Anxiety after stroke: the importance of subtyping

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Anxiety After Stroke
The Importance of Subtyping

Ho-Yan Yvonne Chun, MBBS; William N. Whiteley, PhD; Martin S. Dennis, MD; Gillian E. Mead, MD; Alan J. Carson, MD

Background and Purpose—Anxiety after stroke is common and disabling. Stroke trialists have treated anxiety as a homogenous condition, and intervention studies have followed suit, neglecting the different treatment approaches for phobic and generalized anxiety. Using diagnostic psychiatric interviews, we aimed to report the frequency of phobic and generalized anxiety, phobic avoidance, predictors of anxiety, and patient outcomes at 3 months poststroke/transient ischemic attack.

Methods—We followed prospectively a cohort of new diagnosis of stroke/transient ischemic attack at 3 months with a telephone semistructured psychiatric interview, Fear Questionnaire, modified Rankin Scale, EuroQol-5D5L, and Work and Social Adjustment Scale.

Results—Anxiety disorder was common (any anxiety disorder, 38 of 175 [22%]). Phobic disorder was the predominant anxiety subtype: phobic disorder only, 18 of 175 (10%); phobic and generalized anxiety disorder, 13 of 175 (7%); and generalized anxiety disorder only, 7 of 175 (4%). Participants with anxiety disorder reported higher level of phobic avoidance across all situations on the Fear Questionnaire. Younger age (per decade increase in odds ratio, 0.64; 95% confidence interval, 0.45–0.91) and having previous anxiety/depression (odds ratio, 4.38; 95% confidence interval, 1.94–9.89) were predictors for anxiety poststroke/transient ischemic attack. Participants with anxiety disorder were more dependent (modified Rankin Scale score 3–5, [anxiety] 55% versus [no anxiety] 29%; P<0.0005), had poorer quality of life on EQ-5D5L, and restricted participation (Work and Social Adjustment Scale: median, interquartile range, [anxiety] 19.5, 10–27 versus [no anxiety] 0, 0–5; P<0.001).

Conclusions—Anxiety after stroke/transient ischemic attack is predominantly phobic and is associated with poorer patient outcomes. Trials of anxiety intervention in stroke should consider the different treatment approaches needed for phobic and generalized anxiety. (Stroke. 2018;49:00-00. DOI: 10.1161/STROKEAHA.117.020078.)

Key Words: anxiety ■ ischemic attack, transient ■ neuropsychiatry ■ phobic disorders ■ stroke
Our Aims
To determine the target for anxiety treatment after stroke, we need to know the proportions of anxiety subtypes; if phobic, the specific stimuli; the predictors for anxiety; the impact of anxiety on functional outcomes and quality of life. We aimed to report (1) the frequency of phobic disorder and GAD at 3 months after stroke and TIA, (2) avoidant behavior of specific anxiety-provoking situations, (3) the predictors of anxiety, and (4) the associations with dependence, quality of life, and social participation.

Methods
The data that support the findings of this study are available from the corresponding author on reasonable request as per the journal’s Transparency and Openness Promotion Guidelines.

Sampling and Recruitment
Prospective Recruitment
We screened consecutive eligible patients admitted to the acute stroke unit and TIA clinics in National Health Service Lothian—the sole provider of stroke and TIA services for the city of Edinburgh, Midlothian, and East Lothian regions in Scotland, between September 9, 2015, and June 28, 2016. We included participants who (1) were aged ≥18, (2) had a new clinical diagnosis of stroke or definite or probable TIA, (3) had mental capacity to give informed consent, and (4) were able to communicate in English on the telephone. We excluded patients with subarachnoid hemorrhage, subdural and extradural hematoma, ocular TIA, patients at terminal stage of life, or who were difficult to follow-up—no fixed abode, current illicit, or alcohol dependence.

Definitions of Stroke and TIA
We used clinical diagnosis of stroke or TIA made by consultant stroke clinicians according to the following strokes—to the sudden loss of focal cerebral function, lasting ≥24 hours, thought to be caused by an inadequate blood supply to part of the brain (ischemic stroke), or spontaneous hemorrhage into the brain substance (primary intracerebral hemorrhagic), where brain imaging was normal or showed evidence of recent ischemia or hemorrhage. A TIA—a clinical time-based definition of symptoms lasting <24 hours; TIA was definite when a diagnosis of TIA was the only one considered for the symptoms and probable when a diagnosis of TIA was the most likely of several differential diagnoses.

