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Journal Club

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Readiness Potential and Neuronal Determinism: New Insights on Libet Experiment

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Review of Emmons et al.

"*Philosophy may in no way interfere with the actual use of language; it can in the end only describe it . . . it leaves everything as it is.*" — L. Wittgenstein.

Am I writing this piece because I am consciously willing or am I just the vehicle of inevitable natural forces and laws that, given my current context as well as biological and social backgrounds, compel me unconsciously to write down this essay? For centuries, such questions have occupied theologians, philosophers, and scientists alike. In the early 1980s, the neurologist Benjamin Libet performed landmark experiments aimed at investigating the role of consciousness in the generation of a motor action (Libet et al., 1983). Libet et al. (1983) measured the time when subjects became consciously aware of the decision to move. Using a clock with a rapidly rotating dot, the subjects were asked to note the position of the moving dot when he/she was aware of the conscious decision to move a finger (Fig. 1). Scalp EEG was used simultaneously to monitor brain activity during the experiment. Libet et al. (1983) found a premovement buildup of electrical potential called readiness potential (RP) starting ∼550 ms before the movement. Unexpectedly, the conscious awareness of the decision or "the urge to move" emerged only 200 ms before movement, leaving therefore a time lag of ∼350 ms between the initial rising of the RP and the conscious awareness of the decision to flex (Fig. 1). Libet et al. (1983) interpreted the early rise in the RP as a reflexion of neuronal computation that unconsciously prepare for the voluntary action. The conscious will emerging at ∼−200 ms could either allow or block the volitional process to go to completion, resulting, respectively, in the execution or withholding of the motor act (Libet et al., 1983). Therefore, according to Libet et al. (1983), our brain unconsciously plans our behavior but allows for a conscious "veto" to alter the outcome of our volition. The findings of Libet et al. (1983) have had an unrivalled influence on the prevailing view that both our conscious will and subsequent actions are caused by prior neural activity. Recent studies, however, have falsified the causal assumption behind the RP and fine-tuned the notion and the possibility of a volitional "veto."

Two questions directly linked to the conclusions of Libet et al. (1983) are central in understanding the relationship between the RP and the conscious agency of our actions. First, what kind of information does RP neurally encode? And second, is the RP causally linked with the behavioral outcome? Within the context of the experiment by Libet et al. (1983), the main limitation in understanding the meaning of RP is the concomitant modulation of several factors during the execution of the action. These include action preparation, general anticipation of the occurrence of an action, variable waiting time intervals between the onset and the end of the experiment, choice of whether and when to move, and the impulsive urge to move (Mele, 2017). All these factors could be potentially reflected in the RP. In a recent study published in *The Journal of Neuroscience*, Emmons et al. (2017) conducted elegant behavioral and electrophysiological experiments to show that the potential underlying neuronal correlates of the RP encode the temporal component of action control.

Although the RP described by Libet et al. (1983) was recorded at the level of the EEG, the results were replicated at the single-neuron level in human MFC (Fried et al. 2011). At the single-cell level, RP reflects an average signal from two populations of neurons with increasing and decreasing patterns of neuronal firing (Fried et al., 2011). Given the functional homol-

