MATHEMATICAL ASSESSMENT OF EPHAPTIC INTERACTION AND THE RECORDING OF TRANSMEMBRANE POTENTIAL SHIFTS

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A theoretical analysis is given of ephaptic interaction between nerve cells. The larger cells must be more exposed to ephaptic effects. Intracellular studies of transmembrane potential shifts induced by ephaptic action show that the position of the reference electrode is very important. The efficiency of ephaptic interaction is proportional to the specific impedance of the nerve tissue.

KEY WORDS: nerve cells; ephaptic interaction.

Ephaptic interaction between nerve cells is the name given to the influence of currents generated by neurons on the excitability of neighboring neurons. Since ephaptic interaction takes place by the direct shift of potential on the membrane by currents of external origin as regards the neuron concerned, and not synaptically, the latent period of this interaction must theoretically be equal to zero. A latent period of almost zero for ephaptic interaction has been found, for example, in the work of Rosenthal et al. [7]. In addition, currents of external origin differ in their effects on the excitability of diametrically opposite regions of the neuron membrane: that part of the cell membrane through which the electric current enters the cell is hyperpolarized, whereas the opposite part of the membrane, through which the current leaves the neuron, is depolarized. If, therefore, a region with increased excitability exists in a neuron, the same external electric field may produce different effects on the excitability of the neuron depending on its orientation [8, 9].

In this paper the dependence of the transmembrane potential change (ΔV_t) as a result of ephaptic action on the density of the external current, the dimensions of the cell, and the specific impedance of the external medium is deduced. Some theoretical aspects of the recording of ΔV_t are also examined.

METHODS OF CALCULATING AND DISCUSSION OF THE RESULTS

To simplify the calculation of the value of ΔV_t it was considered that the cell is spherical and that the electrolyte surrounding it is infinitely large. It was also assumed that before the spherical cell was placed in the electrolyte, the latter had a uniform current field with density $\vec{j}_0$. With this model of ephaptic interaction the following expression can be obtained for the value of the transmembrane potential change (ΔV_t) in relation to the level of the resting potential:

$$\Delta V_m = -\frac{3}{4}\vec{j}_0 \cdot \rho_0 \cdot D \cdot \mathrm{Cos}\,\theta, \tag{1}$$

where ρ_0 is the specific resistance of the medium surrounding the cell, D the diameter of the cell, and θ the angle between the direction and the radius drawn from the center of the cell (Fig. 1).

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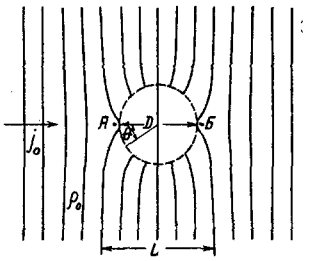

Fig. 1

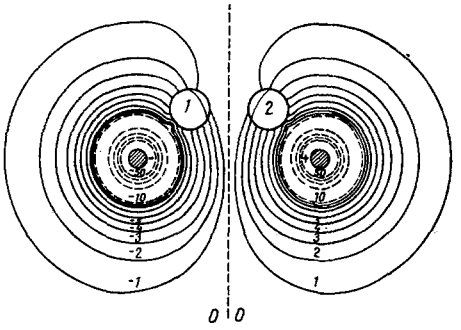

Fig. 2

Fig. 1. Model of nerve cell in homogeneous field of electric current: $\vec{j}_0$) vector of current density sufficiently far from the cell; ρ_0) specific resistance of surrounding electrolyte; D) diameter of cell; θ) angle between direction of $\vec{j}_0$ and radius drawn from the center of the cell; L) distance between equipotential lines on which points A and B lie.

Fig. 2. Nerve cell in field of current of ephaptic dipole. Shaded circles represent poles of dipole; 1 and 2) two symmetrical positions of nerve cell; numbers on isopotential curves are equal to values of potential on them in conventional units.

The calculations showed that the change in transmembrane potential (ΔV_t) during ephaptic action is proportional to the size of the cell (D). This can be explained qualitatively as follows. A decrease in voltage between the points A and B (Fig. 1) must be equal to the potential difference between the equipotential lines on which these points lie. These equipotential curves can be taken as parallel a short distance from the cell, and the distance between them is L. The potential difference sought between the points A and B is thus $j_0 \cdot \rho_0 \cdot L$. The voltage drop between A and B must be divided between three resistors connected in series (the resistance of the membrane for the inward current, the resistance of the intracellular medium, and the resistance of the membrane for the outward current). Since the first and third resistances are many times greater than the second, essentially the whole potential drop between A and B is divided half and half between the resistance of the membrane for the inward current and its resistance for the outward current. The expression $\Delta V_t = (1/2) j_0 \rho_0 L$ can thus be obtained for the magnitude of ΔV_t. Let us estimate L. It is evident that L is greater than D, but it is a value of the same order as D. This follows from the general argument that the distortion of the field (i.e., the deviation of its equipotential curves) is a value of the same order as the size of the object as a result of which the distortion took place. Accordingly, L in the last expression for ΔV_t can be replaced approximately by D, and the resulting expression for ΔV_t now has the form $\Delta V_t = j_0 \rho_0 D$, from which it follows that ΔV_t is proportional to D.