Baseline Characteristics
We used hospital electronic health records to gather data on age, sex, diagnosis on discharge, vascular territory of stroke/TIA, and the National Institutes of Health Stroke Scale score—a measure of neurological impairment on admission. We assigned a National Institutes of Health Stroke Scale score of zero to all TIA. We recorded whether the participants lived alone prestroke or TIA, had a history of stroke or TIA, or had a history of stroke/TIA, (2) had a new clinical diagnosis of stroke or definite or probable TIA, (3) had mental capacity to give informed consent, and (4) were able to communicate in English on the telephone. We excluded patients with subarachnoid hemorrhage, subdural and extradural hematoma, ocular TIA, patients at terminal stage of life, or who were difficult to follow-up—no fixed abode, current illicit, or alcohol dependence.

Assessment of Anxiety and Other Neuropsychiatric Disorders
At 3 months, a trained member of medical staff (H.-Y.Y.C.) performed a semistructured psychiatric interview (SCID) using the telephone version of the Structured Clinical Interview for Diagnostic Statistical Manual-IV-Text Revision of mental disorders. The SCID has fair-to-excellent interrater agreement for diagnosing both anxiety disorders and depression between experienced and newly trained clinicians and between its telephone and face-to-face versions. The following conditions were screened using the relevant SCID modules: panic disorder, agoraphobia, social phobia, specific phobia, GAD, obsessive-compulsive disorder, post-traumatic stress disorder (PTSD), and minor and major depressive episodes. All SCID diagnoses were made according to the SCID coding system and after confirmation with a consultant neuropsychiatrist (A.J.C.) at weekly meetings. Participants who were unable to talk on the telephone had face-to-face interviews at home or at an outpatient clinic. We measured cognition with the telephone Montreal Cognitive Assessment.

Assessment of Avoidant Behavior in Specific Anxiety-Provoking Situations
One week before the SCID interview, we sent the participant a Fear Questionnaire (FQ) for completion by post or online. The FQ consists of an agoraphobic subscale (5 items), a social phobia subscale (5 items), and a blood/injury phobia subscale (5 items). Each item denotes a situation and is rated according to the level of avoidance from zero (would not avoid it) to 8 (always avoid it). We replaced the blood/injury items with 6 other specific situations that we encountered in our clinical practice—(1) physical exertion, (2) having sex, (3) being alone at home, and any of your normal day-to-day activities for fear of having a headache (4) another stroke, or (5) a fall. During the interview, we also recorded positive responses to a list of 11 predefined anxiety-provoking stimuli, similar to the ones on the FQ (Table I in the online-only Data Supplement). We derived these additional anxiety-provoking stimuli from the shared clinical experience of our multidisciplinary stroke team in neuropsychiatry and post-stroke settings.

Potential Predictors for Anxiety Disorder at 3 Months After Stroke/TIA
We prespecified age, sex, living alone prestroke/TIA, and a past diagnosis of anxiety or depression as potential predictors for having anxiety disorder at 3 months after stroke/TIA.

Measures of Dependence, Quality of Life, and Social Participation
Measures of dependence, quality of life, and social participation were completed at the time of SCID with the modified Rankin Scale, the EuroQol-5D5L, and the Work and Social Adjustment Scale.

Statistical Analyses
We used descriptive statistics to summarize data, exact confidence intervals for proportions, and univariable and multivariable logistic regression to calculate unadjusted and adjusted odds ratios for associations. Group differences were assessed using univariable logistic regression, t tests, and Mann–Whitney U tests as appropriate to data type. Only returned FQs were analyzed for avoidant behavior. All items on the online questionnaire must be scored to permit submission, preventing any unscored items. Any unscored item on a returned postal questionnaire was given the most conservative interpretation and imputed zero, assuming that the item was irrelevant or did not elicit any anxiety symptoms. We performed all statistical analyses using STATA14. We aimed for a target sample size of ≥200 to achieve a desired precision of ±0.05 around our estimated frequency of poststroke anxiety of 0.20.

Reporting Standards and Ethics Approval
We reported the study in accordance with Strengthening the Reporting of Observational Studies in Epidemiology guidelines. We obtained approval from the South East Scotland Research Ethics Committee (15/SS/0087) on September 1, 2015. All participants gave written informed consent.

