Dendritic calcium spikes that are related to behavior and cognitive function

Re-interpretation based on the IPL mechanism

Similar to the action potentials (axonal spikes or neuronal firing) occurring at the axonal hillock, there are spikes occurring at the dendrites. These are called dendritic spikes. Based on the strength of summated potentials, a rough estimate shows that they constitute synchronous activation of nearly 10 to 50 neighboring glutamatergic synapses triggering a local regenerative potential (Antic et al., 2010). Depending on the channels involved, there are different types of dendritic spikes. Recently, it was found that distal dendrites generate dendritic spikes whose firing rate is nearly five times greater than at the cell body (Moore et al., 2017). Another group of investigators who have previously shown that dendritic spikes are related to behavior and cognitive function recently found that dendritic calcium spikes contribute to surface potentials that are recorded as electroencephalogram (EEG) (Suzuki et al., 2017). Surface EEG recording is generated by current sink that reflects the net potential changes within the extracellular matrix space. This is expected to be contributed by several factors. It is known that the surface positive potentials are generated mainly by synaptic inputs from other cortical and subcortical regions to the pyramidal neurons located between L2/3 to L4 regions (Douglas and Martin, 2004). Recent studies by Suzuki et al., has found that dendritic calcium spikes at the main bifurcation points of the apical dendrites of L5 pyramidal neurons (note that L5 pyramidal neurons are upper motor neurons that direct motor movement of the body) also generate the surface positive potentials (Suzuki et al., 2017).

The last two findings lead to these questions. “How can two different sources of potentials provide similar surface positive potentials?" "Can we provide an interconnected explanation?" Since dendritic spikes are related to both behavior and cognitive functions and since IPL mechanism can explain generation of concurrent internal sensation of memory and behavioral motor action, can IPL mechanism explain the above findings? Since the apical tuft regions of all the pyramidal neurons are anchored to the pial surface, the dendritic arbor of all the pyramidal neurons overlapped at the recording location of Suzuki et al., (Suzuki et al., 2017). In this context, it is necessary to examine the potential changes occurring at the neuronal processes around the recording electrode. In the context of the IPL mechanism, it is anticipated that the dendritic spines of different neurons have formed a large number of islets of IPLs between them at these locations. By examining the zone from where low-threshold calcium spikes were recorded (Suzuki et al., 2017; Larkum and Zhu, 2002), the following is possible.

Spatially, the main bifurcation points of the apical dendrites of L5 pyramidal neurons are also locations where spines of the L2/3 pyramidal neurons receive their input. Based on the IPL mechanism, several of these spines are expected to be inter-LINKed to form large islets. These islets are also expected to be inter-LINKed with spines of L5 pyramidal neurons for initiating or controlling motor actions. The potentials through the IPLs are expected to arrive at the axon hillock of the L5 motor neurons that are kept at a sub-threshold state (see figure 5 in the FAQ section of this website) for the motor action (**Fig.2**). For a system that operates to generate internal sensations and initiates or controls concurrent motor actions, the islets at appropriate locations are expected to transmit potentials to the axon hillock of the L5 pyramidal neurons that are upper motor neurons. Calcium spikes are generated at the postsynaptic locations within the islet of inter-LINKed spines, possibly due to an increased density of these channels at these locations. Since the pyramidal neurons are found to be under the influence of an inhibitory blanket (Karnani et al., 2014), a function of dendritic spikes is to generate sufficient potentials to overcome this inhibition. In other words, there is a provision for increasing the inhibitory blanket around an L5 pyramidal neuron axon hillock as the size of the islets of inter-LINKed spines that are connected to these neurons increases. This will make sure that the L5 neuron fires only at the activation of specific sets of IPLs that generates a specific conformation of semblance for both the internal sensation and concurrent behavioral motor actions.

