Epidemiological CLInicoPathological Studies in Europe (EClipSE)

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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.

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.

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

Table 1. Details of studies included in the EClipSE database

<table>
<thead>
<tr>
<th>Study</th>
<th>Baseline</th>
<th>No. at baseline</th>
<th>Age at baseline</th>
<th>No. brain donors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vantaa 85+</td>
<td>1991</td>
<td>553</td>
<td>85+</td>
<td>290</td>
</tr>
<tr>
<td>CC75C</td>
<td>1985</td>
<td>2,600</td>
<td>75+</td>
<td>190*</td>
</tr>
<tr>
<td>MRC CFAS</td>
<td>1989/1991</td>
<td>18,226</td>
<td>65+</td>
<td>456*</td>
</tr>
</tbody>
</table>

*Collective ongoing

Figure 1. 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