Normal Aging of the brain

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Introduction

With the increase of the mean age of our populations, neurodegenerative diseases are becoming more and more important. This is also true for the early diagnosis of neurodegeneration and to allow for an early therapeutic intervention since degenerative diseases begin long before the patient experiences any symptoms. It can be months or years before clinical symptoms become obvious. Imaging with its sensitivity to detect even suitable changes in the brain may be of vital importance in this scenario. Even with the fact that the radiolocical evaluation of neurodegenerative diseases has markedly improved with the introduction of modern MRI techniques, the differential diagnosis between the different diseases is still a challenge. It requires a detailed analysis of the normal aging changes and always includes the assessment of the clinical findings and labora tory tests.
Beside conventional MRI imaging with volumentric analysis, the assessment of the brain microstructure using diffusion tensor imaging (DTI) has become a promising toll in aging research.

The aging brain

In the normal aging brain we see changes in the iron content, the volume of the brain and the amount of white matter changes. These changes may vary and are influenced by a large number of factors, including lifestyle, blood pressure, diabetes etc. Normally one can not clearly differentiate normal from early pathological changes. However, to detect changes one should know about the normal findings.

Several studies have shown that there is an increase in the cerebral iron deposition with age – the cause, however, is poorly understood. MRI is a sensitive method to visualize iron deposition in the brain, mainly in the basal ganglia. Taking into account that the higher the field strength of the MRI the more sensitive is the detection of iron, one should be aware of the fact that subjects age 70 or younger should be further evaluated for neurodegenerative disease if there is a stronly deminshed T2 signal in the basal ganglia (Figure 1), suspective for pathologic iron deposition.

Focal or even diffuse white matter hyperintensities are common findings in the elderly population. They increase with age and are described to be more common in patients with dementia. To decide weather they are still normal or already pathologic is not possible in the majority of cases. They should be described as punctate, patchy or confluencing (Figure 2). Some of them may be attributed to Virchow-Robin spaces.

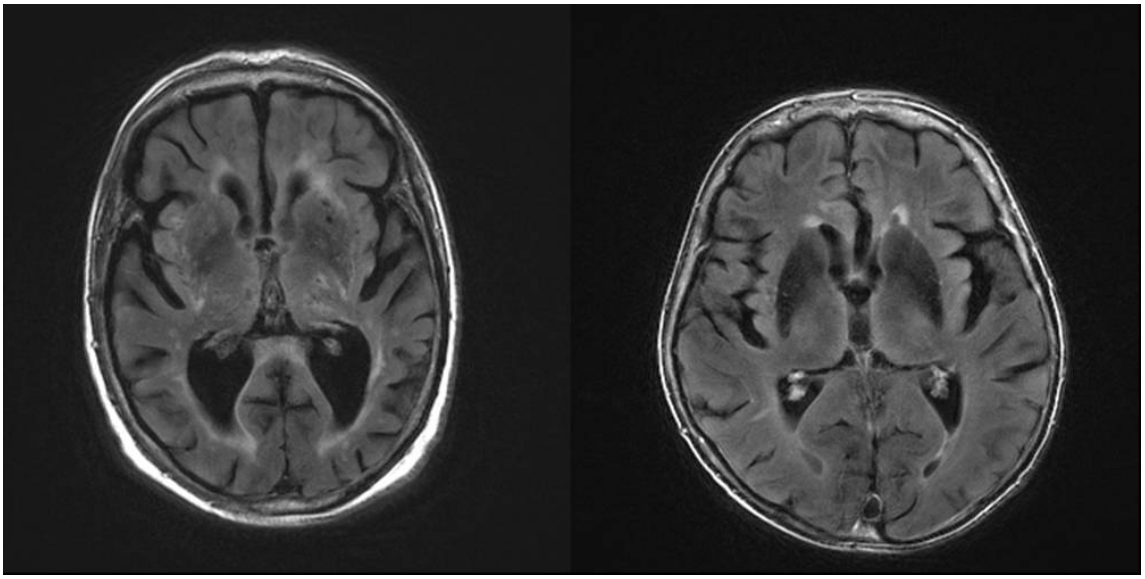

Figure 1: Left: Normal iron deposition in a patient with global cerebral atrophy (72 year and cogonitive impairment) on 3T-FLAIR MRI. The patient on the right also presented with mental decline but did not present atrophic changes (69 year old patient – 3T FLAIR MRI). However, the signal in the putamen is substantially reduced which is suspicious for iron deposition and therefore the presence of a neurodegenerative disesase

