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BEYİNDEKİ SİNİR HÜCRELERİNİN DİLİ: ZAMANSAL ATEŞLEME PATERNLERİ

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A Language of the Neurones in the Brain: Temporal Firing Patterns

Summary

Neurons in vertebrate and invertebrate brains use characters that are unique to encode the things happening in the external world. The coding characters are the electrical signals to process all types of information, such as visual, auditory, taste, smell. The only electrical signal that neurons produce, transmit, recognize and use is action potential, with which for example, brain knows what a word means or how cold the weather is. The temporal characteristics of action potentials generated by neurons is important in coding different modules of information. In this review, an attempt for understanding the higher functions of the brain is made by correlating the temporal activity of individual nerve cells to the coding the information.

Keywords: Neuron, coding information, firing patterns, PSTH

Özet

Omurgalı ve omurgasızların beyni, dış dünyada meydana gelen değişiklikleri kodlamak için çok özel karakterler kullanırlar. Bu kodlama karakterleri, görme, işitme, tat ve koklama duyu organlarının duyarlı olduğu bilgileri işleyebilen elektrik sinyalidir. Aksiyon potansiyeli, sinir hücrelerinin ürettiği, taşıdığı, tanıdığı ve kullandığı elektriksel sinyallerdir. Bu sayede beyin, bir kelimenin ne manaya geldiğini veya havanın ne kadar soğuk olduğu gibi bilgileri anlayabilir. Sinir hücreler tarafından meydana getirilen aksiyon potansiyellerin zamansal özellikleri değişik bilgi türünü kodlamada önemlidir. Bu derlemede, sinir hücrelerinde meydana gelen zamansal aktiviteleriyle bilgi kodlama arasında bir bağlantı kurularak yüksek beyin fonksiyonlarının anlatılması amaçlanmıştır.

Anahtar Kelimeler: Sinir hücresi, bilgi kodlama, ateşleme paterni, PSTH

Introduction

Brain is consisted of individual unit-neurons that continually receive, analyzes and perceives. Upon making decisions, it can initiate actions in response to various senses to regulate their performance. In other words, brain has tasks of monitoring the environment and taking steps accordingly and of determining numerous aspects of behavior. However, neurons and their connections are simply the fundamental tools for all its functions. Individual neurons and neuronal arrays can encode complex information and concept into simple electrical signals, which consists of potential changes produced by ionic currents flowing through cell membrane (19,20,21). The Na^+, K^+, Ca^{2+} and Cl^- ions appear to be responsible for the signaling of various neurons (16). There are two kinds of electrical signals in the nervous system. The first kind is **localized potentials**, which are graded in size. In sensory endings, it is called **receptor potentials** and at synapses, local potential are known as **synaptic potentials**. The second kind is the **action potentials**, which are regenerative impulses and can travel rapidly along an axon without attenuation and distortion (19,20,21). These two types of signals are the conventional language of nerve cells in the animal kingdom (31). The localized potential is not within the scope of this review article.

What is the need for the temporal coding?

In other words, for processing all kinds of information, such as, auditory, visual, motor, mental and emotional, neurons in the brain use stereotyped electrical signals regardless of the modules of information. Most likely, the quality of information is coded in temporal response patterns or frequency of action potentials, i.e., different neurons with different temporal firing pattern highly likely to process different aspects of information. The former

one is called **temporal coding** and the latter one is called **frequency coding** (17,35,37,39,41,42). The frequency coding is used to convey information only about the intensity of a stimulus by the nervous system. There are few exceptions to this rule; in the sense of vibration, the frequency of firing can follow the frequency of the source of the stimulation. Much of the information carried, processed and manufactured by the brain is hidden in the temporal firing patterns of neurons (9).

The information in frequency coding may be carried by the rate of the discharge of a neuron. However it has to be noted that the temporal firing patterns or frequency of action potential discharging do not suffice on its own for coding different modules of information. The content or module of the information that a nerve cell carry and process within the brain are determined by the origins of the nerve fibers and their destinations. Different sensory modalities are connected to different part of the brain; this is termed as **labeled line coding** (9). What this means is that the contents of information are entirely different in the neurons responding to sound or light even if the frequency and the temporal firing patterns may be similar. These coding systems are the known major ones operating in the brain faculties. Processing information for hearing a spoken language, or seeing a delicate art cannot be accounted for only by the labeled line coding or by the frequency or temporal coding. In fact, it is currently believed that these codes operate in various combinations depending upon complication of the information to be processed (22,31).

There is a notion that the central nervous system (CNS) preserves temporal information in firing patterns as cues. Firing patterns in neurons are governed by biophysical properties of the neuron together with the interaction of the synaptic inputs (6,7,18,26-28,32-34). Branching patterns of neurons and the spatial patterns of synaptic inputs may also contribute to the formation of different firing patterns (8,40,44). The temporal characteristics of a neuron's response can be demonstrated by the shape of the prestimulus time histogram (PSTH). The shape of a PSTH gives information about the firing probability around and during a stimulus. It is not yet entirely clear what role these temporally different firing patterns play in the CNS. However, evidence will be discussed below about the known PSTH firing patterns (22).

