_a and R_c) and is reinforced if the IRT is greater than *t*. Importantly, LTIs (the time between R_c and R_a) and not IRTs are sensitive to pre-feeding. By contrast, in DRL, R_a and R_c are both lever presses at the same location, differentiated only as a function of time. In DRL, LTIs only follow reinforcement and IRTs are sensitive to pre-feeding (Daniels, Stephens, et al. 2018; Romero et al., 2016).

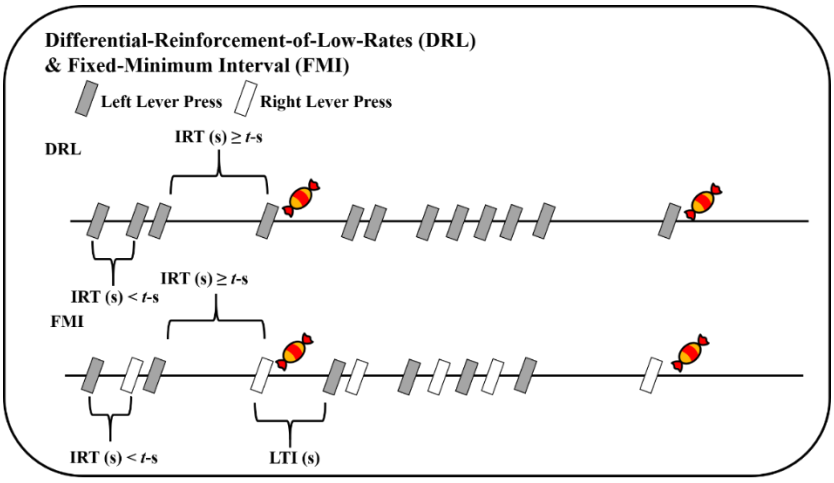

Figure 1.5. Schematic of response-initiated (RI) schedules of reinforcement: differential-reinforcement-of-low-rates (DRL) and fixed-minimum-interval (FMI), respectively. Performance indices are indicated by a bracket and labeled (i.e., IRTs).

The comparison of FMI with DRL suggest how RI may dissociate interval timing and motivation. First, R_a must produce the time-maker and activate the interval. Second, R_a, R_b, and R_c must be discriminable from each other. Differentiating responses by both timing and location ensures that transitions into each behavioral mode are associated with a specific and easily discriminated response. Maintaining the discriminability of initiating-responses and target responses ensures that initiating-responses and target responses are accurately encoded. That is, preserving discriminability of initiating and target responses ensures that there is no fluctuation in whether initiating and target responses are controlled by their respective associations: trial activation and time, respectively.

Discriminability of initiating and target responses is likely a positive function of the number of dimensions on which initiating-responses and target responses differ. Thus, as initiating-responses become progressively different from target responses, RI is expected to increasingly enhance temporal control and dissociate interval timing and motivation. This revised RI hypothesis is referred to as the *discriminative RI hypothesis*.

The purpose of the present dissertation is to test the discriminative RI hypothesis, and thus whether interval timing and motivation are dissociable.

General Outline of Experiments

In the present dissertation, three experiments were conducted to test the discriminative RI hypothesis and, thus, whether interval timing and motivation are dissociable. In all experiments, rats were trained and tested in RI and EI variants of the switch-timing procedure and the location variant of the temporal bisection procedure. These procedures were chosen because of (a) the dearth of data on whether pre-feeding affects overt and latent LTSs, and (b) the similarity of the behavioral sequences entrained by both procedures. The dearth of data allows for the present dissertation to assess the generality of pre-feeding effects across immediate and retrospective timing procedures. And the similarity of performance entrained in the switch-timing and location variant of the temporal bisection procedures facilitates comparison of pre-feeding effects between procedures.

Experiment 1 (Chapter 2), tested whether initiating-responses differing from target responses as a function of time and location would enhance temporal control of overt LTSs and protect overt LTSs from pre-feeding in rats trained in the switch-timing procedure (Figure 1.1B). Experiment 2 (Chapter 3) replicated experiment 1 and tested whether initiating-responses differing from target responses as a function of time, location, and form would enhance temporal control of overt LTSs and protect overt LTSs from pre-feeding and extinction in rats trained in the switch-timing procedure. Experiment 3 (Chapter 4) tested the generalizability of the discriminative RI hypothesis by testing whether initiating-responses differing from target responses as a function of time, location, and form would enhance temporal control of latent LTSs and protect

latent LTSs from pre-feeding and extinction in rats trained in the location variant of the temporal bisection procedure (Figure 1.1B). It was expected that as initiating-responses become progressively more discriminable from target responses, temporal control of LTSs and robustness of LTSs to pre-feeding would increase.

Extinction probes were included to determine whether RI selectively dissociates interval timing and motivation, or generally dissociates interval timing and non-timing processes. Previous research indicates that extinction does not result in unlearning. Instead, extinction results in a context dependent reduction in motivation and new, inhibitory learning (Bouton, 2004; Redish, Jensen, Johnson, & Kurth-Nelson, 2007). Motivation is reduced because the reinforcer supporting interval timing is no longer delivered at the end of trials. New, inhibitory learning occurs as subjects engage in other non-timing behaviors that become associated with no-reinforcement. The reduction in motivation presumably occurs before subjects engage in new behaviors (e.g., Brackney, Cheung, Herbst, Hill, & Sanabria, 2012; Katz, 1981), suggesting that extinction effects, like pre-feeding effects, should be circumscribed to post-food focal search and, thus, to LTIs. It was expected that initiating-responses should protect LTSs from extinction. Thus, as initiating-responses become progressively discriminable from target responses it was expected that RI would increasingly and generally dissociate interval timing and non-timing processes rather than selectively dissociate interval timing and motivation.

A secondary purpose of the present dissertation was to clarify the results of previous RI studies. Previous studies conducted by Fox and Kyonka (2013, 2015, 2016) suggest that RI reduces rather than enhances temporal control of FI and peak-timing performance. In Experiments 1 and 2, rats are trained to initiate some switch-timing trials via a single response on the Short FI (Short FI lever response-initiation, SL-RI).

SL-RI is discriminable from target responses denoting Long FI performance (i.e., LTSs) as a function of time and location, but is only discriminable from target responses denoting Short FI performance as a function of time. Generalization between SL-RI and Short FI performance is expected to occur more readily than generalization between SL-RI and Long FI performance. Thus, SL-RI is expected to reduce temporal control of Short FI performance but enhance temporal control of LTSs and protect LTSs from pre-feeding and extinction.

Another secondary purpose of the present dissertation was to test the generalizability of the conclusions of Daniels & Sanabria (2017a). They found that pre-feeding increased the mean and variability of FI latencies because it increased the prevalence and mean of non-timed latencies. Pre-feeding did not alter parameters of timed latencies. Fitting Equation 1.2 to LTSs is expected to reveal the same pattern of effects in EI but not RI. Specifically, that pre-feeding increases the prevalence and mean of non-timed LTSs without affecting timed LTSs.

Chapter 2: Experiment 1 - Response-Initiated Discrete-Trials Switch-Timing

Introduction

Mechner and Guevrekian (1962) developed two RI procedures that dissociate schedule performance from changes in motivation: fixed-consecutive number (FCN) and fixed-minimum interval (FMI). In both procedures, initiating-responses are distinct from target responses denoting performance indices. In FMI (Figure 1.5), a lever press at one location starts an IRT (initiating-response) and a lever press at another location terminates the IRT (target response). In FCN, a lever press starts (initiating-response) and counts towards completion of an FR requirement (target responses) that, once completed, is terminated at another lever. These original implementations of FMI and

FCN (also see Çavdaroğlu & Balci, 2016) suggest that initiating-responses discriminable from target responses as a function of time and location should dissociate interval timing and motivation processes.

Experiment 1 sought to test whether initiating-responses discriminable from target responses as a function of time and location dissociate interval timing and motivation processes. To test this hypothesis, rats were trained in a discrete-trials switch-timing FI 8-s FI 16-s (Figure 2.1A). Some rats were trained to initiate trials via a single response on the Short FI (SL-RI group) and other rats were trained with initiation yoked to SL-RI rats (EI group). Following acquisition of stable performance, rats were exposed to a single 1 h pre-feeding probe.

Compared to EI, SL-RI was expected to enhance temporal control of LTSs and yield LTSs robust to pre-feeding. SL-RI LTIs were expected to lengthen following pre-feeding. Additionally, SL-RI was expected to reduce temporal control of Short FI performance. Fits of the gamma-exponential mixture model (Equation 1.2) to LTSs were expected to reveal that the pre-feeding-induced longer and more variable LTSs is explained by an increase in the prevalence and mean of non-timed LTSs without affecting timed LTSs in EI but not SL-RI.

Methods

Subjects

Twenty-four male Wistar rats (Charles River Laboratories, Hollister, CA) served as subjects. Rats arrived on postnatal day 60 and were triple-housed immediate upon arrival. Rats were housed on a 12:12 h light cycle, with dawn at 1900 h; all behavioral training was conducted during the dark phase of the light cycle starting at approximately 0800 h and ending at approximately 1000 h. Following four days of acclimation to the

colony room, food access was reduced daily from 24 to 18, 12, and finally 1 hour per day. Food was placed on home-cages 30 min after the end of each experimental session and taken away 1 hour later. This ensured that at the beginning of the next session weights were, on average, 85% of *ad libitum* weights, as estimated from growth charts provided by the breeder. Water was always available in home-cages. All animal handling procedures used during this study followed National Institutes for Health Guidelines and were approved by the Arizona State University Institutional Animal Care and Use Committee.

Apparatus

Experiments were conducted in 12 MED associates (ST. Albans, VT, USA) modular test chambers (8 chambers measured 305 mm long, 241 mm wide, and 210 mm high; 4 chambers measured 305 mm long, 241 mm wide, and 292 mm high), each enclosed in a sound- and light-attenuating box equipped with a ventilation fan that provided masking noise of approximately 60 dB. The front and back walls and the ceiling of test chambers were made of Plexiglas; the front wall was hinged and served as a door to the chamber. One of the two aluminum side panels served as a test panel. The floor consisted of thin metal bars positioned above a catch pan. The reinforcer receptacle was a square opening (51-mm sides) located 15 mm above the floor and centered on the test panel. The receptacle provided access to a dipper (MED Associates, ENV-202M-S) fitted with a cup (MED Associates, ENV-202C) that could hold 0.01 cc of a liquid reinforcer (~33% sweetened condensed milk diluted in tap water; Kroger, Cincinnati, OH). The receptacle was furnished with a head-entry detector (ENV-254-CB). A multiple-tone generator (MED associates, ENV-223) was used to produce a 15-kHz tone at approximately 75 dB through a speaker (MED Associates, ENV-224 AM) centered on the

top of the wall opposite the test panel and 240 mm above the floor of the chamber. Two retractable levers (ENV-112CM) flanked the reinforcer receptacle. Lever presses were recorded when a force of approximately 0.2 N was applied to the end of the lever. Three-color light stimuli (ENV-222 M) were mounted above each lever; they could be illuminated yellow, green, and red (only yellow was used in the present experiment). A house light located behind the wall opposite to the test panel could dimly illuminate the test chambers. Experimental events were arranged via a MED PC® interface connected to a PC controlled by MED-PC IV® software.

Procedure

Training sessions occurred 7 days/week during the dark phase at 0800 h, 1 h after the end of the light phase. Each session began with a 3-min warmup period during which the houselight was illuminated.

Lever shaping. Immediately following the warmup, the houselight was turned off and the first trial began with the delivery of 5 s of access to reinforcement, which was counted from the detection of a head-entry into the reinforcement receptacle. Further reinforcement was scheduled on a variable time 45-s inter-trial interval (ITI). Both the left and right levers were extended for 8 s prior to the delivery of and retracted just before reinforcement. If either lever was pressed during the 8-s presentation, the levers were immediately retracted, and reinforcement delivered. This phase continued until rats were reliably obtaining reinforcement from the reinforcement receptacle and pressing at least one of the levers. The houselight remained lit throughout the entire session.

Yoked-Trials Training. Rats were randomly assigned to group Short FI-lever response-initiated (SL-RI; n = 12) and externally-initiated (EI; n = 12). Trials in groups

SL-RI and EI were mutually yoked: For each yoked pair of SL-RI and EI rats, the SL-RI rat initiated every trial for both rats but could not initiate trials until both the SL-RI and the EI rat had completed the preceding trial and ITI. Trial availability was signaled to SL-RI rats by turning off the houselight and extending both levers. One lever was designated the initiation lever (left for half of the SL-RI rats, right for the other half). Initiating-responses illuminated the yellow light above both levers for the SL-RI and yoked EI rat and turned off the houselight and extended both levers for the yoked EI rat. Initiating-responses also activated a fixed-interval (FI) 2-s schedule of reinforcement on either the left or right lever (selected by sampling without replacement from a 6-item list) for both rats; extinction was programmed in the other lever. Completion of the schedule turned off the houselight; a subsequent head-entry activated the dipper for 2.5 s. After reinforcement, a lit ITI commenced that was at least 2-s long but continued until both rats completed the preceding trial. SL-RI rats then initiated the next trial as described above. The ITI was thus equal to the time it took SL-RI rats to initiate trials. ITIs of SL-RI rats are also referred to as the latencies-to-initiate (LTIs). Taken together, ITIs and LTIs are referred to as the time-to-initiate. This phase continued until SL-RI rats were reliably initiating trials and all rats in both groups were reliably lever pressing.

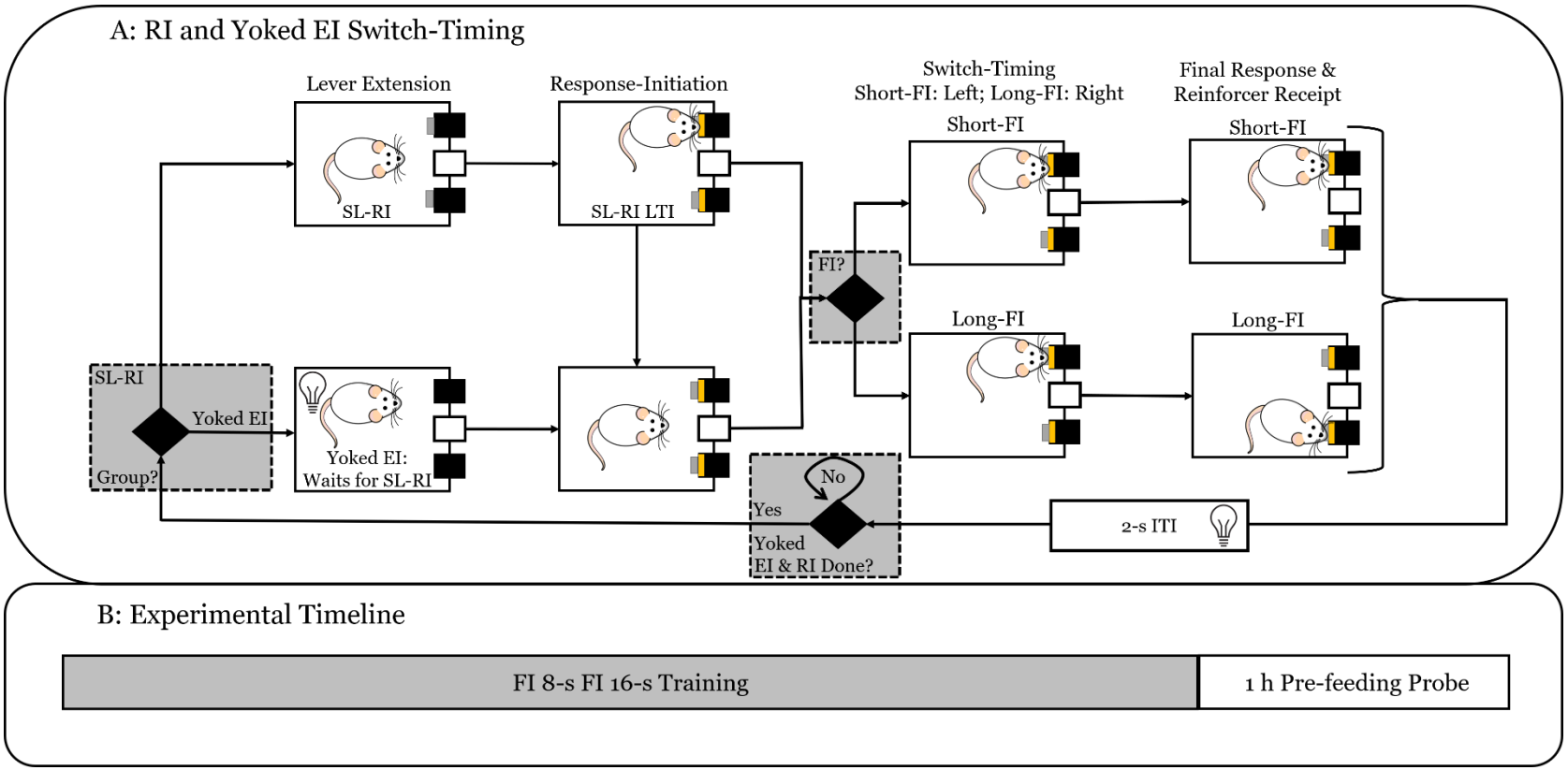

Figure 2.1. Experiment 1 Schematic of the SL-RI and yoked EI switch-timing procedures and timeline of experiment 1. At the beginning of the session (Panel A), levers were extended for SL-RI but not EI rats. Following a single Short FI response by an SL-RI rat, either the Short FI or Long FI was activated for SL-RI and yoked EI rats. For SL-RI rats, activation of either FI was signaled by turning on the yellow LEDs above both levers, and for yoked EI rats, turning off the house-light, extending the levers, and turning on the yellow LEDs above both levers. After the active FI elapsed, the first response on the lever associated with the active FI retracted the levers, turned off the yellow LED, and activated the dipper. Once a head-entry into the reinforcement receptacle confirmed reinforcer receipt, the dipper was lowered 2.5-s later. After a lit 2-s ITI had elapsed and both SL-RI and yoked EI rats completed the preceding trials, the house-light was turned off and levers were extended for SL-RI rats to initiate the next trial. Once switch-timing performance stabilized (Panel B), rats were exposed to a single session 1 h pre-feeding probe.

FI 8-s FI 16-s Baseline Training. Figure 2.1 shows a schematic and timeline of training. Rats were trained on a dependent concurrent FI 8-s FI 16-s schedule of reinforcement. Trials were organized as described in *Yoked-Trials Training*, except that the FI 2-s FI 2-s was replaced with FI 8-s FI 16-s. For SL-RI rats, FI 8-s was programmed on the initiation lever; for half of the EI rats, FI 8-s was programmed on the left lever; for the other half, FI 8-s was programmed on the right lever. This training continued for a minimum of 20 sessions and until the median, interquartile range (IQR = difference between third and first quartile, or Q3-Q1), and coefficient of quartile variance (CQV = Q3 + Q1) of latencies to switch (LTSs; first response on the FI 16-s) were deemed stable. Stability was defined as a non-significant regression over the last 5 days for LTS medians, IQRs, and CQVs.

Prefeeding Probe. In a single session immediately following detection of stability rats were provided access to food for an hour prior to, instead of after, the session.

Data Analysis

LTSs stabilized after 29 training sessions. The last five days of training were used to characterize baseline performance and the single session pre-feeding probe characterized the effect of pre-feeding. For each feeding regimen (baseline, pre-feeding), the dependent measures listed in Table 2.1 were directly tagged or calculated from the distribution of responses across the Short FI and Long FI in Long FI trials; Short FI trials were not included because LTSs are not observed in Short FI trials.

Table 2.1

Switch-timing performance dependent measures

Dependent Measure	Definition
Time-to-initiate	**Time to initiate a trial (LTIs and ITIs) following onset of initiation stimulus***
Discrimination Ratio**	Proportion of trials in which the first response was the correct initiating-response
Latency-to-First Response (LFR)†	Time to first response on the Short FI after trial initiation
Latency-to-Depart (LTD) †	Time to last response on the Short FI after trial initiation
Latency-to-Switch (LTS) †	**Time to first response on the Long FI after trial initiation**
Start Ratio	Proportion of trials in which the LTS was longer than the LFR
Persistence Ratio	Proportion of trials in which the LTS was longer than the LTD

Note. Bolded dependent measures test the primary predictions of the discriminative RI hypothesis. All other dependent measures are either of relevance to secondary predictions (e.g., SL-RI will reduce temporal control of short FI performance) or are control variables that can clarify and/or qualify interpretations. *The initiation stimulus was lever extension in experiment 1 (Chapter 2) and tones differing in frequency (3-, 8-, and 15-kHz) in experiments 2 (Chapter3) and 3 (Chapter 4). **Discrimination ratios are not reported in experiment 1 (Chapter 2) because rats were exposed to only one initiation type or experiment 3 (Chapter 4) because rats did not have as many responses available during the ITI. †For LFRs, LTDs, and LTSs, the median, inter-quartile range (IQR: 3rd quartile – 1st quartile), and coefficient of quartile variation [CQV: [IQR/(3rd quartile + 1st quartile)]] were calculated to characterize LFR, LTD, and LTS distributions because such metrics are robust to outliers and proportional to the mean, standard deviation (SD), and coefficient of variation (CV) when data are approximately normally distributed (Huber, 1972).

Analysis of Descriptive Statistics

All dependent measures were log or log-odds transformed and then analyzed via Bayesian variants of traditional null hypothesis significance tests (ANOVA and *t*-tests) in JASP (Love et al. 2016). Bayesian analyses were conducted because they reduce the impact of outliers, missing data, and allow for evidential support to be quantified for both the alternative and null hypotheses (for in-depth descriptions of these tests, see Kruschke, 2014; Rouder, Morey, Speckman, & Province, 2012; Rouder, Morey, Verhagen, Swagman, & Wagenmakers, 2016). Briefly, in Bayesian analyses, posterior distributions of parameters of a likelihood function are generated through the convolution of a likelihood function (e.g., the equations and distributions specified by ANOVA and *t*-tests) and prior distributions characterizing prior knowledge about the parameters of those likelihood functions. Although JASP allows for some level of control over the prior distribution in these tests, default settings of JASP were retained. The default settings assume diffuse priors reflecting little knowledge of potential effects, thereby letting the data determine the outcome of analyses.

A model-selection approach was implemented wherein information from the Bayesian analyses are used to calculate Bayes Factors (BF)—a model selection metric that characterizes the strength of evidence for a given alternative (*i*) model relative to the null model (0). More formally, a BF is the ratio of the probability of a model given the data over the probability of a competing alternative model, such as the null hypothesis, given the same data (Kass & Raftery, 1995). Importantly, each potential effect contained within an analysis can be recast as a model embodying that effect. For example, in a dependent samples *t*-test assessing the effect of feeding regimen (baseline, pre-feeding)

there is a null-hypothesis model that assumes no effect of feeding regimen, and an alternative hypothesis model that assumes an effect of feeding regimen. Similarly, in a 2 (initiation type: EI, SL-RI) × 2 (feeding regimen: baseline, pre-feeding) repeated measures Bayesian ANOVA there are five potential models: a null-hypothesis model, an initiation type model, a feeding regimen model, an initiation type + feeding regimen model, and an initiation type × feeding regimen model.

Typically, a BF ≥ 3 is taken as an indication of substantial evidence for a specific model. BFs were natural-log transformed such that models with a natural-log BF ($ln\text{BF}_{io}$, nomenclature adopted from Jarosz & Wiley, 2014) ≥ +1.098 were considered as having substantial evidential support and models with a $ln\text{BF}_{io} \leq -1.098$ were considered as having no substantial evidential support and in fact indicate substantial evidential support for the null model. Any $ln\text{BF}_{io}$s between +1.098 and -1.098 were considered as not providing enough evidential support to make any strong claims; however, the direction may indicate a tendency toward supporting the alternative or null hypothesis.

In each analysis, each *i*th model was compared to the null (0) model; models with a $ln\text{BF}_{io} \geq 1.098$ were considered candidate models. If there was more than one candidate, the $ln\text{BF}_{io}$s were compared among candidate models, with the simplest candidate model, the candidate model with fewest free parameters[6], serving as a reference. For a more complex model to be chosen, the $ln\text{BF}_{io}$ of the more complex model had to be at least 1.098 units larger than the $ln\text{BF}_{io}$ of the simpler model. This process

[6] Whereas a model containing only a feeding regimen parameter has 1 free parameter, a model containing an initiation type × feeding regimen parameter has 3 free parameters. This is because of the hierarchical nature of ANOVA, a model with an interaction parameter must also contain parameters for the main effects.

continued until the model with the largest $ln\text{BF}_{io}$ and the fewest number of free parameters was selected.

Note that wherever there existed *a priori* predictions in baseline, models were selected in two stages. In the first stage, models were selected from an omnibus ANOVA or *t*-tests describing performance with parameters only available in baseline (e.g., initiation type). In the second stage, models were selected from an omnibus ANOVA describing performance with parameters available in both feeding regimens (e.g., initiation type and feeding regimen); however, the null model of this analysis included all the parameters from the baseline analysis such that what was estimated was whether adding feeding regimen to or having feeding regimen interact with parameters of the previous model improved the overall fit. Otherwise, tests were conducted in a manner consistent with experimental design and available data.

Mixture Model Analysis

To assess the secondary prediction that LTS sensitivity to pre-feeding in EI is explained by a pre-feeding-induced increase in the prevalence and mean of non-timed LTSs rather than parameters of timed LTSs, Equation 1.2 was rewritten below as Equation 2.1,

$$
\begin{aligned}
&p(\text{performance index} = \tau \mid \tau < \delta) = 0 \\
&p(\text{performance index} = \tau \mid \tau \geq \delta) = q\frac{1}{\Gamma(\varepsilon)c^{\varepsilon}}(\tau-\delta)^{\varepsilon-1}e^{-\frac{\tau-\delta}{c}} + (1-q)\frac{1}{K}e^{-\frac{\tau-\delta}{K}} \\
&\varepsilon \geq 1; c, K, \delta > 0; 0 \leq q \leq 1
\end{aligned}
\tag{2.1}
$$

where parameters are as described for Equation 1.2, except $\varepsilon = \theta M$ and is thus the criterion pulse count for emitting a target response denoting an LTS.

Parameters of Equation 2.1 were estimated for each rat via maximum likelihood estimation (MLE; Myung, 2003) using custom written Matlab® code. From these parameter estimates, the following derived statistics were calculated: the mean timed LTS ($\varepsilon c+\delta$), standard deviation of timed LTSs (SD; $c\varepsilon^{0.5}$), timed LTS coefficient of variation (CV; $\varepsilon^{-0.5}$); also calculated from Equation 2.1 is the mean non-timed LTS ($K+\delta$). Parameter estimates, and derived statistics were log or log-odds transformed for statistical analysis via Bayesian *t*-tests and ANOVA. MLE parameter estimation can sometimes yield extreme estimates (Cheung, Neisewander, & Sanabria, 2012); thus, prior to analysis, parameter estimates, and derived statistics were submitted to two-tailed Grubb's tests with $\alpha = .01$. Outliers were removed until none were detected.

Results

Is switch-timing performance differentially sensitive to initiation type as a function of feeding regimen?

Figure 2.2 shows the median, IQR, and CQV of LFRs, LTDs, and LTSs of each rat as a function of initiation type (EI, SL-RI). SL-RI was predicted to enhance temporal control of LTSs. To assess this prediction, LTS dependent measures were submitted to independent samples *t*-tests comparing initiation type (EI, SL-RI). There was little evidence for an initiation type model describing either LTS IQRs ($ln\text{BF}_{io} = -0.892$) and CQVs ($ln\text{BF}_{io} = -0.931$) suggesting that SL-RI and EI rats produced similarly variable LTSs. Likewise, there was little evidence for an initiation type model describing LTS medians ($ln\text{BF}_{io} = -0.985$), suggesting that SL-RI and EI rats produced similar median LTSs.

Figure 2.3 shows the pre-feeding – baseline median, IQR, and CQV of LFRs, LTDs, and LTSs of each rat as a function of initiation type (SL-RI, EI). SL-RI was also predicted to result in LTSs robust to changes in motivation. To assess this prediction, LTS dependent measures were submitted to a 2 (initiation type: SL-RI, EI) × 2 (feeding regimen: baseline, pre-feeding) Bayesian repeated measures ANOVA. There was little evidence supporting the addition of an initiation type × feeding parameter to the model describing LTS medians, IQRs, or CQVs (largest $ln\text{BF}_{io}$ = -0.407), suggesting that the effect of pre-feeding on LTSs did not depend on initiation type. Indeed, there was substantial evidence for adding a feeding regimen parameter to the model describing LTS medians ($ln\text{BF}_{io}$ = 2.184), indicating that pre-feeding increased LTS medians regardless of initiation type. In contrast, there was little evidence for adding a feeding regimen parameter to the model describing LTS IQRs or CQVs (largest $ln\text{BF}_{io}$ = -0.285), suggesting that LTS variability was robust to pre-feeding.

