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EXTRACELLULAR LOCAL FIELD POTENTIALS IN MEN AND WOMEN BASED ON A THEORETICAL MODEL OF VOLTAGE DECREASE AS A FUNCTION OF DISTANCE

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ABSTRACT

Extracellular microelectrodes determine the field potential difference adjacent to the neuron and depend on the composition of the tissue, including ohmic resistance and distance from the source. Based on theoretical aspects, a reciprocal voltage versus distance model is postulated, which was assessed by means of clinical neurographical data in men and women. Data of women showed higher voltages and could be slightly better fitted to the model. Voltage amplitude and to a lesser extent rise time (RT) were the only action potential characteristics which could predict the gender in a discriminant analysis model. In conclusion, neurographical studies may be a suitable option to assess ohmic resistance of tissue and composition of tissue in addition to bioimpedance (BIA) methods.

Keywords: *field potential; voltage amplitude; action potential; gender difference*

INTRODUCTION

Local field potentials (LFP) are defined as the electrical field around active neurons in the ambient extracellular space. In general, LFPs can be recorded in central or peripheral neurons [1, 2, 3, 4]. We concentrate on the recordings of single peripheral neuronal activity using adjacent metal electrodes. We admit that the resistance of the perineuronal tissue is mainly ohmic resistance, and that reactance, i.e., cellular components of the tissue, do not play a substantial

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role [3, 5]. Ohmic resistance is determined by the composition of tissue and water or electrolyte contents, respectively.

We consider the neuron as a time dependent dipole, which generates a remote potential difference [6, 7]. As the angle between the neuron and the microelectrode remains constant during the recording and is not known to us, we chose a simplified electrophysiological model [1]. Ohmic resistance ρ and conductivity σ are defined as follows: $\sigma = \frac{1}{\rho}$. In general terms, we can define the current density J in Ohm's law as a function of the electrical field $J = E * \sigma$ (note: J and E are vectors), if we admit the spherical structure of the electrical field around the source (neuron). According to the law of current conservation, the current density in the sphere is given by the equation $= i * \frac{r}{(4\pi r^2)}$, where r is a unit vector and r the distance between source and recording i the current. As the voltage dV is given by $dV = E * dr$, we can substitute and integrate (for details see 5) the equation from r1 to r2.

$$dV = \frac{1}{\sigma}\int_{r1}^{r2} J = \frac{1}{\sigma}\int_{r1}^{r2} \frac{i}{4\pi r^2}$$

The voltage V(r) is then defined as $V(r) = \frac{1}{4\pi\sigma} * \frac{i}{r}$, if we assume V(∞) = 0.

The first objective of this study was to fit the data to the quite simple reciprocal theoretical model – although exponential models may also be suitable – which can be written as follows: $y = \frac{1}{(A + BX)}$, where Y denotes the voltage and X the distance. A and B are the corresponding model parameters, preventing zero division [2, 8].

The second criterion was to look for differences between men and women with regard to additional criteria of the field potentials such as slope or rise time. The following action potential (AP) characteristics were determined electronically (see Figure 1): Latency (stimulus – AP), amplitude (positive to negative tip of the spike, slope (maximum upstroke of tangent), rise time (RT, time from 10 to 90% of the action potential).

Fitting of clinical data to the model

Routine clinical recordings of adult patients (12 men, 16 women) who agreed to the neurophysiological investigation with normal peripheral neuron potentials were evaluated retrospectively. In addition to the recording, the distance between the microelectrode and the nerve was estimated by means of sonography. In addition, anthropometric data (body weight, height) were determined. The detailed technique of needle neurography (extracellular

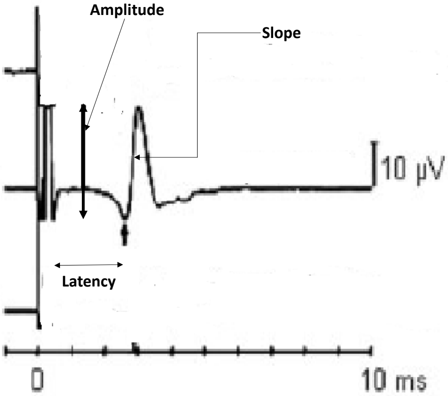

Figure 1. Qualitative characteristics of a sensory action potential (modified according to 15)

recording of sensory action potentials of the *nervus suralis*) and the theoretical background have been published elsewhere [9, 10, 11]. In brief, the nerve was repeatedly stimulated on both legs with a bipolar surface electrode. The recording metal electrode was placed approximately 1 to 10 mm, a reference electrode was positioned about 5 cm proximal to the recording site.

Figures 2a and 2b show the fit of the data to the theoretical field potential model in women and men. The model parameters showed a better curve fit in women compared to men. Moreover, the mean voltage was slightly higher in women than in men (Table 1). Nonparametric preliminary comparison showed no significant difference between men and women (Mann-Whitney *U* test). Nevertheless, the data show that the theoretical model of field potentials delineates the naturalistic data of clinical practice.

