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BRAIN RESEARCH

Research Report

The adult rat hippocampal slice revisited with multi-electrode arrays

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ABSTRACT

The multi-electrode arrays (MEA) technology for the recording of brain slices is available for more than 10 years. However, despite its relative simplicity, this recording technique is not widely used in academic or pharmaceutical research laboratories. We illustrate here that MEA provide multiple possibilities to investigate some network physiological properties as well as to evaluate the pharmacological effects of compounds. We first document that MEA allow to trigger and to record conventional FP which are inhibited by the block of action potential propagation (with 500 nM TTX). FP recorded with MEA are sensitive to ionic substitutions, to ionotropic glutamate receptor antagonists (CNQX or NBQX) and to energetic failure. Second, we illustrate that different "classical" protocols (paired-pulse, LTP, chemical LTD), revealing synaptic plasticity mechanisms, could be performed. Third, we document that MEA allow spatial and temporal discriminations for the effects of known pharmacological compounds such as competitive antagonist (gabazine, bicuculline) and allosteric modulators (steroids) of $GABA_A$ receptors. In conclusion, we illustrate that MEA recordings of adult rat hippocampal slices constitute a powerful and sensitive system to evaluate the effect of molecules on basic synaptic propagation/transmission and on synaptic plasticity processes.

1. Introduction

More than 200 years ago, the fundamental experiments of Galvani revealed that "bioelectric forces" exist in living tissues such as nerve and muscles. In 1843, Du Bois-Reymond demonstrated that the "nerve impulse" is a wave-like propagation of negative charges in the nerve trunk. But it took almost one additional century before Huxley proposed the first model of the nerve axon (1938). The demonstration of the ionic mechanisms supporting nerve conduction was achieved by Hodgkin and Huxley (1952a,b) in 1952. Since these pioneering studies, the glass electrode has been considered as the "standard" for electrophysiological recordings, and the refinement of this technique has culminated by the development of the patch-clamp (Hamill et al., 1981). However, alternative approaches for the non-invasive recording of neurons have been developed: multi-electrode arrays (MEA) made of metal electrodes or semi-conductors (Hutzler and Fromherz, 2004) and two-photon imaging technologies. One of the main problems when using metal electrodes to record extracellular signals is to minimize redox phenomena that could interfere with biological processes and signals. Electrodes of MEA are made of inert metal such as indium tin oxide (ITO), platinum or gold that could be additionally coated

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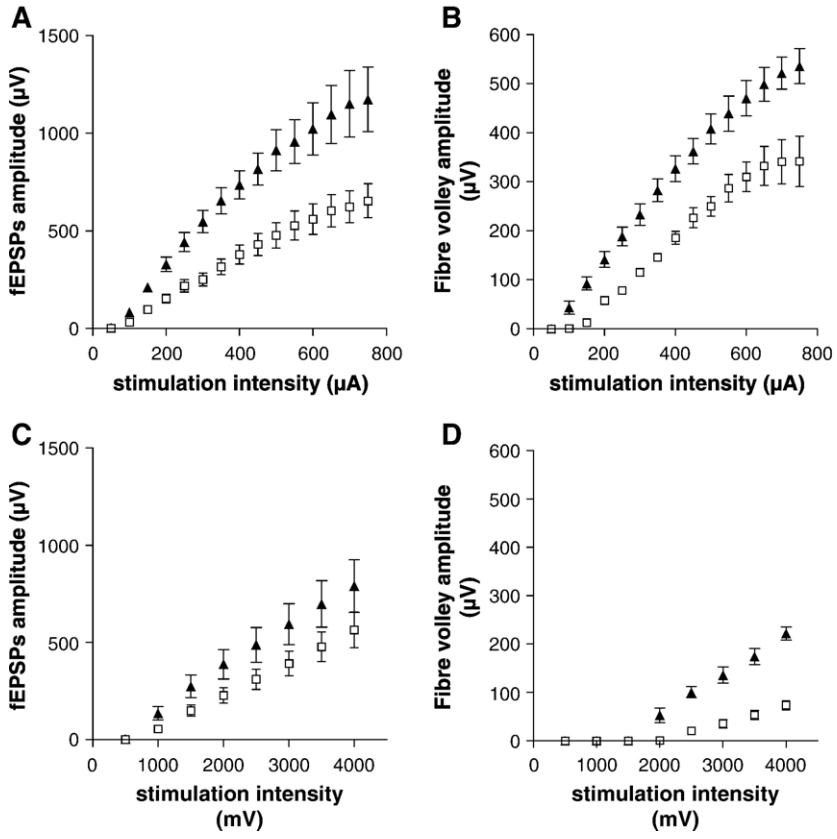

Fig. 1 – Amplitude of Field Potentials and Fiber Volley as a function of stimulus intensity (either current or voltage). Slices were stimulated either with symmetric bipolar current (A, B) or voltage (C, D) pulses in the CA3 region. Field Potentials (FP) or Fiber Volley (FV) was recorded in CA1 (stratum radiatum). Mean values of FP or FV amplitudes (in μV) were plotted as a function of the stimulation intensity. In the same slices (A or B), increasing current stimuli were first applied between one MEA electrode and the reference electrode (squares) and then between two adjacent MEA electrodes (triangles) including the electrode that was used initially against the ground. Evoked FP and FV were twice bigger when the current stimulus is applied between two MEA electrodes. A good linearity of the responses versus stimuli is observed for current intensity between 50 and 600 μA (A, B). For stimuli >600 μA, a clear rectification appears for the FV amplitude which might indicate that whole fibers have been recruited. In the same slices (C or D), increasing voltage stimuli were first applied between one MEA electrode and the reference electrode (squares) and then between two adjacent MEA electrodes (triangles) including the electrode that was used initially against the ground. Voltage stimuli (C) did not evoke responses as large as the ones observed with current stimuli (A), but the voltage–response relationship is linear over the range of values investigated (C). As previously observed for current stimulations, the amplitude of the FV is larger for bipolar stimulations (D). (A and C) Mean of 6 electrodes/slice and 2 slices for each protocol. (B and D) Mean of 8 electrodes in 3 independent slices. Error bars correspond to SEM.

by a biologically inert metal layer of black platinum, or titanium nitride. There are now a growing number of publications that demonstrate that neuron cultures as well as nervous tissue slices could be recorded and stimulated with MEA. If technical and methodological works describing the realization and the basic use of MEA are now well documented, their use in extensive biological studies has been documented in only a few studies (Meister et al., 1991; Tscherter et al., 2001; Shimono et al., 2002; Wirth and Luscher, 2004). We present here multiple ways for the use of MEA in the rat adult hippocampal slice to demonstrate that such technique could be easily used for physiological and pharmacological studies. Finally, and may be of most importance, we would like to shed light on the fact that MEA allow multi-sites recording within a single slice enabling powerful statistical analysis and observation of region-specific phenomenon.

2. Results

2.1. *Current versus voltage stimulation with MEA*

MEA electrodes display the unique advantage to be used either as active or as passive electrodes. To document the signals that could be triggered by the MEA, we have performed in the same slices different stimulating protocols based on current or voltage pulses applied between one electrode and the ground reference electrode (monopolar) or between two adjacent