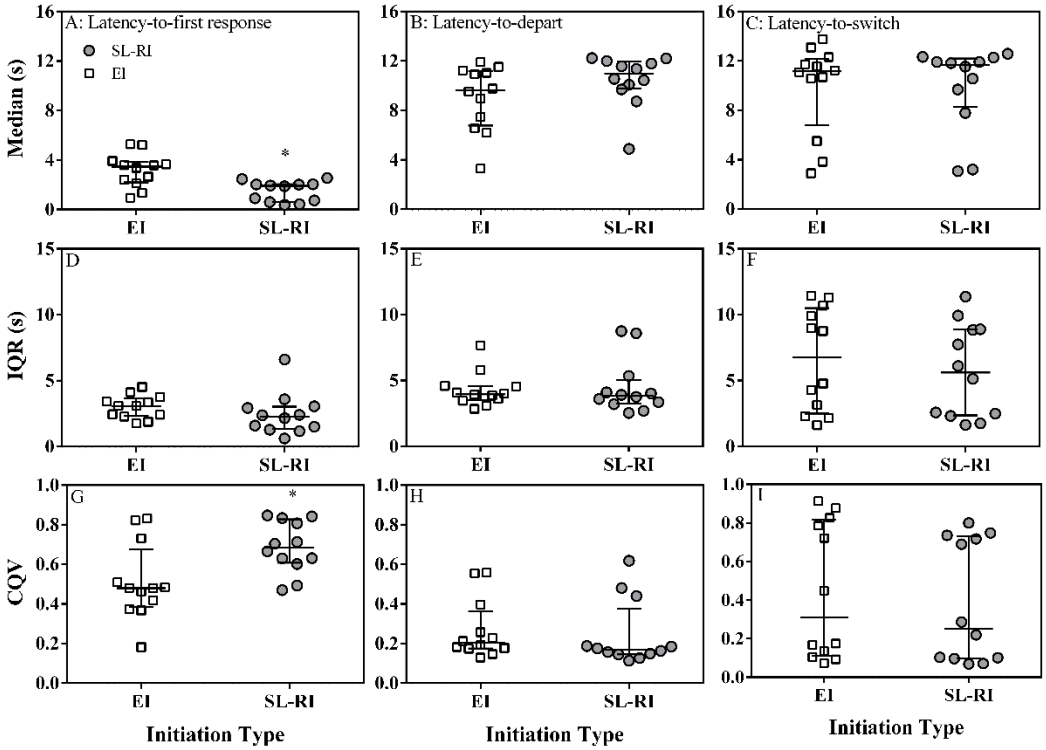

Figure 2.2. Experiment 1 baseline switch-timing performance. Median (Panels A-C), IQR (Panels D-F), and CQV (Panels G-I) of LFRs (Panels A, D, and G), LTDs (Panels B, E, and H), and LTSs (Panels C, F, and I) of each rat as a function of initiation type (EI = white squares; SL-RI = grey circles) overlaid with the median and inter-quartile range. *Indicates substantial evidence (i.e., $ln BF_{io} = 1.098$) for an initiation type model describing the difference between SL-RI and EI.

SL-RI was also predicted to reduce temporal control of Short FI performance (Figure 2.2). To assess this prediction, LFR and LTD dependent measures submitted to independent samples *t*-tests comparing initiation type (EI, SL-RI). These revealed substantial evidence for an initiation type model describing LFR medians ($ln BF_{io} = 2.503$) and CQVs ($ln BF_{io} = 1.327$), indicating that SL-RI rats started responding on the Short FI sooner and produced more variable LFRs than EI rats. There was little evidence for an initiation type model describing LFR SDs ($ln BF_{io} = 0.062$), suggesting that the higher variability of LFRs produced by SL-RI rats is explained by the shorter LFR

medians rather than larger LFR IQRs. In contrast, there was little evidence for an initiation type model describing LTD medians, IQRs, or CQVs (largest $\ln BF_{io} = 0.713$), suggesting that though SL-RI rats started responding on the Short FI before EI rats, SL-RI rats stopped responding on the Short FI around the same time as EI rats.

The sensitivity of LFRs and LTDs to pre-feeding (Figure 2.3) was also assessed by submitting LFR and LTD dependent measures to 2 (initiation type: EI, SL-RI) × 2 (feeding regimen: baseline, pre-feeding) Bayesian repeated measures ANOVAs. These analyses revealed little evidence for adding a feeding regimen parameter to the models describing LFRs and LTDs (largest $ln\text{BF}_{io} = 0.566$), suggesting that neither LFRs or LTDs were sensitive to pre-feeding.

Taken together, these data suggest that SL-RI does not result in LTSs under greater temporal control or robust to pre-feeding compared to EI. Consistent with predictions, SL-RI reduced temporal control of Short FI performance: LFRs following SL-RI were much shorter and variable than LFRs following EI. LTDs were not affected by initiation type; Short FI performance was insensitive to pre-feeding.

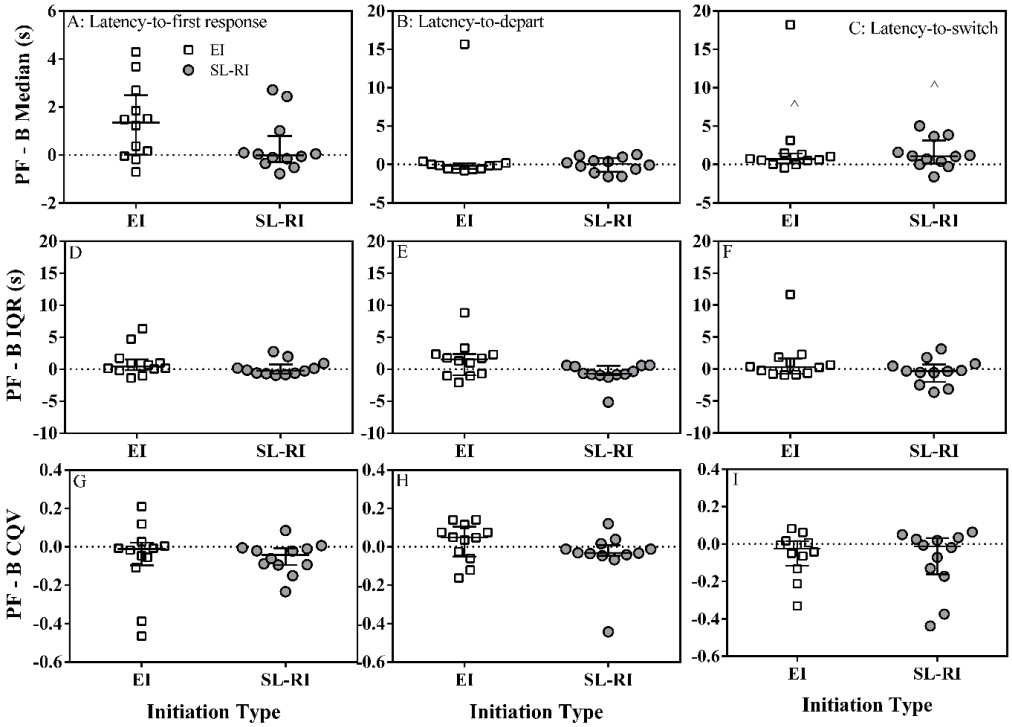

Figure 2.3. Experiment 1 pre-feeding switch-timing performance. Pre-feeding (PF) – baseline (B) median (Panels A-C), IQR (Panels D-F), and CQV (Panels G-I) of LFRs (Panels A, D, and G), LTDs (Panels B, E, and H), and LTSs (Panels C, F, and I) of each rat as a function of initiation type (EI = white squares; SL-RI = grey circles) overlaid with the median and inter-quartile range. Dotted lines indicate differences equal to zero. ^Indicates substantial evidence (i.e., $ln BF_{10} = 1.098$) for a feeding regimen model describing the difference between pre-feeding and baseline.

Are times-to-initiate, start ratios, and persistence ratios affected by initiation type or feeding regimen?

Figure 2.4 shows the median and pre-feeding – baseline median LTI and mean and pre-feeding – baseline mean start and persistence ratios of each rat as a function of initiation type (EI, SL-RI). LTIs were predicted to increase with pre-feeding. To assess this prediction, median LTIs were submitted to a Bayesian dependent samples *t*-test comparing feeding regimens (baseline, pre-feeding). This revealed substantial evidence

for the null model describing LTIs (lnBF$_{io}$ = -1.246), indicating that LTIs were robust to pre-feeding.

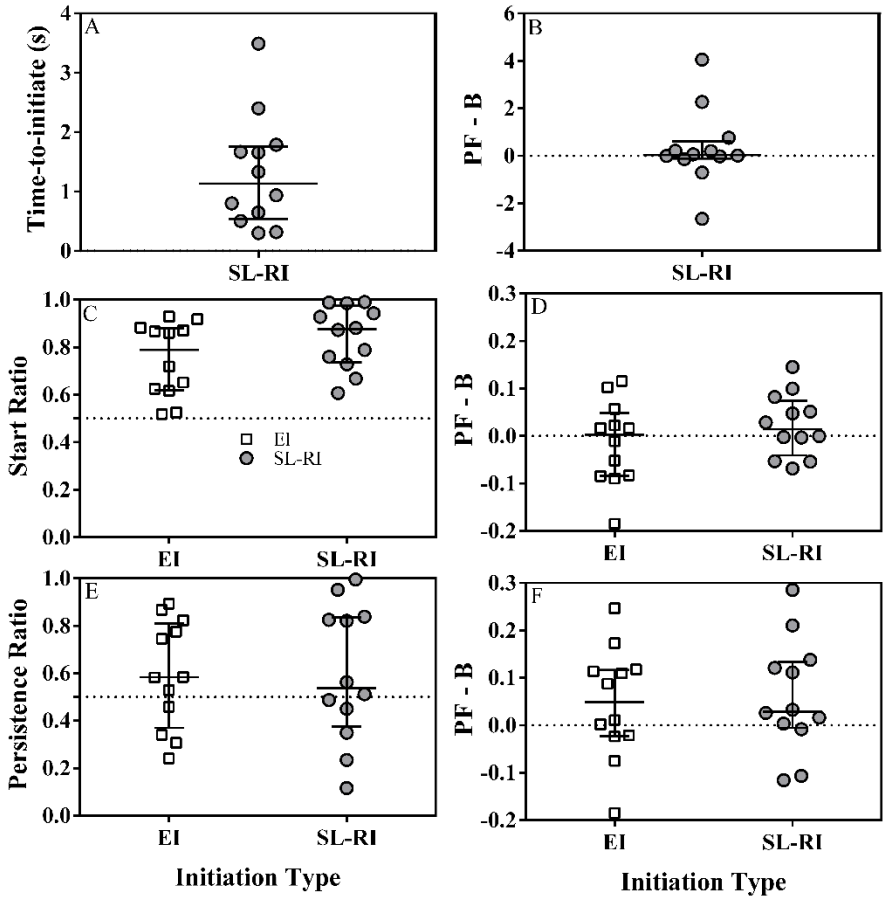

Figure 2.4. Experiment 1 baseline and pre-feeding times-to-initiate, start ratios, and persistence ratios. Median and pre-feeding (PF) – baseline (b) median time-to-initiate (Panel A & B) and mean and PF – B mean start ratio (Panel C & D) and persistence ratio (Panel E & F) of each rat as a function of initiation type (EI = white squares; SL-RI = grey circles) overlaid with the median and inter-quartile range. Note that whereas dotted lines in Panels C & E indicate ratios equal to 0.5, dotted lines in Panels B, D, & F indicate differences equal to zero.

It is possible that the feeding regimen model describing LTSs or initiation type model describing LFRs is due to a difference in start or persistence ratios. To assess this possibility, start ratios and persistence ratios were submitted to 2 (initiation type: EI, SL-

RI) × 2 (feeding regimen: baseline, pre-feeding) Bayesian repeated measures ANOVAs. These analyses revealed little evidence for a feeding, initiation type, or initiation type × feeding regimen model describing start or persistence ratios (largest $ln BF_{io} = 0.076$), suggesting that SL-RI and EI rats started just as often on the short FI and switched back to the short FI after an LTS equally as often.

Taken together, these data suggest that LTIs were not sensitive to pre-feeding as predicted. Importantly, however, the effect of feeding regimen on LTSs or initiation type on LFRs is not attributable to differences in how frequently rats started on the Short FI or switched back to the Short FI after an LTS.

Is the sensitivity of LTS medians to pre-feeding explained by an increase in the prevalence and mean of non-timed LTSs?

Grubb's test revealed a few outliers: rat 3 (SL-RI rats) for q in baseline; rat 10 (EI rats) for ε, mean timed LTS, timed LTS SD, and timed LTS CV in pre-feeding; rat 16 (EI rats) for q, c, mean timed LTS and timed LTS SD in pre-feeding; and rat 24 (EI rats) for ε, the mean timed LTS, and non-timed LTS in pre-feeding. These data were removed from analysis.

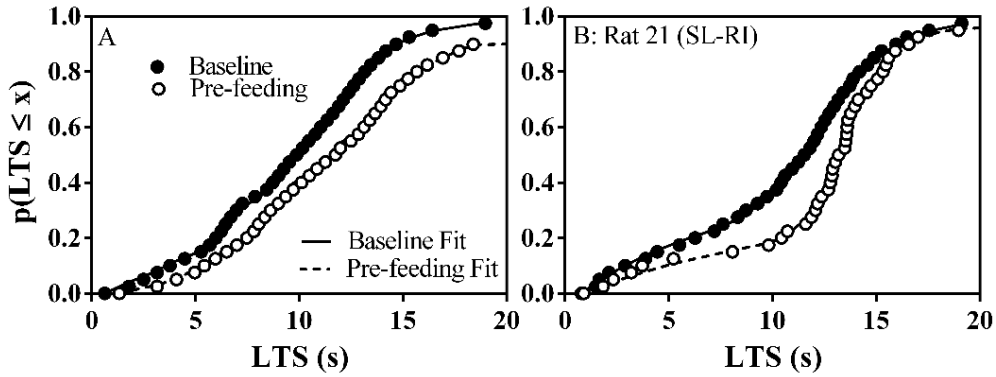

Figure 2.5. Experiment 1 gamma-exponential mixture model fits to empirical cumulative LTS distributions. Mean LTS cumulative distributions (Panel A), LTS cumulative distribution of a representative rat (Panel B) and fits of Equation 2.1 as a function of feeding regimen (baseline = filled black circles, solid line; pre-feeding = filled white circles, dashed line). Representative rat was defined as the rat with the median pre-feeding-induced increase in median LTS.

Figure 2.5 shows the mean LTS cumulative distribution, LTS cumulative distribution of a representative rat and fits of Equation 2.1 as a function of feeding regimen (baseline, pre-feeding); data were collapsed across initiation types because there was no evidence for an initiation type model describing LTSs in the previous analysis. Table 2.2 shows median (IQR) baseline and the median (IQR) pre-feeding - baseline parameter estimates. Equation 2.1 appears to adequately track the data, showing little deviation from the observed mean cumulative distribution of LTSs or the cumulative distribution of LTSs of the representative rat.

Table 2.2

Experiment 1 Median (IQR: 1st Quartile, 3rd Quartile) baseline and pre-feeding – baseline Parameter estimates of Equation 2.1

Parameter	Baseline	Pre-feeding - Baseline
q	.66 (.46, .81)	0.06 (-0.01, 0.11)
ε (pulses)	**37.69 (28.09, 52.28)**	**-15.88 (-22.26, 0.14)**
c (s)	0.32 (0.21, 0.42)	0.11 (0.03, 0.27)
δ (s)	**0.38 (0.16, 0.83)**	**0.57 (0.09, 0.92)**
Derived Statistics		
Mean Timed LTS (s)	12.37 (11.83, 12.82)	0.66 (-0.26, 1.09)
Timed LTS SD (s)	**1.89 (1.51, 2.24)**	**0.41 (-0.09, 0.87)**
Timed LTS CV	**0.16 (0.14, 0.20)**	**0.04 (-0.01, 0.07)**
Mean non-timed LTS (s)	5.83 (2.94, 7.91)	1.75 (-0.05, 66.42)

Note. Parameter estimates and derived statistics in bold indicate substantial evidence for a feeding regimen model describing those parameters and derived statistics.

The effect of pre-feeding on median LTS was predicted to be explained as an increase in the prevalence and mean of non-timed LTSs. To assess this prediction, parameter *q* and the mean non-timed LTS were submitted to Bayesian dependent *t*-tests comparing feeding regimens (baseline, pre-feeding). These analyses revealed little evidence for a feeding regimen model describing either parameter (largest $ln BF_{io}$ = -0.150), suggesting that both the probability of entering a timing state and the mean non-timed LTS were insensitive to pre-feeding.

To further isolate the potential mechanism by which pre-feeding lengthens LTSs, the remainder of the parameters and derived statistics were submitted to Bayesian

dependent *t*-tests comparing feeding regimens (baseline, pre-feeding). These revealed substantial evidence for a feeding regimen model describing ε ($ln\text{BF}_{io}$ = 1.789), indicating that pre-feeding reduced the criterion pulse count for emission of a target response. Consistent with this model, there was substantial evidence for a feeding regimen model describing the timed LTS SD ($ln\text{BF}_{io}$ = 1.328) and CV ($ln\text{BF}_{io}$ = 1.789), indicating that the pre-feeding-induced reduction in the criterion pulse count increased timed LTS variability. There was little evidence for a feeding regimen model describing the mean timed LTS ($ln\text{BF}_{io}$ = -0.315), suggesting that the pre-feeding-induced reduction in the criterion pulse count was not enough to alter the mean timed LTS. That is, the mean timed LTS was insensitive to pre-feeding.

The effects observed thus far do not explain the pre-feeding-induced lengthening of LTSs. Thus, the minimum LTS was also submitted to a Bayesian dependent *t*-test comparing feeding regimens (baseline, pre-feeding). This revealed that there was substantial evidence for a feeding regimen model describing the minimum LTS ($ln\text{BF}_{io}$ = 4.748), indicating that pre-feeding increased the minimum LTS.

Taken together, these data suggest that pre-feeding-induced lengthening of LTSs is not due to an increase in the prevalence and mean of non-timed LTSs. Instead it appears that much of the increase in LTSs is due to a lengthening of the minimum LTS, shifting the entire distribution of LTSs by about .60 s. Interestingly, pre-feeding increased the variability but not the mean of timed LTSs by reducing the criterion pulse count.

Discussion

Experiment 1 revealed little evidence for the discriminative RI hypothesis. LTSs in SL-RI were not under greater temporal control or robust to pre-feeding compared to LTSs in EI. Indeed, LTS medians and variability were similar in both SL-RI, and LTS medians in both SL-RI and EI were equally sensitive to pre-feeding. Additionally, LTIs were not sensitive to pre-feeding. SL-RI did not dissociate interval timing and motivation.

The insensitivity of SL-RI LTIs to pre-feeding suggests that Short FI initiating-responses are not sensitive to changes in motivation. This insensitivity is incongruent with FMI and FCN procedures developed by Mechner & Guevrekian (1962), which also required a lever initiating-response. The critical difference between the present implementation of the SL-RI switch-timing procedure and the RI procedures developed by Mechner & Guevrekian (1962) is that in their procedures, the manipulanda are always available and in the present implementation of SL-RI switch-timing the manipulanda are not always available. That is, whereas in Mechner & Guevrekian (1962) the levers did not serve as discrete cues for reinforcement, in the present study the levers did serve as discrete cues for reinforcement. Lever insertion signals to both SL-RI and EI rats that food will arrive in either 8-s or 16-s. Associating lever insertion with imminent reinforcement is known to promote the attribution of value to levers (Beckmann & Chow, 2015; Davey & Cleland, 1982; Holland, 1977), which in turn promotes interaction with the levers and facilitation of habit development (Everitt & Robbins, 2005; Vandaele, Pribut, & Janak, 2017); habits are insensitive to manipulation by disruptors such as pre-feeding (Dickinson & Balliene, 1994; Vandaele, Pribut, & Janak, 2017). Given that habit development is also facilitated with extended training (Dickinson & Balliene, 1994; Yin &

Knowlton, 2006), it is likely that Short FI initiating-responses were insensitive to pre-feeding because (a) the SL-RI switch-timing procedure was programmed as a procedure in which lever insertion was a reliable cue for both trial initiation and imminent reinforcement, and (b) the Short FI initiating-response was extensively trained prior to pre-feeding. This suggests that a design in which initiating-responses are unlikely to become habits would restore the sensitivity of SL-RI, and thus SL-RI LTIs, to pre-feeding.

Habit development of Short FI initiating-responses may also explain why SL-RI did not protect LTSs in SL-RI from changes in motivation. Habit development of initiating-responses likely fail to circumscribe the effect of pre-feeding to the post-food focal search mode. As a result, pre-feeding effects on post-food focal search are expected to perturb general search and subsequently pre-food focal search (Figure 1.4B). Such effects predict that performance indices become longer and more variable. Although it is unclear why initiating-responses but not target responses became habits, target responses denoting performance indices appear to require substantial training to become habits. For example, Cheng, Hakak, & Meck (2007) found peak-times were most sensitive to methamphetamine administration after 20 sessions of training, less sensitive after 60 sessions of training and not sensitive after 120 sessions of training. In the present study, rats were only trained for 29 sessions prior to the single session pre-feeding probe. This suggests that target responses were not trained long enough to become habits, allowing pre-feeding to affect target responses and thus performance indices.

It is also possible that there was still some generalization between Short FI initiating-responses and target responses. Short FI initiating-responses are

discriminable from Long FI target responses as a function of time and location but identical as a function of form. Indeed, Short FI and Long FI responses are both measured as lever presses. Despite turning on a localized yellow LED easily detected by rats (Burn, 2008; Graham & Riggs, 1935; Prusky, Harker, Douglas, & Whishaw, 2002; Walton, 1933) to signal an effective initiating-response, the identical form of the response may have promoted generalization between Short FI initiating-responses and target responses[7]. This suggestion is also consistent with the observation that pairing discriminative cues with initiating-responses does not enhance temporal control of RIFI and RI peak performance relative to EIFI and EI peak performance (Fox & Kyonka, 2016). Thus, it may be that discriminability of initiating-responses from target responses needs to be a function of time, location, *and form*.

Chapter 3: Experiment 2 - Response-Initiated Free-Operant Switch-Timing

Introduction

The results of experiment 1 suggest that (a) the discrete-trials switch-timing procedure or (b) the identical form of Short FI initiating-responses and target responses resulted in a failure to demarcate post-food focal search from general search. Whereas the discrete-trials switch-timing procedure may have facilitated Short FI initiating-responses becoming habits, the identical form of Short FI initiating-responses and target responses may have facilitated generalization between Short FI initiating-responses and

[7] An alternative hypothesis may be offered from the perspective of PA models. In Figure 1.2, every Short FI response is followed by another query of the timing process to determine whether it is time to switch over to the Long FI. Subjects may thus encode every Short FI response as a query of the timing process. That is, as a prelude to completing an LTS.

target responses. Regardless of the route by which Short FI initiating-responses failed to demarcate the post food-focal search from general search, this failure suggests either that interval timing and motivation are not dissociable or that initiating-responses need to differ from target responses as a function of time, location, and form.

Comparison of contemporary implementations of FMI to DRL confirms that this other dimension is likely the form of the response. IRTs of both rats (e.g., Hill et al. 2012) and mice (e.g., Daniels et al., 2018; Romero, 2016) trained in FMI relative to DRL are under greater temporal control and robust to pre-feeding (Daniels et al., 2018; Romero et al. 2016; Mazur et al., 2014; Watterson et al., 2015). The critical difference between contemporary implementations of FMI and DRL, is that in contemporary implementations of FMI, IRTs are initiated, for example, via a lever-press and terminated via a head-entry. That is, initiating-responses in FMI differ from target responses as a function of time, location, and form. In DRL, IRTs are both initiated and terminated via the same response (e.g., lever press, nose-poke, head-entry). The exact form of initiating-responses in FMI does not appear to be important, as IRTs initiated via nose-pokes are similar to IRTs initiated via lever-presses (Daniels et al., 2018; Romero et al., 2016).

Thus, experiment 2 sought to test whether initiating-responses discriminable from target responses as a function of time, location, and form dissociate interval timing and motivation. To test this hypothesis, rats were trained in a multiple RI EI switch-timing procedure (Figure 3.1) in which manipulanda were always available, and active manipulanda were signaled by discriminative stimuli. Initiating-responses were discriminable from target responses as a function of either two or three dimensions. Rats were trained with EI, SL-RI and nose-poke RI (NP-RI) where SL-RI is discriminable

from target responses as a function of time and location (as in experiment 1, Chapter 2), and NP-RI is discriminable from target responses as a function of time, location, and form. Motivation was manipulated via 1 h and 24 h pre-feeding probes; the different pre-feeding durations were included to determine whether effects differed with 1 h and 24 h pre-feeding. Extinction probes were also included to determine whether RI selectively dissociates interval timing and motivation or more generally dissociates interval timing and non-timing processes.

Compared to EI, NP-RI was predicted to improve temporal control of LTSs and protect LTSs from pre-feeding and extinction. SL-RI was predicted to have the same effects, but to a lesser degree. NP-RI and SL-RI LTIs were predicted to be sensitive to pre-feeding and extinction, but LTIs in NP-RI were predicted to be more sensitive to pre-feeding and extinction than SL-RI. Additionally, SL-RI was predicted to reduce temporal control of Short FI performance. Fits of Equation 2.1 to LTSs was expected to reveal that pre-feeding increases the prevalence and mean of non-timed LTSs in EI but not SL-RI or NP-RI.

Methods

Subjects

Eight naïve male Sprague Dawley rats (Charles River Laboratories, Hollister, CA) served as subjects. Subjects arrived on post-natal day (PND) 61 and were immediately pair-housed in a vivarium on a reverse 12:12 h light cycle, with lights on at 1900 h. All behavioral training was conducted during the dark phase of the cycle, starting at approximately 1130 h and ending approximately at 1330 h. Following four days of acclimation to the colony room, food access was reduced daily from 24 to 18, 12, and finally 1 hour per day. Food was placed on home-cages 30 min after the end of each

experimental session and taken away 1 hour later. This ensured that at the beginning of the next session weights were, on average, 85% of *ad libitum* weights, as estimated from growth charts provided by the breeder. Water was always available in home-cages. All animal handling procedures used during this study followed National Institutes for Health Guidelines and were approved by the Arizona State University institutional Animal Care and Use Committee.

Apparatus

Experiments were conducted in 8 of the 12 MED Associates (St. Albans, VT, USA) modular test chambers detailed in Experiment 1 (Chapter 2; 2 chambers were 305 mm long, 241 mm wide, and 210 mm high; 4 chambers were 305 mm long, 241 mm wide, and 292 mm high). Chambers were modified to include a nose-poke device (ENV-114M) at the bottom of the panel opposite the response panel containing the levers and reinforcement receptacle, flush with the floor. This device could be internally illuminated with green, yellow, and/or red LEDs.

Procedure

All experimental sessions were 2 hours in duration and began with a 3-min warm-up. During this warm-up period, no stimuli were activated.

Reinforcer Shaping. Rats were initially acclimated to the operant chambers and trained to obtain reinforcement. After the 3-min warm-up, a single reinforcer was delivered by raising the liquid dipper. A single head-entry into the reinforcement receptacle broke an infrared beam, 10 s later the liquid dipper was lowered and a fixed-time 90-s inter-trial interval (ITI) commenced.

Manipulandum Shaping. After a single day of *Reinforcer Shaping*, rats were shaped to press levers and nose poke the nose-poke device using a Pavlovian conditioned approach procedure. After the 3-min warm-up, a 1-kHz tone was activated, and a single reinforcer was delivered. A single head-entry into the reinforcement receptacle broke an infrared beam; 5 s later the liquid dipper was lowered, the 1-kHz tone deactivated, and a variable-time 45-s ITI commenced. At the end of each ITI, a single manipulandum (i.e., left lever extended, right lever extended, or turning on all lights in the nose-poke device) was pseudo-randomly selected from a list, such that no manipulandum could be selected in more than six consecutive trials; the selected manipulandum was activated. If 8 s elapsed after manipulandum activation, the manipulandum was deactivated (i.e., left lever retracted, right lever retracted, all lights in the nose-poke device turned off), the 1-kHz tone was turned on, and a single reinforcer delivered. Alternatively, if a response was made on the active manipulandum before 8-s elapsed (i.e., a lever press on the activated lever, or a nose poke on the nose-poke device) the manipulandum was deactivated, the 1-kHz tone was turned on, and a single reinforcer delivered.

Lever Press and Nose Poke Training. After four days of *Manipulandum Shaping*, rats were trained to press the left and right lever and nose poke the nose-poke device for reinforcement. After the 3-min warmup, a single manipulandum was pseudo-randomly selected and activated, as described in *Manipulandum Shaping*. Following a single response on the active manipulandum, the manipulandum was deactivated, the 1-kHz tone was activated, and a single reinforcer delivered. A head-entry into the reinforcement receptacle deactivated the 1-kHz tone and lowered the liquid dipper 2.5 s later. After the liquid dipper was lowered, a fixed-time 5-s ITI commenced.

Response-Initiated Switch-Timing Shaping: Response-Initiation. Figure 3.1 shows a schematic of the multiple RI EI switch-timing procedure. After four days of *Lever Press and Nose Poke Training*, rats were trained to initiate switch-timing trials. After the 3-min warmup, both levers and the nose-poke device were activated. Initiation types were signaled by activating one of three tones (3-kHz, 8-kHz, or 15-kHz), pseudo-randomly sampled from a list such that no initiation type could occur in more than six consecutive trials. Each tone indicated whether the trial was initiated by nose poking the nose-poke device (NP-RI), pressing the Short-FI lever (SL-RI; see *Switch Timing* below), or waiting for the experimenter to initiate the trial (EI). EI trials were initiated after 2.5 s since tone onset, and until rats had ceased to press the levers and nose poke the nose-poke device for 0.25 s. The initiation type signaled by each tone was counterbalanced across all rats such that no tone served as the signal for a specific initiation type in more than 2-3 rats.