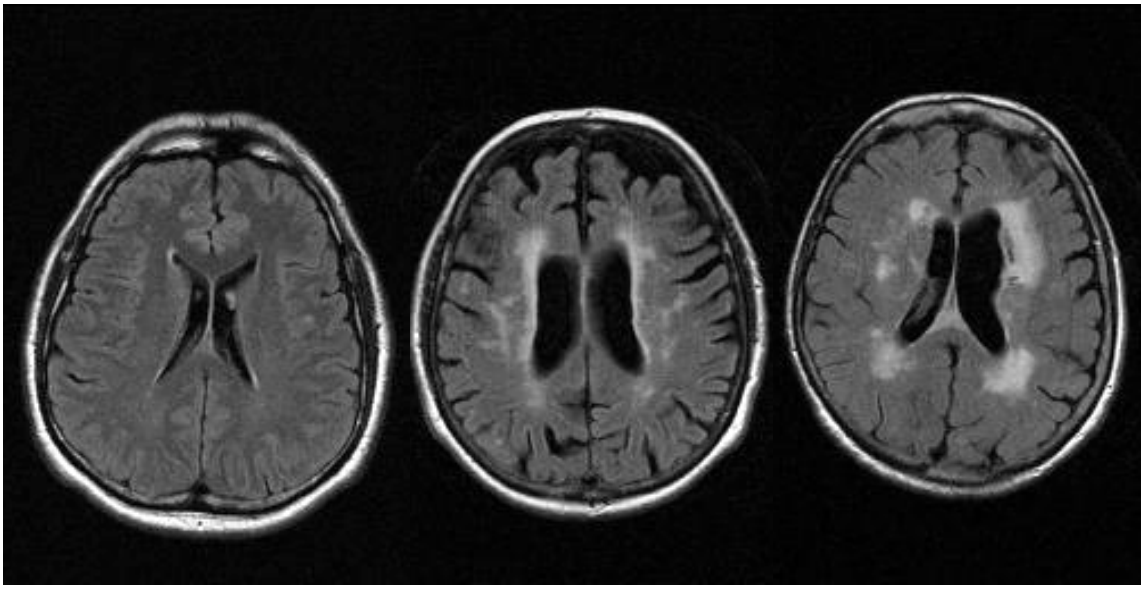

Figure 2*: White matter hyperintensities on routine FLAIR imaging in 3 subjects at the age of 70. On the left a normal finding is shown with only solitary lesions, in the middle a mixed stage with solitary and partially confluencing lesions. The case on the right represents major confluencing lesions mixed with makroangiopathic changes hydrocephalus e vacuo.*

Risk factors for an increased number of white matter hyperintensities are hypertension, diabetes and previous treatments. Pathologically they represent arteriosclerotic atrophic demyelination in combination with dilated vascular spaces. The corpus callosum is normally not affected, wich allows a differentiation from inflamatory diseases which normally include the corpus callosum. The changes present normaly without enhancement.

To better categorize these findings diffusion imaging may be helpful to differentiate between acute, subacute or chronic changes.

Volumetric changes of the brain also correlate with age. With a maximum weight in the third decade of age, a gradually decline of brain volume can observed thereafter. Using MRI as volumetric tool these changes can be assessed and serve as early indicator for a neurodegenerative disease. A widening of the sylvian fissure, the basal cisterns and later also the interhemispheric fissures with an associated widening of the ventricles can be observed after the age of 65-70. The normal atrophic changes normally affect the frontal lobes first, followed by the parietal lobes with consecutive enlargement of the lateral ventricles, but sparing the temporal horns. A change in the temporal horns is therefore a sensitive marker of a neurodegenerative disease (Figure 3).

