

Unravelling the pathology of dementia

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Combination therapies to tackle multiple changes in the brain may be needed to combat the growing problem of dementia in ageing societies, according to a study published this week in the open access journal *PLoS Medicine*. The study shows that multiple abnormal processes in the brain are often involved in cases of dementia, and that the drugs currently in development to treat individual brain pathologies may have a limited impact on the overall burden of dementia in the population.

Dementia - which can involve problems with memory, language and judgement - is a growing social and clinical problem affecting a quarter of people 85 years or older and an estimated 35 million people worldwide. Paul Ince, of the University of Sheffield, and colleagues at the University of Cambridge, conducted the study to estimate the relative contribution of known causes of [dementia](#) in the [brain](#) to dementia at death. Their research drew upon data from the Medical Research Council's Cognitive Function and Ageing Study - a major investigation into dementia in England and Wales that began in 1990.

In this study, the researchers used statistical methods to establish the proportion of dementia directly attributed to each specific change in the brain and other factors. 456 participants in the study donated their brains for post-mortem examination which enabled estimation of the contribution of each type of pathology to dementia in the population as a whole. The main pathological contributors to dementia were clumps of proteins called plaques and neurofibrillary tangles (19%) - which are regarded as the hallmarks of Alzheimer's disease -and blood vessel disease (21%). Other factors contributing to the risk of dementia across

the population included age, markers of reduced brain size and atrophy of a structure called the [hippocampus](#) which is involved in [learning](#) and [memory](#).

The researchers conclude that dementia is often associated with mixed pathological changes - in other words, at death many people had changes in the brain consistent with Alzheimer's and those linked to vascular dementia. The findings may be difficult to extrapolate to the living population because most changes in the brain can only be established by post-mortem, whilst the abnormal changes in the brains of people living with dementia may alter over time. Nevertheless, the findings suggest that drugs focusing on specific pathologies - whilst having a profound effect in some the smaller proportion of cases in which a single disease process predominates - may do little to reduce the overall burden of dementia in societies with ageing populations. An effective strategy for the population will need a range of protective strategies linked to biomarkers for each major risk factor.

More information: Matthews FE, Brayne C, Lowe J, McKeith I, Wharton SB, Ince P. (2009) Epidemiological Pathology of Dementia: Attributable-Risks at Death in the Medical Research Council Cognitive Function and Ageing Study. PLoS Med 6(11): e1000180.
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