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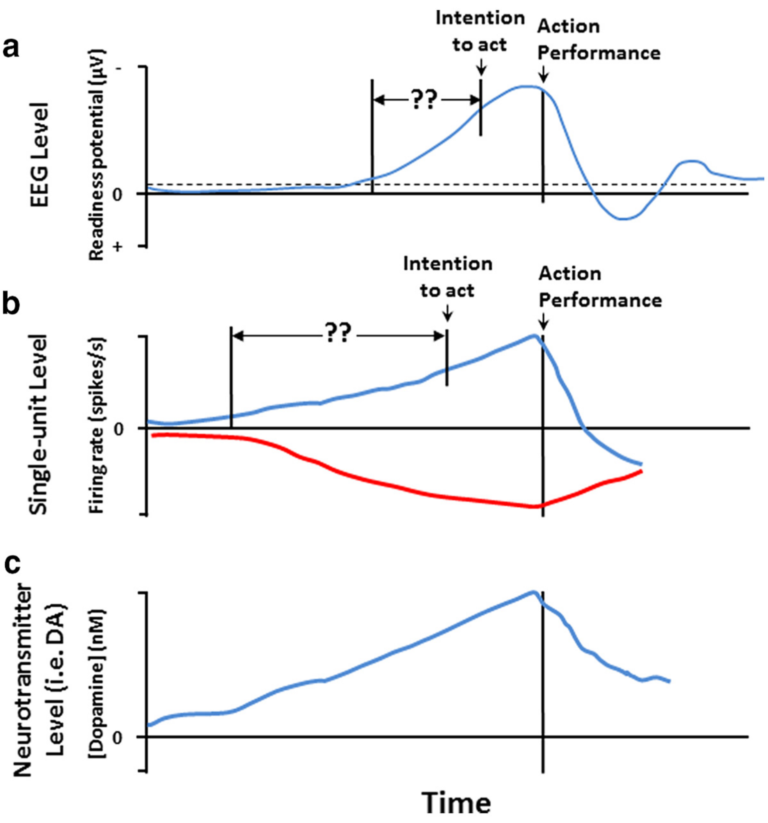

Figure 1. Neuronal basis of RP. Because premovement building of the RP both at the EEG (***a***) (Libet et al., 1983) and single-unit (***b***) (Fried et al., 2011) levels precedes the emergence of the intention to act, it was originally considered to reflect causal and subconscious neuronal preparation of the action. Emmons et al. (2017) suggested that such ramping activity encodes time intervals. Recent studies have revealed dopamine as a potential neuromodulatory system mediating the encoding of time intervals as well as action-related cognitive processes through similar ramping patterns of activity (***c***) (Soares et al., 2016; Howard et al., 2017; Kim et al., 2017).

ogy of the frontal cortex between humans and rodents (Barthas and Kwan, 2017), Emmons et al. (2017) recorded single-cell activity from MFC of rats engaged in a behavioral task involving computation of interval timing (Emmons et al., 2017, their Fig. 2). Rats were trained to press a lever either 3 or 12 s after the onset of an instructional cue in exchange for a reward. Like the up and down ramping patterns of neuronal activity described in human MFC (Fried et al., 2011), Emmons et al. (2017) found two populations of neurons with, respectively, increasing and decreasing neuronal firing rates across time (Emmons et al., 2017, their Fig. 3). Importantly, the authors showed that the ramping of neuronal activity followed similar patterns during trials with 3 and 12 s waiting intervals, but the ramping scaled differently to represent elapsed time (Emmons et al., 2017, their Figs. 3, 7). These results demonstrate that the premovement ramping of neuronal activity in the MFC encodes temporal processing during the execution of a behavioral action. To further confirm this conclusion, Emmons et al. (2017) used a naive Bayesian model to predict time from firing rates of ramping neurons (Emmons et al., 2017, their Fig. 8). Emmons et al. (2017) found that the pattern of neuronal activity in the MFC predicted time of waiting intervals with a high degree of accuracy (Emmons et al., 2017, their Fig. 8). These results explain why Fried et al. (2011) found that the ramping rate in MFC was better able to predict the timing of a voluntary decision to move relative to the decision to move alone (98% vs 80%, respectively). Together, these results provide evidence that premovement ramping activity is a key neuronal signal for processing temporal information within the MFC.