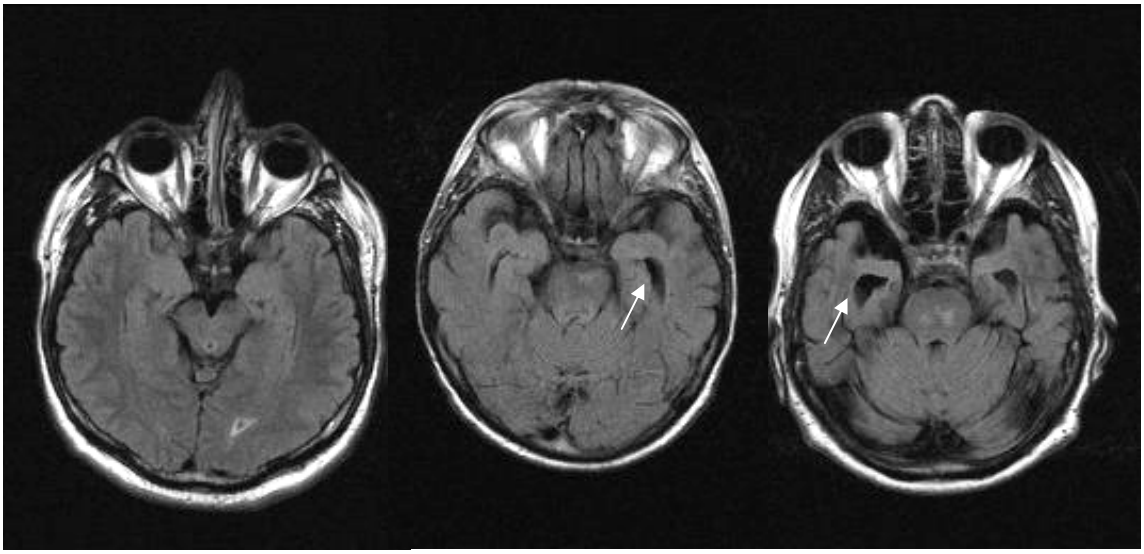

Figure 3*: Normal finding on the left and increasing atrophy of the temporal lobes with consecutive widening of the temporal horns (arrows) of the lateral ventricles (all subjects age 71).*

DTI – Microstructure analysis

DTI allows for a robust quantification of cerebral microstructures by the microscopic stochastic movement modelled as Brownian motion within each voxel of the data set. In regions with few or no constraints imposed by physical boundaries, such as CSF in the ventricles, water movement is random, i.e. freely diffusing, and is therefore isotropic. By contrast, the path of a water molecules, for example in a white matter fiber tissue, is constrained by the physical boundaries, such as the axon sheath, causing the movement to be greater along the long axis of the fibre than across it and is anisotropic, typically measured as fractional anisotropy (FA) and ranging between 0 and 1 on a normalized scale. Thus, DTI is selectively sensitive to the detection of tightly packed fibres in locally parallel orientation, characterizing white matter commissures, bundles and fasciculi of the brain. The method is also sensitive in the detection of disturbances in the fiber integrity thus allowing for an early diagnosis of degenerative dieases. Studies of normal ageing have benefited immeasurably by the introduction of quantitative DTI, which has successfully revealed evidence of microstructural disruption of regional white matter even in regions appearing normal on bulk volume imaging.

Since the initial quantitative DTI study of normal aging by Pfefferbaum in 2000, several studies have replicated the original finding of decline in FA and complementary increase in diffusivity in brain white matter with advancing age, and this ageing pattern is similar in men and women. Although the FA decline with age is linear from about 20 years onwards, the rise in diffusivity is not and accelerates in older age. To date, however, studies of normal ageing have relied on cross-sectional examination of healthy men and women drawn from either contrasting age groups (young vs elderly adults) or a continuous age distribution. The lack of longitudinal results limits generalization of available studies.

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