Results
We recruited 201 participants between September 9, 2015, and June 28, 2016. Twenty-six of 201 participants did not have
Table 1. Baseline Characteristics of Sample, by Anxiety Disorder at 3 Months

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>Prospective Cohort</th>
<th>SCID Diagnosis</th>
<th>Univariable Logistic Regression</th>
<th>Likelihood Ratio Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>Any Anxiety Disorder</td>
<td>No Anxiety Disorder</td>
<td>OR</td>
</tr>
<tr>
<td>Demographics</td>
<td>175</td>
<td>38</td>
<td>22%</td>
<td>137</td>
</tr>
<tr>
<td>Age, y; mean (SD)</td>
<td>69.6</td>
<td>(11.6)</td>
<td>64.2</td>
<td>(12.3)</td>
</tr>
<tr>
<td>Age group, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>62</td>
<td>35%</td>
<td>23</td>
<td>61%</td>
</tr>
<tr>
<td></td>
<td>0.08–0.56</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65–75</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>55</td>
<td>31%</td>
<td>6</td>
<td>16%</td>
</tr>
<tr>
<td></td>
<td>0.79–2.21</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;75</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>58</td>
<td>33%</td>
<td>9</td>
<td>24%</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>70</td>
<td>40%</td>
<td>18</td>
<td>47%</td>
</tr>
<tr>
<td>Men</td>
<td>105</td>
<td>60%</td>
<td>20</td>
<td>53%</td>
</tr>
<tr>
<td>Recruitment setting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinic</td>
<td>95</td>
<td>54%</td>
<td>21</td>
<td>55%</td>
</tr>
<tr>
<td>Acute stroke unit</td>
<td>80</td>
<td>46%</td>
<td>17</td>
<td>45%</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>109</td>
<td>62%</td>
<td>24</td>
<td>63%</td>
</tr>
<tr>
<td>Primary intracerebral hemorrhage</td>
<td>5</td>
<td>3%</td>
<td>3</td>
<td>8%</td>
</tr>
<tr>
<td>TIA (probable or definite)</td>
<td>61</td>
<td>35%</td>
<td>11</td>
<td>29%</td>
</tr>
<tr>
<td>Hemisphere of stroke/TIA symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left anterior circulation</td>
<td>82</td>
<td>47%</td>
<td>17</td>
<td>45%</td>
</tr>
<tr>
<td>Right anterior circulation</td>
<td>53</td>
<td>30%</td>
<td>13</td>
<td>34%</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>35</td>
<td>20%</td>
<td>6</td>
<td>16%</td>
</tr>
<tr>
<td>Uncertain</td>
<td>5</td>
<td>3%</td>
<td>2</td>
<td>5%</td>
</tr>
<tr>
<td>Neurological impairment (NIHSS)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>0 (0–2)</td>
<td>0</td>
<td>(0–2)</td>
<td>0</td>
</tr>
<tr>
<td>TIA</td>
<td>61</td>
<td>35%</td>
<td>11</td>
<td>29%</td>
</tr>
<tr>
<td>Stroke, NIHSS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>30</td>
<td>17%</td>
<td>9</td>
<td>24%</td>
</tr>
<tr>
<td>1–4</td>
<td>71</td>
<td>41%</td>
<td>16</td>
<td>42%</td>
</tr>
<tr>
<td>&gt;4</td>
<td>13</td>
<td>7%</td>
<td>2</td>
<td>5%</td>
</tr>
<tr>
<td>Prestroke status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lived alone before stroke/TIA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>60</td>
<td>34%</td>
<td>15</td>
<td>39%</td>
</tr>
<tr>
<td>No</td>
<td>115</td>
<td>66%</td>
<td>23</td>
<td>61%</td>
</tr>
<tr>
<td>Independent before stroke/TIA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>169</td>
<td>97%</td>
<td>37</td>
<td>97%</td>
</tr>
<tr>
<td>No</td>
<td>6</td>
<td>3%</td>
<td>1</td>
<td>3%</td>
</tr>
<tr>
<td>Past diagnosis of depression or anxiety disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>123</td>
<td>70%</td>
<td>15</td>
<td>39%</td>
</tr>
<tr>
<td>Depression only</td>
<td>30</td>
<td>17%</td>
<td>10</td>
<td>26%</td>
</tr>
<tr>
<td>Anxiety only</td>
<td>11</td>
<td>6%</td>
<td>6</td>
<td>16%</td>
</tr>
<tr>
<td>Both depression and anxiety</td>
<td>11</td>
<td>6%</td>
<td>7</td>
<td>18%</td>
</tr>
</tbody>
</table>

(Continued)
SCID at 3 months—3 had died, 1 was on palliation for terminal cancer, 4 had lost mental capacity, 9 withdrew consent for SCID, and 9 were not contactable (Figure I in the online-only Data Supplement). Participants lost to follow-up were more likely to live alone (losses: 15 of 26, 58%; analyzed: 60 of 175, 34%; \( P = 0.024 \)); otherwise, they were similar to those who were analyzed (Table II in the online-only Data Supplement).

