Explanatory factors for the association between depression and long-term physical disability after stroke

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Abstract

Objectives: to identify explanatory factors for the association between depression at 3 months after stroke and physical disability at 3 years.

Methods: data from the South London Stroke Register (1998–2013) were used. Patients (n = 3,612) were assessed at stroke onset. Follow-up at 3 months included assessment for depression with the Hospital Anxiety and Depression scale (scores ≥ 7 = depression), physical disability (Barthel index) cognitive function, smoking habit, selective serotonin reuptake inhibitors (SSRIs) use, perception of recovery and social support. Physical disability was reassessed at 3 years. The associations between depression at 3 months and physical disability at 3 years were estimated with multinomial regression adjusting for age, gender, ethnicity, stroke severity and possible explanatory factors for the association (introduced in the models first individually and then sequentially): pre-stroke medical history and physical disability, cognitive function, smoking, SSRIs, perception of recovery and social support at 3 months.

Results: one thousand three hundred and seven survivors were assessed at 3 months, of which 418 (32.0%) had depression. Survivors with depression had a higher physical disability rate at 3 years. These associations remained significant after adjustment for individual explanatory factors but were not significant after adjustment for combined explanatory factors. Physical disability at 3 months was a relevant explanatory factor for this association. SSRIs were associated with severe, relative risk: 6.62 (2.92–15.02) P < 0.001, and moderate physical disability, relative risk: 3.45 (1.58–7.52) P = 0.002, at 3 years.

Conclusion: the association between depression and physical disability appears to be multifactorial. The use of SSRIs after stroke requires further research.

Keywords: stroke, depression, disability, antidepressive agents, cohort studies, older people
Factors for the association between depression and long-term disability

**Introduction**

Depression has a prevalence of around 30% in the long term after stroke, with most patients developing their first symptoms shortly after the acute event [1, 2]. It is also an independent predictor of long-term disability [3, 4]. A number of medical and social factors have been proposed to underlie the relationship between depression and disability including other co-morbidities, such as diabetes, poor health behaviours (e.g. smoking), cognitive impairment, negative perception of coping strategies and poor socialisation. However, these are only hypothetical factors raised in studies that observed the association between depression and disability and in a systematic review of depression and risk of stroke [5–7]. A better understanding of the association between depression and disability would strengthen the evidence for causality, management and prognosis, of depression and disability, in the long term after stroke. This study investigates potential explanatory factors for the association between depression 3 months after stroke and physical disability at 3 years.

**Methods**

The study conformed to the recommendations of the STROBE statement [8]. First in a lifetime, stroke patients were recruited from the South London Stroke Register (SLSR), a prospective population-based cohort study [9]. Data from patients, registered in the SLSR between the 1 January 1998 and 30 June 2012, and followed up until the 30 June 2013, were used. The WHO definition of stroke was used [10]. Patients were registered during the acute phase of stroke. Data on age, gender and ethnicity were collected. Stroke severity measures were also recorded including Glasgow Coma Scale (GCS), categorised as severe (3–8), moderate (9–12) and mild (13–15), levels of impairment, urinary incontinence and paresis. Other data collected at baseline included medical history of diabetes, hypertension, ischaemic heart disease, congestive heart failure and atrial fibrillation.

Follow-up assessments were conducted by postal questionnaire or interview, depending on the capacity of the patient to fill in the questionnaire, at 3 months, 1 year after stroke and annually thereafter. At 3 months, patients were screened for depression using the Hospital Anxiety and Depression scale (HADS) [11]. HADS has been validated in stroke patients showing good performance both when it is used in a face-to-face interview and when it is self-administered [12] (optimum performance when the scores >7 in the HADS depression subscale are used to identify depression: sensitivity 0.82, specificity 0.74) [11]. As HADS cannot be answered by proxy, no data could be collected from patients with communication impairment that the fieldworker or next of kin, in case of postal questionnaire, judged would give invalid responses. Physical disability was assessed at 3 months using the Barthel Index (BI) [13]. To make physical disability measures clinically meaningful it was categorised: scores of 0–14 for severe, 15–19 moderate disability and 20 independent. Cognitive function was assessed at 3 months with the Mini-Mental State Examination (MMSE) [14] between 1997 and 2001 and with the Abbreviated Memory Test (AMT) [15] between 2001 and 2012. MMSE scores under 24 or AMT scores under 8 considered cognitive impairment [14, 15]. Other data collected at 3 months included smoking habit (smoker or non-smoker) and social support: Do you see as much of your relatives or friends as you would like? (Yes/No). Subjective perception of recovery from stroke was also recorded at this time point: Do you think that you have made complete recovery from stroke? (Yes/No). Medication taken regularly at the time of follow-up was recorded as well. This included use of selective serotonin re-uptake inhibitors (SSRIs), first-line drugs for the management of depression in adults [16]. Follow-up at 3 years included reassessments for physical disability (BI).