Switch-Timing. Following trial initiation, the active tone was deactivated, the houselight illuminated for either a fixed-interval (FI) 1-s (Short FI) or a FI 4-s (Long FI), pseudo-randomly sampled from a list such that neither FI occurred in more than four consecutive trials within an initiation type, and in no more than 12 consecutive trials across initiation types. For some rats, the left lever delivered reinforcement according to the Short FI and the right lever delivered reinforcement according to the Long FI, and vice versa for the other rats. This assignment was also counterbalanced across tone-initiation assignment, such that within each pattern of tone-initiation assignment there was at least one rat for which the Short FI was programmed on the left lever and one rat for which the Long FI was programmed on the left lever. The first press on the active FI lever after the active FI elapsed turned off the houselight and delivered a single reinforcer. A head-entry into the reinforcer receptacle broke an infrared beam and then

deactivated the dipper 2.5 s later. This was immediately followed by a tone signaling the next initiation type. The ITI was thus equal to the time it took rats to initiate trials in NP-RI and SL-RI, and equal to the time it took rats to quit lever pressing or nose poking in EI, with a minimum ITI of 2.5 s. The SL-RI and NP-RI ITIs are also referred to as the latency-to-initiate (LTI). Taken together, ITIs and LTIs are referred to as the time-to-initiate.

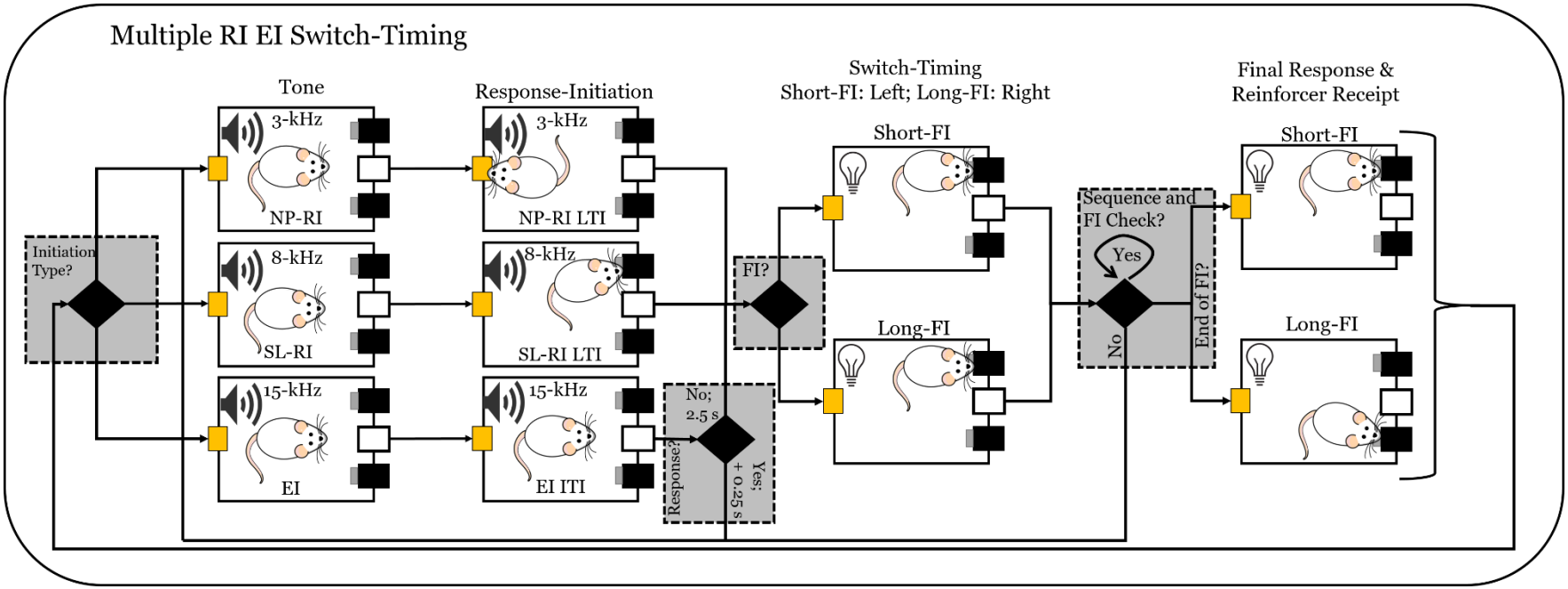

Figure 3.1. Experiment 2 Schematic of the multiple RI EI switch-timing procedure. At the beginning of the session, the nose-poke device was illuminated, and the levers extended. The initiation type was then selected and indicated by a tone. Following correct initiating-responses, the tone was turned off and either the Short FI or Long FI was activated, nondifferentially signaled by turning on the houselight. In nose-poke (NP-RI) and Short FI (SL-RI), rats nose-poked and responded on the Short FI, respectively, to initiate trials; in externally-initiated (EI), nose-pokes and lever presses delayed trial initiation by 0.25 s but were otherwise initiated after 2.5 s. Once a trial was initiated, performance was checked against the optimal behavioral sequence (see text for details); if the optimal sequence was not followed, the trial was terminated, and the trial reinitiated either by the subject or the experimenter, depending on the initiation type. After the active FI elapsed, the first response on the lever associated with the active FI turned off the houselight and activated the dipper. Once a head-entry into the reinforcement receptacle confirmed receipt of the reinforcer, the dipper was lowered 2.5 s later and the next initiation type selected.

Punishment. Optimal performance in the switch-timing procedure involves responding first on the Short FI and eventually switching over to the Long FI. To encourage this sequence, trials were terminated without reinforcement if (a) the first response after trial initiation was on the long FI, (b) if the Short FI was active and a response was made on the Long FI at any point during the trial, or (c) if the Long FI was active and a response was made on the Short FI after a response on the Long FI.

Training Order. Rats were trained such that reinforcement was initially contingent upon FI 1-s FI 4-s only in EI; NP-RI and SL-RI were terminated with reinforcement following initiating-responses. Reinforcement contingent upon FI 1-s FI 4-s in NP-RI and SL-RI was slowly introduced as rats learned to correctly respond in the presence of the tone and engage in switch-timing FI 1-s FI 4-s in the presence of the houselight. This was assessed by inspecting the number of obtained reinforcers in the previous two sessions; if rats earned more than 600 reinforcers, FI 1-s FI 4-s was introduced following SL-RI and then following NP-RI.

Switch-Timing Training. Once rats were trained on FI 1-s FI 4-s in all initiation types, rats were trained up to the timing conditions of interest in the following order: FI 4-s FI 12-s A, FI 6-s FI 18-s, and FI 4-s FI 12-s B. All rats experienced the same order of conditions; the two FI 4-s FI 12-s conditions allowed for assessment of potential order effects. Punishment continued as described in *Response-Initiation and Switch-Timing Shaping*, until subjects had experienced a minimum of 5 sessions of training with punishment in each condition and until performance was deemed stable. Punishment was then removed, and subjects were trained for a minimum of 7 sessions and until performance was again deemed stable. Stability was assessed visually and confirmed via

a non-significant regression of the critical dependent measures listed in *Data Analysis & Results* over the last 5 sessions of training.

Single-Initiation Type Testing: Pre-feeding. Figure 3.2 shows a schematic of training and testing. Table 3.1 shows the order of testing for each rat. Following confirmation of stable performance in the FI 4-s FI 12-s A and the FI 6-s FI 18-s timing conditions, rats were tested for 15 sessions in a counterbalanced order within each timing condition for 5 sessions within each initiation type. In each single-initiation type testing condition, the first, second, and fifth sessions served as baselines and the third and fourth sessions served as 1-h and 24-h pre-feeding probes, respectively. In the 1-h PF, rats were given continual access to food at their home-cages 1 h immediately prior to testing. In 24-h PF, rats were given continual access to food at their home-cages 24 h prior to testing. To return to baseline performance on the fifth session, rats were not given 1 h of post-experimental feeding after the 24 h pre-feeding probe. At the end of testing, rats were returned to *Switch-Timing Training*.

Single-Initiation Type Testing: Yoked-ITI Pre-feeding. Following confirmation of stable performance in the FI4-s FI 12-s B schedule, rats were tested as described in *Single-Initiation Type Testing: Pre-feeding*. However, EI ITIs for each rat were changed from 2.5 s to a list containing the 1st, 2nd (median), and 3rd quartiles of the same rats' NP-RI LTIs during the pre-feeding portion of *Single-Initiation Type Testing: Pre-feeding* in the FI 4-s FI 12-s (first determination) condition.

Single-Initiation Type Testing: Extinction. Immediately following*: Single-Initiation Type Testing: Yoked-ITI Pre-feeding*, rats started another round of *Single-Initiation Type Testing*; EI ITIs were returned to their original length of 2.5 s. However,

pre-feeding probes were substituted with extinction sessions, wherein the liquid dipper normally containing sweetened condensed milk was empty.

Data Analysis and Results

Single-Initiation Type Testing began on session 51 for FI 4-s FI 12-s A, session 104 for FI 6-s FI 18, and session 136 for FI4-s FI 12-s B. Dependent measures were analyzed and calculated as described in experiment 1 (Chapter 2). Note that dependent measures calculated based on LFRs were not included for rat 1, because almost all LFRs for rat 1 were equal to 0.2 s, indicating most LFRs were the product of lever bounces following SL-RI. To determine whether the sensitivity of LTSs to pre-feeding can be explained by an increase in the prevalence and mean of non-timed LTSs in EI, parameter estimates, and derived statistics of the gamma-exponential were estimated and analyzed as described in experiment 1 (Chapter 2).

The number of completed trials under 1 h and 24 h pre-feeding was substantially less than baseline, on average a 2- to 3-fold decrease. To determine whether 1 h and 24 h pre-feeding sessions could be collapsed into a single pre-feeding factor for analysis, the effect of feeding duration on LTSs and LTIs was assessed via Bayesian dependent *t*-tests within each switch-timing condition and initiation type. There was little evidence for a feeding duration model describing LTS dependent measures or LTIs (largest $\ln BF_{io} = -0.300$), suggesting that switch-timing performance was similar across pre-feeding durations. Thus, the 1 h and 24 h pre-feeding sessions were collapsed into a single factor of pre-feeding for all dependent measures. Data were analyzed as described in experiment 1 (Chapter 2).

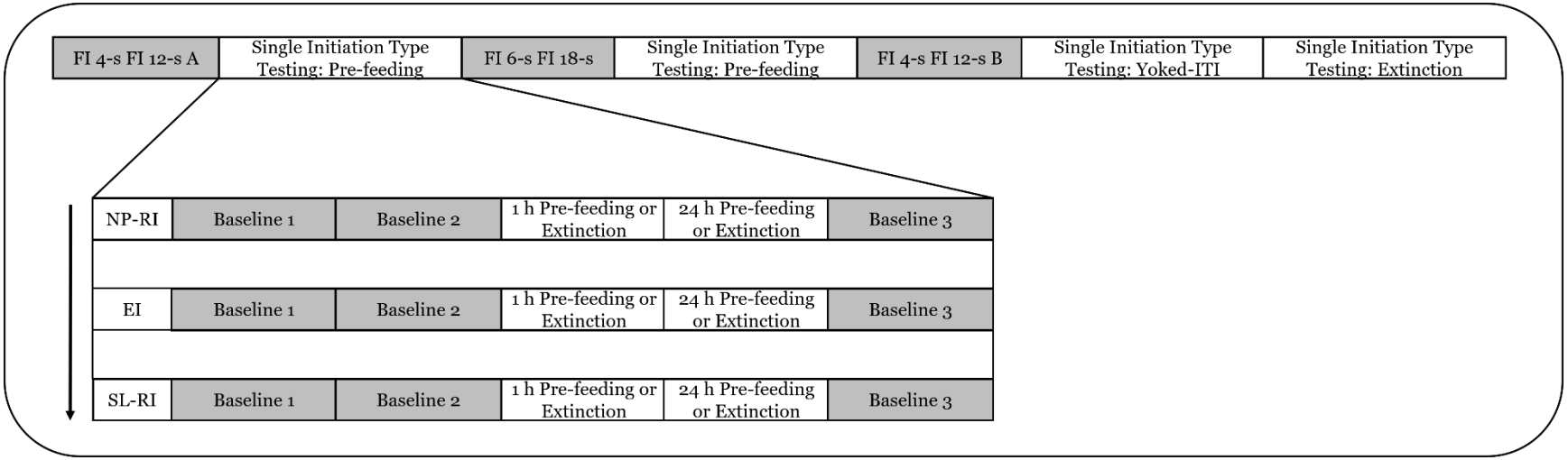

Figure 3.2. Experiments 2 and 3 schematic of training and testing timeline. In experiment 2 (multiple RI EI Switch-Timing), rats were trained in a fixed order on FI 4-s FI 12-s A, FI 6-s FI 18-s, and then FI 4-s FI 12-s B. In experiment 3 (multiple RI EI Temporal Bisection), rats were trained in a fixed order on Short 4-s Long 12-s A, Short 6-s Long 18-s, and then Short 4-s Long 12-s B. At the end of the first two timing conditions, rats were tested in Single-Initiation Type Testing: Pre-feeding with the order of initiation types counterbalanced within and across rats. In the Single-Initiation Type Testing: Yoked-ITI Pre-feeding, EI ITIs during the 1 h and 24 h pre-feeding probes were yoked to NP-RI LTIs from the 1 h and 24 h pre-feeding probes the Single-Initiation Type Testing: Pre-feeding condition. In the Single-Initiation Type Testing: Extinction, pre-feeding probes were replaced with extinction probes, and EI ITIs were reprogrammed to 2.5 s. Note that the experimental timeline is not to scale.

Table 3.1

Experiment 2 Order of Single-Initiation Type Testing

		Rat							
Single-Initiation Type Testing Condition	Session	1	2	3	4	5	6	7	8
FI 4-s FI 12-s A: Pre-feeding	1-5	NP-RI	SL-RI	EI	NP-RI	SL-RI	EI	EI	NP-RI
	6-10	SL-RI	NP-RI	NP-RI	EI	EI	SL-RI	NP-RI	EI
	11-15	EI	EI	SL-RI	SL-RI	NP-RI	NP-RI	SL-RI	SL-RI
FI 6-s FI 18-s: Pre-feeding	1-5	EI	EI	SL-RI	SL-RI	NP-RI	NP-RI	SL-RI	SL-RI
	6-10	NP-RI	SL-RI	EI	NP-RI	SL-RI	EI	EI	NP-RI
	11-15	SL-RI	NP-RI	NP-RI	EI	EI	SL-RI	NP-RI	EI
FI 4-s FI 12-s B: Yoked-ITI Pre-feeding	1-5	SL-RI	NP-RI	NP-RI	EI	EI	SL-RI	NP-RI	EI
	6-10	EI	EI	SL-RI	SL-RI	NP-RI	NP-RI	SL-RI	SL-RI
	11-15	NP-RI	SL-RI	EI	NP-RI	SL-RI	EI	EI	NP-RI
FI 4-s FI 12-s B: Extinction	1-5	NP-RI	EI	EI	SL-RI	NP-RI	SL-RI	NP-RI	SL-RI
	6-10	EI	NP-RI	SL-RI	NP-RI	SL-RI	EI	SL-RI	EI
	11-15	SL-RI	SL-RI	NP-RI	EI	EI	NP-RI	EI	NP-RI

Note. The third and fourth sessions in each Single-Initiation Type Testing condition (i.e., sessions 3, 4, 8, 9, 13, and 14) were preceded by 1 h and 24 h pre-feeding, respectively.

Is switch-timing performance differentially sensitive to initiation type as a function of feeding regimen?

Figure 3.3 shows the median, IQR, and CQV of LFRs, LTDs, and LTSs for each rat as a function of the Long FI in each timing condition (FI 12-s A, FI 18-s) and initiation type (EI, SL-RI, NP-RI). NP-RI was predicted to enhance temporal control of LTSs relative to SL-RI and EI, SL-RI was predicted to enhance temporal control of LTSs relative to EI. To asses this prediction, LTS dependent measures were submitted to a 3 (initiation type: EI, SL-RI, NP-RI) × 2 (timing: FI 4-s FI 12-s A, FI 6-s FI 18-s) Bayesian repeated measures ANOVAs. These revealed substantial evidence for a timing model describing LTS medians ($ln BF_{io}$ = 43.275) and IQRs ($ln BF_{io}$ = 7.508), indicating that LTS medians and IQRs scaled with the timing condition; there was substantial evidence against an initiation type model describing LTS IQRs ($ln BF_{io}$ = -1.104), indicating that LTSs were equally variable across initiation types. Consistent with these models, there was no substantial evidence for a timing, initiation type, timing + initiation type, or a timing × initiation type model describing LTS CQVs (largest $ln BF_{io}$ = -0.055), suggesting that CQVs were invariant to both initiation type and timing conditions.

Figure 3.4 shows the pre-feeding – baseline median, IQR, and CQV of LFRs, LTDs, and LTSs for each rat as a function of the Long FI in each timing condition (FI 12-s A, FI 18-s), and each initiation type (EI, SL-RI, NP-RI). NP-RI was also predicted to protect LTSs from changes in motivation more than SL-RI and EI, SL-RI was predicted to protect LTSs from changes in motivation more than EI. To assess these predictions, LTS dependent measures were submitted to 3 (initiation type: EI, SL-RI, NP-RI) × 2 (feeding regimen: baseline, pre-feeding) × 2 (timing: FI 12-s A, FI 18-s) Bayesian repeated measures ANOVAs. These analyses revealed substantial evidence for adding an initiation type × feeding regimen parameter to the model describing LTS medians

(lnBF$_{io}$ = 16.681), indicating that whether LTSs were affected by pre-feeding depended on initiation type. Dependent *t*-tests probing this interaction revealed substantial evidence for adding a feeding regimen parameter to the model describing LTS medians in EI (lnBF$_{io}$ = 7.960) and SL-RI (lnBF$_{io}$ = 2.677) but not NP-RI (lnBF$_{io}$ = 0.259), indicating that pre-feeding increased the median LTSs in EI and SL-RI but not NP-RI. In contrast, there was substantial evidence for adding a feeding regimen parameter to the model describing LTS IQRs (lnBF$_{io}$ = 24.870) and CQVs (lnBF$_{io}$ = 20.528), indicating that pre-feeding resulted in more variable LTSs in all initiation types. Thus, only LTS medians were robust to pre-feeding in only NP-RI.

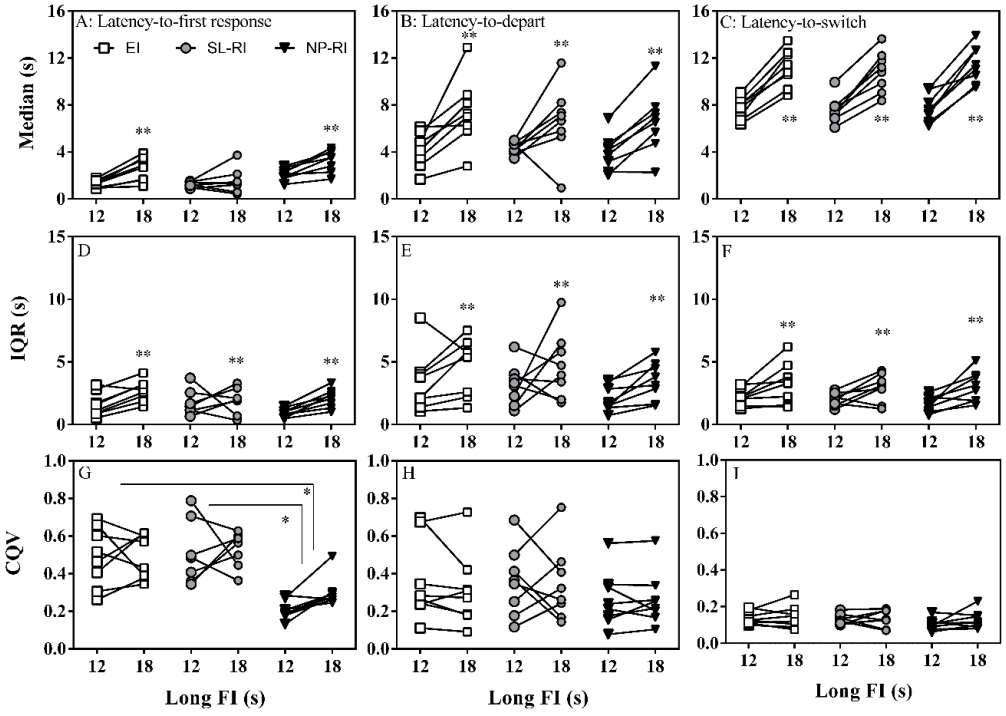

Figure. 3.3 Experiment 2 baseline switch-timing performance. Median (Panels A-C), IQR (Panels D-F), and CQV (Panels G-I) of LFRs (Panels A, D, & G), LTDs (Panels B, E, & H), and LTSs (Panels C, F, & I) for each rat as a function of Long FI in each timing condition (12-s A, 18-s) and each initiation type (EI = white squares; SL-RI = grey circles; NP-RI = black triangles). *Indicates substantial evidence (i.e., lnBF$_{io}$ = 1.098) for an initiation type model. **Indicates substantial evidence for a timing condition model.

SL-RI was predicted to reduce temporal control of Short FI performance (Figure 3.3). To assess this prediction, LFR and LTD dependent measures were submitted to 3 (initiation type: EI, SL-RI, NP-RI) × 2 (timing: FI 12-s A, FI 18-s) Bayesian repeated measures ANOVAs. These revealed substantial evidence for an initiation type × timing condition model describing LFR medians (lnBF$_{io}$ = 11.634), indicating that whether LFRs increased with the timing condition depended on initiation type. Probes of the initiation type × timing model describing LFR medians revealed substantial evidence for a timing model describing LFR medians in EI (lnBF$_{io}$ = 5.426) and NP-RI (lnBF$_{io}$ = 3.969) but not SL-RI (lnBF$_{io}$ = 0.446), indicating that median LFRs scaled with the timing condition in EI and NP-RI but not SL-RI. There was substantial evidence for a timing condition model describing LFR IQRs (lnBF$_{io}$ = 1.612), indicating that LFR IQRs scaled with the timing condition. Interestingly, there was substantial evidence for an initiation type model describing LFR CQVs (lnBF$_{io}$ = 15.521). Post-hoc dependent samples *t*-tests probing the initiation type model describing LFR CQVs revealed substantial evidence for initiation type models describing LFR CQVs when comparing EI to NP-RI (lnBF$_{io}$ = 6.596) and SL-RI to NP-RI (lnBF$_{io}$ = 8.207) but not EI to SL-RI (lnBF$_{io}$ = 8.207, indicating the LFR CQVs were higher in EI and SL-RI than NP-RI. Additionally, there was substantial evidence for a timing model describing LTD medians (lnBF$_{io}$ = 7.292) and IQRs (lnBF$_{io}$ = 3.225) but not CQVs (lnBF$_{io}$ = -1.159) indicating that LTDs scaled with the timing condition.

LFR and LTD dependent measures were also assessed for their sensitivity to pre-feeding (Figure 3.4) by submitting LFR and LTD dependent measures to 3 (initiation type: EI, SL-RI, NP-RI) × 2 (feeding regimen: baseline, pre-feeding) × 2 (timing: FI 12-s A, FI 18-s) Bayesian repeated measures ANOVAs. These analyses revealed substantial evidence for adding a feeding regimen parameter to the model describing LFR medians

($ln\text{BF}_{io}$ = 19.384) and IQRs ($ln\text{BF}_{io}$ = 14.188) indicating that LFR median and variability increased with pre-feeding in all initiation types. There was also substantial evidence for adding a feeding regimen × timing condition parameter to the model describing LFR CQVs ($ln\text{BF}_{io}$ = 1.127), indicating that whether LFR CQVs increased with pre-feeding depended on timing condition. Post-hoc dependent *t*-tests probing this interaction revealed substantial evidence for adding a feeding regimen parameter to the model describing LFR CQVs in FI 4-s FI 12-s A ($ln\text{BF}_{io}$ = 2.629) but not FI 6-s FI 18-s ($ln\text{BF}_{io}$ = -1.074), indicating that LFR CQVs increased with pre-feeding in FI4-s FI 12-s A but not FI 6-s FI 18-s. Additionally, there was substantial evidence for adding a feeding regimen parameter to the model describing LTD medians ($ln\text{BF}_{io}$ = 10.776), IQRs ($ln\text{BF}_{io}$ = 18.439), and CQVs ($ln\text{BF}_{io}$ = 5.329), indicating that LTDs also increased with pre-feeding.

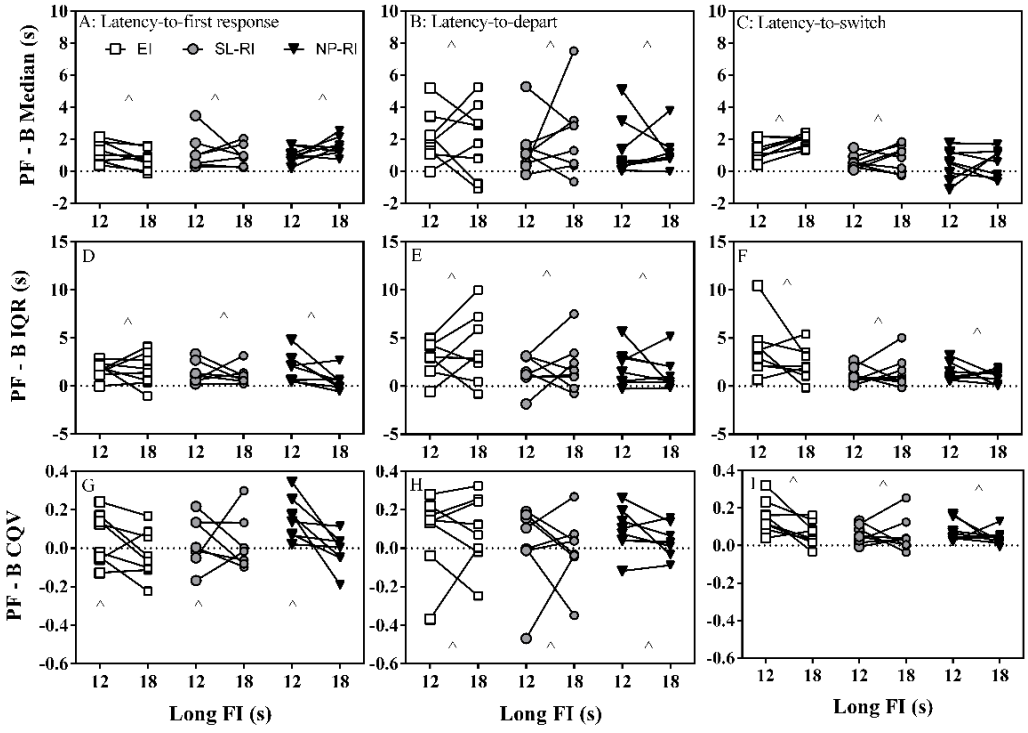

Figure. 3.4 Experiment 2 pre-feeding switch-timing performance. Pre-feeding (PF) – baseline (B) median (Panels A-C), IQR (Panels D-F), and CQV (Panels G-I) of LFRs (Panels A, D, & G), LTDs (Panels B, E, & H), and LTSs (Panels C, F, & I) for each rat as a function of the Long FI in each timing condition (12-s A, 18-s) and each initiation type (EI = white squares; SL-RI = grey circles; NP-RI = black triangles). ^Indicates substantial evidence (i.e., $ln BF_{io} = 1.098$) for a feeding regimen describing the difference between pre-feeding and baseline. Dotted lines indicate differences equal to zero.

Taken together, these data suggest that LTSs, LTDs, and to an extent LFRs scaled as expected from FI 4-s FI 12-s A to FI 6-s FI 18-s. Although LTSs in SL-RI and NP-RI were not under greater temporal control relative to LTSs in EI, LTS medians in NP-RI but not SL-RI or EI were robust to pre-feeding. LTS medians in SL-RI were less robust to pre-feeding than LTS medians in NP-RI but more robust to pre-feeding than LTS medians in EI. Interestingly, LTS variability increased with pre-feeding in all three initiation types. Consistent with predictions, temporal control of Short FI performance in SL-RI was reduced relative to Short FI performance in EI and NP-RI: LFR medians did

not increase from FI 4-s FI 12-s to FI 6-s FI 18-s. Short FI performance was also affected by pre-feeding: LFR and LTD medians, IQRs, and CQVs were all elevated with pre-feeding.

Are times-to-initiate, discrimination ratios, start ratios, and persistence ratios affected by initiation type, feeding regimen, or timing condition?