In the analyzed sample (Table 1), 175 participants (mean age [SD], 70 [12]; women, 70 of 175; 40%) had SCID at 3 months poststroke/TIA. The majority had ischemic stroke, a third had TIA, and few had primary intracerebral hemorrhage (ischemic stroke: 109 of 175, 62%; TIA: 61 of 175, 35%; primary intracerebral hemorrhage: 5 of 175, 3%). We recruited similar numbers from the acute stroke unit and TIA clinic (acute stroke unit: 80 of 175, 46%; TIA clinics: 95 of 175, 54%). Our sample, therefore, consisted of patients with mild stroke and TIA (National Institutes of Health Stroke Scale: median [interquartile range], 0 [0–2]). Nearly all participants were interviewed by telephone (telephone: 168 of 175, 96%; face to face: 7 of 175, 4%).

**Frequency of Anxiety Disorders and Psychiatric Comorbidity at 3 Months After Stroke/TIA**

A fifth of our sample had at least 1 anxiety disorder at 3 months after stroke/TIA (38 of 175, 22% [95% confidence interval, 16–29]). Phobic disorder was the most frequent anxiety subtype (phobic disorder only: 18 of 175, 10%; both phobic disorder and GAD: 13 of 175, 7%; GAD only: 7 of 175, 4%; Figure 1A; Table 2). PTSD appeared as a comorbidity in phobic disorder-only cases (6 of 18), GAD-only cases (1 of 7), and both phobic disorder and GAD cases (4 of 13; Table 2). Half of all people with anxiety disorder also had a minor or major depressive episode (20 of 38, 53%; Figure 1B). We found no difference in cognitive function between patients with anxiety disorder and those without (telephone Montreal Cognitive Assessment median, interquartile range: [anxiety disorder] 18, 16–21; [no anxiety disorder] 19, 17–20; \( P = 0.692 \)). Of the TIA patients, 18% (11 of 61) had an anxiety disorder, 10% (6 of 61) had phobic disorder only, 3% (2 of 61) had both phobic disorder and GAD, and 5% (3 of 61) had GAD only.

**Avoidant Behavior and Anxiety-Provoking Situations/Stimuli**

Eighty-four percent (147 of 175) returned completed FQ for analysis. Nonresponders were younger than the FQ sample analyzed (mean age: nonresponders, 64.8±14.9; FQ analyzed, 70.5±10.6; \( P = 0.017 \)) but did not differ statistically in other characteristics (Table III in the online-only Data Supplement). Participants with an anxiety disorder at 3 months reported significantly higher level of avoidant behavior across all situations on the FQ compared with participants without (Figure 2). Similarly, during SCID, positive responses to all of the 11 predefined situations were more common in participants with anxiety disorder compared with those without (Figure II in the online-only Data Supplement). The fear of stroke recurrence had the most positive responses in those with anxiety disorder (31 of 38; 82%) and in those without (40 of 137; 29%).

---

**Table 1.** Continued

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>Prospective Cohort</th>
<th>SCID Diagnosis</th>
<th>Univariable Logistic Regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>Any Anxiety Disorder</td>
<td>No Anxiety Disorder</td>
</tr>
<tr>
<td>History of stroke</td>
<td>175</td>
<td>38</td>
<td>22%</td>
</tr>
<tr>
<td>Yes</td>
<td>22</td>
<td>13%</td>
<td>7</td>
</tr>
<tr>
<td>No</td>
<td>153</td>
<td>87%</td>
<td>31</td>
</tr>
<tr>
<td>History of ischemic heart disease</td>
<td>175</td>
<td>38</td>
<td>22%</td>
</tr>
<tr>
<td>Yes</td>
<td>30</td>
<td>17%</td>
<td>8</td>
</tr>
<tr>
<td>No</td>
<td>145</td>
<td>82%</td>
<td>30</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; SCID, Structured Clinical Interview for Diagnostic Statistical Manual-IV-Text Revision; and TIA, transient ischemic attack.

