Pathways common to brain development and aging

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Research question and background

The increasing number of elderly people will have a major impact on the prevalence of age-related diseases like Alzheimer's disease (AD), which will pose major challenges to keep health systems in Europe sustainable. Current knowledge is insufficient to identify the transition of normal brain ageing into AD-like brain damage. The aim of the DEVELAGE project is to characterize shared molecular pathways between early development processes in the brain and brain ageing. The concept is based on the hypothesis that disorders of neural development contribute to age-related neurodegeneration, that developmentally essential proteins might have a role in neurodegeneration and that neurodegeneration related proteins and genes are important during the development of the brain. In this regard, Down's syndrome (DS, trisomy 21) represents a complex genetic abnormality that leads to pathology in later life that is similar to AD, and provides a good model to study neurodegenerative changes occurring in brain development disorders. DS is a strong risk factor for dementia that is very similar to AD. DS prevalence of dementia increases with age: 8% before age of 50, 55% before age of 60, and 75% after age of 60 years.

Methods and tissues used

The project will carry out a detailed neuropathological and molecular analysis of the spectrum of developmental and ageing changes in humans as well as in experimental models at genetic, epigenetic, transcription and protein levels. To gain a better understanding of the role of neurodegeneration-related proteins during human brain development, the expression and cellular distribution of these proteins will be studied in early and post-natal development stages and developmental disorders including DS. This will be compared with their expression in neurodegenerative diseases like AD. Further, the study will examine the relation between neurodegeneration-related proteins specific developmental pathways.

Results and conclusion

The study will improve our understanding of abnormal (re-)activation of pathways essential to neurodevelopment and how this might contribute to early events in neurodegeneration. This knowledge will provide novel avenues of investigation into suitable therapeutic approaches to target critical pathways at a stage when pathological progress can still be reverted. The study is ongoing at the moment and results/articles arising from the project will be presented to the Brain Bank when available.