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Vyskočil F, Kříž N & Bureš J. Potassium-selective microelectrodes used for measuring the extracellular brain potassium during spreading depression and anoxic depolarization in rats. *Brain Res.* 39:255-9, 1972.

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Extracellular potassium concentration $[K^+]e$ was monitored with potassium-selective microelectrodes in the cerebral cortex of anesthetized rats. Waves of Leão's spreading EEG depression were accompanied by a steep increase of neocortical $[K^+]e$ from the resting level (3 mM) to 60 mM and by slower recovery. Terminal anoxia raised $[K^+]e$ first slowly to 11 mM, then abruptly to 75 mM, and finally again slowly to 100 mM. The results imply gross changes of brain microenvironment during the above states. [The *SCI*® indicates that this paper has been cited in over 235 publications.]

Potassium-Selective Microelectrodes Reveal Excessive Changes of Brain $[K^+]e$

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This short article described the application of a new technique to a well-recognized but yet unsolved problem. Potassium-selective microelectrodes with a liquid ion-exchanger membrane were developed in 1970 by J.L. Walker,[1] and the technology was brought from Salt Lake City to Prague by our colleague and friend Dr. Pavel Hník. Two of us (FV and NK), having rapidly mastered the production of the microelectrodes, put together the necessary equipment (with the assistance of engineer E. Ujec) and developed various modifications of the technique[2] for recording extracellular potassium concentration in muscles (with Hník) and spinal cord (with Eva Syková and L. Vyklický). At the same time we were looking for other meaningful applications of the technique and accepted the proposal of the third author (JB) to use the electrodes for testing the hypothesis that the self-propagating wave of Leão's spreading depression of EEG activity is due to accumulation of potassium released from depolarized neurons to an extracellular concentration causing depolarization of adjacent nerve cells. Such $[K^+]e$ increase had been postulated since 1956 and demonstrated by indirect methods, but its absolute magnitude remained unknown (see reference 3 for a review).

The actual experiments were performed in a small, crowded laboratory at our institute during two weeks of intensive work in the late summer of 1971. Already the first results confirmed our expectations: intracortical $[K^+]e$ rose in a few seconds from the resting level of 3 mM to over 60 mM during spreading depression and up to 100 mM during terminal anoxia. We were fascinated by the reproducibility of results and by the power of the method, which offered definitive answers to speculations about brain microenvironment. We were sure that other groups were hot on the same trail. The feeling that we were participating in a race contributed to the exhilarating atmosphere of those days as well as to the decision to expedite publication by submitting the results in the short-communication format. Indeed, results of similar research in Munich, 400 kilometers from Prague, were published only a year later,[4] and publications from six other laboratories followed in 1974-1975. Our paper thus became the first of a series marking a wave of renewed interest in the mechanism of spreading depression, which was recognized as "a dramatic example of the failure of ionic homeostasis in the CNS [central nervous system]" (C. Nicholson). It was used in scores of later studies employing ion-selective microelectrodes to demonstrate transmembrane shifts not only of K^+, but also of Cl^-, Na^+, H^+, and Ca^{2+} during various physiological and pathophysiological states. This wave crested in the early 1980s,[5] when anoxic depolarization started to be used for testing the role of excitotoxic amino acids and their antagonists in ischemic brain damage.[6]

Our paper was the result of a short-term convergence of three authors with different backgrounds (biology, electrochemistry, medicine), coming from different laboratories and engaged in different types of research, whose subsequent orientation was not significantly influenced by this "episode." The high impact of the paper was already obvious in the late 1970s as it won the contest for the most-cited paper from our institute. Besides this, the study did not receive any particular recognition from the national or international academic establishment.

1. Walker J L. Ion specific liquid ion exchanger microelectrodes. *Anal. Chem.* 43:89A-93A, 1971. (Cited 410 times.)
2. Vyskočil F & Kříž N. Modifications of single and double-barrel potassium specific microelectrodes for physiological experiments. *Pfluegers Arch.—Eur. J. Physiol.* 337:265-76, 1972. (Cited 95 times.)
3. Bureš J, Burešová O & Křivánek J. *The mechanism and applications of Leão's spreading depression of electroencephalographic activity.* Prague, Czechoslovakia: Academia, 1974. 410 p. (Cited 235 times.)
4. Prince D A, Lux H D & Neher E. Measurement of extracellular potassium activity in cat cortex. *Brain Res.* 50:489-95, 1973. (Cited 155 times.)
5. Syková E, Hník P & Vyklický L, eds. *Ion-selective microelectrodes and their use in excitable tissues.* New York: Plenum Press, 1981. 369 p.
6. Somjen G, ed. *Mechanisms of cerebral hypoxia and stroke.* New York: Plenum Press, 1988.

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