Figure 3.5 shows the median and pre-feeding - baseline median time-to-initiate, and mean and pre-feeding – baseline mean discrimination ratio, start ratio, and persistence ratio for each rat as a function of the Long FI in each timing condition (FI 12-s A, FI 18-s), and each initiation type (EI, SL-RI, NP-RI). LTIs were predicted to be sensitive to pre-feeding, but NP-RI LTIs were expected to be more sensitive to pre-feeding than SL-RI LTIs. To assess this prediction, LTIs were submitted to a 2 (initiation type: SL-RI, NP-RI) × 2 (feeding regimen: baseline, pre-feeding) × 2 (timing: FI 12-s, FI 18-s) Bayesian repeated measures ANOVA; EI ITIs were not assessed because despite nose-pokes and lever-presses delaying trial onset in EI, the median ITI was equal to the programmed ITI of 2.5 s. This analysis revealed substantial evidence for an initiation type + feeding regimen + timing model describing LTIs ($ln BF_{io} = 24.676$), indicating that NP-RI LTIs were longer than SL-RI LTIs and that both NP-RI LTIs and SL-RI LTIs increased with pre-feeding and timing conditions. This suggests that NP-RI LTIs and SL-RI LTIs are equally sensitive to pre-feeding.

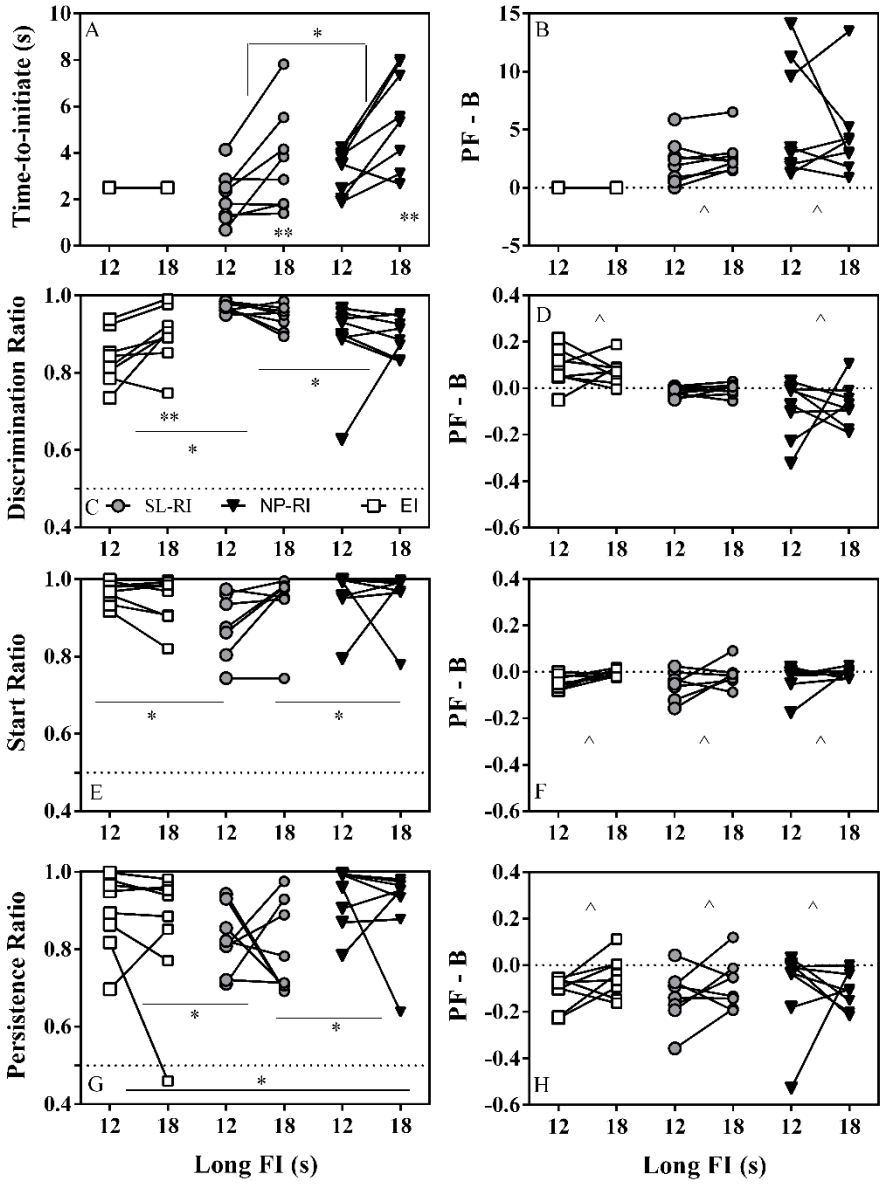

Figure 3.5. Experiment 2 baseline and pre-feeding times-to-initiate, discrimination ratios, start ratios, and persistence ratios. Median and pre-feeding (PF) – baseline (B) median time-to-initiate (Panel A & B), and mean and PF – B mean discrimination (Panel C & D), start (Panel E & F), and persistence ratio (Panel G & H) for each rat as a function of the Long FI in each timing condition (12-s A, 18-s) within each initiation type (EI = white squares; SL-RI = grey circles; NP-RI = black triangles). Note that whereas the dotted line in Panels C, E, and G indicates ratios of 0.5, the dotted line in Panels B, D, F, and H indicate differences equal to zero. *Indicates substantial evidence (i.e., $ln BF_{io}$ = 1.098) for an initiation type model. **Indicates substantial

evidence for a timing condition model. ^Indicates substantial evidence (i.e., lnBF$_{io}$ = 1.098) for a feeding regimen describing the difference between pre-feeding and baseline.

Discrimination ratios were well above 0.5 for all rats in all initiation types. This indicates that rats adequately learned to discriminate tone-initiation type associations. To determine whether discrimination of these tone-initiation type associations was affected by initiation type, feeding regimen, or timing condition, discrimination ratios were submitted to 3 (initiation type: EI, SL-RI, NP-RI) × 2 (feeding regimen: baseline, pre-feeding) × 2 (timing: FI 12-s, FI 18-s) Bayesian repeated measures ANOVAs. These analyses revealed substantial evidence for an initiation type × timing + initiation type × feeding regimen model describing discrimination ratios (lnBF$_{io}$ = 15.791). Probes of the initiation type × timing interaction comparing timing conditions within each initiation type via dependent samples *t*-tests revealed substantial evidence for a timing model describing EI (lnBF$_{io}$ = 1.386) but not SL-RI (lnBF$_{io}$ = 0.423) or NP-RI (lnBF$_{io}$ = -1.085) discrimination ratios, indicating that EI discrimination ratios increased between timing conditions. That is, with extended training the ability of rats to withhold responding for 2.5 s increased. Probes of the initiation type × feeding regimen model comparing feeding regimen within each initiation type via dependent samples *t*-tests revealed substantial evidence for a feeding regimen model describing EI (lnBF$_{io}$ = 5.273) and NP-RI(lnBF$_{io}$ = 2.357) but not SL-RI (lnBF$_{io}$ = -0.091) discrimination ratios, indicating that EI discrimination ratios increased with pre-feeding and NP-RI discrimination ratios decreased with pre-feeding. Thus, whereas pre-fed rats were better able to withhold responding for 2.5 s, pre-fed rats lever pressed more when the initiation tone signaled a nose-poke initiating-responses.

It is possible that some of the selected models containing parameters for initiation type and/or feeding regimen describing LTS, LTDs, and LFRs are attributable

to differences in start and or persistence ratios. To assess whether any of these ratios were sensitive to initiation type, feeding regimen, or timing condition the start and persistence ratios were submitted to 3 (initiation type: EI, SL-RI, NP-RI) × 2 (feeding regimen: baseline, pre-feeding) × 2 (timing: FI 12-s, FI 18-s) Bayesian repeated measures ANOVAs. There was substantial evidence for an initiation type + feeding model describing start ($ln BF_{io} = 6.544$) and persistence ratios ($ln BF_{io} = 15.096$), indicating that both start and persistence ratios were sensitive to initiation type and reduced by pre-feeding. Post-hoc tests revealed that start ratios were well described by an initiation type model when comparing NP-RI and EI ($ln BF_{io} = 1.781$), NP-RI and SL-RI ($ln BF_{io} = 3.318$), but not EI and SL-RI ($ln BF_{io} = 0.724$), indicating that start ratios were higher in NP-RI than EI or SL-RI. Post-hoc tests also revealed that persistence ratios were well described by an initiation type model when comparing EI and SL-RI ($ln BF_{io} = 2.805$), NP-RI and SL-RI ($ln BF_{io} = 7.601$), and NP-RI and EI ($ln BF_{io} = 2.102$), indicating that persistence ratios were highest in NP-RI, lowest in SL-RI, and intermediate in EI.

Taken together, these data suggest that both NP-RI LTIs and SL-RI LTIs increased with pre-feeding and from FI 4-s FI 12-s to FI 6-s FI 18-s. Contrary to expectations, SL-RI LTIs were just as sensitive as NP-RI LTIs to pre-feeding. Importantly, rats learned to respond appropriately in the presence of initiation tones and continued to respond appropriately even with pre-feeding. Although rats adequately learned to discriminate tone-initiation type associations, discrimination ratios were sensitive to the timing condition and pre-feeding. Whereas extended training and pre-feeding improved the ability of rats to wait 2.5 s for trial initiation, pre-feeding increased the probability rats pressed levers when the tone signaled a nose-poke initiating-response. Interestingly, the initiation type models describing LFR and LTD dependent

measures may be attributable to rats starting on the Short FI and persisting on the Long FI less in EI and SL-RI than NP-RI. Likewise, the feeding regimen models describing LTS, LFR, and LTD dependent measures may be attributable to pre-feeding-induced reductions in how often rats started on the short FI and persisted on the long FI after an LTS.

Are LTS medians robust to pre-feeding when EI ITIs are yoked to pre-feeding-induced longer LTIs in NP-RI FI 4-s FI 12-s A?

The previous analysis indicates that LTS medians but not IQRs and CQVs were robust to pre-feeding in NP-RI but not SL-RI or EI. This suggests that RI protects LTS medians from changes in motivation as initiating-responses become progressively more discriminable from target responses. However, it is also possible that such protection was merely due to pre-feeding-induced increase of NP-RI LTIs in the Single Initiation Type: Pre-feeding FI 4-s FI 12-s A condition. To assess this possibility, rats were trained in a second determination of FI 4-s FI 12-s (FI 4-s FI 12-s B) and were then tested in Single-Initiation Type Testing: Yoked-ITI Pre-feeding, wherein EI ITIs in pre-feeding probes were yoked to NP-RI LTIs in pre-feeding probes from Single-Initiation Type Testing: Pre-feeding.

Figure 3.6 shows the median LTI and pre-feeding – baseline LTS as a function of FI 4-s FI 12-s determination (A, B), within each initiation type (EI, SL-RI, NP-RI). To assess the success of the yoking procedure, yoked EI ITI medians and IQRs were compared to NP-RI LTI medians and IQRs in Single Initiation Type Testing: Pre-feeding and Yoked-ITI Pre-feeding conditions via Bayesian dependent *t*-tests comparing initiation types (EI, NP-RI). These revealed substantial evidence for an initiation type model describing the difference between EI ITI medians and NP-RI LTI medians in

Single Initiation Type Testing: Pre-feeding ($ln BF_{io}$ = 5.488), indicating that EI ITI medians were much longer than NP-RI LTI medians. All other comparisons revealed little evidence for an initiation type model (largest $ln BF_{io}$ = -0.183). Thus, the yoking procedure adequately, and to an extent over yoked EI ITIs to pre-feeding lengthened NP-RI LTIs from Single Initiation Type Testing: Pre-feeding.

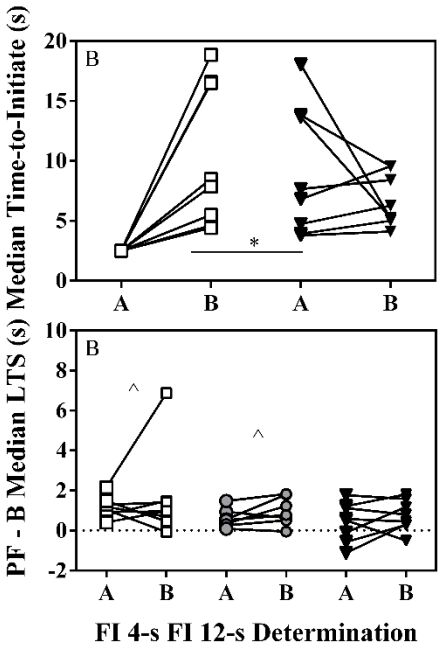

Figure 3.6. Experiment 2 pre-feeding switch-timing performance with yoked EI ITIs. Median LTI and pre-feeding (PF) – baseline (B) LTS as a function of FI 4-s FI 12-s determination (A: EI ITIs = 2.5 s, B: EI ITIs = Pre-feeding Lengthened NP-RI LTIs from FI 4-s FI 12-s A), within each initiation type (EI = white square; SL-RI = grey circles; NP-RI = black triangles). *Indicates substantial evidence (i.e., $ln BF_{io}$ = 1.098) for an initiation type model.

To determine whether LTSs in EI were robust to pre-feeding when EI ITIs were yoked to NP-RI LTIs, LTS medians were analyzed via 3 (initiation type: EI, SL-RI, NP-RI) × 2 (feeding regimen: baseline, pre-feeding) × 2 (determination: FI 4-s FI 12-s A, FI 4-s FI 12-s B) Bayesian repeated measures ANOVAs. The null model of this analysis

contained all the parameters of a 2 (feeding regimen: baseline, pre-feeding) × 3 (initiation type: EI, SL-RI, NP-RI) repeated measures ANOVA to determine the extent to which adding a determination or determination interaction parameter improved model fit. These analyses revealed substantial evidence for adding a determination ($ln BF_{io}$ = 2.429) but not determination × feeding ($ln BF_{io}$ = 1.381) or determination × feeding × initiation type ($ln BF_{io}$ = -1.838) parameter to the initiation type × feeding regimen model describing LTSs, indicating that LTSs increased by 0.5 s between FI 4-s FI 12-s determinations but that the effect of pre-feeding within each initiation type was independent of FI 4-s FI 12-s determinations. Thus, the robustness of LTS medians in NP-RI to pre-feeding is attributable to response initiation per se rather than longer and more variable NP-RI LTIs.

Figure 3.7 shows the average pre-feeding – baseline median LTS as a function of feeding regimen for each rat following initiation type; data were collapsed across determinations and timing conditions because of the lack of evidence for an interaction with either determination or timing condition. These data were submitted to Bayesian dependent measures *t*-tests to characterize the overall magnitude of the effect of pre-feeding on LTS medians. These analyses revealed substantial evidence for a feeding regimen model describing median LTSs in EI ($ln BF_{io}$ = 4.039) and SL-RI ($ln BF_{io}$ = 3.247) but not NP-RI ($ln BF_{io}$ = 0.523), indicating that LTSs were sensitive to pre-feeding in EI and SL-RI but not NP-RI. Interestingly, $ln BF_{io}$s scaled as predicted by the discriminative RI hypothesis: EI > SL-RI > NP-RI.

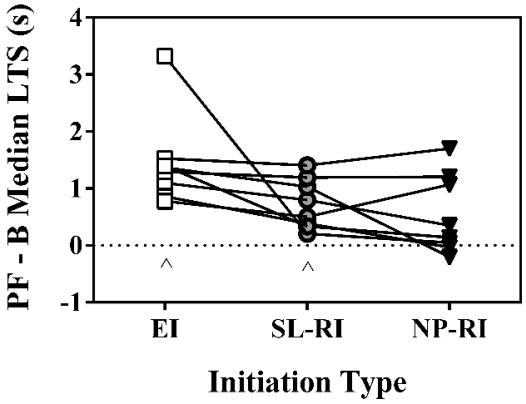

Figure 3.7. Experiment 2 average pre-feeding effect on median LTS in each initiation type. Pre-feeding (PF) – baseline (B) median LTS collapsed across FI 4-s FI 12-s determinations and FI 4-s FI 12-s, FI 6-s FI 18-s timing conditions for each rat as a function of each initiation type (EI = white squares; SL-RI = grey circles; NP-RI = black triangles).

Are times-to-initiate and LTSs differentially sensitive to extinction as a function of initiation type?

In addition to yielding LTSs robust to pre-feeding, NP-RI was predicted to yield LTSs robust to extinction more than SL-RI and EI, SL-RI was predicted to yield LTSs robust to extinction more than EI. Additionally, NP-RI LTIs were expected to be more sensitive to extinction than SL-RI LTIs; although nose-pokes and lever-presses delay trial onset following EI, EI ITIs were not expected to be sensitive to extinction. These predictions were assessed visually because inspection of performance under extinction revealed that idiosyncratic changes in LTIs and LTSs.

Figure 3.8 shows the mean median LTI and LTS as a function of trial under both baseline and extinction sessions in all three initiation types. Whereas NP-RI LTIs and SL-RI LTIs lengthened with extinction, EI ITIs did not. EI ITIs are initially longer than the programmed 2.5 s under baseline and extinction sessions, indicating that at the

beginning of the session subjects respond on the levers and nose-poke device when EI is signaled and thus delay onset of trials following EI. NP-RI LTIs were initially 7-s and then stepped up to about 35-s. SL-RI LTIs were initially 1.5-s but did not lengthen in a systematic manner, oscillating between very short and very long LTIs. Both NP-RI and SL-RI LTIs returned to 1.5-s and 7-s, respectively, at the beginning of the second extinction session, suggesting the spontaneous recovery of LTIs between consecutive extinction sessions. LTIs do not appear to show evidence of extinction bursts, which would be indicated by a transient shortening of LTIs at the beginning of extinction. Taken together, these data suggest that both NP-RI LTIs and SL-RI LTIs are sensitive to extinction; NP-RI LTIs may be more sensitive to extinction than SL-RI LTIs.

LTSs in all three initiation types lengthened with extinction. LTSs were initially 8 s and then increased to about 50 s by the end of each extinction session. LTSs returned to 8 s at the beginning of the second extinction session, suggesting spontaneous recovery of LTSs. Although the rate of the extinction process was not characterized, there appears to be a difference in the rate at which LTSs lengthen, with LTSs in EI lengthening faster in the first extinction session than LTSs in SL-RI or NP-RI. Despite the possibility that the rate of extinction depends on initiation type, these data indicate that neither NP-RI or SL-RI yield LTSs robust to extinction.

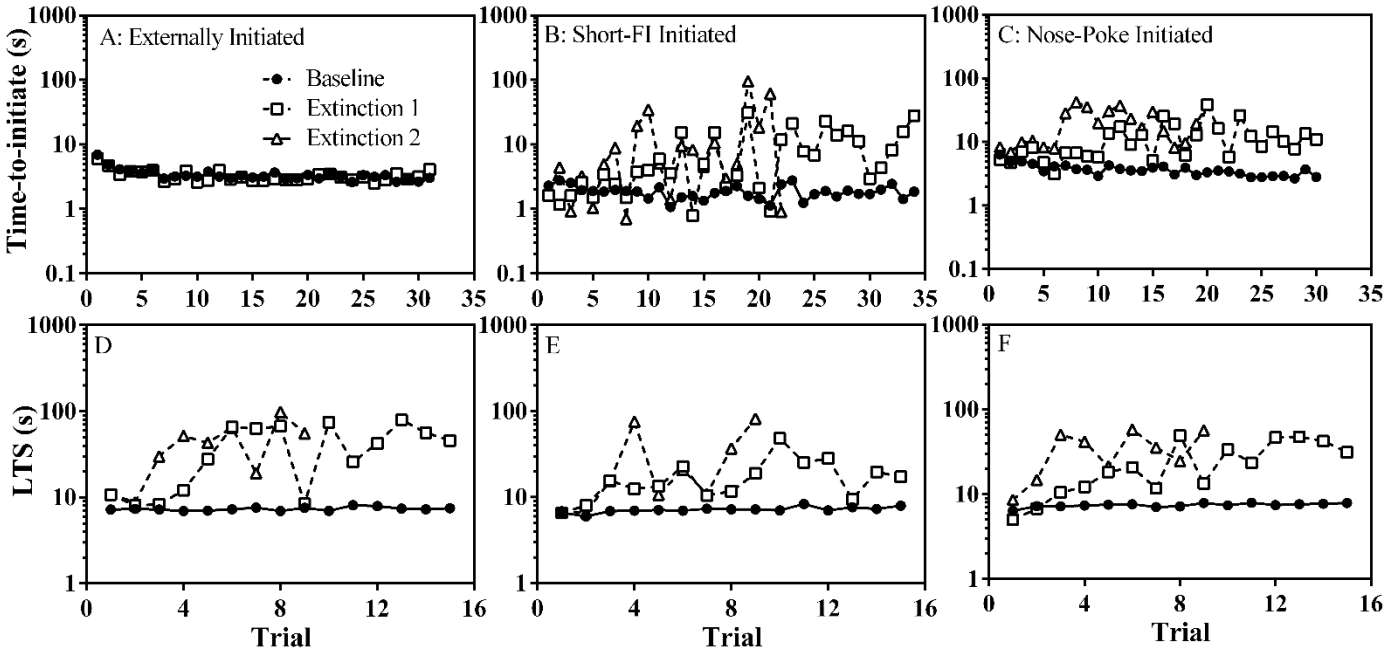

Figure 3.8. Experiment 2 extinction switch-timing performance. Mean median LTI (Panels A-C) and LTS (Panels D-F) back transformed from the log scale as a function of trial in FI 4-s FI 12-s Baseline (filled circles, solid line) and Extinction sessions 1 (white squares, dashed line) and 2 (white triangles, dashed line) within EI (Panels A & D), SL-RI (Panels B & E), and NP-RI (Panels C & F). Note that the data was truncated at the median number of trials completed within each initiation type, and thus the data for the last trial shown is the mean median of four rats.

Is the sensitivity of LTS medians and variability to pre-feeding following EI and SL-RI explained by an increase in the prevalence and mean of non-timed LTSs?

Grubb's test revealed a few outliers: rat 3 for *K* in SL-RI FI 4-s FI 12-s baseline, *q* and *K* in EI FI 6-s FI 18-s baseline; rat 2 for *q* and *K* in SL-RI FI 4-s FI 12-s pre-feeding; rat 4 for *K* in NP-RI FI 6-s FI 18-s baseline; and rat 6 for *q* in SL-RI FI 6-s FI 18-s pre-feeding. These data were removed.

Figure 3.9 shows the mean LTS cumulative distribution and fits of Equation 2.1 as a function of feeding regimen (baseline, pre-feeding) within each initiation type. Table 3.2 shows median (IQR) baseline parameter estimates and Table 3.3. shows the median (IQR) pre-feeding – baseline parameter estimates. Equation 2.1 appears to adequately track the data, showing little deviation from the observed cumulative distribution of LTSs.

The effect of pre-feeding on LTS medians and variability was predicted to arise from an increase in the prevalence and mean of non-timed LTSs. To assess this prediction parameter *q* and the mean non-timed LTS were submitted to 3 (initiation type: EI, SL-RI, NP-RI) × 2 (feeding regimen: baseline, pre-feeding) × 2 (timing: FI 12-s, FI 18-s) Bayesian repeated measures ANOVAs. These analyses revealed substantial evidence for a feeding regimen model describing *q* ($ln\text{BF}_{io}$ = 2.225) indicating that pre-feeding reduced the probability with which rats entered timing states regardless of initiation type. There was also substantial evidence for a feeding regimen model × initiation type describing the mean non-timed LTS ($ln\text{BF}_{io}$ = 9.531) indicating that whether pre-feeding increased the mean non-timed LTSs depended on initiation type. Dependent *t*-tests probing this interaction revealed substantial evidence for a feeding regimen model describing the mean non-timed LTS in EI ($ln\text{BF}_{io}$ = 2.750) but not SL-RI

($ln\text{BF}_{io}$ = 0.706) or NP-RI ($ln\text{BF}_{io}$ = 0.371), indicating that pre-feeding-induced increases in the mean non-timed LTSs in EI but not SL-RI or NP-RI. Thus, at least some of the effects of pre-feeding on LTS medians and variability are due to a reduction in the probability of entering a timing state in all initiation types and an increase in the mean non-timed LTS following EI.

To further isolate the potential mechanism by which pre-feeding lengthens LTSs, the remainder of the parameters and derived statistics were submitted to 3 (initiation type: EI, SL-RI, NP-RI) × 2 (feeding regimen: baseline, pre-feeding) × 2 (timing: FI 4-s FI 12-s, FI 6-s FI 18-s) Bayesian repeated measures ANOVAs. These revealed substantial evidence for a feeding regimen model describing ε ($ln\text{BF}_{io}$ = 14.792), indicating that pre-feeding reduced the criterion pulse count.

There was also substantial evidence for a timing + initiation type × feeding regimen model describing *c* ($ln\text{BF}_{io}$ = 20.502) indicating that the speed of the clock decreased between timing conditions and whether it changed with pre-feeding depended on initiation type. Dependent *t*-tests probing the initiation type × feeding interaction parameter revealed substantial evidence for a feeding regimen model describing *c* in EI ($ln\text{BF}_{io}$ = 3.772), SL-RI ($ln\text{BF}_{io}$ = 2.602), and NP-RI ($ln\text{BF}_{io}$ =2.676), indicating that although pre-feeding reduced the speed of the clock following all initiation types, the speed of the clock was most sensitive to pre-feeding following EI. To clarify these effects, further dependent *t*-tests probing the interaction revealed substantial evidence for an initiation type model describing *c* when comparing EI to SL-RI ($ln\text{BF}_{io}$ = 2.312), EI to NP-RI ($ln\text{BF}_{io}$ = 2.855), but not NP-RI to SL-RI ($ln\text{BF}_{io}$ = 0.732), confirming that the speed of the clock was most sensitive to pre-feeding in EI. In baseline, there was little evidence for an initiation type model describing estimates of *c* (largest $ln\text{BF}_{io}$ = 0.437), suggesting that in baseline the speed of the clock was similar across initiation types.

Thus, some of the effects of pre-feeding on LTS medians and variability are also explained by reductions of speed of the clock.

Consistent with the effects observed on the criterion pulse count and speed of the clock, there was substantial evidence for a timing + initiation type × feeding regimen model describing the mean timed LTS ($ln\text{BF}_{io}$ = 86.597), indicating that LTS means scaled with timing condition and increased with pre-feeding depending on initiation type. Dependent *t*-tests probing the interaction parameter revealed substantial evidence for a feeding regimen model describing the mean timed LTS in EI ($ln\text{BF}_{io}$ = 3.842) and SL-RI ($ln\text{BF}_{io}$ = 3.855) but not NP-RI ($ln\text{BF}_{io}$ = 0.641), indicating that despite pre-feeding slowing down the speed of the clock in all initiation types, pre-feeding only lengthened the mean timed LTS in EI and SL-RI.

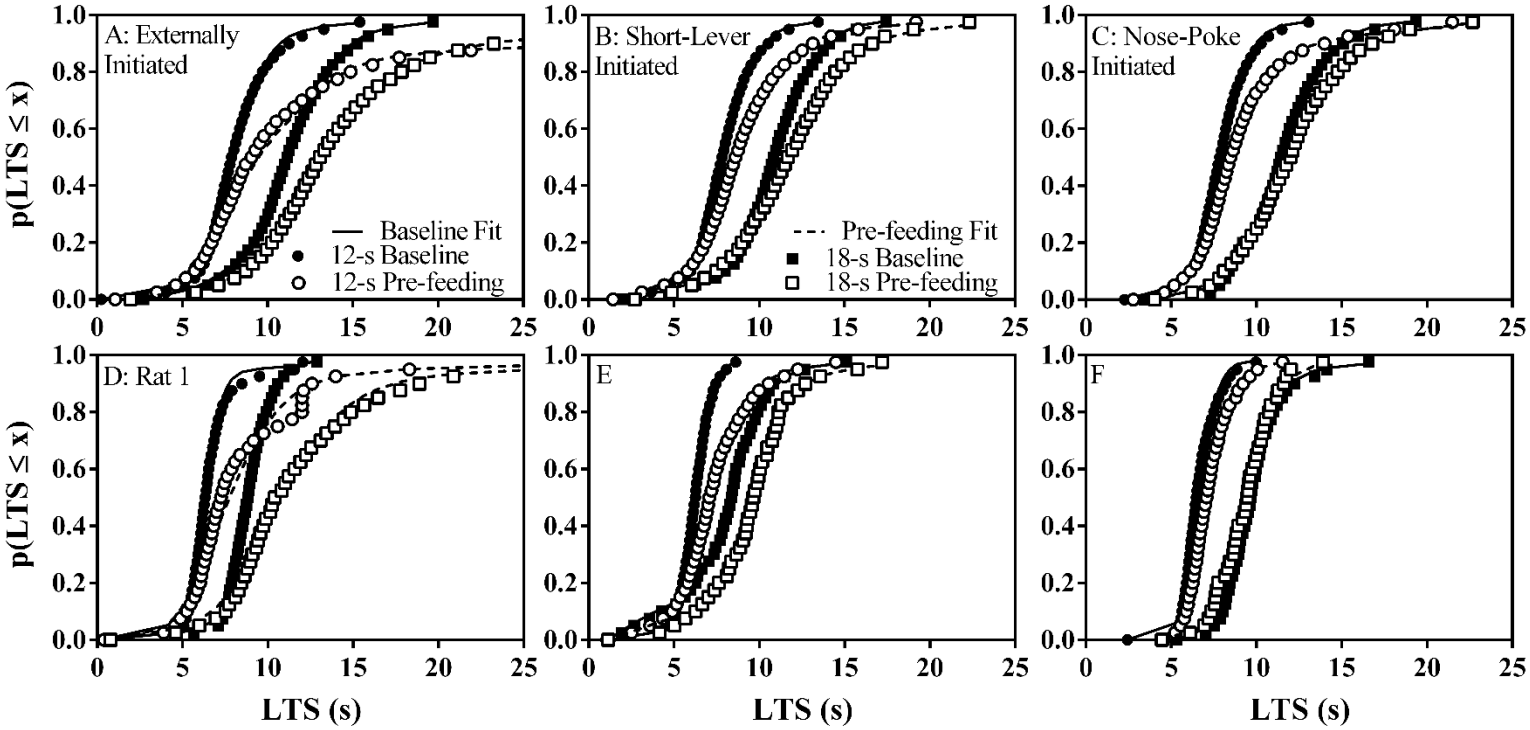

Figure 3.9. Experiment 2 gamma-exponential mixture model fits to empirical cumulative LTS distribution. Mean LTS cumulative distributions, LTS cumulative distributions of a representative rat, and fits of Equation 2.1 as a function of feeding regimen (baseline = black symbols, solid line; pre-feeding = white symbols, dashed line) and Long FI in each timing condition (12-s = circles, 18-s = squares) within EI (Panel A & D), SL-RI (Panel B & E), and NP-RI (Panel C & F) initiation types. Representative rat was defined as the rat with the median pre-feeding-induced increase in median LTS in all three initiation types.

