

EClipSE

Epidemiological Clinicopathological Studies in Europe

CFAS
CC75C
Vantaa 85+

Epidemiological CLInicoPathological Studies in Europe (EClipSE)

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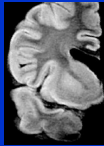
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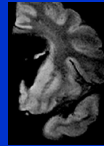
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Background

Studies that have examined the neuropathological basis of dementing disorders in the population have found that neuropathological markers are neither necessary nor sufficient in explaining clinical dementia in a substantial proportion of cases.



The Epidemiological Clinicopathological Studies in Europe (EClipSE) project aims to investigate why some individuals clinically dement without displaying neuropathological markers sufficient for a classification of dementia whilst others never clinically dement despite displaying neuropathological markers sufficient for a classification of dementia?



Methods

There are three European population-based prospective longitudinal studies of ageing and dementia which include a brain donation program: Cambridge City over-75s Cohort (CC75C), MRC Cognitive Function and Ageing Study (CFAS) and Vantaa 85+. The basic details on each of the three studies are displayed in Table 1.

The harmonisation of clinical and neuropathological data from brain donors in each of the three European studies forms the EClipSE database.

EClipSE is the largest population-based neuropathological resource in the world. A description of the development process for the EClipSE database is displayed in Figure 1.

Table 1. Details of studies included in the EClipSE database

	Baseline	No. at baseline	Age at baseline	No. brain donors
Vantaa 85+	1991	553	85+	290
CC75C	1985	2,600	75+	190*
MRC CFAS	1989/1991	18,226	65+	456*

*Collection ongoing

EClipSE aims and research questions identified

Clinical and neuropathological data mapped across the three studies

Common data identified (common defined as apparent in two or all of the studies)

Common data obtained and harmonised

Clinical and neuropathological data stored in a common format for statistical analyses

Figure 1. Development process

Before data was obtained from each study and harmonised to form the EClipSE database, research questions were identified and refined based on identified available and common data.

Study aims

- To determine the percentages of old people who display dementia-related neuropathological markers (e.g. plaques, tangles, cerebral amyloid angiopathy) relative to the population as a whole and clinical dementia status.
- To investigate the effects of apolipoprotein E (APOE) genotype, age and sex on the relationships between neuropathological markers and clinical dementia status.
- To investigate the effects of 'brain reserve' factors such as education, social networks and social class on the relationships between neuropathological markers and clinical dementia status.
- To investigate the relationships between neuropathological markers and behavioural and psychological symptoms of dementia (e.g. anger and irritability).
- To characterise those who age and die without developing clinical dementia in terms of neuropathological markers and longitudinal clinical symptomatology.

What data are available?

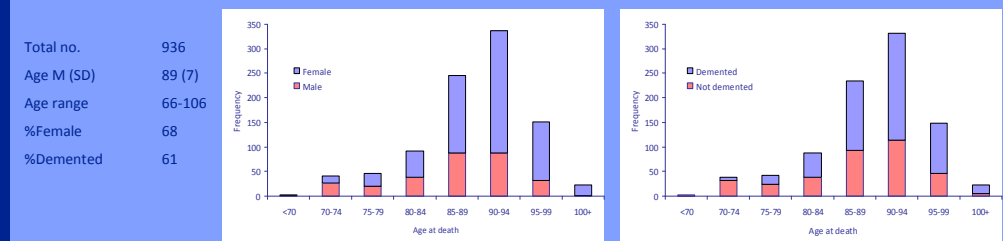
Demographic: age at interviews and death, sex, education, marital status, social class, social networks and accommodation.

Clinical: demented status, cognition (e.g. Mini Mental State Examination and self-reported memory impairment), activities and instrumental activities of daily living, health conditions and psychiatric symptomatology.

Neuropathological: all participants have Braak stage. CC75C and CFAS participants have full Consortium to Establish a Registry for Alzheimer's Disease (CERAD) data and Vantaa 85+ participants have neuritic plaques, atherosclerosis, haemorrhage, lesions and cerebral amyloid angiopathy (all overlap with CERAD measures).

Genetic: APOE genotype.

Figure 2. EClipSE participants: age at death, sex and dementia status



Future plans

Brain tissue (frozen and fixed) and blood samples were collected in each of the three studies involved in EClipSE. It is hoped that EClipSE will have funding to enable access to these samples to carry out further neuropathological and genetic work. Of particular interest is:

- the investigation of relationships between genome wide analysis results and gene expression in the brain
- the investigation of new pathological markers of dementia such as TAR DNA binding protein (TDP-43)
- better characterisation of neuropathological markers already part of the EClipSE database such as vascular pathologies