\( ^* P < 0.05 \).
Table 2. Sample Frequencies of SCID-Diagnosed Phobic Disorder, GAD, and Psychiatric Comorbidity (n=175)

<table>
<thead>
<tr>
<th>SCID Diagnosis</th>
<th>Total (n=175)</th>
<th>Sample Frequency, %</th>
<th>95% Confidence Intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any anxiety disorder</td>
<td>38</td>
<td>22</td>
<td>16–29</td>
</tr>
<tr>
<td>Phobic disorder only</td>
<td>18</td>
<td>10</td>
<td>6–16</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Panic disorder</td>
<td>5</td>
<td>3</td>
<td>1–7</td>
</tr>
<tr>
<td>PTSD</td>
<td>6</td>
<td>3</td>
<td>1–7</td>
</tr>
<tr>
<td>OCD</td>
<td>0</td>
<td>0</td>
<td>0–2</td>
</tr>
<tr>
<td>Depressive episode (minor+major)</td>
<td>7</td>
<td>4</td>
<td>2–8</td>
</tr>
<tr>
<td>GAD only</td>
<td>7</td>
<td>4</td>
<td>2–8</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Panic disorder</td>
<td>2</td>
<td>1</td>
<td>0–4</td>
</tr>
<tr>
<td>PTSD</td>
<td>1</td>
<td>0.5</td>
<td>0–3</td>
</tr>
<tr>
<td>OCD</td>
<td>0</td>
<td>0</td>
<td>0–2</td>
</tr>
<tr>
<td>Depressive episode (minor+major)</td>
<td>5</td>
<td>3</td>
<td>1–7</td>
</tr>
<tr>
<td>Both phobic disorder and GAD</td>
<td>13</td>
<td>7</td>
<td>4–12</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Panic disorder</td>
<td>7</td>
<td>4</td>
<td>2–8</td>
</tr>
<tr>
<td>PTSD</td>
<td>4</td>
<td>2</td>
<td>1–6</td>
</tr>
<tr>
<td>OCD</td>
<td>2</td>
<td>1</td>
<td>0–4</td>
</tr>
<tr>
<td>Depressive episode (minor+major)</td>
<td>8</td>
<td>5</td>
<td>2–9</td>
</tr>
<tr>
<td>All depressed (minor or major depressive)</td>
<td>27</td>
<td>15</td>
<td>11–22</td>
</tr>
<tr>
<td>Depressed with an anxiety disorder</td>
<td>20</td>
<td>11</td>
<td>7–17</td>
</tr>
<tr>
<td>Depressed without anxiety disorder</td>
<td>7</td>
<td>4</td>
<td>2–8</td>
</tr>
<tr>
<td>Not depressed</td>
<td>148</td>
<td>85</td>
<td>79–90</td>
</tr>
</tbody>
</table>

GAD indicates generalized anxiety disorder; OCD, obsessive-compulsive disorder; PTSD, Post-traumatic stress disorder; and SCID, Structured Clinical Interview for Diagnostic Statistical Manual-IV-Text Revision.

listed any additional anxiety-provoking situations reported during SCID (Table IV in the online-only Data Supplement).

Associations With Dependence, Health-Related Quality of Life, and Social Participation at 3 Months

Despite similar baseline neurological impairment (National Institutes of Health Stroke Scale 0–4, [anxiety disorder] 95% versus [no anxiety disorder] 92%; P=0.575), participants with anxiety disorder were more dependent (modified Rankin Scale score 3–5, [anxiety disorder] 55% versus [no anxiety disorder] 29%; P<0.0005), reported more problems across all health-related quality of life domains on the EQ-5D5L (Figure 3), and more restriction in social participation (Work and Social Adjustment Scale: median, interquartile range: [anxiety disorder] 19.5, 10–27; [no anxiety disorder] 0, 0–5; P<0.001).

Predictors of Anxiety Disorder at 3 Months After Stroke/TIA

The odds of having an anxiety disorder at 3 months after stroke or TIA decreased by a third per decade increase in age (adjusted odds ratio, 0.64; 95% confidence interval, 0.45–0.91) and increased 4-fold when there was a past diagnosis of anxiety or depression (adjusted odds ratio, 4.38; 95% confidence interval, 1.94–9.89; Table 3). Sex or living alone prestroke/TIA were not statistically associated with anxiety disorder at 3 months.

