



# Possible functions of prefrontal cortical neurons in duration discrimination

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The physical duration of a stimulus can be held invariant in different sensory modalities, such as vision and audition. The prefrontal cortex (PFC) is a region for convergence of inputs that originate in distinct sensory areas, and is considered an area of cross-modal association (Fuster et al., 2000). Assuming that the PFC participates in duration discrimination, such cross-modal integration appears crucial in support of an “amodal” clock used to time intervals in the seconds-to-minutes range (Meck and Church, 1982; Cordes et al., 2007). Indeed, brain-imaging studies have demonstrated that the PFC contributes to duration discrimination (for a review, see Meck et al., 2008). However, the actual roles of PFC neurons remain unclear. Although single-unit recording is effective in terms of elucidating the functional roles of each area, only a few investigations have been made of PFC neurons in interval-timing tasks in primates (for a rodent homolog of the role of PFC neurons in timing see Matell et al., 2003, 2011). Here, we review recent results of single-unit recording from monkey PFC neurons, discuss their possible functions, and then comment on future directions.

We recorded single-unit activity while monkeys were performing a duration discrimination task in a series of studies (Oshio et al., 2006, 2008). In the task, red and blue cues were presented consecutively on a computer monitor for different durations ranging from 0.2 to 2.0 s, and the monkeys were then required to choose which color cue had lasted longer. Each cue was followed by a delay period of 1.0 s. The first cue, first delay, second cue, and second delay are referred to as C1, D1, C2 and D2, respectively. First, we found that PFC neurons showed significantly different activity during either the D1 or D2 period when comparing activity in C1-longer (LS) and C2-longer (SL) trials (Oshio et al., 2006). As for the D1 activity, the result indicates that the PFC neurons responded as if they

encoded the duration category (e.g., “long” or “short”) of the C1 cue as early as the D1 period. Taken together with the correlated D2 activity, our findings suggest that PFC neurons not only encode duration category, but also implement strategic processes such as the representation of trial type (LS or SL) and the retention of cue information. Next, we analyzed neurons that were responsive during the C1 period, and found that phasic (transient) activity was the most common mode of activity (Oshio et al., 2008). Peak time of this phasic activity was broadly distributed with a delay of approximately 0.8 s after cue onset. Such phasic activity following a constant delay after cue onset might serve as a mechanism to filter or separate the current trial’s cue duration from the peak time in activity. The most frequent peak time was close to the time separating cue durations into “long” and “short” categories. As a consequence, the activity of this peak time might have played a role in filtering or selecting the appropriate response for the duration discrimination. Outputs of this temporal filtering, as a function of the phasic activity, would have been represented as the categorical response in the D1 period. Recently, two other research groups have successfully recorded single-unit activity in the monkey PFC during an interval-timing task, and found neuronal activities with various temporal profiles, including phasic, tonic, ramping, and so on, during cue and/or delay periods. As a consequence, it was proposed that PFC neurons may play a variety of roles in temporal processing, including the monitoring of cue duration and memory encoding (Sakurai et al., 2004; Genovesio et al., 2009 – see also Matell et al., 2011).

There is considerable agreement among the above-mentioned studies that PFC neurons represent the absolute cue duration as well as other types of temporal information during ensuing delay periods. Scalar timing theory postulates three stages of

temporal processes in duration discrimination: clock, memory, and comparison (Gibbon et al., 1984). The reported delay period activity suggests that PFC neurons contribute to the memory stage. This is reasonable, because PFC activity is well-known to support working memory function (e.g., Miller et al., 1996). Slight differences in PFC activity across various experiments have been attributed to differences in behavioral tasks, i.e., differences in the strategy that monkeys use to solve the task, etc. This also seems reasonable given that the PFC is considered to also serve strategic function. Moreover, subjects may actually adopt different strategies based on the nature of the timing task. The exact strategies taken by subjects can be inferred from behavioral data to some extent, but neuronal data may be more informative in this case and should be taken into consideration when analyzing the behavioral data.

There is controversy over whether the internal clock is modality-specific or modality-independent and centralized or distributed (see Buhusi and Meck, 2005; Buetti and Walsh, 2009). The PFC, an area of cross-modal association, is a candidate for a centralized, amodal timing mechanism. Experiments with timing tasks using unimodal and bimodal sensory stimuli, including vision and audition, should be carried out to clarify whether the PFC serves as a centralized clock or not. In addition, neuroimaging studies have revealed that other brain areas also participate in timing tasks, for example, the basal ganglia, the parietal cortex, the cerebellum, and the supplementary motor area (Buhusi and Meck, 2005). However, the contributions of these areas to duration discrimination are much less understood than the PFC. The PFC has anatomical connections with all of these areas, and is known to cooperate with those areas in cognitive and motor functions (Fuster, 2008). Therefore, further elucidation of the roles of the PFC would be helpful to uncover

their contributions to timing and time perception. In summary, the PFC is a key area to determine the functional and neural mechanisms of interval timing. More extensive research on the properties of PFC neurons is required in order to construct and test neurophysiological models of interval timing (see Matell and Meck, 2004; Lustig et al., 2005; Karmarkar and Buonomano, 2007).

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