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BRAIN RESEARCH

Research Report

Neurophysiological properties of cells filling the neonatal medial prefrontal cortex lesion cavity

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ABSTRACT

Removal of the medial prefrontal cortex (mPFC) of the rat during the initial 7–12 days of life results in spontaneous filling of lesion cavity that is accompanied by recovery of cognitive and motor functions. To date, it remains uncertain whether tissue filling the lesion cavity is actually supporting the functional improvement. In the present study, we examined whether spontaneous neuronal activity could be recorded in adulthood from the tissue that fills the lesion cavity. We recorded EEG and multiunit activity in adulthood from the mPFC and the motor cortex of rats that had received neonatal mPFC lesions on post-natal day 10 (P10) or their non-lesioned littermate controls. We found similarities in both the firing pattern and firing rate of cells from the filled-in region compared to that of controls, although the power associated with peak frequencies in the delta, alpha, and beta range in the EEG recorded from the filled-in region was lower compared to controls. Overall, our results suggest that the cells found in the lesion cavity have similar neurophysiological properties to those found in normal tissue and thus should be capable of at least partially supporting the observed recovery of function.

1. Introduction

Rats given medial prefrontal cortical (mPFC) lesions during the initial 7–12 days of life show remarkable functional improvement (Kolb, 1990; Kolb and Gibb, 1991, 1993; Kolb et al., 1996b; Lois and Alvarez-Buylla, 1994) that is accompanied by spontaneous filling of lesion cavity observed as soon as 7–14 days following injury (Kolb et al., 1996b). The most extensive recovery of function occurs if the injury is inflicted between postnatal days 7 and 12 and if the adjoining motor cortex is largely spared, but not if the tissue is removed before postnatal day (P) 7 or at any point after P15 (Kolb et al., 1996b). In addition, similar damage to other cortical regions, such as the parietal, visual, and motor cortices, does not result in spontaneous filling of the lesion cavity at any point in development (Kolb et al., 1987, 1996a; Monfils et al., 2005).

Although functional improvements have been consistently reported, it remains uncertain whether the tissue filling the lesion cavity is actually supporting the observed recovery of function. The tissue is only about 60% of normal volume and the cortex is much thinner than normal. Retrograde tracing from two regions (striatum and posterior parietal cortex) known to be connected to medial frontal cortex in normal adult rats revealed the tracer in the cells that were also co-labeled with a marker of proliferating cells in the midline filled-in region, suggesting that the newly formed cells develop at least some normal connections (Kolb et al., 1998). Moreover, the neurons residing in the filled region show a

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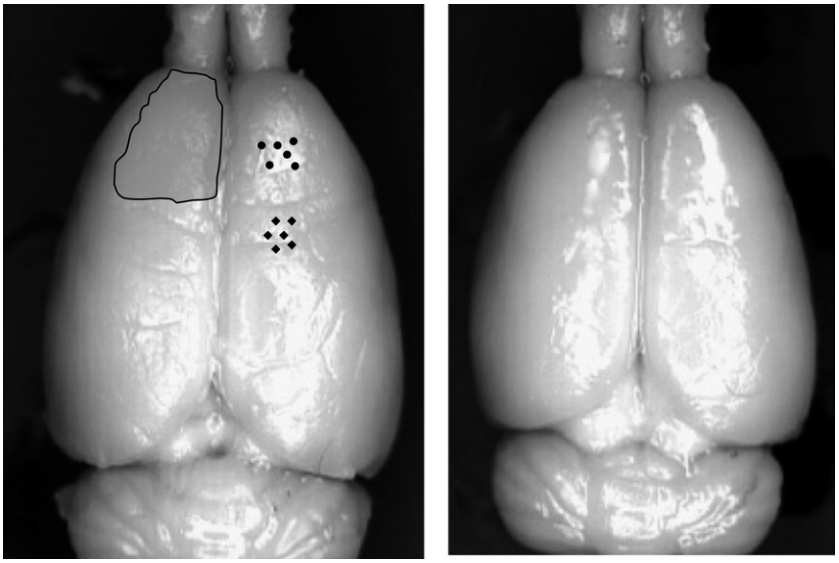

