Journal of Theoretical Biology 438 (2018) 133–142

Contents lists available at ScienceDirect

Journal of Theoretical Biology

journal homepage: www.elsevier.com/locate/jtbi

Scalar timing in memory: A temporal map in the hippocampus

Sorinel A. Oprisan[a,*], Tristan Aft[a], Mona Buhusi[b], Catalin V. Buhusi[b]

[a] Department of Physics and Astronomy, College of Charleston, 66 George Street, Charleston, SC 29624, U.S.A
[b] Interdisciplinary Program in Neuroscience, Department of Psychology, Utah State University, Logan UT, U.S.A

ARTICLE INFO

Article history:
Received 19 June 2017
Revised 19 October 2017
Accepted 15 November 2017
Available online 16 November 2017

Keywords:
Memory
Topological map
Interval timing

ABSTRACT

Many essential tasks, such as decision making, rate calculation and planning, require accurate timing in the second to minute range. This process, known as interval timing, involves many cortical areas such as the prefrontal cortex, the striatum, and the hippocampus. Although the neurobiological origin and the mechanisms of interval timing are largely unknown, we have developed increasingly accurate mathematical and computational models that can mimic some properties of time perception. The accepted paradigm of temporal durations storage is that the objective elapsed time from the short-term memory is transferred to the reference memory using a multiplicative "memory translation constant" K^*. It is believed that K^* has a Gaussian distribution due to trial-related variabilities. To understand K^* genesis, we hypothesized that the storage of temporal memories follows a topological map in the hippocampus, with longer durations stored towards dorsal hippocampus and shorter durations stored toward ventral hippocampus. We found that selective removal of memory cells in this topological map model shifts the peak-response time in a manner consistent with the current experimental data on the effect of hippocampal lesions on time perception. This opens new avenues for experimental testing of our topological map hypothesis. We found numerically that the relative shift is determined both by the lesion size and its location and we suggested a theoretical estimate for the memory translation constant K^*.

1. Introduction

The perception and use of durations in the supra-second range (interval timing) is essential for survival and adaptation, and is critical for fundamental cognitive processes like decision making, rate calculation, and planning of actions (Gallistel, 1990). In the vast majority of species, protocols, and manipulations to date, interval timing is time-scale invariant: time-estimation errors increase linearly with the estimated duration (Buhusi and Meck, 2005; Buhusi et al., 2016; Gibbon, 1977; Gibbon et al., 1984; Mauk and Buonomano, 2004) (Fig. 1). Time-scale invariance is ubiquitous in many species (Buhusi and Meck, 2005; Gallistel, 1990) from invertebrates to fish, birds, and mammals, such as mice (Buhusi et al., 2009), rats (Matell et al., 2004), and humans (Rakitin et al., 1998). Scale invariance is the fundamental property of interval timing, as it is extremely stable over behavioral (Fig. 1), lesion (Meck et al., 1987), pharmacological (Buhusi and Meck, 2002; 2010; Oprisan and Buhusi, 2011), and neurophysiological manipulations (Meck and Malapani, 2004; Oprisan et al., 2014).

One of the most influential theoretical explanation for time perception has been the Scalar Expectancy Theory (SET) (Gibbon, 1977) further augmented with the information-processing theory in the seminal work of Church (1984), Gibbon and Church (1984), and Gibbon et al. (1984). Without further detailing the SET framework, we only mention its key elements: a clock process consisting of a pacemaker and an accumulator, a memory process consisting of short-term and reference memory stores, and a comparator process where decisions are made that lead to behavioral output (Church, 1984; Gibbon, 1977; Gibbon and Church, 1984; Gibbon et al., 1984). The reference memory in SET theory serves two important purposes: (1) provides a temporal reference by storing "important" times, such as the reinforcement time, and (2) holds the key for the observed scalar property of timing, i.e. the standard deviation is proportional to the mean estimated time (Jones and Wearden, 2003).

In SET theory, a multiplicative transformation, the famous "memory translation constant" K^*, was introduced to mediate between the short-term (working) and long-term (reference) memory (Church, 1984; Gibbon and Church, 1984; Gibbon et al., 1984; Meck, 1983). In other words, the difference between the actual duration (clock reading) and the encoded duration stored in the reference memory is determined by the memory transla-

* Corresponding author.
E-mail address: oprisans@cofc.edu (S.A. Oprisan).

https://doi.org/10.1016/j.jtbi.2017.11.012

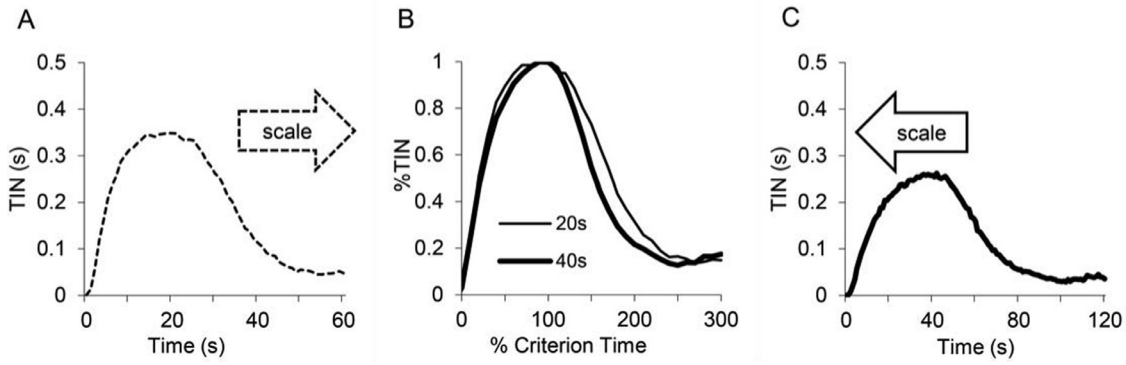

Fig. 1. Time-scale invariant interval timing. The time-in-nosepoke (TIN) curves for mice timing a 20 s interval (A) or 40second interval (C) overlap when normalized by the maximum TIN (vertical axis), and respectively, by the criterion time (horizontal axis); redrawn from (Buhusi et al., 2009).

