Neuronal changes in the dorsolateral prefrontal cortex of post-stroke and other age-related dementias

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Introduction

- Stroke is the second most common cause of dementia in developed countries.¹
- Post-stroke dementia (PSD) is defined as "any dementia occurring after stroke" with approximately 30% of all stroke survivors expected to develop PSD.²
- It remains unknown why only certain individuals go on to develop PSD and others remain cognitively intact.
- Changes in neuronal morphology are thought to be pathological substrates of dementia.
- Interneurones, also termed 'local circuit neurones', make connections in the neocortex between different neuronal domains and account for 20-30% of the total neurone population.³

Aim

To determine if there were any significant differences in layer V GABAergic interneurones of the dorsolateral prefrontal cortex between the disease groups and controls.

Material and methods

- Dorsolateral prefrontal cortex (Brodmann area 9) was immunostained using antibodies to three calcium-binding proteins: parvalbumin (PV), calbindin (CB) and calretinin (CR) (Figure 1).
- Interneurones were selected for counting based on three criteria: size, shape and intensity of staining.
- Two sets of quantitative counts were taken per image; one count for the total interneurones present, and one count for interneurones that were visibly more darkly stained. The percentage of darker stained interneurones was also calculated for each case.

Table 1 shows the demographic of the cohort included in this study ± standard error shown in brackets.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Subjects</td>
<td>Age (Years)</td>
</tr>
<tr>
<td>Controls</td>
<td>10</td>
</tr>
<tr>
<td>PSND</td>
<td>10</td>
</tr>
<tr>
<td>PSD</td>
<td>10</td>
</tr>
<tr>
<td>VaD</td>
<td>10</td>
</tr>
<tr>
<td>Mixed</td>
<td>10</td>
</tr>
<tr>
<td>AD</td>
<td>10</td>
</tr>
</tbody>
</table>

Discussion

- An increase in the number of darker stained interneurones suggests an increase in oxidative stress in demented cases and PSND (Fig.2A).
- An increased volume of pyramidal cells in layer V correlates with an increased number of interneurones, for disorders which have a vascular basis (Fig.3), the higher the number of interneurones the more darker expressing cells will be present and it is thought these damaged interneurones will eventually undergo cellular death.
- Correlation between MMSE scores and VaD interneurone counts suggest that once cell death has occurred, the interneurones which remain will have a lower percentage of darker stained cells; and therefore a reduced burden of damaged interneurones (Fig.2C).

Conclusion

- Intensely stained (darker) interneurones appear to be pathological substrates for dementia.

References