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LETTER TO THE EDITOR

An opinion on the 'delayed spikes' in human motoneurons

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Abstract

This is a note challenging the claim by Kudina and Andreeva's recent publication in Experimental Brain Research. In that publication, Kudina and Andreeva (Exp Brain Res 239:719–730, 2021) put forward a new idea about discovering two spiking modes in human motoneurons. We suggest that what they have shown in their publication maybe is the motor unit firing indicating the end of a net synaptic potential. We reason this challenge from our previous publication in the same journal. In that publication, we have shown that the "second spiking mode" after the H-reflex was a return to the regular prestimulus discharge rate.

Kudina and Andreeva (2021) recently published a paper in Experimental Brain Research claiming that they have discovered two spiking modes in firing human motoneurones. They showed delayed motor unit discharges following the H-reflex in three human muscles, including the tibialis anterior (TA) muscle. We suggest that at least for the TA muscle, they may be looking at the motor unit spikes indicating the end of a net Excitatory Postsynaptic Potential (EPSP) generated by the low threshold stimulation of the common peroneal nerve. We reason this claim from our previous publication in the same journal (Prasartwuth et al. 2008).

In our earlier paper (Prasartwuth et al. 2008), we have shown that low-threshold electrical stimulation of the common peroneal nerve induces a response that can be illustrated using the peristimulus frequencygram (PSF) methodology (Fig. 1). Our publication used both the peristimulus time histogram (PSTH) and the PSF methods to analyze the responses of motor units to electrical stimulation. Our results indicated that the stimulus generated an H-reflex response, which only reflected the rising phase of a net EPSP. Following the short-lasting rising phase of the net EPSP, a period with a low number of discharges was observed (previously referred to as the silent period). As the discharge rates of these spikes were higher than the prestimulus background discharge rate, we thought that this period represented the falling phase of the net EPSP generated by the stimulation. We reason this proposal from our rat brain slice experiments where we injected known currents into regularly discharging motoneurons and analyzed the output using both PSTH and PSF (Türker and Powers 1999, 2005; Fig. 2).

We have also proposed a method for explaining the reason behind the low number of spikes during a falling phase of a net EPSP earlier (Fig. 3).

When the net EPSP finally ended, the firing briefly returned to normal (similar number of spikes to the average prestimulus background discharge level). This brief period resembles the 'peak' that the paper by Kudina et al. claims to have discovered the delayed 'D' excitatory response. However, in our experiments, at least for the TA motor units, this was not an excitatory period as the discharge rates were the same as the prestimulus discharge rate.

The PSF approach also indicated that the brief period of regular firing was followed by a long-lasting inhibitory period. This inhibitory period is likely to originate from the contraction of the TA muscle during the direct motor (M) and H-reflex responses, triggering a combination of net inhibitory postsynaptic potential (IPSP) events, including the tendon organ inhibition and the Renshaw inhibition (Binboga et al. 2011). The PSF illustrates that this inhibitory period lasts much longer than the inhibitory period indicated in the PSTH record.

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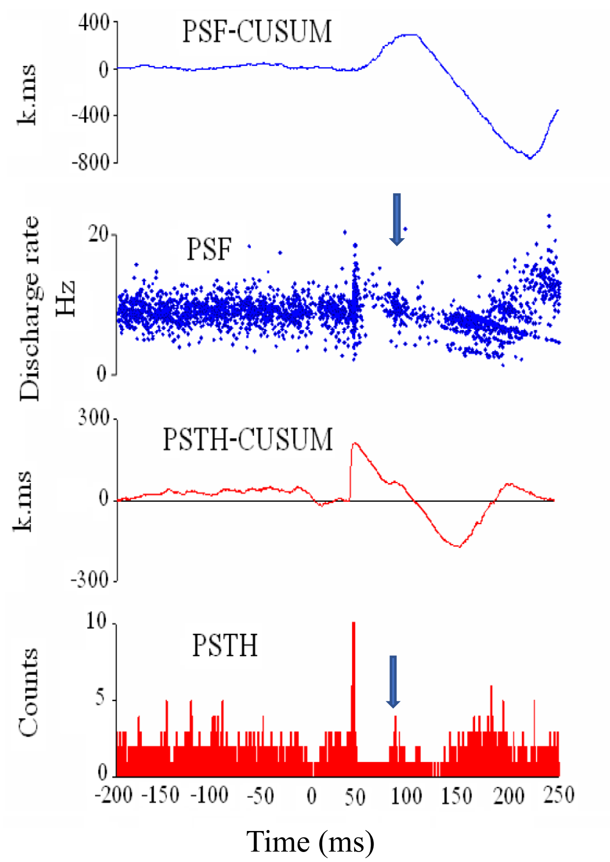