tion constant K* (see Allman et al., 2014 for a detailed review of the SET developed by Gibbon (1977)). It is assumed that the pacemaker/accumulator system faithfully represent the objective elapsed time in terms of the number of pacemaker pulses. At the time the content of the accumulator, i.e. the short-term memory, is transferred to the reference memory its content is multiplied by a "memory translation constant" K^*. K^* is not really a constant but was rather assumed to have a Gaussian distribution, presumably produced because of the accumulation of a large number of presentations of reinforcers (Church, 1984; Gibbon and Church, 1984; Gibbon et al., 1984; Jones and Wearden, 2003). Arguably the two most influential theoretical studies that attempted a mathematical perspective on how the Gaussian K^* produced individual trial responses are Gibbon et al. (1988) and Brunner et al. (1997). In this study, we further investigated the nature of the "memory translation constant" K^* starting from two assumptions: (1) a Gaussian representation of the reinforcement time in the reference memory (see Brunner et al., 1997; Church, 1984; Gibbon and Church, 1984; Gibbon et al., 1988, 1984), and (2) possible peak-interval shifts correlated with the spatial location of hippocampus lesions (see Yin and Meck, 2014; Tam and Bonardi, 2012a,b; Tam et al., 2013, 2015). To bridge the above two paradigms, we suggested here a mathematical model of a topological organization of hippocampus and numerically investigated the effect of lesions in such a model.

Hippocampal lesions and interval timing. Hippocampal lesions have been shown to affect peak time in peak-interval procedures and the subjective equivalence points in temporal bisection procedures (Balci et al., 2009; Meck et al., 1987, 1984; Melgire et al., 2005). Rats with hippocampal damage responded earlier than the scheduled time of reinforcement in a variety of peak-interval procedures (Meck et al., 2013, 1984). Hippocampal lesions also disrupted responses in differential reinforcement of low rates (DRL) schedules. In DRL, rats are trained to withhold responding for food until after a set time has elapsed (e.g. more than 15 s). Rats with dorsal, ventral, or complete hippocampal lesions are highly inefficient at this task because they significantly diminish rats' ablility to wait for the set temporal interval to elapse (Bannerman et al., 1999). Consequently, it has been suggested that the hippocampus plays an important role in temporal memory and/or inhibitory processes (Yin and Troger, 2011).

Importantly, both pre-training and post-training dorsal hippocampal (DH) lesions produced leftward shifts in peak times, confirming previous investigations and suggesting a possible role for the DH in the cortical striatal-based timing mechanisms (Balci et al., 2009; Meck et al., 2013, 1984; Merchant et al., 2013; Tam et al., 2013, 2015). In contrast, ventral hippocampal (VH) lesions produced a temporary rightward shift of peak times (Yin and Meck, 2014). Moreover, when peak times and peak rates were modulated by reversal learning, pre-DH lesions appear to have dramatic effects on the adaptability of temporal associations, whereas VH lesions only affect the response levels. These data suggest that the DH is more closely related to the core timing mechanisms involved in duration encoding (Coull et al., 2011; Matell and Meck, 2004; Meck, 2002; Meck and Malapani, 2002; Merchant et al., 2013) and the VH is more closely related to motivation and context-dependent modulation of timing performance (Drew et al., 2007; Meck, 2006). In a series of experiments investigating the relationship between the DH lesions and peak-interval response, significant leftward (earlier) maximal responses were found when compared to sham-lesioned subjects (Tam et al., 2015). Apart from the order of the surgery with respect to animals' acquired instrumental responses, i.e. surgery first in (Tam and Bonardi, 2012a,b; Tam et al., 2013, 2015) and surgery last in (Yin and Meck, 2014), all studied found that DH lesions produced a leftward shift in peak time. The above brief summary of some experimental results on hippocampus lesions led us to formulating a novel theoretical hypothesis of a topological map of temporal memories stored in the hippocampus.

This paper advances the hypothesis that the long-term storage of temporal memories follows a topological map in the hippocampus, with longer durations stored towards dorsal hippocampus and shorter durations stored toward ventral hippocampus. The hypothesis was evaluated in the framework of two leading models of interval timing: SBF and SBF-ML. The predictions of this hypothesis match current experimental data on the effect of hippocampal lesions on time perception, and open new avenues for further experimental testing.

2. A new hypothesis: A topological temporal map in the hippocampus

2.1. Assumptions: Topological maps in the brain

To mimic the experimentally-observed variability of the memorized criterion time T, we randomly generated a wide range of values around the desired criterion time T using a specified distribution. As an example, in Fig. 2 we generated a Gaussian (normal) distributed criteria around $T = 10$ s (see Brunner et al., 1997; Church, 1984; Gibbon and Church, 1984; Gibbon et al., 1988; 1984). As lesion studies suggested (Yin and Meck, 2014; Tam and Bonardi, 2012a,b; Tam et al., 2013, 2015), we modeled the hippocampus (see Fig. 2A) storage as a spatially distributed map of the Gaussian representation of the reinforcement time values.

Based on the selected memory distribution (see Fig. 2B), different memory cells hold slightly different values of the criterion time in a topologically ordered map. For example, based on Fig. 2B, the relative frequency of memory allocation for $T = 10$ s is maxi-