Transient global brain ischemia in young and aged rats: differences in severity and progression, but not localisation, of lesions evaluated by magnetic resonance imaging

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Abstract

A model of transient global brain ischemia consisting of bilateral occlusion of common carotid arteries for 10 min and mild hypoxia (15% O2–85% N2) for 20 min was studied by means of MRI in young and aged Fischer 344 rats (3–4 and 24–26 months, respectively). Ischemia was assessed by full suppression of spontaneous EEG activity, which reappeared and normalized similarly in the two age-groups. The survival of young with respect to aged rats was considerably higher both at 24 h (20/20, i.e. 100% vs 12/16, i.e. 75%) and at 48 h (16/20, i.e. 80% vs 6/16, i.e. 38%). The localisation of brain lesions, their severity and progression were evaluated by a diffusion-weighted MRI (DWI) sequence at 24 and 48 h post-ischemia. There were no DWI-detectable lesions in eight out of 20 young and two out of 12 aged rats. The localisation of DWI-detected lesions was rather similar in rats of the two age-groups. In fact, the cerebral cortex, mainly parietal, occipital and temporal lobes were damaged in 83% of young and 90% of aged rats. The respective percentages for the thalamus were 83 and 60%, for the striatum 58 and 50%, and for the hippocampus 25 and 30%. The lesions present in the cerebral cortex and the thalamus were considerably more severe in aged than in young rats. In conclusion, in spite of similar localisation of ischemic lesions in the two age-groups, their incidence was higher, appearance more rapid and severity more pronounced in aged with respect to young rats. This resulted in a considerably higher mortality of the former. The overall data indicate that the age issue is very important in experimental ischemia research. © 1998 Elsevier Science B.V. All rights reserved.

Keywords: Global brain ischemia; Magnetic resonance imaging; Ageing; Rat

1. Introduction

Epidemiological research shows that the incidence of ischemic stroke, in Italy cause of 15% of deaths, is about 130 times greater and the course of disease more severe in the aged with respect to the young population (65–74 as compared to 25–34 years) [1]. However, although more than 95% of human strokes occur in late middle or in the geriatric age range, up to a few years ago young and healthy animals were usually utilized for modelling stroke [2–6]. In an important editorial [7] the avoidance of the age issue in experimental stroke research has been found amazing. In fact, various biochemical age-related modifications in the brain, observed also by us [8–13] may influence the outcome of stroke in terms of recovery and plasticity, as well as efficacy of potential interventional strategies. More recently a reproducible model of focal brain ischemia (middle cerebral infarct) in aged rats has been described [14]. Very recently, an increased vulnerability of aged brain tissue to anoxic damage has been associated with age-related alterations in pH regulation [15].
In one of our recent investigations a relatively simple model of transient global ischemia consisting of bilateral common carotid arteries (CCA) ligation associated with mild hypoxia (15% O2-85% N2) has been developed in young adult rats [16,17,28]. This resulted in an immediate suppression of spontaneous EEG activity followed after 7 days by a neuronal damage accompanied by gliosis, mainly in the cerebral cortex, thalamus and hippocampus, detected by histological and immunohistochemical methods [16].

Several studies demonstrated that magnetic resonance imaging (MRI), and in particular diffusion-weighted imaging (DWI), provides powerful means to detect in a non-invasive manner, in terms of voxel signal hyperintensity, the localisation, extension and temporal evolution of brain lesions, induced by ischemic insult [18-24]. Moreover, it is well known that there is a good correlation between the MRI hyperintensity and the impairment of bioenergetic metabolism in various brain areas [18,20,23]. Several MRI investigations utilised different focal brain ischemia models but only a few studies were devoted to global ischemia models in the rat [25-27]. Very recently, using the previously mentioned model of hypoxia-ischemia, we evaluated by MRI the spatial distribution and progression of brain lesions in young rats. The lesions were mainly localised in the cerebral cortex and, to a lesser extent, in the thalamus and/or striatum or hippocampus [28].

To our knowledge, there are no available MRI data on the severity and early evolution of DWI-detectable brain lesions induced by transient global ischemia in aged rats. The purpose of the present investigation was to extend the previous study to aged rats in order to assess, by means of MRI, possible similarities and differences in the localisation of brain lesions, their severity and progression at 24 and 48 h following an episode of hypoxia-ischemia.

Preclinical results of this study were presented at the 5th Scientific Meeting of the International Society for Magnetic Resonance in Medicine held in Vancouver, April 1997 [29].

2. Materials and methods

2.1. Animals

The directives of the Council of the European Communities (86/609/EEC) on animal care and use have been duly followed. Twenty-five male Fischer 344 rats of 3–4 months (250–300 g) and 22 rats of 20–24 months (350–450 g) were obtained from Charles River, Italy (Calco, Como).