Fig. 1 Response of a regularly discharging TA single motor unit to low-threshold common peroneal nerve stimulation. The top panel shows a net long-lasting excitatory effect followed by a net long-lasting inhibitory period. The second is the PSF, which shows increased discharge rates after the H-reflex response. There was a brief period when the discharge rate returned to prestimulus values (downward arrows). In contrast, the third panel (PSTH-CUSUM) and the fourth panel (PSTH) indicate an apparent reduction in spike counts immediately following the H-reflex (the so-called silent period) and a minor peak (the 'D' response; in Kudina and Andreeva, 2021). The stimulus was delivered at time zero. These data come from a single motor unit during an isometric TA contraction at about 3% MVC. The figure was modified from Fig. 3 of Prasartwuth et al. 2008, with permission from Springer Nature

We have shown that the secondary effects of the M-wave and the H-reflex induced muscle contraction in the soleus

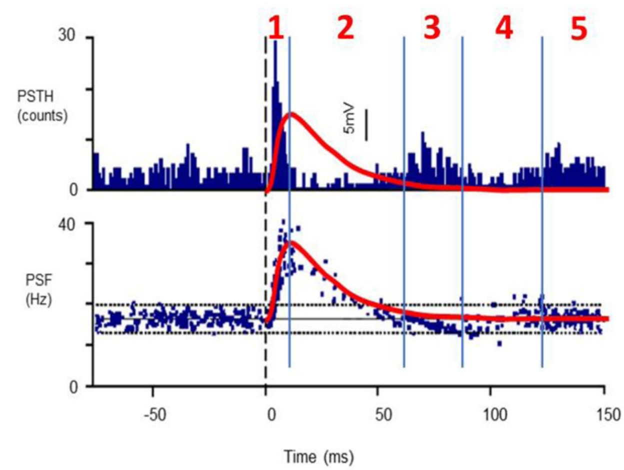

Fig. 2 Direct comparison of the two methods used to study neuronal networks in human subjects indirectly. Pre-determined potentials (shown in continuous red line here) were inserted into regularly discharging motoneurons in rat brain slices. Action potential output from the motoneuron was analyzed using both PSTH and PSF methods. Although a simple EPSP was inserted into the neuron, the PSTH analysis indicated five separate significant peaks and troughs (1–5). On the other hand, the PSF approach indicated only a single long-lasting excitatory event, correctly illustrating the input potential. The figure was modified from Fig. 2 of (Türker and Powers 2005) with permission from TINS

motor units (Binboga et al. 2011). We, therefore, claim that when one examines the entire period of the stimulus-induced response using the PSF, all significant changes in the membrane potential will be observed as the discharge rate indicates the net current flows into a motoneuron for restricted firing ranges (Granit et al. 1966; Schwindt and Calvin 1973; Powers et al. 1992). Despite some limitations, the PSF method is used successfully in several studies and commented highly (discussed in Türker and Powers 2003, 2005). For example, Nordon et al. 2008 noted that: "In summary, the PSF appears to be an accurate representation of the underlying PSP in contrast to the PSTH (and EMG), which is influenced by the synchronization of motoneuron firing following a rapid excitation…. Thus, unlike the PSTH, the PSF provides information concerning the amplitude of the PSP given that the firing rate is linearly

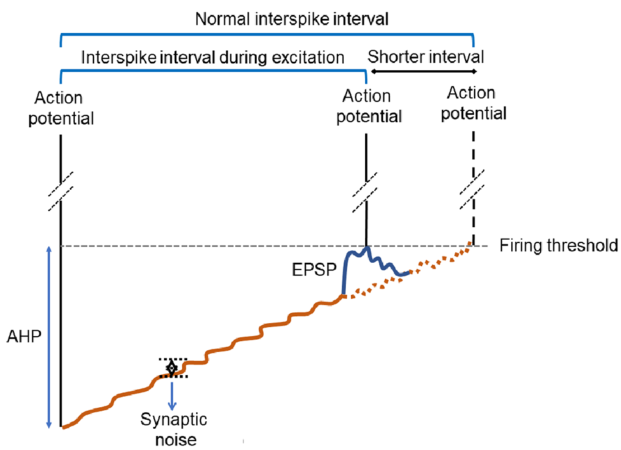

Fig. 3 Hypothetical motoneuron discharge illustrates the effect of low-threshold stimulation of the common peroneal nerve induced net EPSP on ongoing action potentials. The rising phase of the EPSP crosses the firing threshold in most cases as it is larger than the synaptic noise and rapidly rising. Threshold crossing by rapidly-rising phase of EPSP effectively brings action potentials that were to occur later to an earlier time (phase advance of spikes). This creates a period of low firing probability (silent period; SP) immediately after the rising phase of EPSP as spikes that were to fire in that period moved to occur earlier, generating the H-reflex response. Threshold crossing during the falling phase of an EPSP is only possible when the fast-rising phase fails to cross the threshold, and the falling phase of the EPSP crosses the threshold with the help of an up-going synaptic noise. This is an extremely rare event, and hence most of the threshold crossings will be achieved during the rising phase of an EPSP, especially when the EPSP is large. The figure was modified from Özyurt et al. 2019 with permission from PLos ONE

related to the amplitude of the membrane potential at the motoneuron soma".

Data availability Upon a reasonable request, the data will be provided.

Declarations

Conflict of interest The author declares that he has no conflict of interest.

Ethical approval The protocols of the experiments mentioned in this paper are approved by local ethics committees.

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