

The pathology-dementia relationship: evidence of modification from human epidemiological studies

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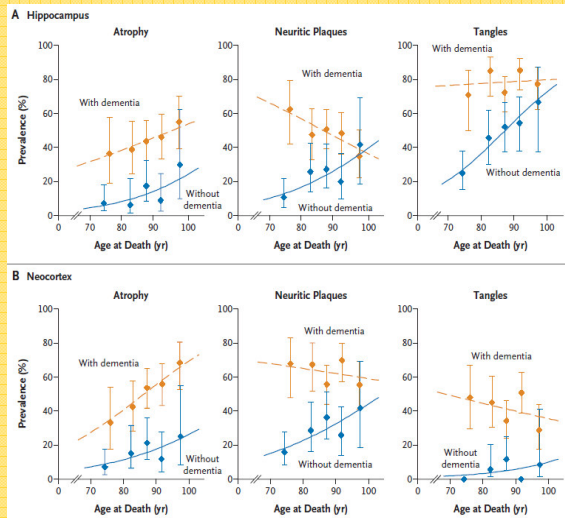
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Background

- Dementia is a clinical syndrome associated with many underlying pathologies. It is often defined in animal models as the presence of insoluble protein aggregates in association with behavioural impairments.
- In humans, as pathological burden increases so does the risk of clinical dementia during life. However, there is much variability around these risk estimates suggesting that other factors modify the relationship between pathological burden and clinical dementia.
- We present two recent epidemiological examples for late onset dementia: the effects of age and formal years of education.

The effect of age on the pathology-dementia relationship [Savva et al. (2009). N Engl J Med;360:2302-09]

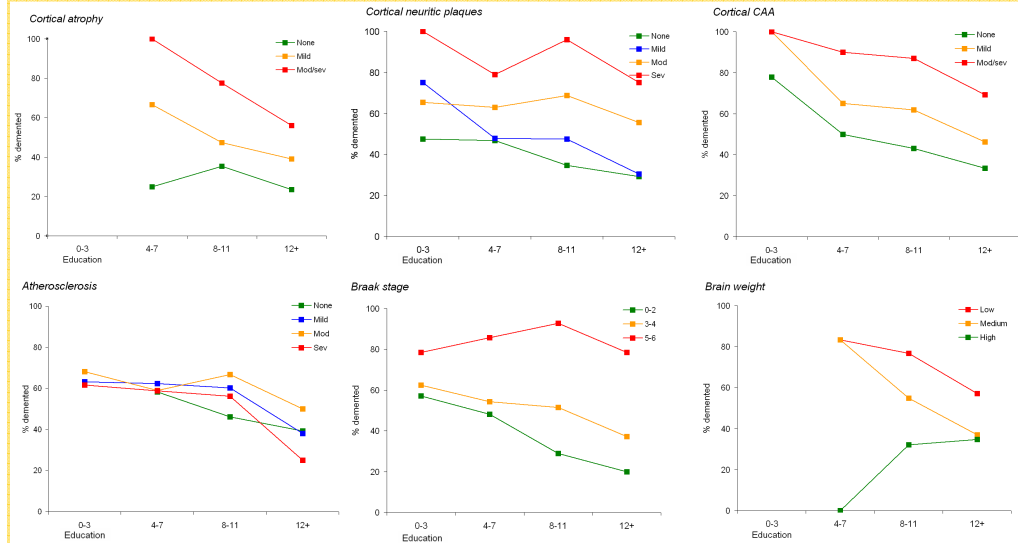
The relationship between Alzheimer's type pathology (neuritic plaques and tangles) and clinical dementia attenuates with increasing age, but this is not the case for atrophy (hippocampal or cortical). The association between the pathological features of Alzheimer's disease and dementia is therefore stronger in younger old persons than in older old individuals.



Modelled and observed prevalence of moderate/severe pathological burden (y-axis) relative to age (x-axis). Persons who died with clinical dementia (yellow) are compared with those who died without dementia (blue).

The effect of education on the pathology-dementia relationship [ECLIPSE (2010). Brain;133:2210-6]

Higher education (e.g. primary, secondary and tertiary education) confers a decreased risk of dementia during life, taking into account pathological burden. This effect is not entirely due to those with higher education having less neuropathology.



Percentage of demented individuals (y-axis) relative to years of education (x-axis). Pathological severity is indicated by colour. Each graph illustrates how education attenuates the association between pathology and dementia. For Braak stage and brain weight, this protective education effect varied with pathological severity.

Key points

- The relationship between pathological burden and dementia is not straightforward.
- Epidemiological and animal model approaches to investigate the underlying biology of dementia are complementary. Some animal models and experiments are integrating epidemiological findings but more integration could improve the relevance of animal models to humans.