Discussion

Key Findings

In our sample of stroke and TIA patients, a fifth had an anxiety disorder diagnosed at psychiatric interview at 3 months. We found phobic disorder to be the predominant anxiety subtype after stroke or TIA. Anxious patients reported more avoidance in agoraphobia-related, social, and other specific situations or stimuli—physical exertion, having sex, being alone at home, activities related to fear of having a headache, another stroke, or a fall. PTSD was more common than we had anticipated. Younger age and having a history of anxiety or depression increased the likelihood of developing anxiety poststroke/TIA. Despite having a similar level of neurological impairment at baseline, participants with anxiety disorder were more dependent, had poorer health-related quality of life, and were more restricted in social participation at 3 months after stroke or TIA compared with those without anxiety disorder.

Potential Bias in Our Methodology

Our trained interviewer was a stroke clinician who received training in performing the SCID. We minimized any variability in diagnosis by having all final diagnoses discussed and confirmed with a consultant neuropsychiatrist at weekly meetings. A systematic review of studies assessing the agreement between diagnostic telephone and face-to-face psychiatric interviews found good agreement (κ=0.69–0.84) between the 2 versions in psychiatric populations,22 supporting the use of telephone SCID for anxiety disorders and depression. However, there are no such comparability data in stroke. The use of telephone SCID in our study could have influenced the accuracy of the true estimates of our SCID diagnoses. SCID diagnosis was made based on formal diagnostic criteria and coding system, taking into account detailed narrative of the patient’s experience. Temporary distress experienced by the participant at the time of SCID, if any, was unlikely to influence the final diagnosis. Our final sample size of 175 fell short of the 200 we intended to recruit. This impacted slightly on the precision of our frequency estimate for any anxiety disorder, from ±0.05 to ±0.06.

We note a high proportion of previous anxiety or depression in our sample. Case ascertainment relied on participants’ recollection of any past diagnosis made throughout their lifetime, potentially leading to overestimates. We had losses to follow-up in the prospective cohort. More people lived alone in the
losses compared with those who underwent SCID. This could have led to underestimates of anxiety disorder and depression because living alone is associated with a higher psychiatric morbidity in the general population. We lost FQ data through nonresponders, and they were younger compared with the FQ sample analyzed. Although over a quarter of participants completed the FQ online as their preferred method, we did not test the agreement between the 2 versions. Our population was at the milder end of the stroke spectrum.

**Interpretation**

Our frequency estimate falls within the range of frequencies reported in a recent meta-analysis of anxiety poststroke: 18% to 25%. We found phobic disorder to be the predominant anxiety subtype poststroke/TIA and quantified for the first time, the avoidant behavior of specific anxiety-provoking situations in people with anxiety poststroke/TIA. Our study is the first to have assessed the frequency of anxiety subtypes using diagnostic interview in TIA patients. Similar to our main analysis, phobic disorder was the most frequent anxiety subtype post-TIA. Our frequency estimate of anxiety disorder post-TIA is similar to that reported using a rating scale cutoff for definite anxiety in a regional stroke registry.

Earlier studies suggested phobic anxiety might be present after stroke, yet clinical trials of anxiety intervention did not translate this finding, treating anxiety poststroke as a unitary phenomenon. Thus far, only general approaches, such as relaxation and antidepressants, have been evaluated in stroke, which are unlikely to be effective in patients with predominantly phobic anxiety. Our findings suggest the need to evaluate exposure techniques—an approach known to be effective in phobic disorder in nonstroke populations but one that has never been evaluated in stroke. We identified the specific situations/stimuli avoided in our anxious participants, which could be potential targets for psychotherapy; for example, CBT.