Multinomial regression was used to analyse the association between depression at 3 months and physical disability at 3 years after stroke adjusting for age, gender and stroke severity measures (GCS, incontinence and hemiparesis) These case-mix variables were chosen because of their clinical relevance and also because of their reported prognostic value [3, 17–19]. Potential explanatory factors for the association between depression and physical disability were then included in the model one at a time. In a second stage, these variables were sequentially included in the model, first, pre-stroke medical history (hypertension, diabetes, ischaemic heart disease and atrial fibrillation), then physical disability at 3 months [17] was added, cognitive impairment at 3 months was next, followed by smoking habit at 3 months, then use of SSRIs, subjective perception of recovery and finally social support [20, 21]. Only patients with complete outcome data were included in the analysis. Patients who were assessed or not for depression and for physical disability at follow-up were compared for age, gender and stroke severity using \( X^2 \) tests.

Most explanatory variables, including depression, had some missing data. A separate category was assigned to it, e.g. Paresis 0 (No), 1 (Yes) and 2 (Missing). Sensitivity analysis was conducted to compare estimates obtained when the category for missing data was included and when it was not included. All estimates were consistent with those based on complete data, so the results obtained using missing data categories were reported.

**Results**

The SLSR recruited 3,612 patients between 1998 and 2012, 1,014 (26.4%) of them died before the 3-month assessment and 954 (26.4%) were lost to follow-up. Among the 1,644 (45.5%) survivors who were followed up, 1,307 (79.5%) were able to complete the HADS and 418 of them (32.0%) were categorised as depressed. The characteristics of these patients are presented in Supplementary data, Table S1, available in Age and Ageing online. There was a higher proportion of patients with GCS <13 and urinary incontinence among those not screened for depression, and a higher proportion
of white patients among those assessed for physical disability in Year 3. No other differences were observed.

Depression at 3 months was associated with severe physical disability at 3 years, and this association remained significant after adjusting individually for past medical history, cognitive impairment, smoking, SSRIs use, perception of recovery and social support. The association became weaker after adjusting for physical disability at 3 months (Table 1).

SSRIs use at 3 months was independently associated with severe and moderate physical disability at 3 years; relative risk: 6.62 (2.92–15.02) \( P < 0.001 \) and 3.45 (1.58–7.52) \( P = 0.002 \), respectively.

When potential explanatory factors were included sequentially in the models, the inclusion of physical disability at 3 months made the association between depression and severe physical disability not significant (Table 2).

The associations between depression and severe physical disability were consistent with the ones observed for severe physical disability (Supplementary data, Tables S2 and S3, available in *Age and Ageing* online).

**Table 1.** Associations between depression at 3 months and severe physical disability (individual adjustment)

<table>
<thead>
<tr>
<th>RR (95% CI)</th>
<th>P value</th>
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<tbody>
<tr>
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<tr>
<td>Univariate analysis</td>
<td>4.22 (2.68–6.65) ( P &lt; 0.001 )</td>
</tr>
<tr>
<td>Model adjusted for age, gender, ethnicity and stroke severity</td>
<td>4.11 (2.51–6.74) ( P &lt; 0.001 )</td>
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<tr>
<td>Model adjusted for age, gender, ethnicity, stroke severity and past medical history of diabetes hypertension, ischaemic heart disease heart failure or atrial fibrillation</td>
<td>4.01 (2.43–6.62) ( P &lt; 0.001 )</td>
</tr>
<tr>
<td>Model adjusted for age, gender, ethnicity, stroke severity and physical disability at 3 months</td>
<td>1.72 (0.96–3.06) ( P = 0.065 )</td>
</tr>
<tr>
<td>Model adjusted for age, gender, ethnicity, stroke severity and cognitive function at 3 months</td>
<td>3.94 (2.39–6.52) ( P &lt; 0.001 )</td>
</tr>
<tr>
<td>Model adjusted for age, gender, ethnicity, stroke severity and smoking habit at 3 months</td>
<td>4.07 (2.48–6.69) ( P &lt; 0.001 )</td>
</tr>
<tr>
<td>Model adjusted for age, gender, ethnicity, stroke severity and use of SSRI at 3 months</td>
<td>3.72 (2.25–6.14) ( P &lt; 0.001 )</td>
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<tr>
<td>Model adjusted for age, gender, ethnicity, stroke severity and subjective perception of recovery at 3 months</td>
<td>3.88 (2.35–6.40) ( P &lt; 0.001 )</td>
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<tr>
<td>Model adjusted for age, gender, ethnicity, stroke severity and social support at 3 months</td>
<td>3.95 (2.39–6.52) ( P &lt; 0.001 )</td>
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**Table 2.** Association between depression 3 months after stroke and severe physical disability (sequential adjustment)