Fig. 1 – Photographs of representative brains from each group. The adult brain of a rat given midline frontal cortex lesions on postnatal day 10 (left) and the brain of a normal adult rat (right). The lesion cavity is significantly filled, although the hemispheres of the lesioned rat are smaller, narrower, and the colliculi are more visible. In addition, on the left hemisphere of the control brain (left panel), the extent of what the lesion area normally would be in adulthood is traced. On the right hemisphere of the control brain, some approximate recording sites in the mPFC (circles) and the control motor cortex (diamonds) are indicated. Actual recordings were performed bilaterally.

progressive dendritic development in the weeks after the injury, although they remain simpler than that in an intact mPFC. Taken together these data suggest a functional incorporation of this tissue with the surrounding environment (De Brabander and Kolb, 1997). Perhaps the most convincing evidence for the possible role of the filled region in functional recovery comes from the demonstration that blocking 're-growth' by pre-treating the rats embryonically with the mitotic marker bromodeoxyuridine (BrdU) results in no functional improvement (Kolb et al., 1996b) whereas removing the 're-grown' tissue reverses functional improvement (Dallison and Kolb, 2003; Kolb et al., 2007).

An important requirement for the demonstration that the tissue filling the lesion cavity functions is to show neural activity in 're-grown' tissue is physiologically normal and resembles normal tissue. To date, this has not been demonstrated despite the impressive amount of circumstantial evidence that suggests the involvement of the filled region in recovery of function. In the present study, we aimed to establish whether spontaneous neuronal activity could be recorded in adulthood from the tissue that fills the previously lesioned cavity. We gave rats mPFC or sham lesions on P10 and recorded EEG and multiunit activity in adulthood (P100) from the mPFC and the motor cortex.

2. Results

2.1. *EEG and multi unit recordings*

Fig. 1 is a photograph of a representative brain of a control rat (A) and a representative adult brain of a rat that received mPFC lesion at P10 with a mostly filled lesion cavity (B). We characterized the firing pattern of the cells in the mPFC (or the tissue filling the previously lesioned mPFC area) and the motor cortex, which in this case served as a control region. We were able to acquire multiunit activity and EEG recordings in all rats that received mPFC lesion at P10, and in all control rats. A representative multiunit activity recorded from 're-grown' tissue in mPFC-lesioned rat and an example of a spike from an isolated cell are presented in Fig. 2. A total of 22 cells in the

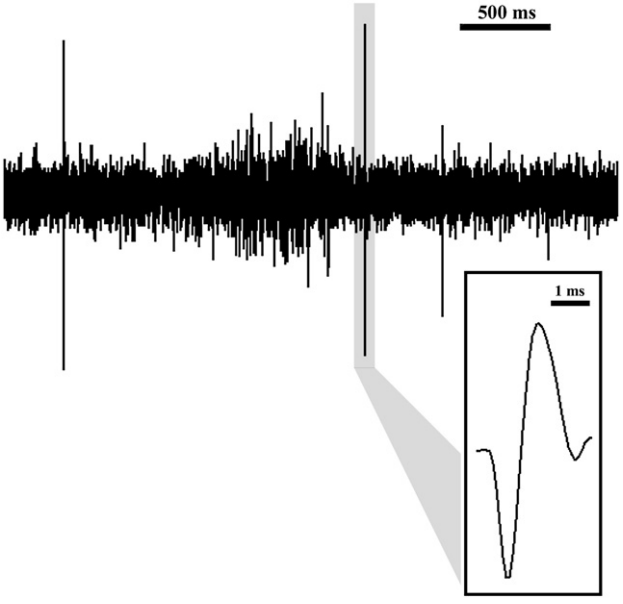

Fig. 2 – A representative multiunit activity (top) recorded from tissue found in the lesion cavity in mPFC-lesioned rat and (bottom) an example of a spike from an isolated cell.