Table 3.2

Experiment 2 Median (IQR: 1st Quartile, 3rd Quartile) baseline parameter estimates of Equation 2.1

	FI 4-s FI 12-s			FI 6-s FI 18-s		
Parameters	EI	SL-RI	NP-RI	EI	SL-RI	NP-RI
q	.88 (.84, .94)	.90 (.89, .92)	.91 (.93, .88)	.88 (.80, .91)	.88 (.83, .93)	.92 (.88, .95)
ε (pulses)	28.09 (19.52, 36.35)	22.37 (20.93, 24.71)	24.85 (33.32, 17.03)	15.24 (13.06, 24.37)	22.10 (18.69, 29.67)	16.70 (12.32, 20.98)
c (s)	**0.27 (0.22, 0.47)**	**0.29 (0.25, 0.33)**	**.20 (0.47, 0.17)**	**0.57 (0.38, 0.68)**	**0.45 (0.28, 0.56)**	**0.48 (0.36, 0.74)**
δ (s)	0.16 (0.05, 0.33)	1.31 (1.24, 1.52)	1.70 (2.60, 1.52)	1.74 (0.46, 5.03)	1.91 (1.16, 2.27)	3.19 (1.52, 5.08)
Derived Statistics						
Mean Timed LTS (s)	**8.13 (7.62, 8.89)**	**7.83 (7.54, 8.42)**	**7.98 (7.46, 8.89)**	**12.08 (10.48, 12.92)**	**11.60 (9.75, 12.27)**	**12.21 (10.48, 12.97)**
Timed LTS SD (s)	**1.48 (1.23, 2.07)**	**1.37 (1.20, 1.51)**	**1.13 (0.89, 1.63)**	**2.26 (1.41, 2.70)**	**2.14 (1.42, 2.50)**	**2.31 (1.38, 2.76)**
Timed LTS CV	0.19 (0.17, 0.23)	0.21 (0.20, 0.22)	0.20 (0.17, 0.25)	0.26 (0.20, 0.28)	0.21 (0.18, 0.23)	0.24 (0.22, 0.28)
Mean non-timed LTS (s)	10.22 (8.76, 11.67)	8.04 (6.96, 9.13)	9.02 (8.65, 10.68)	10.75 (9.33, 12.55)	10.15 (7.18, 15.51)	15.51 (11.82, 17.35)

Note. Parameter estimates and derived statistics in italics indicate substantial evidence for an initiation type model and in bold indicate substantial evidence for a timing condition model describing those parameters and derived statistics.

Table 3.3

Experiment 2 Median (IQR: 1st Quartile, 3rd Quartile) pre-feeding – baseline parameter estimates of Equation 2.1

	FI 4-s FI 12-s			FI 6-s FI 18-s		
Parameters	EI	SL-RI	NP-RI	EI	SL-RI	NP-RI
q	**-.02 (-.12, .06)**	**-.11 (-.12, -.04)**	**-.12 (-.16, -.06)**	**-.04 (-.13, -.01)**	**-.05 (-.12, -.01)**	**-.09 (-.16, -.01)**
ε (pulses)	**-23.75 (-26.42, -13.17)**	**-7.62 (-9.94, -6.71)**	**-6.93 (-17.89, -3.85)**	**-5.10 (-11.16, -1.57)**	**-6.18 (-16.07, 1.32)**	**-6.33 (-10.22, -1.11)**
c (s)	**0.72 (0.60, 1.67)**	**0.27 (0.19, 0.38)**	**0.22 (0.06, 0.31)**	**0.63 (0.38, 0.78)**	**0.31 (0.03, 0.50)**	**0.19 (0.09, 0.33)**
δ (s)	0.73 (0.33, 1.16)	-0.55 (-2.05, 0.13)	0.43 (0.01, 1.16)	0.08 (-0.89, 0.45)	0.5 (0.19, 1.24)	0.54 (-0.04, 1.89)
Derived Statistics						
Mean Timed LTS (s)	**1.29 (0.83, 1.67)**	**0.91 (0.55, 1.26)**	**0.58 (0.15, 0.98)**	**1.86 (1.68, 2.09)**	1.26 (0.73, 1.47)	0.76 (-0.17, 1.12)
Timed LTS SD (s)	**1.38 (0.99, 2.67)**	**0.68 (0.48, 0.84)**	**0.34 (0.21, 0.54)**	**1.30 (1.09, 1.76)**	**0.54 (0.19, 0.81)**	**0.32 (0.06, 0.60)**
Timed LTS CV	**0.19 (0.11, 0.27)**	**0.05 (0.04, 0.09)**	**0.07 (0.01, 0.08)**	**0.07 (0.01, 0.10)**	**0.06 (-0.01, 0.12)**	**0.05 (0.01, 0.07)**
Mean non-timed LTS (s)	**60.44 (11.76, 168.58)**	2.43 (0.96, 5.55)	5.37 (0.79, 7.03)	16.36 (8.18, 19.73)	2.71 (1.38, 5.17)	(-2.46, 4.78)

Note. Parameter estimates and derived statistics in bold indicate substantial evidence for a feeding regimen model describing those parameters and derived statistics.

Correspondingly, there was also substantial evidence for a timing + initiation type × feeding regimen model describing timed LTS SDs (lnBF$_{io}$ = 28.859), indicating that timed LTS variability scaled with timing conditions and that whether timed LTS variability increased with pre-feeding depended on initiation type. Dependent *t*-tests probing the initiation type × feeding regimen interaction parameter revealed that there was substantial evidence for a feeding regimen model describing the timed LTS SDs in EI (lnBF$_{io}$ = 4.442), SL-RI (lnBF$_{io}$ = 3.256), and NP-RI (lnBF$_{io}$ = 1.269), indicating that the pre-feeding-induced reduction in clock speed increased LTS variability for all initiation types, but that the LTS variability was most sensitive to pre-feeding in EI and least sensitive to pre-feeding in NP-RI. To clarify these effects, further dependent *t*-tests probing the interaction revealed substantial evidence for an initiation type model describing LTS SDs when comparing EI and SL-RI (lnBF$_{io}$ = 1.314), EI and NP-RI (lnBF$_{io}$ = 2.176), and SL-RI and NP-RI (lnBF$_{io}$ = 1.269) in pre-feeding but not baseline (largest lnBF$_{io}$ = -0.049), indicating that timed LTS SDs were similar across initiation types in baseline but that timed LTS SDs increased following pre-feeding in EI.

Additionally, there was substantial evidence for a feeding regimen model (lnBF$_{io}$ = 14.784) but not a timing model (lnBF$_{io}$ = -1.553) describing the timed LTS CVs, indicating that pre-feeding increased timed LTS CVs following all initiation types; the LTS CV was also invariant across timing conditions.

In contrast to experiment 1, there was substantial evidence for a timing + initiation type model describing the minimum LTS (lnBF$_{io}$ = 17.537), but no evidence for a feeding regimen model (lnBF$_{io}$ = -0.285).

Taken together, these data indicate that pre-feeding reduced the prevalence of timed LTSs in all initiation types and increased the mean of non-timed LTSs in EI. However, there were also effects on parameter estimates and derived statistics of timed

LTSs. These effects were similar or greater in magnitude to the effects observed on *q* and the mean non-timed LTS. Interestingly, effects on the mean non-timed LTS and mean timed LTS were largely observed only in EI. In contrast, effects on timed LTS variability were observed across all initiation types, but these effects scaled as predicted by the discriminative RI hypothesis: EI > SL-RI > NP-RI. Thus, these data suggest that pre-feeding effects on LTSs are not exclusively attributable to an increase in the prevalence and mean of the non-timed LTS but reinforce the hypothesis that as initiating-responses become progressively discriminable from target responses, interval timing and motivation are increasingly dissociated.

Discussion

Experiment 2 revealed some evidence supporting the discriminative RI hypothesis. Although temporal control of LTSs in baseline was similar across initiation types, the sensitivity of LTS medians, and to a lesser degree LTS variability, to pre-feeding increased with discriminability of initiating-responses from target responses, such that LTS medians and variability in EI > SL-RI > NP-RI. Despite NP-RI and SL-RI LTIs having a similar sensitivity to pre-feeding, only pre-feeding effects in NP-RI were circumscribed to LTIs. LTS medians in SL-RI were sensitive to pre-feeding. In contrast, LTSs were sensitive to extinction regardless of initiating-responses. These data suggest that, as initiating-responses become progressively discriminable from target responses, initiating-responses increasingly and selectively dissociate interval timing and motivation.

The present data also indicate that the data obtained in Experiment 1 are consistent with the discriminative RI hypothesis. Although the sensitivity of SL-RI LTIs to pre-feeding depends on whether the switch-timing procedure is programmed as a

discrete-trials or free-operant procedure, the sensitivity of LTSs in SL-RI does not. Indeed, pre-feeding lengthened SL-RI LTIs in experiment 2 but lengthened LTSs in SL-RI in both experiments 1 and 2. Short FI initiating-responses in experiment 1 likely became habits because of an interaction between prolonged training and the levers acting as time-markers. This suggests that, for initiating-responses to be sensitive to motivation, they must be emitted on manipulanda that do not also serve as time-markers. In contrast, LTSs in SL-RI are likely sensitive to pre-feeding because Short FI initiating-responses and target responses are identical in form, which promotes generalization between Short FI initiating-responses and target responses. Initiating-responses thus need to be highly discriminable and uniquely associated with trial activation.

Although NP-RI protected LTS medians from pre-feeding, pre-feeding increased LTS variability in all initiation types. Fits of Equation 2.1 revealed that the effect of pre-feeding on timed LTS variability scaled such that EI > SL-RI > NP-RI. A similar effect has been observed on IRTs of rats and mice trained in FMI: pre-feeding increases IRT variability without affecting its average (e.g., Daniels et al., 2018; Watterson et al., 2015). This consistent sensitivity of performance index variability to pre-feeding suggests that initiating-responses may only partially dissociate interval timing and motivation. However, the discriminative RI hypothesis and, more generally, the differences in RI and EI performance, has thus far only been tested in immediate timing procedures. This limits the generalizability of the conclusion that initiating-responses partially dissociate interval timing and motivation and calls for a need to evaluate the discriminative RI hypothesis in other interval timing procedures.

Chapter 4: Experiment 3 - Response-Initiated Discrete-Trials Temporal Bisection

Introduction

The discriminative RI hypothesis states that as initiating-responses become progressively different from target responses, initiating-responses increasingly enhance temporal control of performance indices and protect performance indices from fluctuations in motivation. Although neither experiment 1 (Chapter 2) nor experiment 2 (Chapter 3) revealed evidence supporting the notion that RI enhances temporal control of LTSs in rats trained in the switch-timing procedure, experiment 1 and 2 revealed that the robustness of median LTS to pre-feeding was proportional to the discriminability of initiating from target responses. NP-RI protected LTSs more than SL-RI, SL-RI protected LTSs more than EI. Although such scaling was also evident in timed LTS variability, LTS variability in general and timed LTS variability in particular increased with pre-feeding, regardless of initiating-responses. This outcome is consistent with recent research on the effects of pre-feeding on IRTs in FMI: average IRT, but not IRT variability, is robust to pre-feeding (e.g., Daniels et al., 2018; Watterson et al., 2015). This suggests RI schedules may only partially dissociate interval timing and motivation.

It is currently unclear, however, whether this conclusion generalizes to other interval timing procedures. Studies of RI have focused on immediate rather than retrospective timing procedures, thus limiting current conclusions to interval timing procedures in which subjects continuously judge whether to start responding (as in FI) or whether to switch from a Short FI to a Long FI (as in the switch-timing procedure; Figure 1.2). A retrospective timing procedure complementary to the switch-timing procedure is the temporal bisection procedure (Figure 1.1B). Briefly, subjects are trained to classify a just-elapsed interval as ‘short’ or ‘long’ compared to some Short and Long

intervals. Interestingly, pre-feeding lengthens the mean LTS in the location variant of the temporal bisection procedure, which promotes behavioral sequences analogous to those observed in animals trained in the switch-timing procedure because choices 'long' and 'short' are associated with manipulanda in fixed locations (Gouvêa et al. 2014; McClure et al., 2009; cf. Ward & Odum, 2006). Thus, training rats in the location variant of the temporal bisection procedure provides an opportunity to test the generalizability of the discriminative RI hypothesis. It is expected that as initiating-responses become progressively discriminable from target responses, initiating-responses will enhance temporal control of latent LTSs and protect latent LTSs from pre-feeding.

Choices 'short' and 'long' are thought to be the output of a PA-like model in which choices 'short' and 'long' are embedded within the timing process (Figure 1.2B); that is, as the subject continually evaluates whether to choose 'long' or 'short' as pulses accumulated and are compared to memory. Recent work suggests, however, that choices 'long' and 'short' are the output of a timing process that subsequently influences a decision process (Balci & Simen, 2014). In the timing process, pulses accumulate as described by the PA-family of timing models. In the decision process, the rate at which information accumulates, and thus drives a subject to choose 'short' or 'long', is a function of (a) the pulses accumulated in the first stage and (b) the effort and costs associated with each choice. The time it takes for the decision process to complete is indexed by choice latencies. Whereas the timing process is sensitive to the Short and Long intervals (Balci & Simen, 2014), the decision-making process is sensitive to stimulus probability (Akdoğan & Balci, 2016; Çoşkun, Sayalı, Gürbüz, & Balci, 2015) and differences in reinforcement associated with choices 'short' and 'long' (Akdoğan & Balci, 2016). This model predicts that choice latencies should be relatively longer when

categorizing intermediate intervals than the Short and long intervals. Additionally, when taken together with the behavioral systems model (Figure 1.4) and the discriminative RI hypothesis it follows that highly discriminable initiating-responses also protect choices latencies from pre-feeding.

Experiment 3 thus sought to test the generalizability of the discriminative RI hypothesis. To test the discriminative RI hypothesis, rats were trained in a multiple RI EI discrete-trials temporal bisection procedure (Figure 4.1). In this procedure, levers served as choice manipulanda and were thus in fixed locations to promote behavioral sequences akin those observed in animals trained in the switch-timing procedure. Rats were trained with EI and NP-RI, where NP-RI is discriminable from target responses denoting LTSs as a function of time, location, and form. Motivation was manipulated via 1 h and 24 h pre-feeding probes; the different pre-feeding durations were included to determine whether effects differed with 1 h and chronic 24 h pre-feeding. Extinction probes were also included to determine whether RI selectively dissociates interval timing and motivation, or more generally dissociates interval timing and non-timing processes.

Compared to EI, NP-RI was predicted to improve temporal control of LTSs and to yield LTSs and choice latencies robust to pre-feeding and extinction. NP-RI LTIs were predicted to be sensitive to pre-feeding and extinction. Equation 2.1 was rewritten such that what was fit to the choice data was a mixture of a cumulative gamma and cumulative exponential distribution. Fits of the cumulative gamma-exponential mixture to choice data was expected to reveal that the pre-feeding increases the prevalence and mean of the mean non-timed LTS in EI but not in NP-RI.

Methods

Subjects

Eight naïve male Sprague Dawley rats (Charles River Laboratories, Hollister, CA) served as subjects. Subjects arrived on post-natal day (PND) 61 and were immediately pair-housed in a vivarium on a reverse 12:12 h light cycle, with lights on at 1900 h. All behavioral training was conducted during the dark phase of the cycle (i.e. the active phase) starting at approximately 1330 and ending approximately at 1530 h. Following four days of acclimation to the colony room, food access was reduced daily from 24 to 18, 12, and finally 1 hour per day. Food was placed on home-cages 30 min after the end of each experimental session and taken away 1 hour later. This ensured that at the beginning of the next session, weights were, on average, 85 % of ad libitum weights, as estimated from growth charts provided by the breeder. Water was always available in home-cages. All animal handling procedures used during this study followed National Institutes for Health Guidelines and were approved by the Arizona State University Institutional Animal Care and Use Committee.

Apparatus

Experiments were conducted in the same 8 modified MED Associates (St. Albans, VT, USA) modular test chambers described in Experiment 2 (Chapter 3).

Procedure

Experimental sessions, the 3-min warm-up, *Reinforcer Shaping, Manipulandum Shaping, and Lever Press and Nose Poke Training* were conducted as in Experiment 2 (Chapter 3).

Response-Initiated Temporal Bisection Shaping: Response-Initiation. Figure 4.1 shows a schematic of the multiple RI EI temporal bisection procedure. After

four days of *Lever Press and Nose Poke Training*, rats were trained to initiate temporal bisection trials. After the 3-min warmup, the nose-poke device was activated. Initiation types were signaled by activating one of two tones (3-kHz or 15-kHz) pseudo-randomly by sampling from a list such that no initiation type could occur in more than six consecutive trials. Each tone indicated whether rats initiated the trial by nose-poking the nose-poke device (NP-RI) or waiting for the experimenter to initiate the trial (EI). In EI, trials started 2.5 s after tone onset and if rats were not nose poking the nose-poke device for 0.25 s. The initiation type signaled by each tone was counterbalanced across all rats such that no tone served as the signal for a specific initiation type in more than 4 rats.

Temporal Bisection. Following trial initiation, the active tone was deactivated, and the houselight illuminated for either a Short interval 1-s or a Long interval 4-s. Intervals were selected by pseudo-randomly selecting from a list such that neither interval occurred in more than four consecutive trials within an initiation type, or in more than 8 consecutive trials across initiation types; the selected interval is referred to as the active interval. At the end of the active interval, the houselight was turned off and both the left and right levers extended. For some rats, choice of the left lever was reinforced following the Short interval and choice of the right lever was reinforced following the Long interval; and vice versa for the other rats. This assignment was counterbalanced across tone-initiation assignment such that, within each pattern of tone-initiation assignment, there were two rats for which choice of the left lever was reinforced following the Short interval and two rats for which choice of the left lever was the reinforced following the Long interval. Correct choices following the active interval resulted in a single delivery of reinforcement by activating the dipper. A head-entry into the reinforcer receptacle broke an infrared beam and then deactivated the dipper 2.5 s later. Incorrect choices following the active interval resulted in a 2.5-s timeout. Both outcomes were immediately followed

by a tone signaling the next initiation type. The ITI was thus equal to the time it took rats to initiate trials following NP-RI, and equal to the time it took rats to quit nose poking preceding trials in EI, with a minimum ITI of 2.5 s. The ITI preceding NP-RI is also referred to as the latency-to-initiate (LTI). Taken together, ITIs and LTIs are referred to as the time-to-initiate.

Punishment. Because temporal bisection performance is indexed via choices at the end of intervals rather than continuously throughout FIs, no punishment was needed as in Experiment 2 (Chapter 3) to ensure rats engaged in an optimal behavioral sequence.

Training Order. Rats were trained such that initially reinforcement was contingent upon choosing 'short' or 'long following EI; NP-RI terminated in reinforcement following initiating-responses. Reinforcement contingent upon choosing 'short' or 'long' following NP-RI was slowly introduced as rats learned to correctly respond in the presence of the tone and the houselight. This was assessed by inspecting the number of obtained reinforcers in the previous two sessions; if rats earned more than 600 reinforcers, choosing 'short' or 'long' following NP-RI was introduced.

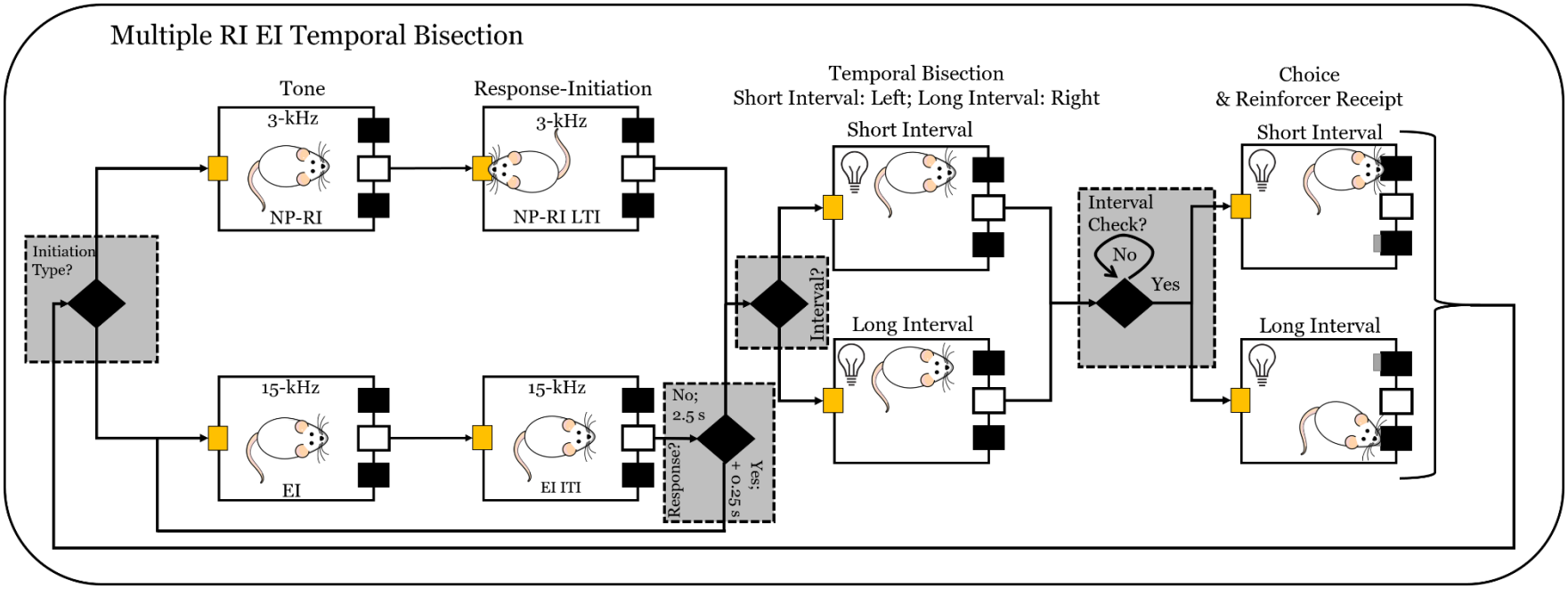

Figure 4.1. Experiment 3 schematic of the multiple RI EI temporal bisection procedure. At the beginning of the session, the nose-poke device was illuminated, and the initiation type was then selected and indicated by a tone. Following correct initiating-responses, the tone was turned off and either the Short, Long, or an intermediate interval was activated, nondifferentially signaled by turning on the houselight. In nose-poke (NP-RI), rats nose-poked to initiate trials; in externally-initiated (EI), nose-pokes delayed trial initiation by 0.25 s but were otherwise initiated after 2.5 s. After the active interval elapsed, the houselight turned off and the levers extended. If the interval was the Short or Long interval, choice of the lever associated with the active interval retracted the levers and activated the dipper; once a head-entry into the reinforcement receptacle confirmed reinforcer receipt, the dipper was lowered 2.5 s later and the next initiation type selected. If the interval was the Short or Long interval, choice of the lever not associated with the active interval retracted the levers and started a 2.5-s timeout, which was immediately followed by selection of the next initiation type. If the interval was an intermediate interval, choice of either lever retracted the levers and started a 2.5-s timeout, which was immediately followed by selection of the next initiation type.

Temporal Bisection Training. Once rats were initiating temporal bisection Short 1-s Long 4-s trials following all initiation types, rats were trained up to the timing conditions of interest in the following order: Short 4-s Long 12-s A, Short 6-s Long 18-s, and Short 4-s Long 12-s B. All rats experienced the same order of conditions; the Short 4-s Long 12-s A and B conditions allowed for assessment of potential order effects. Training with only Short and Long intervals continued until subjects had experienced a minimum of 5 sessions of training in each timing condition and until performance was deemed stable. After performance was deemed stable, training with intermediate intervals commenced; Table 4.1 shows the intermediate intervals, which were equally spaced on a logarithmic scale. Non-reinforced intermediate intervals were added two per session, starting with the extremes and continuing until all 6 intermediate intervals were added to the daily experimental sessions. As intermediate intervals were added, pseudo-randomly sampling of intervals within each initiation type (NP-RI and EI) was altered such that within a block of trials, each intermediate interval was presented once, and each Short and Long interval was presented four times. Thus, after all intermediate intervals had been added to the session, blocks of trials consisted of 14 intervals: 4 Short intervals, 4 Long intervals, and 6 non-reinforced intermediate intervals. Subjects were trained with intermediate intervals for a minimum of 7 sessions and until performance was again deemed stable. Stability was assessed visually and confirmed via a non-significant regression of the critical dependent measures listed in *Data Analysis & Results* over the last 5 sessions of training.

Table 4.1

Intervals of each Timing Condition

Timing Condition	Intervals (s)							
Short 4-s Long 12-s A & B	4	4.68	5.47	6.41	7.49	8.77	10.26	12
Short 6-s Long 18-s	6	7.02	8.21	9.61	11.24	13.15	15.39	18

Note. The intervals corresponding to the Short and Long durations were differentially reinforced as described in the text; intermediate intervals were tested in extinction.

Single-Initiation Type Testing: Pre-feeding. Following confirmation of stable performance in each timing condition, rats were tested for 10 sessions in a counterbalanced order within each timing condition for 5-sessions in each initiation type as described in Experiment 2 (Chapter 3). Figure 3.2 shows a schematic of training and testing. Table 4.2 shows the order of testing for each rat. At the end of testing, rats were returned to *Temporal Bisection Training*.

Single-Initiation Type Testing: Yoked-ITI Pre-feeding. Following confirmation of stable performance in the Short 4-s Long 12-s B timing condition, rats were tested with longer ITIs as described in Experiment 2 (Chapter 3).

Single-Initiation Type Testing: Extinction. Immediately following *Single-Trial Type Testing: Yoked-ITI Pre-feeding*, rats started another round of *Single-Trial Type Testing* and tested in an extinction procedure rather than pre-feeding probes as described in Experiment 2 (Chapter 3).

Table 4.2

Experiment 3 Order of Single-Initiation Type Testing

		Rat							
Temporal Bisection Condition	Sessions	1	2	3	4	5	6	7	8
Short 4-s Long 12-s A	1-5	EI	NP-RI	NP-RI	EI	EI	EI	NP-RI	NP-RI
	6-10	NP-RI	EI	EI	NP-RI	NP-RI	NP-RI	EI	EI
Short 6-s Long 18-s	1-5	NP-RI	EI	EI	NP-RI	NP-RI	NP-RI	EI	EI
	6-10	EI	NP-RI	NP-RI	EI	EI	EI	NP-RI	NP-RI
Short 4-s Long 12-s B-Yoked EI ITIs	1-5	EI	EI	NP-RI	NP-RI	NP-RI	EI	NP-RI	EI
	6-10	NP-RI	NP-RI	EI	EI	EI	NP-RI	EI	NP-RI
Short 4-s Long 12-s B-Extinction	1-5	EI	NP-RI	EI	NP-RI	EI	EI	NP-RI	NP-RI
	6-10	NP-RI	EI	NP-RI	EI	NP-RI	NP-RI	EI	EI

Note. In each Single-Initiation Type Testing condition, sessions 1,2, and 5 served as Baselines (B1, B2, and B3) sessions 3 and 4 served as 1 h and 24 h pre-feeding probes (1 h PF, 24 h PF).

Data Analysis

Single-Trial Type Testing began on session 40 for FI 4-s FI 12-s A, session 93 for FI 6-s FI 18, and session 129 for FI4-s FI 12-s B. To estimate dependent measures of latent LTSs, a psychophysical function relating choices 'long' to the Short, Long, and intermediate intervals was fit to trial-by-trial data of each rat from the two baseline sessions immediately preceding and including the pre-feeding and extinction probes via MLE. To keep analyses of temporal bisection performance consistent with analyses of switch-timing performance, while maintaining parsimony and consistency with previous temporal bisection research (e.g., Blough, 1996; McClure et al., 2009), the following psychophysical function was fit,

$$p(Choice = 'Long' \mid \tau) = m + (1-m)r\left[\frac{1}{\Gamma(\varepsilon)}\gamma(\varepsilon, \frac{\tau}{c})\right],$$
$$m, r, c > 0; \varepsilon \geq 1 \qquad (4.1)$$

where the probability of choosing 'long' given some interval (τ) is described by a shifted (m) and scaled (r) cumulative gamma distribution. Γ is the gamma function, γ is the lower incomplete gamma function, $\varepsilon = \theta M$ and is thus the criterion pulse count, c is the average inter-pulse interval ($1/c$ is the speed of the clock), m is the minimum probability of choosing 'long'; r is the range, and $m + r$ is the maximum probability of choosing long. From the cumulative gamma distribution, the same derived statistics—LTS mean, SD, and CV—were calculated as described for Equation 2.1 (Chapter 2); unlike Equation 2.1, Equation 4.1 does not contain parameter δ because LTSs are latent rather than overt. Calculated directly from initiating-responses and choices 'short' and 'long' were latencies-to-initiate in NP-RI and choice latencies.