The true value of ΔV_t, incidentally, can be measured when the potential difference is measured between the intracellular and extracellular electrodes, the last of which must be placed as near as possible to the membrane of the cell concerned. In that case the potential difference between the intracellular and extracellular electrodes will be equal to the sum of the resting potential and ΔV_t of that part of the cell membrane that lies closest to the extracellular electrode. The potential drop in the intracellular medium between the point where the electrode is situated and the inner surface of the membrane is a negligibly small magnitude compared with ΔV_t.

To measure the value of ΔV_t, the position of the reference electrode thus becomes extremely important. If this electrode is sufficiently far, compared with the size of the current ephaptic dipole, from that dipole the reference electrode can be regarded as lying on the zero isopotential curve (Fig. 2). If, therefore, a sufficiently distant reference electrode is used the potential difference between the intracellular and reference electrodes will depend only on the position of the investigated cell in the field of potentials generated by the current ephaptic dipole. The same potential difference (but differing in resting potential) could be recorded from the active electrode after the cell had been removed but the active electrode was left in its old position. The potential difference recorded by this distant reference electrode can even change its sign, whereas the ephaptic influence on the cell (proportional to the potential gradient) may remain unchanged (see positions 1 and 2 of the cell in Fig. 2).

This disparity between the intracellular potentials (relative to the distant reference electrode) and the changes in excitability of the neuron under the influence of the ephaptic field is shown by the records illustrating the paper by Nelson [6].

Complete agreement between the intracellularly recorded potential change (relative to the distant reference electrode) and the change in the level of excitability of the neuron during ephaptic action was also found by Belenkov and Chirkov [1, 3] when investigating ephaptic excitability of pyramidal neurons during electrical stimulation of the surface of the cortex. These workers assert that the intensification and inhibition of activity of the tested neuron after electrical stimulation of the cortical surface coincided with depolarization and hyperpolarization respectively during intracellular recording. This complete agreement between the changes in the intracellular potential and the level of excitability can only be explained on the assumption that the latency of the intracellular response, as these workers themselves state, was not less than 1-2 msec. The response itself must therefore be regarded, not as ephaptic, but as evoked synaptically, for which the change in the intracellular potential does not correspond to the level of excitability.

It must be mentioned in particular that the ephaptic effect on the cell membrane does not show itself as the potential of the external electric field, but as the density of the electric current in the region where the neuron lies. The conclusion that the ephaptic effect on a neuron depends on the size of the extracellular potential of the ephaptic field, reached by Belenkov and Chirkov in their investigation [1], is therefore incorrect. The ephaptic action of the external electric field on a neuron must be proportional to the extracellular potential gradient in the region where the neuron lies (the density of the electric current is proportional to the potential gradient at a given point). This dependence of the ephaptic action of an external electric field on the spontaneous discharge frequency was found by Terzuolo and Bullock [9].

Comparison of the ephaptic action of high-frequency and low-frequency currents arising during generation of the action potential (AP) and postsynaptic potential (PSP) respectively is usually made on the basis of comparison of the impedance values of the nerve tissue for these frequencies. Chirkov et al. [4] assert that frequencies of 50-20 Hz must spread over the cortex with greater difficulty than frequencies of 500-1500 Hz, for the impedance for low frequencies is almost three times greater than that for the high frequency. However, this assertion is valid only if the generator of ephaptic currents has an internal resistance much smaller than the load resistance. The cell is known to be a "current generator". In fact, during excitation of any part of the neuron membrane an electric current "begins" to flow inside the cell from the region of excitation toward the neighboring unexcited regions of the membrane, it crosses the membrane of the unexcited regions, and it then flows along the volume conductor toward the excited part of the membrane where, crossing the membrane in the opposite direction, it "closes" its circuit. The volume conductor surrounding the cell can be regarded as a load resistance connected to the neuron membrane between the excited and unexcited regions. The resistance of the volume conductor is evidently many times smaller than the resistances overcome by the current as it crosses the membrane and moves inside the cell. The magnitude of the current sent by the excited region of the membrane into the volume conductor is thus practically independent of its impedance, for far higher resistances are connected to it in series in the electric circuit.

Ephaptic action, as follows from equation (1) must be proportional to the specific resistance of the tissue surrounding the neuron. Low-frequency currents, for which brain tissue presents a greater resistance, must therefore have a greater ephaptic action.

When the ephaptic effects of currents generated by APs and PSPs are compared, this must also be done on the basis of 1) the combined value of the current sent by the cell into the volume conductor and 2) the fact that the density of this current falls rapidly with increasing distance from the excited area of the membrane. The first criterion gives priority to the AP, whereas the second gives priority to ephaptic interaction during the PSP [2, 5]. Ephaptic action of the cell, it will be noted, is independent of the specific resistance of its membrane, as follows from equation (1).

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