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<th>RR (95% CI)</th>
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<tr>
<td>Model adjusted for age, gender, ethnicity, stroke severity and past medical history of diabetes hypertension, ischaemic heart disease heart failure or atrial fibrillation</td>
<td>4.01 (2.42–6.63) ( P &lt; 0.001 )</td>
</tr>
<tr>
<td>Previous model further adjusted for physical disability 3 months after stroke</td>
<td>1.73 (0.97–3.11) ( P = 0.063 )</td>
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<tr>
<td>Previous model further adjusted for cognitive impairment at 3 months</td>
<td>1.74 (0.97–3.13) ( P = 0.064 )</td>
</tr>
<tr>
<td>Previous model further adjusted for smoking habit at 3 months</td>
<td>1.63 (0.90–2.94) ( P = 0.106 )</td>
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<tr>
<td>Previous model further adjusted for use of SSRI at 3 months</td>
<td>1.59 (0.87–2.88) ( P = 0.130 )</td>
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<tr>
<td>Previous model further adjusted for subjective perception of recovery at 3 months</td>
<td>1.45 (0.79–2.66) ( P = 0.226 )</td>
</tr>
<tr>
<td>Previous model further adjusted for social support at 3 months</td>
<td>1.57 (0.85–2.90) ( P = 0.146 )</td>
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**Discussion**

Depression 3 months after stroke is associated with higher rate of physical disability at 3 years. This association appears to have a multifactorial pathway with physical disability at 3 months being a relevant explanatory factor. In addition, SSRI use was associated with higher rates of physical disability.

The SLSR is a population-based cohort of stroke patients with large sample size and long-term follow-up. It provides the least biased sampling frame and good statistical power, allowing for an in-depth investigation of the nature of the association between depression and physical disability, in contrast to many previous studies [3]. It would have been better to assess depression with a diagnostic tool [22]. However, the HADS has a good performance in non-psychiatric patients according to a systematic review [11]. The BI does not discriminate well between patients with high degree of disability and does not capture relevant disabling issues such as dysphasia, which is a limitation of this study. Patients with communication impairment were excluded from the study, and this represents another limitation. Those with complete and incomplete data could not be compared for unmeasured factors, which may result in some patients being more likely to have incomplete follow-up. Nonetheless, the sensitivity analysis suggests that while some sociodemographic groups are more likely to be missing than others, this had little impact when analysing the association between depression and physical disability.

A combination of factors seems to explain most of the association between depression and physical disability. These include medical factors associated with both depression and...
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disability (e.g. diabetes) [23], psychological mechanisms, such as subjective perception of recovery from stroke and sociological factors, such as social isolation. However, it seems that the combination of depression, stroke severity and physical disability in the short term after stroke [19] has the highest impact not only on mood [2] but also on functionality in the long term. Therefore, holistic interventions addressing neurological deficit, mood and functionality shortly after stroke could have the highest beneficial effect in the long term.

The association between SSRI use at 3 months and physical disability could be explained, because patients on SSRIs may suffer from more severe depression [5]. It may also be that using SSRIs at 3 months is associated with depression shortly after stroke, which is strongly associated with both depression and disability in the long term [3, 19]. Another possibility is that the SSRIs have adverse effects that increase physical disability in the long term. Previous studies on the non-psychological effects of antidepressants report contradictory results [5, 24–28]. Further research is needed to clarify the therapeutic effects and safety of SSRIs in the long term after stroke.

Key points

- Depression at 3 months after stroke is associated with physical disability at 3 years, and this association remained significant after adjusting individually for past medical history, cognitive impairment, smoking, SSRIs use, perception of recovery and social support.
- This association appears to have a multifactorial pathway, with the combination of depression, stroke severity and physical disability in the short term after stroke having the highest impact on functionality in the long term.
- SSRIs use at 3 months was independently associated with physical disability at 3 years.

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Ethical approval

Written informed consent was obtained from patients or their relatives. The ethics committees of Guy’s and St. Thomas’ Hospital National Health Service Foundation Trust, King’s College Hospital Foundation, National Hospital for Nervous Diseases, Queen’s Square Hospital, St. George’s Hospital and Westminster Hospital approved the study.

References


Supplementary data

Supplementary data mentioned in the text are available to subscribers in Age and Ageing online.

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Conflicts of interest

None declared.
Delusions of pregnancy in older women: a case series

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Abstract

Background: delusions of pregnancy have been reported in a wide variety of functional and organic psychiatric conditions but rarely with dementia. Most such delusions arise in women of child-bearing age. We report five cases in older women all of whom had severe constipation that probably precipitated this delusion.

Case reports: of the five women (age 74–89 years), two had dementia, two had delirium and one had both. All patients had borne healthy children. Three women reported that they were in labour, and one was concerned that the baby was not moving. All had severe constipation on examination or imaging, and three had faecal impaction. All were treated with laxatives or enemas, and only one patient required brief antipsychotic therapy. The delusions lasted from a few hours to 5 days. In general, resolution of the delusion occurred in concert with improvement in bowel function, although in one case a large bowel movement was followed by the delusion that a baby had been born.

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