Types of Firing Patterns

The PSTH firing patterns of neurons are studied with extracellular, and also intracellular recording techniques in response to sense specific stimuli and current injection respectively. Intracellular recording has its own nomenclature for firing patterns. However they have very similar classification but not as elegant and elaborated as done for extracellular recordings. This is because the firing patterns recorded using intracellular technique *in vitro* reflects only biophysics of individual neurons, whereas the firing patterns recorded extracellularly reflects a comprise of biophysics of individual neurons, integration of excitation and inhibition and influence of morphology of individual neurons (24,39). From extracellular recordings *in vivo*, neurons in the brain exhibits a range of PSTH firing patterns, which have been broadly divided into ***onset (phasic)* pattern** in which a neuron responds only at the onset of a stimulus and or ***sustained (tonic)* pattern** in which neuron continues to fire action potentials for the duration of a stimulus (5,7,8). Within these two broad groups, subgroups for each group and combinations of onset and sustained response patterns (generally separated by a pause) have also been reported (25,39). An **onset chopper pattern** had three distinct peaks limited to the first 30 ms of the stimulus. A **chopper pattern** is characterized by a PSTH with three or more distinct, regularly timed peaks near the onset of the stimulus or regularly spaced peaks during the stimulus. **Pauser pattern** is characterized by an initial peak, followed by several milliseconds (ms) of pause, which is either a complete cessation or marked reduction in the firing, lasting up to about 25 ms. **On-sustained pattern** is characterized by a peak at the onset of the stimulus and a sustained component lasting throughout the stimulus (10,22).

Intracellular recordings yielded the following major firing patterns. ***Onset neurons*** fire only one AP at the onset of a stimulus irrespective of the amplitude of the current injected ***Regular neurons*** fire trains of APs with a constant interspike interval to current injection. ***Adapting neurons*** fire trains of APs with regular or irregular adaptation during the stimulus. ***Bursting neurons*** fire bursts of APs on depolarizing current injections (1,2,6,7,18,28,32,36). Not all intracellularly recorded neurons with regular firing in vitro corresponds to the extracellularly recorded chopper units in vivo. For example D-stellate cell fire regularly in slice preparation when stimulated with DC current. They, in fact, are a subset of onset PSTH units (40,41). This results from integration of biophysics of neuron, inhibition and excitation that they receive and morphology of neurons (24).

Possible Roles of Neurons with Different Firing Patterns

Tonic (Sustained) Firing: The precise role of neurons with different temporal firing patterns is not clearly understood. The regularly firing neurons might play an important role in encoding the temporal aspect of the stimulus, such as sound information, providing a reliable time base to encode the timing of a sound, for example, onset, offset, duration and intensity of the sound. It is also suggested that the tonic firing might be associated with discrimination of different stimulus levels, because it has been shown that, in comparison to other PSTH types, regularly chopping neurons showed larger increase in spike rate with increasing sound pressure level (10,22).

Onset (Phasic) Firing: Onset responsive neurons have been associated with encoding the timing information or encoding cues driven from time information. For example in auditory pathway, Rhode *et al* (40) hypothesized that onset neurons might work in neural pathways that encode sound localization and might initiate arousal because occurrence of the action potential are well timed and restricted to the onset of the stimulus. After years it has been demonstrated that bushy cells located in the ventral nucleus of cochlear nucleus convey timing information to the superior olivary complex that is necessary for the localization of sound in the azimuth (10,22). It is interesting that their morphology and the biophysical properties of the bushy cells, which is onset responsive are well suited to carry precise timing information (2,36).

Most interesting member of the onset neurons may be octopus cell in the posterio-ventral cochlear nucleus, which detects synchronous firing in large groups of auditory nerve fibers and conveys timing of the coincidence with temporal precision. This cell type anatomically and biophysically is well suited for this job. The dendrites of octopus cells spread perpendicularly across the paths of large number of auditory nerve fibers representing big range of frequencies (13,14,33). Octopus cells has the lowest input resistance ever recorded (about 7 mOhm) (6,32). The low input resistance in octopus cell has two functionally important consequence in the signaling of octopus cells: firstly this enable octopus cells to produce rapid and brief synaptic potentials, contributing to the precision in timing of signaling and secondly low input resistance cause voltage changes in response to synaptic currents to be small. This is consistent with the statement by Golding *et al.* (14) that octopus cell fire action potential if synchronous firing in a large numbers of auditory nerve fibers, which is the basis of the coincidence detection theory (6,13,14,35).

How the temporal firing patterns are produced biophysically?

Neuronal membranes in the nervous system are equipped with large number of ion channels, mediating ionic currents carried by sodium, potassium, calcium and chloride ions. For processing different aspects of information that we are involved, there is a requirement for a large repertoire of firing patterns in encoding, for which, in turn, the diversity of ion channels is essential. Sodium channels do not seems to have very much diversity; cross the many cells types studied a stereotype sodium channel has been reported. There are several types of calcium current reported (16). The diversity in particularly potassium channels is well documented; at least 30 different potassium channels have been characterized biophysically and also genetically. Each cell types posses sets of ion channels to produce particular firing pattern (3,4,5,11,12,23,43).

Those neurons that are capable of firing regularly at high frequencies appear to posses dense Kv3.3 alpha subunit, which is reported to be molecular substrates for delayed rectifier (K_{DR}). This subunit in expression systems has been shown to deactivate rapidly, which enable cell to fire more frequently (13,38). Voltage clamp experiments in cells from the different region of the brain proved that adaptation in the firing usually comes from the calcium activated potassium currents (16). It has been demonstrated that low threshold calcium current causes the purkinje neurons of cerebellum to fire bursts of action potential (26,27,28).

For onset neurons, there are accumulating evidence that transient potassium outward current is the major current that makes these cells to fire only one action potential (13,14,29,45). Manis *et al.* (30) showed that regularly firing fusiform cells can turn into pauser pattern when preconditioning hyperpolarization used. This is consistent with the notion that neurons with pauser firing pattern are not a distinct group of neurons different from regular neurons and the regular neurons with A-current can modulate firing patterns from regular to the pauser pattern (30).

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