In line with other studies showing the involvement of several cortical and subcortical structures in tracking time intervals (Bhattacharjee, 2006), Emmons et al. (2017) found that neurons in the dorsomedial striatum also encode waiting time intervals through up and down ramping activity (Emmons et al., 2017). What could be the common underlying neuromodulatory system behind the time-related modulation of neuronal activity in these areas? Both MFC and dorsomedial striatum are densely innervated by midbrain dopaminergic neurons, and three recent studies have directly implicated DA in the control of judgment and estimation of time (Soares et al., 2016; Howard et al., 2017; Kim et al., 2017). Soares et al. (2016) measured and manipulated DA neurons in mice trained, as in the Emmons et al. (2017) study, to perform a behavioral task in which they have to estimate the duration of time intervals. In addition to showing that DA neurons encode information about trial-to-trial variability in time estimates, the authors found that pharmacogenetics and optogenetic manipulation of DA neurons were sufficient to slow down or speed up time estimation (Soares et al., 2016). Conversely, depletion of DA in the MFC has been shown to impair temporal control of action (Kim et al., 2017). Interestingly, optogenetic stimulation of pyramidal neurons expressing Type 1 DA receptors compensates for interval timing deficits by normalizing the ramping patterns of neuronal activity in the MFC (Kim et al., 2017). These results corroborate and extend the last experiment performed by Emmons et al. (2017) showing the critical role of MFC in encoding and conveying temporal information to striatal neurons (Emmons et al., 2017, their Fig. 11). In the third study implicating dopamine in time estimation, Howard et al. (2017) used an operant behavioral task in which mice were trained to track time intervals (2 or 8 s and 4 or 16 s) and found that both activity of DA neurons and DA concentration in the dorsal striatum displayed increasing and decreasing ramping patterns that scaled with interval duration. In this study, however, DA signaling did not simply reflect timing or even reward prediction or value alone. Rather, changes in the pattern of DA were associated with internal processes of choice and action selection (Howard et al., 2017). Collectively, all these studies point to the ramping DA signal (Howe et al., 2013) as a potential neuromodulatory system underlying the encoding of interval timing estimation and cognitive processes of action selection by MFC.

What kind of action-related cognitive processes are encoded in the ramping neuronal activity of the MFC? This question brings us back to the question of causality between RP and the behavioral outcome. Originally, Libet et al. (1983) interpreted the RP as representing the brain decision “to initiate or, at least, prepare to initiate the act at a time before there is any reportable subjective awareness that such a decision has taken place." According to this model, once the ramping activity in the frontal cortex reaches a threshold, the motor command is inevitably executed (Libet et al., 1983; Fried et al., 2011). Using slightly modified versions of Libet et al. (1983) experiment, two recent studies have challenged this interpretation (Alexander et al., 2016; Schultze-Kraft et al., 2016). The first demonstrated that humans can still cancel the initiation of a movement, even after the onset of the RP up to a point of no return ~200 ms before movement onset. Importantly however, it was found that, even after the onset of the movement, it is still possible to alter and abort the movement as it unfolds (Schultze-Kraft et al., 2016). Alexander et al. (2016) revealed that robust RPs occur, even in the absence of movement. Together, these two studies demonstrate that premovement RP is not sufficient for the enactment of a motor action. Therefore, the RP must encode processes other than motor-action preparation. Results from Emmons et al. (2017) suggest that such ramping activity encodes self-monitored time intervals. This hypothesis is particularly pertinent given that self-monitoring of the passing of time by the experimental subjects is intrinsic to the Libet et al. (1983) experiment. Alternatively, although not mutually exclusive, RP might reflect general anticipation (i.e., the conscious experience that an event will soon occur) (Alexander et al., 2016) or simply background neuronal noise (Schurger et al., 2016). Future studies are needed to test these alternatives.

Although the philosophical implications of these results are open for debate, neural determinism defined as the mediation of all mental states by brain processes is the inevitable paradigm, even if we assume the centrality of conscious awareness in action control. This view, however, remains compatible with both physicalism (i.e., all mental states are caused by brains) and interactionism (i.e., brain and mind, while distinct and independent, exert causal effects on one another). This makes the philosophical debate about free will and determinism in a state of underdetermination by current neuroscientific findings. Consequently, and referring to the quotation that started this essay, we might conclude by saying that: *Neuroscience may in no way interfere with our first-person experience of the will, it can in the end only describe it . . . it leaves everything as it is.*

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