Descriptive Statistics Analysis

Log or log odds transformed parameter estimates (m and r), derived statistics (LTS mean, SD, and CV), and dependent measures (LTIs, choice latencies) were analyzed via Bayesian variants of t-tests and ANOVAs as described in experiment 1 (Chapter 2). MLE parameter estimation can sometimes yield extreme estimates; thus, prior to analysis, parameter estimates, and derived statistics were submitted to two-tailed Grubb's tests with $\alpha = .01$. Outliers were removed until none were detected.

Mixture Model Analysis

To assess the secondary prediction that LTS sensitivity to pre-feeding in EI is explained by a pre-feeding-induced reduction in the prevalence of timed LTSs and an increase in the mean of non-timed LTSs, Equation 2.1 was rewritten such that what was estimated were parameters of a mixture of a cumulative gamma and cumulative exponential distributions with $\delta = 0$. Parameter estimates, and derived statistics were analyzed as described in experiment 1 (Chapter 2).

Results

The number of completed trials under 1 h and 24 h pre-feeding was substantially less than baseline, on average a 2- to 3-fold decrease. To determine whether 1 h and 24 h pre-feeding sessions could be collapsed into a single pre-feeding factor for analysis, the effect of pre-feeding duration on LTSs and LTIs was assessed via Bayesian dependent t-tests within each condition and initiation type. There was little evidence supporting the feeding duration model (largest $\ln BF_{10} = 0.684$) suggesting that temporal bisection performance was similar across pre-feeding durations. Thus, the 1 h and 24 h pre-

feeding sessions were collapsed into a single factor of pre-feeding for all dependent measures.

Grubb's test revealed rat 3 as an outlier for *m* in EI and NP Short 4-s Long 12-s A baseline and LTS CV in EI Short 4-s Long 12-s B; rat 2 for *r* in EI Short 4-s Long 12-s B pre-feeding; rat 4 for *m* in NP Short 4-s Long 12-s B pre-feeding; rat 5 for the LTS mean in NP Short FI 4-s Long 12-s A pre-feeding, in NP Short 6-s Long 18-s baseline and pre-feeding, and for *r* in NP Short 6-s Long 18-s. pre-feeding; rat 8 for *m* in EI Short 4-s Long 12-s A baseline. These data were removed.

Is temporal bisection performance differentially sensitive to initiation type as a function of feeding regimen?

Figure 4.2 shows the mean psychophysical functions, psychophysical functions of a representative rat, and fits of Equation 4.1. The cumulative gamma distribution adequately described choice behavior on average and for the representative rat in both timing conditions and feeding regimens. Indeed, there were no substantial deviations from the obtained psychophysical functions.

Figure 4.3 shows the pre-feeding – baseline derived statistics of Equation 4.1 for each rat as a function of the Long interval in each timing condition (12-s A, 18-s) and initiation type (EI, NP-RI). NP-RI was predicted to enhance temporal control of LTSs relative to EI. To asses this prediction, parameter estimates, and derived statistics were submitted to a 2 (initiation type: EI, NP-RI) × 2 (timing: 12-s A, 18-s) Bayesian repeated measures ANOVAs. These analyses revealed substantial evidence for a timing model describing *r* ($ln\text{BF}_{io}$ = 1.592) and mean LTSs ($ln\text{BF}_{io}$ = 30.117), indicating that maximum probability ($m+r$) decreased between timing conditions and that the mean LTS scaled with the timing condition. Interestingly, there was also substantial evidence for an

initiation type + timing model describing LTS SDs (lnBF$_{io}$ = 5.761), indicating that LTS SDs were smaller in NP-RI compared to EI and scaled with the timing condition. Consistent with these selected models, there was substantial evidence for an initiation type (lnBF$_{io}$ = 1.731) but not a timing model (lnBF$_{io}$ = -1.314) describing LTS CVs, indicating that CVs were invariant across timing conditions, but smaller in NP-RI compared to EI.

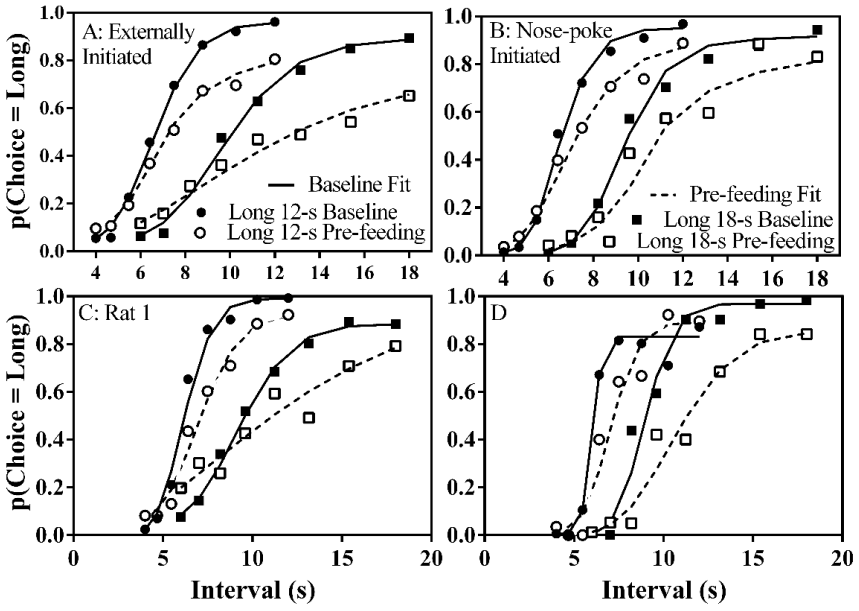

Figure 4.2. Experiment 3 fits of the cumulative gamma to baseline and pre-feeding psychophysical functions. Mean psychophysical functions (Panels A & B), psychophysical functions of a representative rat (Panels C & D) and fits of Equation 4.1 within each initiation type (EI: Panels A & C; NP: Panels B & D) as a function of timing condition (12-s A: circles; 18-s: squares) and feeding regimen (baseline = filled symbols, solid line; pre-feeding = white symbols, dashed line). Representative rat was defined as the rat with the median pre-feeding-induced increase in mean LTS in both initiation types.

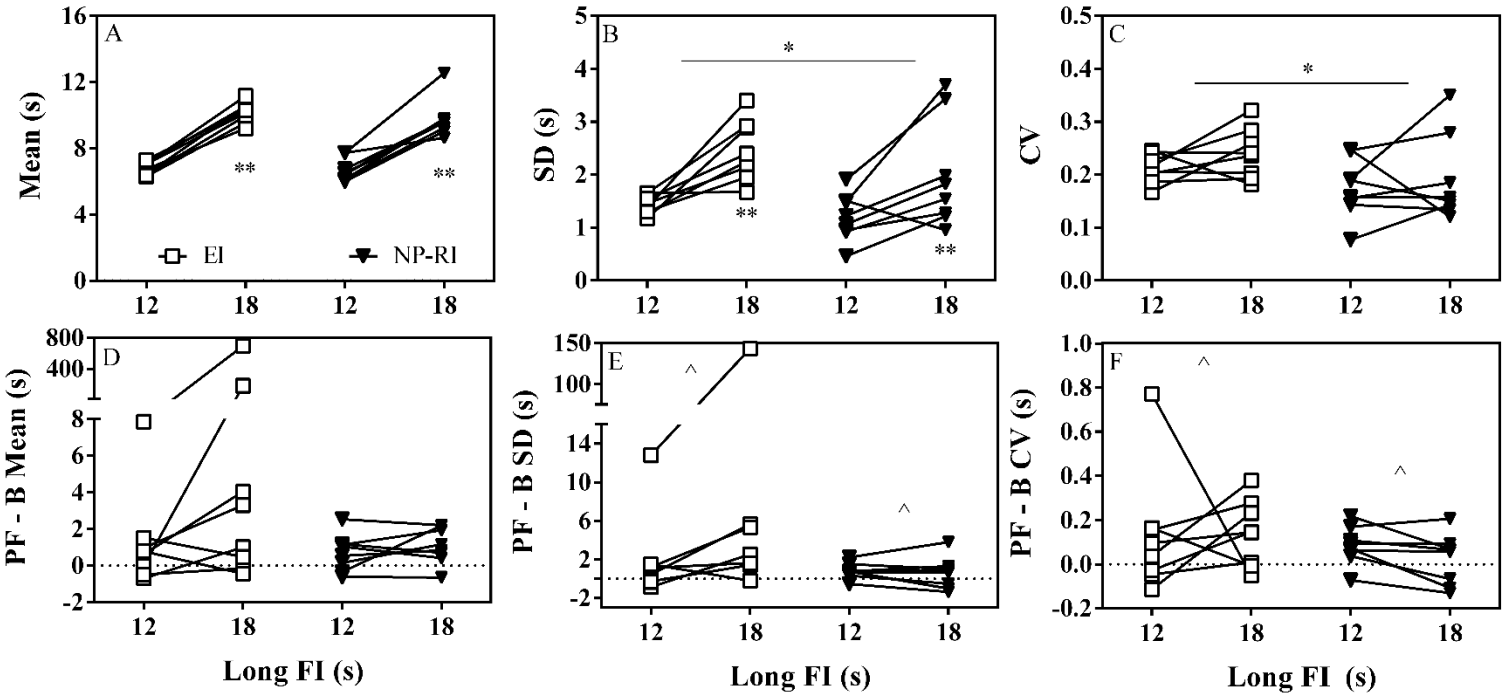

Figure 4.3. Experiment 3 **baseline and pre-feeding temporal bisection performance**. Derived statistics (Panels A-C: mean LTS, LTS SD, and LTS CV, respectively) and pre-feeding (PF) – baseline (B)derived statistics (Panels D-F: mean LTS, LTS SD, and LTS CV, respectively) for each rat as a function of the Long interval in each timing condition (12-s, 18-s) and initiation type (EI = white squares, NP-RI = black triangles)[5]. *Indicates substantial evidence (i.e., $ln BF_{io} = 1.098$) for an initiation type model. **Indicates substantial evidence for a timing condition model. ^Indicates substantial evidence (i.e., $ln BF_{io} = 1.098$) for a feeding regimen describing the difference between pre-feeding and baseline.

NP-RI was also predicted to protect LTSs from changes in motivation compared to EI. To test this prediction, parameter estimates, and derived statistics were submitted to 2 (initiation type: EI, NP-RI) × 2 (feeding regimen: baseline, pre-feeding) × 2 (timing: FI 4-s FI 12-s, FI 6-s FI 18-s) Bayesian repeated measures ANOVAs within each initiation type. These analyses revealed substantial evidence for adding a feeding regimen parameter to the models describing LTS SDs (lnBF$_{io}$ = 3.127) and CVs (lnBF$_{io}$ = 1.179), indicating that pre-feeding increased LTS variability regardless of initiation type. There was little evidence for adding an initiation type × feeding regimen or feeding regimen parameter to the model describing the mean LTS, *m* or *r* (largest lnBF$_{io}$ = 0.427) [8].

Taken together, these data suggest that LTSs scaled with the timing condition and that NP-RI enhances temporal control of LTSs. Interestingly, parameter *r* decreased between timing condition, suggesting a loss of temporal control as Short and Long intervals increased. LTS variability but not mean reliably increased with pre-feeding regardless of initiation type. This suggests that pre-feeding does not increase the mean latent LTSs in temporal bisection and confirms that NP-RI does not protect against pre-feeding-induced increases in LTS variability.

Are times-to-initiate and choice latencies affected by initiation type, feeding regimen, or timing condition?

[8] Note the EI and sometimes NP-RI psychophysical functions of rats 4 and 5 were mostly flat in pre-feeding. Despite Grubb's test not always detecting rats 4 and 5 as outliers, to determine the reliability of the obtained pre-feeding effects, analyses were reconducted with both rats 4 and 5 removed from analyses. Analysis of LTS SDs (lnBF$_{io}$ = 1.630) and CVs (lnBF$_{io}$ = 1.419) did not depend on whether rat 4 and 5 were included. Analysis of mean LTSs depended on whether rats 4 and 5 were included (lnBF$_{io}$ = 2.123). Thus, the pre-feeding-induced increased in latent LTS variability is reliable and the pre-feeding-induced increase in the latent mean LTS is unreliable.

Figure 4.4 shows the median LTI and choice latency and pre-feeding – baseline median LTI and choice latency for each rat as a function of the Long interval in each timing condition (12-s A, 18-s) and initiation type (EI, NP-RI). NP-RI LTIs were predicted to be sensitive to pre-feeding and NP-RI choice latencies were predicted to be robust to pre-feeding compared to EI choice latencies. To assess these predictions, LTIs were submitted to a 2 (feeding regimen: baseline, pre-feeding) × 2 (timing: 12-s A, 18-s) Bayesian repeated measures ANOVA; EI ITIs were not assessed because despite nose-pokes delaying trial onset in EI, the median ITI was always equal to the programmed EI ITI of 2.5 s. Choice latencies were submitted to a 2 (initiation type: EI, NP-RI) × 2 (feeding regimen: baseline, pre-feeding) × 2 (timing: 12-s A, 18-s) Bayesian repeated measures ANOVA; choice latencies were collapsed across the Short, Long, and intermediate intervals because there was little evidence that choice latencies varied systematically within each subject as predicted by the model proposed by Balci and Simen (2014). These analyses revealed substantial evidence for a timing + feeding model describing NP-RI LTIs ($ln\text{BF}_{io} = 13.393$), indicating that LTIs scaled with the timing condition and increased with pre-feeding. Similarly, there was substantial evidence for a timing + feeding model describing choice latencies ($ln\text{BF}_{io} = 11.585$), indicating that choice latencies also scaled with the timing condition and increased with pre-feeding regardless of initiation type.

Taken together, these data indicate that both LTIs and choice latencies scale with the timing condition and are increased by pre-feeding. Although the sensitivity of LTIs to pre-feeding is consistent with predictions, choice latencies were expected to be insensitive to pre-feeding in NP-RI. This suggests that NP-RI does not protect the decision process from slowing down with pre-feeding.

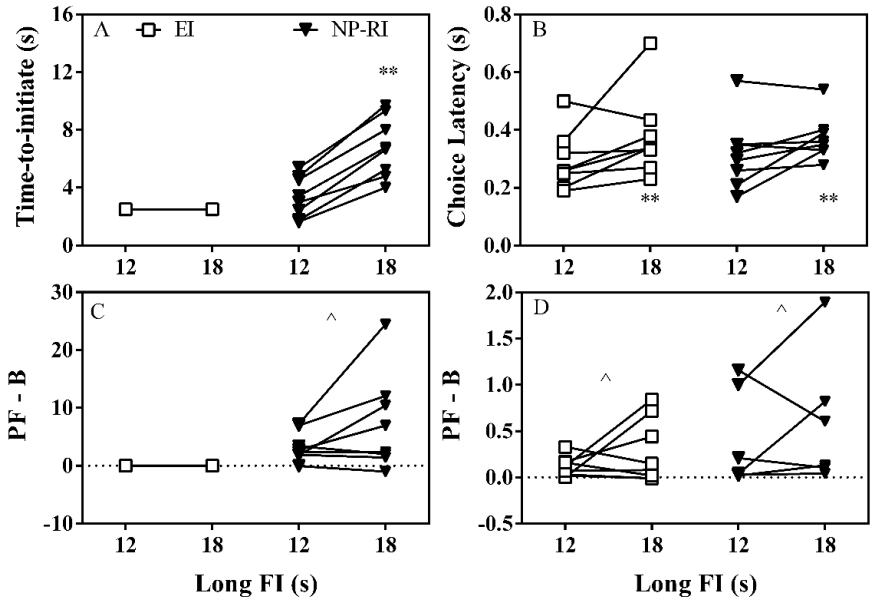

Figure 4.4. Experiment 3 Baseline and pre-feeding times-to-initiate and choice latencies. Median LTI (Panel A) and choice latency (Panel B) and pre-feeding (PF) – baseline (B) median LTI (Panel C) and choice latency (Panel D) for each rat as a function of the Long interval in each timing condition (12-s, 18-s) and initiation type (EI = white squares, NP-RI = black triangles). *Indicates substantial evidence (i.e., $ln BF_{10}$ = 1.098) for an initiation type model. **Indicates substantial evidence for a timing condition model. ^Indicates substantial evidence (i.e., $ln BF_{10}$ = 1.098) for a feeding regimen describing the difference between pre-feeding and baseline.

Does the sensitivity of LTS variability depend on whether EI ITIs are yoked to pre-feeding-induced longer NP-RI LTIs from Short 4-s Long 12-s A?

The previous analyses indicate LTS variability but not the mean LTS was sensitive to pre-feeding. The main effect of pre-feeding suggests that the effect of feeding regimen on LTS variability is not attributable to the pre-feeding-induced lengthening of NP-RI LTIs. To confirm that the effect of feeding regimen does not depend on LTI length, rats were trained in a second determination of Short 4-s Long 12-s (Short 4-s Long 12-s B) and then tested in: Single-Initiation Type Testing: Yoked-ITI Pre-feeding wherein EI ITIs were yoked to pre-feeding-induced longer NP-RI LTIs from Single-Initiation Type Testing: Pre-feeding.

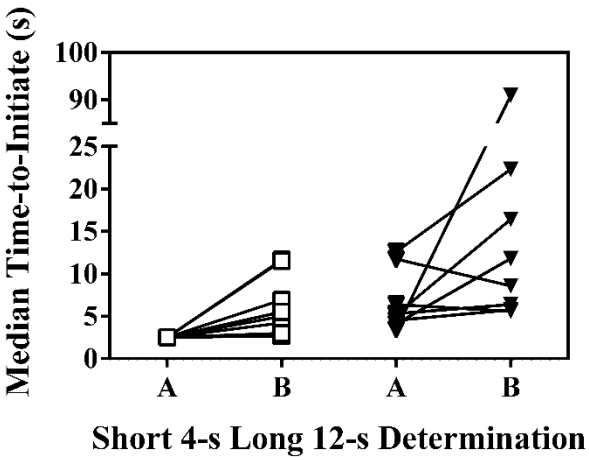

Figure 4.5. Experiment 3 pre-feeding times-to-initiate with yoked EI ITIs. Median LTI as a function of Short 4-s Long 12-s determination (A: EI LTI = 2.5 s, B: EI LTI = Pre-feeding Lengthened NP-RI LTI from Short 4-s Long 12-s A) and initiation type (EI = white squares, NP = black triangles).

Figure 4.5 shows the median LTI for each rat as a function of Short 4-s Long 12-determination (A, B) and initiation type (EI, NP-RI). To assess the success of the yoking procedure, yoked EI ITI medians and IQRs were compared to NP-RI LTI medians and IQRs in Single Initiation Type Testing: Pre-feeding and Yoked-ITI Pre-feeding via Bayesian dependent samples *t*-tests comparing initiation type (EI, NP-RI). These revealed substantial evidence for an initiation type model describing the difference between EI ITI IQRs compared to NP-RI LTI IQRs in Single Initiation Type Testing: Pre-feeding ($ln BF_{io} = 3.539$), indicating that NP-RI LTI IQRs in Single Initiation Type Testing: Pre-feeding were larger than EI ITI IQRs. All other comparisons revealed little evidence for an initiation type model (largest $ln BF_{io} = 0.755$). Thus, the yoking procedure adequately yoked the mean LTI but not LTI variability to pre-feeding lengthened NP-RI LTIs in Single Initiation Type Testing: Pre-feeding.

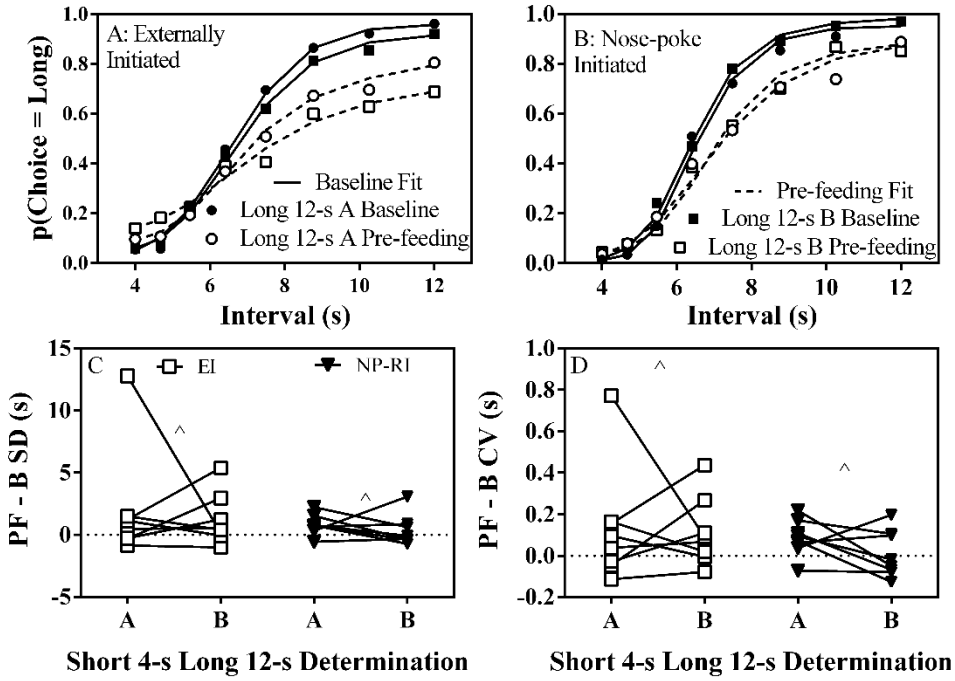

Figure 4.6. Experiment 3 baseline and pre-feeding with yoked EI ITIs fits of cumulative gamma model to psychophysical functions and temporal bisection performance. Mean psychophysical functions (Panels A & B), fits of Equation 4.1 (Panels A & B), and pre-feeding (PF) – baseline (B) LTS SDs (Panel C) and LTS CVs (Panel D) of Equation 4.1 previously affected by pre-feeding as a function of Short 4-s Long 12-s determination (A: EI LTI = 2.5 s, B: EI LTI = Pre-feeding Lengthened NP-RI LTI from Short 4-s Long 12-s A) and initiation type (EI = white squares, NP = black triangles). ^Indicates substantial evidence (i.e., $ln BF_{io} = 1.098$) for a feeding regimen describing the difference between pre-feeding and baseline.

Figure 4.6 shows the mean psychophysical functions, fits of Equation 4.1, and the pre-feeding – baseline LTS SDs and LTS CVs for each rat as a function of Short 4-s Long 12-s determination (A, B) and initiation type (EI, NP-RI). To determine whether the effect of pre-feeding on LTS variability changed when EI LTIs were yoked to NP-RI LTIs, LTS SDs and CVs were analyzed via 2 (initiation type: EI, NP-RI) × 2 (feeding regimen: baseline, pre-feeding) × 2 (determination: Short 4-s Long 12-s A, Short 4-s Long 12-s B) Bayesian repeated measures ANOVAs. The null model of these analyses contained all the parameters of a 2 (feeding regimen: baseline, pre-feeding) × 2 (initiation type: EI, NP-

RI) repeated measures ANOVA to determine the extent to which adding a determination or determination interaction parameter improved model fit. These analyses revealed evidence against adding a determination, determination × feeding regimen, or determination × feeding regimen × initiation type parameter to the model describing LTS SDs (largest $ln\text{BF}_{io}$ = -1.378), or LTS CVs (largest $ln\text{BF}_{io}$ = -1.160) indicating that there were no effects of Short 4-s Long 12-s determination on LTS variability.

Figure 4.7 shows the pre-feeding - baseline LTS SD and CV for each rat; data were collapsed across determinations and timing conditions because of the lack of evidence for an interaction with either determination or timing condition. These data were submitted to Bayesian dependent measures *t*-tests to characterize the overall magnitude of the effect of pre-feeding on LTS variability. These revealed substantial evidence for a feeding-regimen model describing LTS SDs ($ln\text{BF}_{io}$ = 1.109) and CVs ($ln\text{BF}_{io}$ = 1.826) confirming that pre-feeding increased LTS variability.

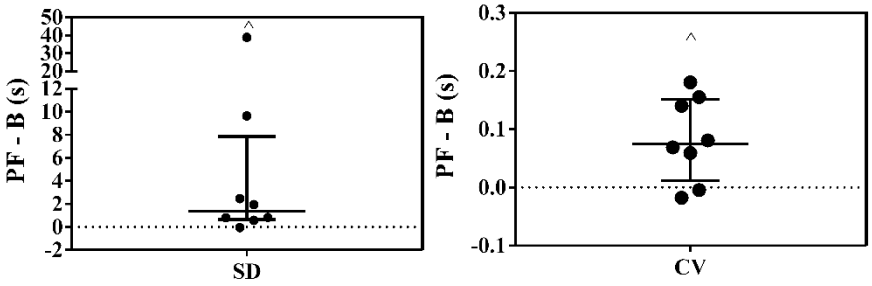

Figure 4.7. Experiment 3 average pre-feeding effect on LTS variability. Pre-feeding (PF) – baseline (B) LTS SD (Panel A) and CV (Panel B) for each rat collapsed across Short 4-s Long 12-s determinations, timing conditions, and initiation types and overlaid with the median and inter-quartile range. ^Indicates substantial evidence (i.e., $ln\text{BF}_{io}$ = 1.098) for a feeding regimen describing the difference between pre-feeding and baseline.

Are times-to-initiate, choice latencies, and LTSs differentially sensitive to extinction as a function of initiation type?

NP-RI was also predicted to yield LTSs and choice latencies robust to extinction. NP-RI LTIs were expected to be sensitive to extinction. Although nose-pokes could delay onset of trials following EI, EI ITIs were not expected to be sensitive to extinction. These predictions were assessed visually because inspection of performance under extinction revealed that changes in LTIs, choice latencies, and probability of choice 'long' across rats were idiosyncratic.

Figure 4.8 shows the mean median LTI and choice latency as a function of trial under both baseline and extinction sessions in EI and NP-RI, and the mean psychophysical function with fits of Equation 4.1 as a function of baseline and extinction (collapsed across trials and sessions). NP-RI LTIs but not EI ITIs increased with extinction. Interestingly, NP-RI LTIs appear to initially shorten and then lengthen; such shortening suggests a kind of 'extinction burst' in NP-RI LTIs. NP-RI LTIs also return to baseline levels at the beginning of the second extinction session, suggesting evidence of spontaneous recovery. Similarly, both NP-RI and EI choice latencies initially shorten and then increase with extinction, returning to baseline levels at the beginning of the second extinction session. Taken together, this suggests NP-RI LTIs and choices latencies in EI and NP-RI are sensitive to extinction.

Interestingly, the effect of extinction on LTSs appears to depend on initiation type. Whereas extinction in EI results in an overall flattening corresponding to an increase in the minimum and reduction in the range of the psychophysical function, extinction in NP-RI results in a less severe flattening corresponding to a smaller increase in the minimum and reduction in the range of the psychophysical function. The

probability of choice 'long' in EI ranges between 0.2 and 0.6, compared to between 0.1 and 0.8 in NP. This suggests that LTSs become more variable in extinction to a greater extent in EI than NP-RI. In NP-RI, there is a clear leftward shift of the psychophysical function, indicating that LTSs lengthen in extinction. In contrast, the severe flattening of the psychophysical function in EI makes it difficult to ascertain any shift in the psychophysical function. Taken together, these data suggest that both mean LTS and LTS variability increases with extinction but LTS variability may do so to a lesser degree in NP-RI.

Is the sensitivity of LTS variability to pre-feeding in EI and NP-RI explained by an increase in the prevalence and mean of non-timed LTSs?

Grubb's test revealed as an outlier rat 5 for ε, *c*, timed LTS SD, and timed LTS CV in NP-RI Short 4-s Long 12-s pre-feeding, the mean timed LTS in NP-RI Short 6-s Long 18-s and *q* in NP-RI Short 6-s Long 8-s pre-feeding; rat 4 for K in EI Short 4-s Long 12-s pre-feeding; rat 8 for *K* in EI Short 4-s Long 12-s baseline and Short 6-s Long 18-s pre-feeding. These data were removed from analysis.

Figure 4.9 shows the mean psychophysical function, psychophysical function of a representative rat, and fits of Equation 2.1 as a function of feeding regimen (baseline, pre-feeding) within each initiation type (EI, NP). Table 4.3 shows the baseline and Table 4.4 shows pre-feeding – baseline parameter estimates of the gamma-exponential (Equation 2.1) mixture model. Equation 2.1 appears to track the data just as well as Equation 4.1, with no significant deviations from the psychophysical functions.