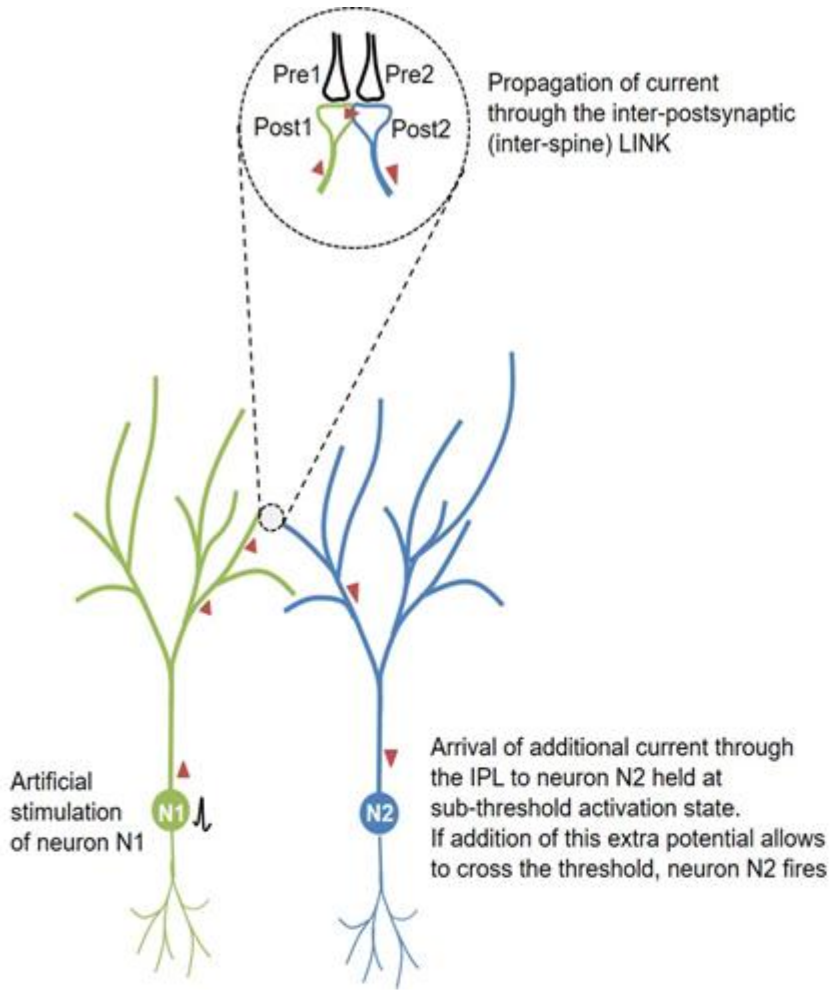

Figure 2. Figure explaining a potential mechanism occurring at the level of the main bifurcation point of an apical dendrite of an L5 pyramidal neuron (based on semblance hypothesis). The circles with different colors represent an islet of inter-LINKed spines (dendritic spines or postsynaptic terminals) that belong to different pyramidal neurons at the level of the main bifurcation point of the apical dendrite of L5 neuron. Note that one of the spines (in violet) belongs to one of the L2/3 pyramidal neurons. Also note that the inter-LINKed spine on the far-right end of the islet (in green) belongs to L5 pyramidal neuron. During development, neurons of different cortical neuronal orders descend from the inner pial surface area by anchoring the apical dendritic terminals to the inner pial region. This allows overlapping of the dendritic arbors of neurons from different orders, which leads to abutting of their spines that eventually leads to the formation of inter-LINKs between these spines during learning. The waveform shown at the level of the inter-LINKed spines indicates that the oscillating extracellular potentials recorded have a major contribution from the

propagation of potentials through the islets of inter-LINKed spines. Secondary factors can determine different wave forms depending on the locations from where recording is carried out. They include a number of neuronal layers, recurrent collaterals, connections with the projection neurons from other areas of the brain, etc. Figure not to scale (spines in the islet are drawn disproportionately large compared to the size of neurons).

The explanation that synaptic transmission and propagation of potentials through the IPLs provide vector components of oscillating extracellular potentials also becomes suitable. If the arrival of potentials from sensory stimuli evokes dendritic calcium spikes along with the reactivation of specific inter-LINKed spines (and their islets) inducing units of specific internal sensations concurrent with activation of specific sets of motor neurons, it can provide an explanation how dendritic calcium spikes are related to behavior and cognitive function. The findings of Suzuki et al., necessitate examining the role of background EEG wave forms, frequency of which correlates with normal level of consciousness. In this regard, the explanation by the IPL mechanism that the net background semblance induced by reactivation of inter-LINKed spines contributes to the internal sensation of consciousness (Vadakkan, 2010) becomes a suitable mechanism that can be subjected to further studies.

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