The secondary objective of this investigation was to assess whether additional characteristics of the sensory action potential may be different between men and women. The descriptive results of model independent analysis are summarized in Table 2. Apart from the expected differences in body weight or height, the only significant (Mann-Whitney *U* test) difference between genders was found for the RT. This result was verified by a discriminant analysis model which assesses the functional association of a dependent variable Y (gender) with different dependent variables Xi (weight, height, slope, rise time, amplitude) [12]. The rise time was the only characteristic of the action potential which markedly allowed the prediction of the gender ($p = 0.04$); to a lesser extent the slope, which correlates with the RT, was a weak predictor of gender ($p = 0.047$). All calculations were done with commercial software (NCSS 12.0.5; NCSS Kaysville 2018, USA).

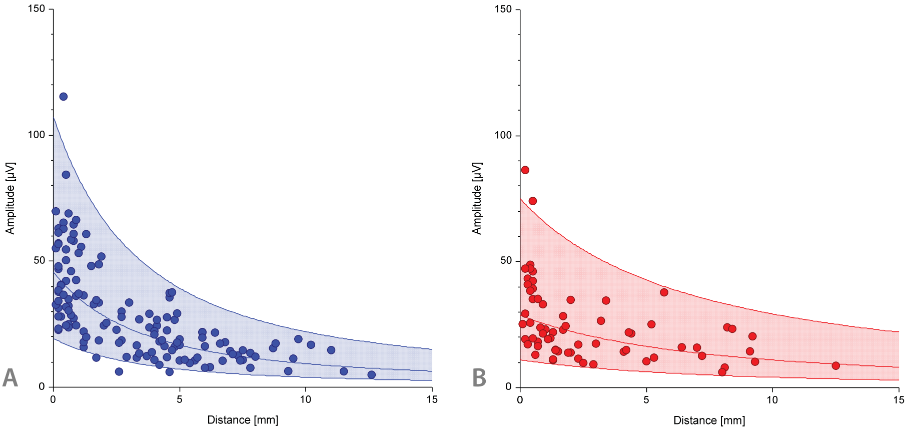

Figure 2a shows the curve fit of women ($r^2 = 0.56$), **Figure 2b** the curve fit of men ($r^2 = 0.27$). Data of both genders could be fitted to a voltage versus distance reciprocal model. Voltages of women were slightly higher with lower degree of variation

Table 1. Estimated model characteristics (A, B) of the reciprocal model of decreasing voltage: $Y = \frac{1}{A + BX}$, including goodness of fit (r^2 coefficient of determination)

	Parameter	Model estimate	95% confidence limits model parameters
Female	A	0.26	0.02–0.22
($r^2 = 0.56$)	B	0.02	0.02–0.22
Male	A	0.30	0.28–0.31
($r^2 = 0.27$)	B	0.12	0.01–0.02

Table 2. Descriptive comparison of characteristics between women and men (BW – body weight) including nonparametric Mann-Whitney *U* test (MW-Test). Amplitude see Table 1

Parameter	Women		Men		MW-Test
	Mean	SD	Mean	SD	
Height (cm)	116.5	6.02	185.1	6.02	$P < 0.05$
BW (kg)	61.4	6.29	77.9	5.30	$P < 0.05$
Rise time (µs)	328.5	78.4	380.1	120.2	$P < 0.05$
Slope (V/ms)	99.4	77.0	77.7	61.0	$P > 0.05$
Amplitude (µV)	28.13	14.94	24.54	18.79	$P > 0.05$

DISCUSSION AND CONCLUSION

The investigation shows that clinical data support the theoretical aspects of decreasing field potentials with increasing distance from the source, i.e., the reciprocal dependence of the voltage recorded in tissue and the distance between the neuron and the recording site. Routine data performed to exclude polyneuropathies do not allow to characterise the electrical properties of the tissue, as both tissue and action potential may be a source of variation. However, the coincidence with previous studies using bioimpedance methods [13] enables us to suppose that the conductivity of the tissue is slightly better in women than in men as the mean RT, amplitude or slope revealed marked differences.

A well-known phenomenon may also be of interest in this context. Experimental studies show that women are more sensitive to pain than men [14, 15]. With a certain heat or pressure stimulus, they estimate the pain intensity to be higher and withstand the pain for a shorter time. In addition, they already perceive lower stimuli as painful. Interestingly, the pain sensitivity changes during pregnancy and after menopause, which corresponds to reciprocal model characteristics and indicates some associations between hormone status and tissue conductivity.

In conclusion, the theoretical reciprocal field potential model could be supported by clinical data. Men and women showed different potential characteristics, particularly with regard to rise time and slightly with regard to voltage amplitude and slope. The data endorse the hypothesis that peripheral tissue conductivity is higher in women than in men.

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