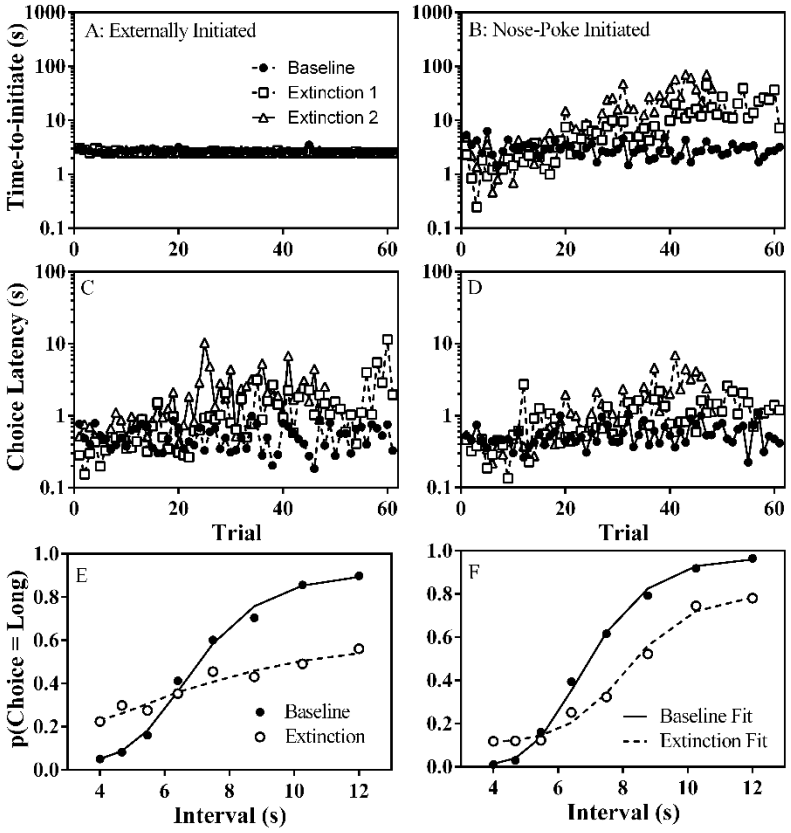

Figure 4.8. Experiment 3 extinction temporal bisection performance. Mean median LTI (Panels A & B) and choice latency (Panels C & D) back transformed from the log scale as a function of trial in Short 4-s Long 12-s Baseline (filled circles, solid line) and Extinction sessions 1 (white squares, dashed line) and 2 (white triangles, dashed line) within EI (Panels A & C) and NP-RI (Panels B & D). Also shown is the mean psychophysical function and fits of Equation 4.1 as a function of Short, Long, and intermediate intervals in Baseline (filled circles, sold line) and Extinction (white circles, dashed line; collapsed across both extinction sessions) within EI (Panel E) and NP-RI (Panel F). Note that for Panels A-D, the number of visualized trials is the median number of trials completed within each initiation type, and thus by the last visualized trial each data point is the mean median of four rats.

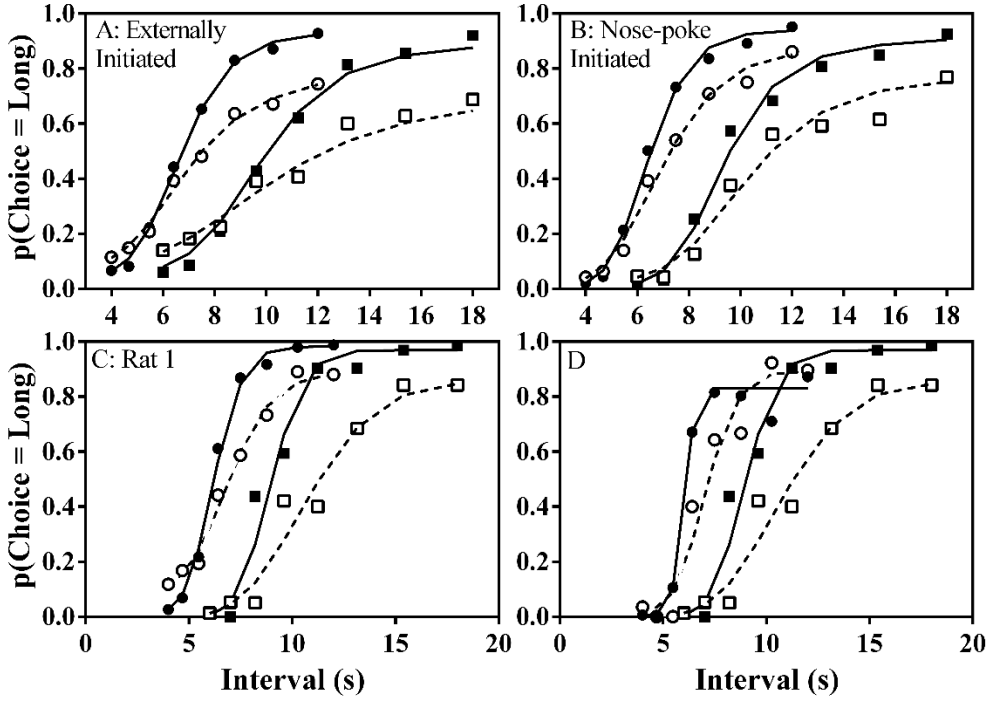

Figure 4.9. Experiment 3 cumulative gamma-exponential mixture model fits to baseline and pre-feeding psychophysical functions. Mean psychophysical functions (Panels A & B), psychophysical functions of a representative rat (Panels C & D) and fits of Equation 2.1 within each initiation type (EI: Panels A & C; NP: Panels B & D) as a function of timing condition (12-s: circles; 18-s: squares) and feeding regimen (baseline = filled symbols, solid line; pre-feeding = white symbols, dashed line). Representative rat was defined as the rat with the median pre-feeding-induced increase in mean LTS in both initiation types. Note that the fits of Eq. 4.1 and 2.1 are not visually distinguishable.

To assess whether pre-feeding effects on LTSs are explained by a reduction in the prevalence of timed LTSs and mean of non-timed LTSs, all dependent measures were submitted to 2 (initiation type: EI, NP-RI) × 2 (feeding regimen: baseline, pre-feeding) × 2 (timing: 12-s, 18-s) Bayesian repeated measures ANOVAs. These analyses revealed substantial evidence for a feeding model ($ln BF_{io} = 5.593$) describing q, indicating that pre-feeding reduced the probability of entering a timing state. Additionally, there was subthreshold evidence for also including an initiation type parameter in the feeding model (initiation type + feeding, $ln BF_{io} = 6.682$; $\Delta ln BF_{io} = 1.089$), suggesting that rats

may enter timing states more often in NP-RI than EI. There was also substantial evidence for an initiation type model (lnBF$_{io}$ = 5.487) describing the mean non-timed LTS, indicating that when not timing rats were less likely to respond 'short' in NP-RI than EI. There was substantial evidence for the null model (lnBF$_{io}$ = -1.155) describing the mean non-timed LTS, suggesting that the mean non-timed LTS is insensitive to pre-feeding.

To further isolate the potential mechanism by which pre-feeding increases LTS variability, the remainder of the parameters and derived statistics were submitted to 2 (initiation type: EI, NP-RI) × 2 (feeding regimen: baseline, pre-feeding) × 2 (timing: 12-s, 18-s) Bayesian repeated measures ANOVAs. These revealed substantial evidence for an initiation type + feeding regimen + timing model (lnBF$_{io}$ = 11.989) describing c, indicating that the speed of the clock was higher in NP-RI than EI, reduced by pre-feeding, and scaled with the timing condition. There was also evidence for an initiation type + feeding regimen (lnBF$_{io}$ = 8.043) model describing ε, indicating that the criterion pulse count was higher for NP-RI than EI and reduced by pre-feeding.

Consistent with the effects observed on the speed of the clock and criterion pulse count, there was substantial evidence for an initiation type + feeding regimen + timing model (lnBF$_{io}$ = 13.636) describing timed LTS SDs, indicating that timed LTS SDs were smaller in NP-RI than EI, increased by pre-feeding, and scaled with the timing condition. There was also substantial evidence for an initiation type + feeding regimen model (lnBF$_{io}$ = 8.013) describing timed LTS CVs, indicating that LTS CVs were higher in NP-RI than EI and increased by pre-feeding. In contrast, there was only substantial evidence for a timing model (lnBF$_{io}$ = 8.711) describing timed mean LTSs, indicating

mean LTSs scaled with the timing condition. There was no substantial evidence for a feeding regimen ($ln BF_{io}$ = -0.224) model describing timed LTS means[9].

Taken together, these data suggest that rats produced more timed and less variable LTSs in NP-RI than EI. The less variable LTSs appears to be due to a faster clock speed in NP-RI than EI. Although pre-feeding reduced the prevalence of timed LTSs, it did not affect the mean non-timed LTS as predicted. Instead, pre-feeding reduced the speed of the clock and the criterion pulse count, suggesting that timed and not non-timed LTSs are sensitive to pre-feeding. Thus, these data suggest that the pre-feeding effects on LTSs are not attributable to an increase in the prevalence and mean of non-timed LTS. Additionally, these data reinforce the notion that although NP-RI enhances temporal control of latent LTSs in rats trained in the temporal bisection procedure, NP-RI does not protect LTSs from motivational fluctuations.

[9] As with analysis of free parameters and derived statistics of fits of Eq. 4.1, to determine the reliability of the obtained pre-feeding effects, analyses were reconducted with both rats 4 and 5 removed. Analysis of timed LTS SDs ($ln BF_{io}$ = 10.156) and CVs ($ln BF_{io}$ = 7.938) did not depend on whether rat 4 and 5 were included. Analysis of timed mean LTSs depended on whether rats 4 and 5 were included ($ln BF_{io}$ = 4.087). Thus, the pre-feeding-induced increased in latent LTS variability is reliable and the pre-feeding-induced increase in the latent mean LTS is unreliable.

Table 4.3

Experiment 3 Median (IQR: 1st Quartile, 3rd Quartile) baseline parameter estimates of Equation 2.1

	Short 4-s Long 12-s		Short 6-s Long 18-s	
Parameters	EI	NP-RI	EI	NP-RI
q	.91 (.82, .93)	.93 (.89, .97)	.80 (.72, .89)	0.93 (0.89, 0.94)
ε (pulses)	*24.03 (19.12, 26.93)*	*27.58 (24.32, 35.82)*	*21.89 (14.29, 45.07)*	*30.02 (24.64, 45.47)*
c (s)	***0.28 (0.26, 0.36)***	***0.24 (0.18, 0.27)***	***0.49 (0.26, 0.68)***	***0.32 (0.21, 0.45)***
Mean non-timed LTS (*K*) (s)	*14.02 (11.98, 27.49)*	*>100 (27.78, >100)*	*32.86 (20.37, >100)*	*>100 (>100, > 100)*
Derived Statistics				
Mean Timed LTS (s)	**6.96 (6.51, 7.09)**	**6.44 (6.27, 6.86)**	**10.15 (9.81, 10.49)**	**9.68 (9.19, 9.80)**
Timed LTS SD (s)	***1.41 (1.29, 1.55)***	***1.25 (1.10, 1.32)***	***2.22 (1.60, 2.54)***	***1.73 (1.41, 2.06)***
Timed LTS CV	*0.20 (0.19, 0.23)*	*0.19 (0.17, 0.20)*	*0.22 (0.16, 0.27)*	*0.18 (0.15, 0.21)*

Note. For temporal bisection Equation 2.1 was expressed as a cumulative density rather than a probability density function with $\delta = 0^6$. Parameter estimates and derived statistics in italics indicate substantial evidence for an initiation type model and in bold indicate substantial evidence for a timing condition model describing those parameters and derived statistics. *The estimate of *K* determines at what duration rats choose 'long' over 'short': durations less than *K* are categorized as 'short' and all durations greater than *K* are categorized as 'long'. Thus, as *K* increases, the bias to categorize a duration as 'short' increases, and as *K* decreases, the bias to categorize a duration as 'long' increases. Estimates of *K* were inordinately large for most subjects, particularly in NP-RI. Nevertheless, estimates were still analyzed and are reported as means or > 100, whichever was most informative.

Table 4.4

Experiment 3 Median (IQR: 1st Quartile, 3rd Quartile) pre-feeding – baseline parameter estimates of Equation 2.1

	Short 4-s Long 12-s		Short 6-s Long 18-s	
Parameters	EI	NP-RI	EI	NP-RI
q	**-.14 (-.19, -.04)**	**-.11 (-.16, -0.01)**	**-.01 (-0.06, .06)**	**-.11 (-.20, -.02)**
ε (pulses)	**-6.79 9(-13.31, -2.57)**	**-13.24 (-22.83, -4.55)**	**-11.01 (-28.73, -4.24)**	**-19.55 (-26.30, -9.7)**
c (s)	**0.16 (0.09, 0.93)**	**0.21 (0.07, 0.33)**	**1.48 (0.85, 3.19)**	**0.37 (0.24, 0.81)**
Mean non-timed LTS (*K*) (s)	-2.24 (-13.71, 7.98)	-1.87 (<-100, >100)	-25.55 (<-100, 2.79)	<-100 (<-100, <-100)
Derived Statistics				
Mean Timed LTS (s)	0.66 (0.29, 1.49)	0.89 (0.20, 1.02)	1.74 (0.28, 29.34)	1.31 (-0.01, 1.99)
Timed LTS SD (s)	**0.68 (0.34, 1.49)**	**0.60 (0.18, 0.92)**	**2.65 (1.49, 8.29)**	**1.06 (0.84, 1.66)**
Timed LTS CV	**0.04 (0.02, 0.16)**	**0.06 (0.02, 0.11)**	**0.14 (0.03, 0.18)**	**0.08 (0.06, 0.13)**

Note. For temporal bisection Equation 2.1 was expressed as a cumulative density rather than a probability density function with δ = 0. Parameter estimates and derived statistics in bold indicate substantial evidence for a feeding regimen model describing those parameters and derived statistics[6]. *The estimate of *K* determines at what duration rats choose 'long' over 'short': durations less than *K* are categorized as 'short' and all durations greater than *K* are categorized as 'long'. Thus, as *K* increases, the bias to categorize a duration as 'short' increases, and as *K* decreases, the bias to categorize a duration as 'long' increases. Estimates of *K* were inordinately large for most subjects, particularly in NP-RI. Nevertheless, estimates were still analyzed and are reported as described for the other parameter estimates or > 100, whichever was most informative.

Discussion

Experiment 3 revealed some evidence supporting the discriminative RI hypothesis. LTS variability was smaller in NP-RI than in EI, indicating that highly discriminable initiating-responses enhance temporal control of latent LTSs in rats trained in the temporal-bisection procedure. Despite the sensitivity of NP-RI LTIs to pre-feeding, NP-RI did not yield mean LTSs or choice latencies robust to pre-feeding or extinction. Whereas pre-feeding consistently and reliably increased LTS variability and choice latency regardless of which outlier data were included in analyses, it did not reliably lengthen LTSs. Pre-feeding increased the mean LTS in both EI and NP-RI only if rats with flat psychophysical functions following pre-feeding in EI were removed despite not being detected by Grubb's test. Thus, it appears that the RI temporal bisection procedure enhances temporal control of interval timing but does not protect interval timing from motivational fluctuations or extinction.

Chapter 5: General Discussion

The present dissertation sought to determine whether interval timing and motivation are dissociable processes. Timing performance appears sensitive to fluctuations in both motivation and time, suggesting that interval timing and motivation are inseparable processes. According to a behavioral systems model of timing performance (e.g., Timberlake, 2000), behavioral modes underlying timing performance are differentially sensitive to fluctuations in time and motivation: post-food focal search is sensitive to motivation, general search and pre-food focal search are sensitive to time (Figure 1.4). This suggests that training subjects to emit a response when transiting from post-food focal search to general search should circumscribe pre-feeding effects to post-food focal search without affecting timing performance. Thus, training subjects to

response-initiate (RI) trials rather than having the experimenter determine when trials are initiated (EI) is expected to dissociate interval timing and motivation processes. Specifically, according to the discriminative RI hypothesis, training subjects to initiate their own trials should dissociate interval timing and motivation processes as a function of the discriminability of initiating-responses from target responses.

This hypothesis was evaluated in three experiments. In experiments 1 (Chapter 2) and 2 (Chapter 3), rats were trained in the switch-timing procedure (Figure 1.1B), an immediate timing procedure in which subjects continuously judge whether to switch from a Short fixed-interval (FI) schedule of reinforcement to a Long FI. In experiment 3, rats were trained in the location variant of the temporal bisection procedure (Figure 1.1B), a retrospective timing procedure in which subjects continuously judge whether to categorize an interval 'short' or 'long', with choice of either 'short' or 'long' expressed after the interval has elapsed. In the switch-timing procedure the latency-to-switch (performance index: LTS; Figure 1.2) is indicated by the first response on the Long FI (target response); in the location variant of the temporal bisection procedure LTSs are latent, only indicated by choosing 'long' over 'short' (target response). Some trials were EI, and others RI, initiated via the first response on the Short FI (SL-RI) or via a nose-poke in a nose-poke device (NP-RI). In two timing conditions (4-s 12-s, 6-s 18-s), subjects were challenged with 1-h and 24-h pre-feeding probes. To control for the possibility that the dissociating effects of RI compared to EI is attributable to pre-feeding-induced longer latencies-to-initiate (LTIs) trials and not RI per se, subjects were also challenged with pre-feeding probes with EI inter-trial intervals (ITIs) yoked to NP-RI LTIs. Additionally, to determine whether initiating-responses generally dissociate interval timing and non-timing processes or selectively dissociate interval timing and motivation processes, subjects were challenged with two-session extinction probes.

Table 5.1 shows a summary of and support for the predictions derived from the discriminative RI hypothesis. Initiating-responses enhanced temporal control of latent LTSs but not of overt LTSs, and SL-RI reduced but NP-RI enhanced temporal control of Short FI performance. The robustness of overt median LTS but not LTS variability from pre-feeding increased with the discriminability of initiating-responses from target responses. Latent mean LTS but not latent LTS variability was robust to pre-feeding in both EI and NP-RI. LTSs were sensitive to extinction in EI, SL-RI, and NP-RI. Importantly, the protective effects of NP-RI were not an artifact of longer NP-RI LTIs, indicating that highly discriminable response-initiation per se protects median LTSs from pre-feeding-induced reductions in motivation. LTIs were sensitive to the timing condition, and pre-feeding so long as manipulanda also did not predict imminent reinforcement. Similarly, a gamma-exponential mixture model provided only a partial dissociation of interval timing and motivation: parameters of timed LTSs were just as sensitive to pre-feeding as parameters of non-timed LTSs. Taken together, these data provide moderate support for the discriminative RI hypothesis, indicating that as initiating-responses become progressively discriminable from target responses, initiating-responses selectively but only partially dissociate interval timing and motivation.

Table 5.1

Summary and support for predictions derived from the discriminative RI hypothesis

		Experiment 1 (Chapter 2)	Experiment 2 (Chapter 3)	Experiment 3 (Chapter 4)
Prediction: As initiating-responses become more discriminable from target responses		Switch-timing	Switch-timing	Temporal Bisection
1	Temporal control of LTSs will increase	No	No	Yes
2	Robustness of LTSs to pre-feeding will increase	No	Moderate*	Moderate**
3	LTIs will be sensitive to pre-feeding	No	Yes	Moderate***
4	Robustness of LTSs to extinction will increase	NA	No	No
5	LTIs will be sensitive to extinction	NA	Yes	Yes
Prediction: Compared to EI, in SL-RI but not NP-RI				
6	Temporal control of Short FI performance will be reduced	Moderate[&]	Moderate[&]	NA
Prediction: In EI,				
7	Interval timing and motivation will be computationally dissociable	No	Moderate[†]	Moderate[†]

Note. NA = Not applicable. *Only overt LTS medians were robust to pre-feeding; pre-feeding increased LTS variability in all initiation types. ** Latent mean LTS but not latent LTS variability was insensitive to pre-feeding. **Despite NP-RI but not SL-RI protecting over LTSs medians from pre-feeding, SL-RI and NP-RI LTIs were equally sensitive to pre-feeding as long as manipulandum on which initiating responses were emitted did not serve as a discriminative stimulus for some other component of the task. [&]Only temporal control of LFRs was reduced. [†]Pre-feeding affected parameters of both timed and non-timed LTSs.

Discriminability of Initiating-Responses Modulates Temporal Control of Target Responses

The differential effects of SL-RI and NP-RI on temporal control of Short FI performance, as indexed by the latency-to-the-first-response (LFR) on the Short FI, indicates moderate support for the notion that the discriminability of initiating-responses modulates temporal control of target responses (Figure 2.2 and Figure 3.3). Whereas SL-RI differs from Short FI target responses only as a function of time, NP-RI differs from Short FI target responses as a function of time, location, and form. As such, generalization between SL-RI and target responses is more likely to occur than between NP-RI and target responses. Such generalization would promote encoding of initiating-responses as target responses and vice versa, thereby reducing control of both responses by their respective associations: starting trials and timing intervals, respectively. In turn, this is predicted to result in poorer temporal control of timing performance. The SL-RI-induced reduction in temporal control of LFRs suggests that the results obtained by Fox and Kyonka (2013, 2015, and 2016)—poor temporal control in RI compared to EI fixed-interval and peak interval performance—is likely due to generalization between initiating-responses and target responses. Pigeons were trained to initiate fixed-interval and peak trials via a single peck on the FI key; initiating-responses differed from target responses only as a function of time.

As expected, NP-RI enhances temporal control of LTSs relative to EI. However, this enhancement is limited to latent LTSs in animals trained in the temporal bisection procedure (Figure 4.3; cf. Figure 3.3), suggesting that initiating-responses enhance temporal control in retrospective but not immediate timing performance. Although consistent with Caetano & Church (2009) and Caetano (2009), such an outcome is inconsistent with the behavioral systems model (Figure 1.4). According to this model,

initiating-responses dissociate post-food focal search and general search in *all* interval-timing procedures, enhancing synchronization of time-markers and general search and, thus, temporal control of target responses. It might be that whether initiating-responses enhance temporal control depends on the extent to which EI retrospective and EI immediate timing procedures gain temporal control over target responses. If temporal control is already relatively high, perhaps at a ceiling, then initiating-responses may not enhance temporal control; if temporal control is relatively low, then initiating-responses may enhance temporal control. This suggests that, when externally initiated, immediate timing procedures gain greater temporal control of target responses than retrospective timing procedures. Consistent with this notion, the probability of entering a timing state appears to be slightly higher in EI switch-timing (Experiment 2: median =.90; IQR = .80-.91) than in EI temporal bisection procedures (median =.85; IQR = .79-.91; cf. Tables 3.3 and 4.3), and the LTS CQVs appear to be smaller in EI switch-timing (Experiment 2: median =.13; IQR = .11-.17) than in EI temporal bisection procedures (median =.22; IQR = .21-.26; cf. Figure 3.3 and Figure 4.3). Thus, temporal control may be a function of the degree of time-marker and general search synchronization and the basal temporal control of target responses gained by an EI interval timing procedure.

There are two critical differences between EI switch-timing and EI temporal bisection procedures that may explain why temporal control was higher in the former than the latter. First, expression of switch-timing performance is less variable than expression of temporal bisection performance. Performance in switch-timing trials is mostly expressed as Short FI or Long FI responding (Daniels et al., 2015b). Performance in temporal bisection trials is expressed as choosing 'short' or 'long' at the end of a trial, and as latent LTSs during a trial. Expression of these latent switches, however, likely consists of many different behaviors including but not limited to grooming, sniffing,

investigating, head-entries, etc. (Gouvêa et al. 2014; Timberlake, 2000; Staddon & Simmelhag, 1971). Increased variability in the expression of these latent LTSs suggests that, when a reinforcer is delivered, more than just target responses (choices 'short' and 'long') compete for reinforcer credit assignment. Increased credit assignment competition decreases temporal control of target responses (Killeen, 2011; Killeen & Pellón, 2013; Sanabria, Thrailkill & Killeen, 2009).

Variability in the expression of performance also potentially explains why temporal control of LFRs but not the latencies-to-depart (LTDs) is differentially sensitive to discriminability of initiating-responses. At the beginning of switch-timing trials the Short FI is the only source of reinforcement. At the end of switch-timing trials both the Short and Long FI are sources of reinforcement. The lack of an alternative source of reinforcement at the beginning but not the end of switch-timing trials suggests that expression of performance is more variable at the beginning than at the end of switch-timing trials. Increased variability in the expression of switch-timing performance at the beginning but not at the end switch-timing trials suggests that more responses compete for reinforcer credit assignment at the end of Short FI but not Long FI trials. Likewise, Sanabria, Thrailkill, & Killeen (2009) showed that providing an alternative source of reinforcement to pigeons trained on the peak procedure resulted in later and less variable start-times, and sooner and less variable stop-times. This strengthens the notion that explicitly programming multiple sources of reinforcement reduces credit assignment competition and thus enhances temporal control of performance indices.

Second, the probability of reinforcement at the end of the switch-timing trials (1.0) is much higher than in temporal bisection trials (.57). Extant theories of attention suggest that attention is a function of either or both reinforcement predictability

(Mackintosh, 1965, 1975; also see Fortes, Pinto, Machado, & Vasconcelos, 2018) and reinforcement uncertainty (Pearce & Hall, 1980; Daniels & Sanabria, 2018; for a review, see Esber & Haselgrove, 2011). For example, according to the predictability theory, attention is a positive function of the probability of reinforcement signaled by a stimulus. Thus, as the probability of reinforcement signaled by a time-marker increases, so does attention; likewise, as the probability of reinforcement signaled by a time-marker decreases, so does attention. Temporal control of LTSs in EI temporal bisection may be lower than in EI switch-timing procedures because of the lower probability of reinforcement at the end of a trial. Future research may explore the relationship between the probability of reinforcement at the end of a trial, the expression of performance during trials, and RI enhancement of temporal control.

Discriminability of Initiating-Responses Modulates the Selective and Partial Dissociation of Interval Timing and Motivation

Interval Timing and Motivation

The selective but partial dissociation of interval timing and motivation (Figure 2.3, Figure 3.4) is moderately consistent with the discriminative RI hypothesis and the posited behavioral systems model (Figure 1.4). Taken together, these predict that as initiating-responses become progressively discriminable from target responses, initiating-responses increasingly dissociate post-food focal search and general search, which is predicted to manifest as an increasing robustness of *both* median LTS and LTS variability to pre-feeding. However, only median LTS was increasingly robust to pre-feeding as initiating-responses became progressively discriminable from target responses.

The consistent effect of pre-feeding on LTS variability suggests that, although pre-feeding increases the time spent in post-food focal search, it also alters the probability of transiting between general search and both the post-food focal search and pre-food focal search. Figure 5.1 shows a schematic of this *ad hoc* revision of the behavioral systems model. In this revised behavioral systems model, pre-feeding still (1) increases the time spent in post-food focal search, but also (2) increases the probability of transiting back to post-food focal search from general search, and (3) decreases the probability of transiting to pre-food focal search from general search. Importantly, this revised model still predicts that pre-feeding increases the mean and variability of performance indices. Taken together with the discriminative RI hypothesis, the revised behavioral systems model predicts that pre-feeding increases both median LTS and LTS variability in EI but only LTS variability in NP-RI.

In addition to accounting for the consistent effect of pre-feeding on LTS variability, this revised model accounts for the concomitant pre-feeding-induced reduction in the probability of entering a timing state (Table 3.3), and the reduction in start and persistence ratios (Figure 3.5). If pre-feeding increases the probability of transiting back to post-food focal search, then synchronization of time-markers and general search will decrease, resulting in subjects entering non-timing states more frequently than in baseline. Additionally, an increase in the probability of returning to post-food focal search entails engaging in post-food focal search behaviors, which includes but is not limited to grooming, digesting, and interacting with still available manipulanda (e.g., Timberlake, 2000). Interaction with manipulanda in post-food focal search, however, is not under the control of time as in general-search and pre-food focal search. Subjects are thus likely to start on the Long FI rather than the Short FI (reduced

start ratio) and persist less on the Long FI than on the Short FI (reduced persistence ratio).