**Fear of Stroke Recurrence**

The fear of stroke recurrence was the most commonly reported anxiety-provoking stimulus in our participants, with or without anxiety disorder. In our interviews, we found this anxious anticipation—the experience of anxiety by thinking about an event in the future, to have led to differential behaviors in our participants. In some, this anticipatory anxiety brought about a desire for better health and increased positive health behaviors; for example, complying to medications and doctor’s advice on lifestyle and giving up smoking. In others, this anticipatory anxiety became
disproportionate and perpetuated maladaptive avoidant behaviors of specific situations; for example, travelling alone, crowds, physical exertion, and social gatherings. The fear of stroke recurrence, accompanied by a sense of complete loss of control in a public place, seemed to underlie the agoraphobia in our participants. These maladaptive thinking patterns and avoidant behaviors are potential targets for cognitive restructuring and exposure therapy in a CBT intervention. In exposure therapy, phobic patients confront their specific feared situation in a graduated hierarchical fashion, until the unpleasant anxiety feelings diminish. The individual’s realization that catastrophe has not occurred, despite confronting his/her feared situation, for example, taking the bus, can be used to help challenge a maladaptive belief; for example, “I am going to have a stroke if I travel on the bus.”
Psychiatric Comorbidity
Psychiatric comorbidity in our sample was common, and its symptoms should be considered in the treatment of anxiety poststroke/TIA. Few studies have estimated the frequency of clinical diagnosis of PTSD poststroke/TIA.25 Like phobic and generalized anxiety, PTSD has specific treatment strategies in nonstroke populations—trauma-focused CBT and eye movement reprocessing.26,27 These now need to be tested in stroke. Our finding on PTSD adds weight to our general thesis that treating anxiety as a unitary condition after stroke will lessen the likelihood of finding effective treatments. In PTSD, individuals persistently reexperience the traumatic event in the form of distressing flashbacks, intrusive thoughts, and nightmares.7 In our cases of PTSD, emotional distress was provoked by bodily sensations or situations that reminded the individuals of their index event; for example, headaches, odd sensation in affected limb, and meeting people who were likely to enquire about the index event. Panic disorder was nested within our phobic and GAD cases. It refers to a tendency to have panic attacks—the most extreme and unpleasant form of anxiety state with marked autonomic symptoms and the feeling of impending catastrophe. Panic disorder is usually managed with CBT or medications. Consistent with the literature,1,28 concurrent depression was common among anxiety cases, reaffirming the need to manage depression in those with anxiety poststroke. Our frequency estimate of poststroke depression was half of what is usually reported.29 This is probably because our sample consisted of mainly mild stroke and TIA patients and that stroke severity and physical disability are the most consistent predictors for poststroke depression.30

Predictors of Anxiety Poststroke/TIA
The likelihood of developing anxiety after stroke or TIA increased in younger people and in those with a history of anxiety or depression, consistent with anxiety in the general population. In contrast to the general population, men were as likely as women to develop anxiety poststroke/TIA. We found no association between lesion location and anxiety poststroke/TIA.

Associations With Dependence, Quality of Life, and Social Participation
Our study findings on dependence, quality of life, and social participation challenge the pervasive view among stroke clinicians that these patients are not disabled by their seemingly minor cerebrovascular event. Anxiety disorders, PTSD, and depression can be profoundly disabling and need to be considered as important outcomes in stroke and TIA.

Implications for Future Research
The lack of evidence-based anxiety interventions is a barrier to improving outcomes in patients with anxiety poststroke/TIA. Trialists must recognize the need for different treatment approaches for phobic and generalized anxiety. Given the predominance of phobic disorder poststroke/TIA, exposure therapy needs to be evaluated in a clinical trial in this population. Individually tailored CBT (augmented CBT) is feasible in clinical trial setting of poststroke depression31,32 and may be similarly applied in anxiety poststroke/TIA.

Generalizability
Our sample is different from the population of patients with stroke, in that all our participants could communicate by telephone, hence in general had mild deficits. Based on the Scottish Stroke Care Audit registry data, we would expect around a fifth of the National Health Service Lothian stroke population to have communication difficulties. Furthermore, competing research studies were recruiting patients with more severe deficits at the same time as this study’s recruitment. We recruited half of our sample from clinic where patients tended to have mild or resolution of neurological symptoms. We, therefore, consider our sample as representative of the mild stroke and TIA population with limited generalizability to severe stroke or those who have significant communication difficulties. The telephone Montreal Cognitive Assessment scores in our sample are consistent with findings in a similar sample of stroke and TIA patients18 and suggest the presence of mild cognitive impairment—a known manifestation of mild stroke and TIA.33

Conclusions
Phobic disorder is the predominant anxiety subtype and can occur in the absence of GAD after a mild stroke or TIA. Future trials of anxiety intervention in stroke must consider the presence of phobic disorder and should consider the use of exposure therapy techniques and augmented CBT.

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References


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