Early anatomical and microstructural changes induced in rat brain by Vitamin A Deprivation: a longitudinal MRI study

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Purpose: Vitamin A Deprivation (VAD) constitutes a nutritional model of accelerated cerebral aging [1]. Retinoids, derivates of vitamin A, are indeed implicated in the adult neuronal system functioning specially in cognitive processes such as neuronal plasticity [2] and associated with memory disorders [3]. After 10 weeks of VAD in weaned rat, cerebral and hippocampal volumes were decreased with dramatic ventricular enlargement [1], followed at 14 weeks by severe impairments in spatial learning and memory task and, at long, β-amyloid deposit [4]. Our aim was to follow-up and characterize the earliest brain changes from the onset of vitamin A deprivation, using Diffusion Tensor Imaging (DTI) and anatomical MRI.

Materials and methods: Male Wistar rats were fed ad libitum with a VAD diet during 6 weeks from the weaning (21 days-old, 45-50 g; n=4). The control group (Ctrl) was fed with usual laboratory food (n=4). Anatomical images (15 coronal slices; RARE acquisition; TE/TR: 70/3700 ms; resolution 210x153x600 μm^3) and diffusion tensor images (B-value 1000; 30 diffusion directions; resolution: 0.312x0.312x1 mm^3) were acquired, using a 4.7T MRI scanner, once a week along the first 6 weeks of VAD. Fraction Anisotropy (FA) and apparent diffusion coefficient were computed for the striatum and hippocampus and corpus callosum using regions of interest manually defined on diffusion maps. The volumes of the total brain, ventricles, hippocampus and striatum were assessed after a semi-automatic segmentation of anatomical images. Post-hoc statistical tests were used to compare values obtained from VAD and control groups.

Results: The earliest change in diffusion parameters was detected on the week 5-6 (data were pooled) in the striatum (FA_{VAD}=0.34; FA_{Ctrl}=0.29; p=0.05). Time-depending volume decrease in the total brain, hippocampus and striatum was revealed between VAD-and Ctrl-groups. The earliest decrease was found on second week (-4.4% of brain volume; -13.9% of hippocampus volume and –22% of striatum volume). On the 6th week, the volume decreases were estimated to: -9% of brain volume; -14.2% of hippocampus volume and –28.5% of striatum volume (Fig.1.A).

Brain volume decrease through the time is coupled by a ventricular enlargement starting at the onset of the VAD. This decrease becomes stronger from 4th week of VAD. On 6th week of VAD, the mean ventricular volume in the VAD-group is 2.65 time higher than that of Ctrl-group (fig.1.B).

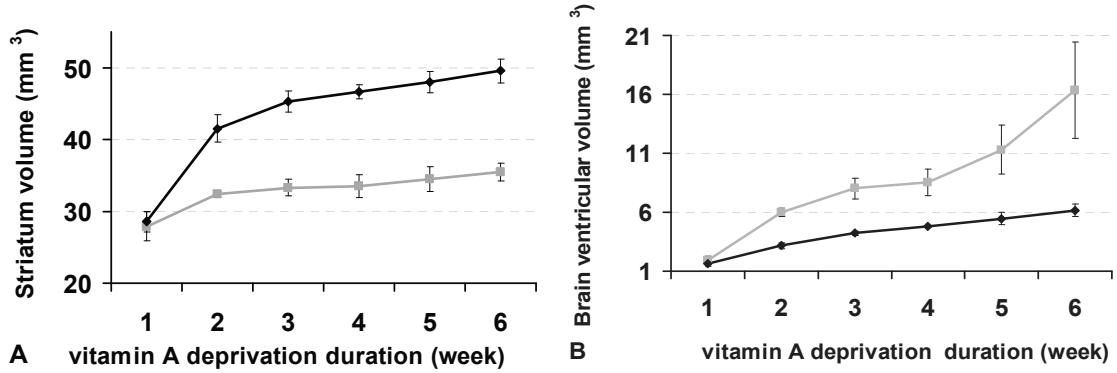

Figure 1: Striatum and ventricular volumes changes in control rats (♦) and in rats with a VAD (■).

Conclusion: Previous study [1] performed only from the 5th VAD week pointed out global changes in cerebral, hippocampal and ventricular volumes. This preliminary study demonstrated for the first time that VAD decreased from the 1st week the growth of total brain, striatum and hippocampus. At the 4rd week of VAD, the dramatic increase in ventricular volumes can be correlated with the 2-fold decrease in serum retinol [1]. Retinoids are proposed as candidates for the treatment of neuroinflammation [5], this latter being detectable in earliest stages of diseases such as Alzheimer [6]. So we could hypothetized an implication of a decrease in VA biodisponibility in the onset of inflammation described in numerous neurodegenerative processes.

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