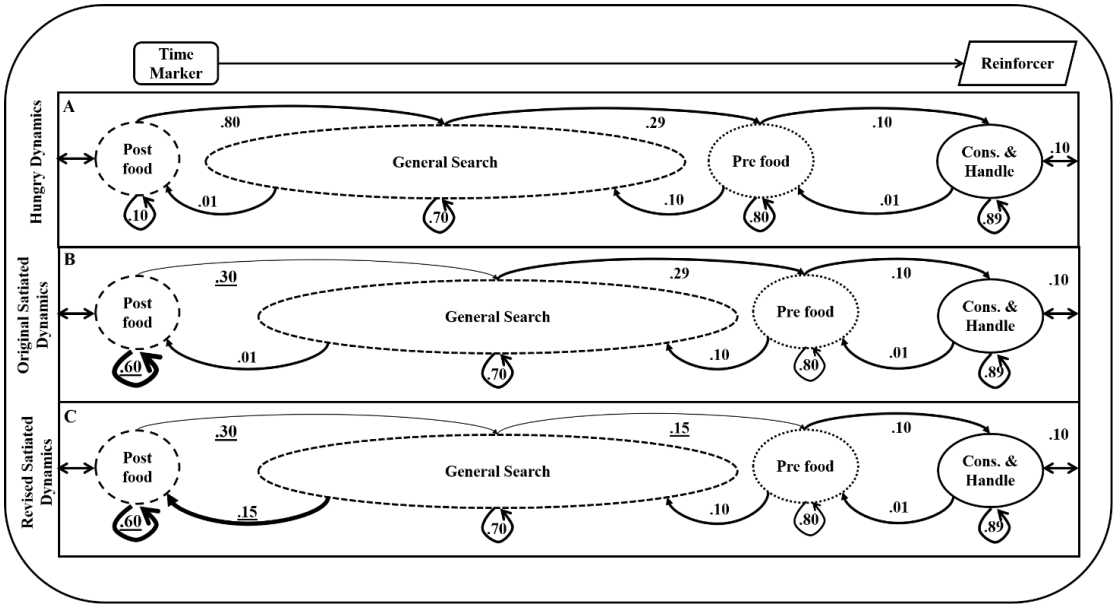

Figure 5.1. Schematic of the ad hoc revision of the predatory subsystem of rats in interval timing procedures. Schematic shows trial dynamics of a hungry rat (Panel A) compared to the original predicted pre-feeding effects (Panel B) and the ad hoc revision of the predicted pre-feeding effects (Panel C). The ad hoc revision of the behavioral systems model is motivated by the consistent effect of pre-feeding on LTS variability across initiation types. See text for details. Note that the static transition probabilities are for illustrative purposes only, some probabilities are likely dynamic and may shift to 1 given certain experimental events, such as the probability of transitioning into the consumption\handling mode upon reinforcer delivery. Underlined transition probabilities illustrate the predicted effect of pre-feeding, with thicker and thinner arrows further indicating whether pre-feeding increased or decreased a specific probability. Note that the shift of general search is intentional, indicating that post-food focal search delays onset of general search.

This revised model also explains the pre-feeding-induced increase in LFR and LTD median and variability (Figure 3.4). The higher probability of transiting back to post-food focal search is followed by spending more time in post-food-focal search. As such, emission of general-search-to-pre-food-focal-search transiting responses (i.e., LFRs, LTDs, and LTSs) becomes delayed. Taken together with the discriminative RI hypothesis, this suggests that the sensitivity of median LFR and LTD should be

proportional to the discriminability of initiating-responses from target responses. Despite analyses revealing only main effects of pre-feeding on median LFR and LTD, *post hoc* analyses within each initiating type indicates that the effect of pre-feeding on LFRs and LTDs scales as expected: EI (average $ln BF_{io}$ = 5.522) > SL-RI (average $ln BF_{io}$ = 2.47) > NP-RI (average $ln BF_{io}$ = 1.69). This is further corroborated by visual inspection of Figure 3.4, where the pre-feeding-induced increase in median LTD is larger for EI than for NP-RI switch-timing procedures; scaling of the effect is less clear for median LFR. Thus, most of the pre-feeding effects observed in this dissertation are explained following a slight *ad hoc* modification of the behavioral systems model.

This revised model also makes a prediction consistent with timing theories that suggest the speed of the clock is a function of arousal (e.g., Killeen & Fetterman, 1988), which is a function of motivation (Killeen, 1995; Killen & Sitomer, 2003). Because general search is more sensitive to conditioning than post-food focal search, the effect of pre-feeding on general search, but not on post-food focal search, is expected to be transient. That is, to the extent that all performance indices (i.e., LFRs, LTDs, and LTSs) are timed (i.e., the output of a PA-like model), extended training under the pre-feeding-induced reduction in motivation is expected to result in recalibration of performance indices to baseline levels. LTIs, in contrast, are expected to remain lengthened. In EI, and to a lesser extent in SL-RI, full recalibration of performance indices is not expected because post-food focal search and general search are still conflated. Likewise, many PA models suggest that clock-speed-induced perturbations in interval timing are transient because reinforcement updates memory with new pulse counts (Meck, 1996). Although it is possible for this recalibration to occur within-session, previous research suggests that such recalibration typically takes 3-7 sessions of training (Meck, 1996), thus testing this prediction is outside the scope of the present dissertation.

Unfortunately, the revised model does not explain why mean LTS but not LTS variability was robust to pre-feeding in both NP-RI and EI temporal bisection (Figure 4.3). This outcome also argues against McClure et al.'s (2009) suggestion that that training subjects in the location variant of temporal bisection, which associates choices 'short' and 'long' with fixed locations and thus facilitates behavioral sequences akin those observed in animals trained in the switch-timing procedure, promotes lengthening of the mean LTS. Indeed, the reliable pre-feeding-induced increases in LTS variability is inconsistent with McClure et al. (2009) but consistent with the data reported by Ward & Odum (2006). Ward & Odum (2006) trained pigeons with choices 'short' and 'long' counterbalanced across locations. Importantly, these equivocal effects are not attributable to differences in the ratio of the Short and Long intervals or variations in pre-feeding protocols. Whereas in the present dissertation the ratio of the Short and Long intervals was 1:3, in Ward & Odum (2006) and McClure et al. (2009) the ratio of the Short and Long intervals was 1:4. Although McClure et al. (2009) conducted single session pre-feeding manipulations and Ward & Odum (2006) conducted 5-session pre-feeding manipulations, in the present dissertation there was little evidence for a difference between 1 h and 24 h pre-feeding. Taken together, these data suggest that the effect of pre-feeding in the temporal bisection procedure depends on some unappreciated procedural variable.

McClure et al. (2009) also suggested that the effect of pre-feeding depends on the complexity of experimental procedures. Complex experimental procedures reduce temporal control of target responses because stimuli signal many different attributes of response-reinforcer associations and control of target responses is likely to fluctuate among attributes within and between stimuli (e.g., Daniels et al., 2015b; Delamater et al. 2014; Stubbs et al., 1994). Such fluctuation may obfuscate potentially interesting effects.

Whereas Ward & Odum (2006) trained and tested pigeons in the temporal bisection procedure, FI, and a color-discrimination task within the same session, McClure et al. (2009) trained and tested pigeons only in the location variant of the temporal bisection procedure. In the present dissertation, despite testing rats with single initiation types, rats were trained with multiple initiation types, making the location variant of the temporal bisection procedure in the present dissertation more complex than the procedure employed by McClure et al. (2009). This increased complexity likely increased fluctuation in the temporal control of target responses. Visual comparison of psychophysical functions across studies suggests that McClure et al. (2009) obtained steeper psychophysical functions (higher slope), and thus less variable performance, than Ward and Odum (2006) and the present dissertation. Despite the inherent problems with such cross-study comparisons, this indicates that training and testing rats in only the EI location variant of the temporal bisection procedure should enhance temporal control of temporal bisection performance and thus promote a pre-feeding-induced lengthening of the mean LTS.

The hypothesis that the effect of pre-feeding depends on the degree of temporal control potentially explains the inconsistent effects of pre-feeding between experiments 1 and 2, and 1 and 3. In experiment 1, pre-feeding only lengthened LTSs (Figure 1.3); in experiment 2 pre-feeding increased LTS variability and, depending on initiation type, also lengthened LTSs (Figure 3.4, 3.7); in experiment 3, pre-feeding only reliably increased LTS variability (Figure 4.3, 4.7). Temporal control was much lower in experiment 1 than in experiments 2 and 3. In experiment 1, rats started on the Short FI and persisted on the Long FI less than rats in experiment 2; in experiment 1 rats entered timing states less frequently than in experiments 2 and 3. These data suggest that temporal control is a function of both task complexity and training regimen. Whereas in

experiment 1 rats had to merely complete the active FI, in experiment 2 rats had to follow a behavioral sequence to obtain reinforcement, and in experiment 3 rats had to correctly categorize the Short and Long intervals. Future research may parametrically investigate the relationship between interval timing procedures, temporal control, and fluctuations in motivation.

Interval Timing and Extinction

The selective but partial dissociation of interval timing and motivation is inconsistent with the expectation that RI generally dissociates interval timing and non-timing processes. RI was expected to dissociate interval timing and extinction because extinction results in a substantial reduction in motivation followed by new, inhibitory learning (Bounton, 2004; Reddish et al., 2007; Katz, 1981). The initial reduction in motivation (e.g., Katz, 1981) was expected to circumscribe new, inhibitory learning to LTIs. If a trial was initiated, interval timing was expected to remain intact. However, extinction lengthened both LTIs and LTSs, which showed evidence of spontaneous recovery by returning to baseline levels at the beginning of the second extinction session (Figure 3.8 and 4.8). Interestingly, LTIs and choice latencies—the time to choose 'short' or 'long' in the temporal bisection procedure— showed evidence of extinction bursts, an initial shortening, prior to extinction (Figure 4.8)-induced lengthening.

The sensitivity of LTIs, LTSs, and choice latencies to extinction indicates that initiating-responses *do not* generally dissociate timing and non-timing process. Extinction is thought to promote exploration of alternative sources of reinforcement while previously learned behaviors remain intact, just not expressed (Gershman, Blei, & Niv, 2010; Lattal, St. Peter, & Escobar, 2013; Todd, Vubric, & Bouton, 2014). For example, following VI schedules of reinforcement, where responding clusters in bouts

(e.g., Brackney et al., 2011; Daniels & Sanabria, 2017b; Shull, 2011), extinction reduces the bout-initiation rate, which also spontaneously recovers between extinction sessions, without altering within-bout responding or the number of responses emitted in a bout (Brackney et al., 2017; Brackney, Cheung, Herbst, Hill, & Sanabria, 2012; Cheung et al., 2012). Bout-initiation responses are thought to demarcate general-search-to-pre-food-focal-search transitions just as initiating-responses demarcate post-food-focal-search-to-general-search transitions and target responses demarcate general-search-to-pre-food-focal-search transitions. Likewise, just as within-bout responding is thought to characterize performance within behavioral modes, response runs in animals trained in the switch-timing procedure should characterize performance within behavioral modes. This suggests that responses demarcating behavioral mode transitions, but not responses within a behavioral mode, are sensitive to extinction, and thus should show classic extinction effects, including but not limited to spontaneous recovery, extinction bursts, and, more generally, context specificity (see Bouton, Winterbauer, & Todd, 2012). Although speculative, this hypothesis predicts that in animals trained in the switch-timing procedure, response runs, but not LTSs, should be robust to extinction. Testing this hypothesis is outside the scope of the present dissertation.

The prevalence of extinction bursts in the temporal bisection procedure, but not in the switch-timing procedure, may be related to the probability of reinforcement associated with lever pressing. Although there is little research investigating the determinants of extinction bursts, these appear to occur when extinction follows training on rich rather than lean schedules of reinforcement (Lattal et al., 2013; Lerman & Iwata, 1995; Lerman, Iwata, & Wallace, 1999). Such schedule effects are likely driven by the relative discriminability of extinction from training: whereas extinction is easily discriminated from training on rich schedules, extinction is not easily discriminated

from training on lean schedules. Consistent with this notion, the probability of reinforcement associated with each individual lever press is higher in the temporal bisection than in the switch-timing procedures. In the temporal bisection procedure, subjects correctly categorize Short and Long Intervals in about 90 and 95 % of trials such that the probability of reinforcement following a lever press is close to the programmed probability of reinforcement at the end of a trial: .57. In switch-timing procedures, subjects typically respond about in bouts 5 responses long (consistent with extant data on the length of response runs in FI, Daniels & Sanabria, 2017a; Guilhardi, Yi, & Church, 2007; Kirkpatrick, 2002) such that in the Short FI only 1-2 bouts occur and in the Long FI 2-4 bouts occur. At the low end of these estimates, this indicates that the probability of reinforcement following a lever press is lower than .57, approximately between .25 and .10. This suggests that extinction is more easily discriminated from training in the temporal bisection procedure than in the switch-timing procedure. Given the relative dearth of basic research on determinants of extinction bursts, future research may seek to determine whether extinction bursts can be explained by extant computational models of extinction that assume that what drives extinction is the discriminability of the training and extinction contexts (e.g., Gershman et al., 2010).

Mixture Models Only Partially Dissociate Interval Timing and Motivation

The observation that pre-feeding affects almost all parameters of the gamma-exponential mixture model (Tables 3.3 and 4.4) indicates that, like initiating-responses, the gamma-exponential mixture model partially dissociates interval timing and motivation. Consistent with Daniels and Sanabria (2017a) and the behavioral systems model (Figure 1.4 and 5.1), pre-feeding increased both the prevalence and mean of non-timed LTSs in EI switch-timing procedures. However, pre-feeding also decreased the

speed of the clock and reduced the criterion pulse count. The magnitude of pre-feeding effects on the prevalence and mean of non-timed LTSs was similar to the magnitude of pre-feeding effects on parameters of timed LTSs. Additionally, the pre-feeding effects on parameters of timed LTSs, such as the speed of the clock, scaled as predicted by the discriminative RI hypothesis: EI > SL-RI > NP-RI. This suggests that, although the gamma-exponential mixture model only partially dissociates interval timing and motivation, the effect of pre-feeding on parameters of timing supports the hypothesis that as initiating-responses become progressively discriminable from target responses, interval timing and motivation become increasingly dissociated.

The sensitivity of the speed of the clock to pre-feeding was inversely related to discriminability of initiating-responses from target responses such that EI > SL-RI > NP-RI. This outcome is consistent with the behavioral theory of timing (Beam, Killeen, Bizo, & Fetterman, 1998; Bizo & White, 1995, 1994; Killeen & Fetterman, 1988). The behavioral theory of timing states that the clock is embodied in behavioral state transitions and that the rate at which subjects transition between behavioral states is proportional to arousal, which is modulated by motivation (Killeen, 1995; Killeen & Sitomer, 2003). As motivation increases, so does arousal and the rate of behavioral state transitions; likewise, as motivation decreases, so does arousal and the rate of behavioral state transitions. From the perspective of the behavioral theory of timing, initiating-responses may be viewed as fixing motivation at a relatively high level prior to trial initiation, thereby reducing the degree to which behavioral state transitions are modified by fluctuations in motivation.

Importantly, reframing the results of the present dissertation within the context of the behavioral theory of timing is consistent with both the proposed revision of the

behavioral systems model (Figure 5.1) and the discriminative RI hypothesis. Indeed, the predicted pre-feeding-induced reduction in the rate of behavioral state transitions may manifest as transiting more often into states weakly associated with reinforcement and remaining in those states for a longer time. Additionally, because initiating-responses dissociate post-food focal search and general search, initiating-responses are expected to attenuate the pre-feeding-induced reduction in the rate of behavioral state transitions. However, it is worth noting that the behavioral theory of timing accounts for fewer effects than the revised behavioral systems model. Whereas both the behavioral theory of timing and the revised behavioral systems model can account for pre-feeding-induced effects on the median and variability of performance indices (i.e., LFRs, LTDs, and LTSs), the behavioral theory of timing cannot explain the reduced start and persistence ratios. Only the revised behavioral systems model can explain all these effects.

The clock-speed account of pre-feeding effects is also incomplete because the pre-feeding-induced reduction in the criterion pulse count likely reflects pre-feeding effects on both the response-threshold and memory. The criterion pulse count is the product of the response-threshold and memory, where memory, but not the response threshold, is expected to recalibrate with feedback following a change in the clock speed (e.g, Daniels et al., 2015a; Meck, 1996). The pre-feeding-induced reduction in the speed of the clock suggests that memory is repopulated with lower pulse counts. However, it is unclear whether the reduction in the criterion pulse count also reflects a reduction in the response-threshold.

To determine whether and how pre-feeding affects the response-threshold, the response threshold under baseline and pre-feeding for each initiation type was estimated by dividing the estimated criterion pulse counts by the pulse counts in memory implied

by the estimated clock speeds. The difference between the pre-feeding and baseline response-thresholds indicates whether pre-feeding increases or decreases the response-threshold. In experiment 2, the differences between the pre-feeding and baseline response-thresholds were 0.17, 0.08, and -0.01 for EI, SL-RI, and NP-RI, respectively. In experiment 3, the differences between the pre-feeding and baseline response-thresholds were 3.51 and 0.09 for EI and NP-RI, respectively. Pre-feeding appears to slow down the clock, which updates memory with smaller pulse counts, and elevates the response-threshold in EI and SL-RI, and to a lesser extent in NP-RI. Thus, from the perspective of timing models, performance does not recalibrate with extended training in pre-feeding because even after memory recalibrates, the response-threshold is still elevated. This is consistent with the behavioral systems model and with recent research suggesting that the administration of dopaminergic agonists and antagonists affects the response-threshold without impairing acquisition of peak-interval performance (Balci 2014; Sanchez-Castillo, Taylor, Ward, Paz-Trejo, Castillo, & Balsam, 2015).

Importantly, this pattern of effects is consistent with the observation that the response-threshold is robust to pre-feeding in FMI but not in DRL (Watterson et al., 2015; Daniels et al., 2018; Romero et al., 2016). In both FMI and DRL, subjects are trained to wait *t*-s between two consecutive responses; the time between the two consecutive responses is an inter-response time (IRT). In FMI, the IRTs are initiated via a lever press (initiating-response) in one location and terminated via a head-entry (target-response) into the reinforcement receptacle. In DRL, IRTs are initiated and terminated as lever presses (initiating-response and target response) on the same lever. Although FMI and DRL are both RI interval timing procedures, only in FMI are initiating-responses highly discriminable from target responses. Thus, just like the speed

of the clock, the degree to which pre-feeding elevates the response-threshold is also a function of the discriminability of initiating-responses from target responses.

Implications for The Study of Cognition and Motivation

The data obtained in the present dissertation informs more than just interval timing research; it also provides guidance on the study of cognition and motivation. First, the selective and partial dissociation of interval timing and motivation suggests that, even if cognition and motivation are inseparable, training subjects in RI procedures still protects cognitive performance from fluctuations in motivation, while providing a within-subject and within-procedure index of motivation independent of cognitive performance. The within-subject and within-procedure index of motivation eliminates the need to estimate motivation in other procedures, which may be unrelated to the cognitive function of interest and may thus inaccurately indicate whether an intervention affects both cognition and motivation. Given such a benefit of RI procedures, it is surprising that, although RI procedures increasingly implemented to reduce idiosyncrasies and biases in behavior (e.g., Hintze et al., 2018), few studies have verified that LTIs are sensitive to fluctuations in motivation, let alone analyze LTIs to qualify obtained effects. An effect on cognition would manifest in post-initiating-response performance; an effect on motivation would manifest in LTIs. For example, in the present dissertation, whereas LTIs were sensitive to both pre-feeding (largest $ln\text{BF}_{io}$ = 17.45) and to reductions in reinforcement rate (interval length; largest $ln\text{BF}_{io}$ = 10.01), LTS medians were substantially more sensitive to interval length (average $ln\text{BF}_{io}$ = 43.28) than to pre-feeding (Figure 3.7, EI $ln\text{BF}_{io}$ = 4.039; SL-RI $ln\text{BF}_{io}$ = 3.247; NP-RI $ln\text{BF}_{io}$ = 0.523). This indicates that, although fluctuations in time and motivation appear

to affect both timing and motivation, LTIs are substantially more sensitive to motivation and LTSs are substantially more sensitive to time.

Second, the relationship between discriminability of initiating-responses and degree of dissociation of interval timing and motivation suggests that, consistent with Mechner's revealed-operant procedure (e.g., Mechner, 1994), initiating-responses must be identifiably different from other procedure-relevant responses. In the present dissertation, only discriminability of initiating-responses from target responses was investigated. It is worth highlighting that the most discriminable initiating-response, NP-RI, was not confounded with any other responses. Recent implementations of RI procedures have used head-entries into the reinforcement receptacle to initiate trials (e.g., Chow, Smith, Wilson, Zentall, & Beckmann, 2017; Hurtubise, Marks, Davies, Catton, Baker, & Howland, 2017; Liu, Wilkinson, & Robbins, 2017). Associating head-entries into the reinforcement receptacle with both trial initiation and reinforcer receipt likely limits the hypothesized benefits of initiating-responses. Such conflicting associations may result in premature trial initiation, or an insensitivity of initiating-responses to fluctuations in motivation. Consistent with this line of reasoning, SL-RI was insensitive to fluctuations in motivation when initiating-responses were emitted on a lever that signaled both trial activation and imminent reinforcement (experiment 1, Chapter 2, Figure 2.3). Thus, to obtain accurate and independent estimates of motivation, initiating-responses should ideally *not* be confounded with other procedure relevant responses, such as reinforcer receipt.

These implications suggest that RI procedures with highly discriminable initiating-responses are necessary for research in which cognition and motivation need to be disentangled. For example, it has been notoriously difficult for researchers to find

behavioral and psychopharmacological therapeutics for the treatment of positive, cognitive, and negative symptoms in individuals diagnosed with schizophrenia (for a review see Aleman, et al. 2017; Downs et al. 2018). For example, antipsychotics attenuate positive and rescue cognitive symptoms via antagonism of D2 dopamine receptors but fail to rescue negative symptoms such as amotivation (Keefe et al. 2007; Krause et al. 2018). This failure may be partially attributable to procedures not providing accurate within-subject and within-procedure indices of motivation and cognition. RI procedures provide such indices and thus would characterize how well novel therapeutics rescue both motivation and cognition while simultaneously reducing the time needed to complete such assessments.

Similarly, RI procedures with highly discriminable initiating-responses may overcome difficulties inherent to testing and developing therapeutics for addiction. Typically, drug self-administration procedures program drug infusion contingent upon responses on an active lever and nothing on an inactive lever; responses on the active lever measure the strength of drug-response associations and responses on the inactive lever measure overall arousal, which is modulated by motivation (Killeen, 1995). However, this procedure does not adequately dissociate the strength of drug associations from motivation for the drug. Previous work indicates that psychostimulants, such as nicotine, increase arousal and motivation for nicotine despite not altering responding on the inactive lever (e.g., Barrett & Bevins, 2013). RI procedures would overcome this limitation by training subjects to activate the active lever via an initiating-response. Whereas changes in responding on the active lever would index the strength of drug-response associations, changes in LTIs would provide an index of motivation for the drug. This index of motivation may also reflect drug craving, which is notoriously difficult to define and model in non-human animals (for reviews see Ahmed, 2010;

Arnold & Roberts, 1997; Drummond, Litten, Lowman, & Hunt, 2000; Katz & Higgins, 2003). Specifically, as with motivation, high craving would be indicated by shorter LTIs and low craving would be indicated by longer LTIs. Importantly, recent research suggests that rats can be trained in relatively complex RI self-administration procedures without noticeable schedule strain (Singer, Fadanelli, Kawa, & Robinson, 2017).

RI procedures with highly discriminable initiating-responses may also be useful in studies leveraging smartphones to increase ecological validity and avoid demand effects common to human studies conducted in laboratories (Bless, Westerhausen, Kompus, Gudmudsen, & Hugdahl, 2014; Dufau et al., 2011; Rutledge, Skandali, Dayan, & Dolan, 2014). A typical study conducted via smartphone alerts subjects on a regular basis to participate in the study. Subjects are alerted via a message on their phone that once tapped with a finger begins the cognitive assessment. In this seminatural experimental setup, the time it takes an individual to start a cognitive assessment is an important variable. Individual differences in the time it takes subjects to start participating may be of theoretical interest, providing an index of motivation that informs observed cognitive performance. When collected simultaneously with other data, including but not limited to daily schedules and stressors, LTIs may provide an opportunity to relate how daily life interferes with cognition. Alternatively, the time it takes subjects to start participating may provide a proxy by which to filter or slice data. Subjects who start the cognitive assessment too fast or too slow may show interesting and informative patterns in their cognitive performance compared to those waiting an average amount of time to start the cognitive assessment.

Limitations and Future Directions

Despite the implications of the present dissertation for research on the relationship between cognition and motivation, there are a few potential limitations. For example, it is possible that some of the obtained effects in the present dissertation are an artifact of the concomitant pre-feeding-induced reduction in the number of completed trials. Rats completed fewer trials in 1 h than in 24 h pre-feeding, and the number of trials completed scaled such that EI > SL-RI > NP-RI in both baseline and pre-feeding. This suggests that LTS variability should have been greater in 1 h than 24 h pre-feeding and scale such that NP-RI > SL-RI > EI. However, it is important to highlight that there was little evidence that LTS variability differed between feeding durations, and LTS variability in NP-RI was similar to or less than LTS variability in SL-RI or EI. Additionally, in other RI procedures such as FMI, IRT variability but not mean IRT was sensitive to pre-feeding even when the number of obtained reinforcers was held approximately constant (e.g., Watterson et al., 2015). Thus, though it is possible, it seems unlikely that the effects of pre-feeding are merely explained by a pre-feeding-induced reduction in the number of completed trials.

The pre-feeding-induced reduction in the number of completed trials, however, may explain some of the difficulties in analyzing temporal bisection performance. Pre-feeding effects on the mean LTS were unreliable, dependent on which rats were included in analyses. In the temporal bisection procedure, latent LTSs are inferred by fitting a psychophysical function to trial-by-trial data informing a limited number of potential LTS lengths (Table 4.1). In contrast, in the switch-timing procedures overt LTSs are observed in every Long FI trial and can be of any length. Whereas in the temporal bisection procedure the distribution of responses may change substantially following a

reduction in sample size, in the switch-timing procedure the shape of the distribution may still be intact following a reduction in sample size. The substantial pre-feeding-induced reduction in the number of completed trials is thus more detrimental for temporal bisection than switch-timing procedures. Indeed, pre-feeding reduced the number of trials comprising each potential LTS from around 20-30 to 5-15 trials and in extreme cases resulted in a complete flattening of the psychophysical function. Because MLE only relies upon the data of each subject to inform parameter estimates, it is highly sensitive to changes in sample size (e.g., Anderson & Gerbing, 1984; Cheung et al., 2012), resulting in extreme, outlier estimates as sample size decreases. Although steps were taken to limit the influence of outlier parameter estimates (i.e., Grubb's test and Bayesian *t*-tests and ANOVAs), MLE parameter estimation likely contributed to the unreliability of pre-feeding effects on the mean LTS in the temporal bisection procedure.

Another limitation of the present dissertation is that it only investigated pre-feeding-induced reductions in motivation. Motivation can be manipulated via many routes, including but not limited to the magnitude of reinforcement, administration of dopaminergic agonists and antagonists, and pairing reinforcers with lithium chloride. Increasing the magnitude of reinforcement on the Long FI appears to result in shorter and more varied LTSs (e.g., Daniels et al., 2015b). Administration of dopaminergic agonists such as methamphetamine appears to yield short and less varied mean LTSs in the temporal bisection procedure (Cheng, Etchegaray, & Meck, 2007; Maricq & Church, 1983). Pairing reinforcers with lithium chloride appear to result in longer peak-times in the peak procedure (Galtress & Kirkpatrick, 2009; cf. Delamater et al., 2014, 2018). The degree to which these changes in performance reflect alterations in interval timing and motivation is currently unclear. Future research may systematically investigate the

degree to which different manipulations of motivation differentially affect LTIs and performance indices.

Additionally, the present dissertation only focused on maintenance of EI, SL-RI, and NP-RI interval timing. As such, there is at least one untested prediction of the discriminative RI hypothesis. As initiating-responses become progressively discriminable from target responses, *acquisition* of target responses is increasingly facilitated. Such facilitation is expected to occur for the same reason RI enhances temporal control of target responses: dissociation of post-food focal search and general search, enhancing time-marker and general search synchronization. Experiment 1 does not provide an adequate test of this hypothesis because SL-RI and EI were differentially signaled by lever insertion and a dark operant chamber, respectively. SL-RI also promotes starting on the Short FI, which is consistent with the optimal behavioral sequence of starting and remaining on the Short FI until reinforcement is not forthcoming and then switching to the Long FI. Any effect of SL-RI on acquisition of target responses thus could be attributable to differential signaling of initiation types between groups or confounding of SL-RI with the optimal behavioral sequence. Experiments 2 and 3 also do not adequately test the acquisition hypothesis because subjects were reinforced for the same behavioral sequence across all initiation types, which were presented within-session for each subject. Given the sensitivity of behavior to training and order effects (e.g., Freeman & Lattal, 1992; Pattij, Broersen, Peter, & Olivier, 2004; Tatham & Wanchisen, 1998), stringent reinforcement contingencies and intermixing initiation types within-subject likely has different effects on acquisition of target responses compared to training single initiation types and loose reinforcement contingencies between-subject.

Conclusion

Nonetheless, the present dissertation provides some evidence in support of the discriminative RI hypothesis, indicating that interval timing and motivation are partially dissociable. Pre-feeding appears to affect the post-food focal search and general search modes of the predatory subsystem entrained by interval timing procedures. As initiating-responses become more discriminable from target responses, RI increasingly dissociates post-food focal search from general search modes. As such, training subjects to initiate their own trials enhances temporal control and largely circumscribes the effect of pre-feeding to the latency to trial initiation, leaving mean post-initiation performance relatively intact. Consistent with the notion of a partial dissociation, fitting a gamma-exponential mixture model to LTSs revealed that pre-feeding affects both timing and non-timing processes. However, the sensitivity of these processes to pre-feeding depends on whether subjects initiate their own trials. These data have potentially important implications for the study of cognition and motivation; specifically, it suggests that subjects should be trained to self-pace experiments via highly discriminable initiating-responses to ensure that fluctuations in motivation can be measured independently of cognitive performance. Thus, to quote Richard Feynman:

> "Maybe it is just as well if we face the fact that time [cognition] is one of the things we probably cannot define… What really matters anyways is not how we define time [cognition], but how we measure it."

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