Does Respiratory Muscle Training Improve Cough Flow in Acute Stroke? Pilot Randomized Controlled Trial

Stefan Tino Kulnik, MRes; Surinder Singh Birring, PhD; John Moxham, MD; Gerrard Francis Rafferty, PhD; Lalit Kalra, PhD

Background and Purpose—Cough protects the lungs from aspiration. We investigated whether respiratory muscle training may improve respiratory muscle and cough function, and potentially reduce pneumonia risk in acute stroke.

Methods—We conducted a single-blind randomized placebo-controlled trial in 82 patients with stroke (mean age, 64±14 years; 49 men) within 2 weeks of stroke onset. Participants were masked to treatment allocation and randomized to 4 weeks of daily expiratory (n=27), inspiratory (n=26), or sham training (n=25), using threshold resistance devices. Primary outcome was the change in peak expiratory cough flow of maximal voluntary cough. Intention-to-treat analyses were conducted using ANCOVA, adjusting for baseline prognostic covariates.

Results—There were significant improvements in the mean maximal inspiratory (14 cmH\textsubscript{2}O; \(P<0.0001\)) and expiratory (15 cmH\textsubscript{2}O; \(P<0.0001\)) mouth pressure and peak expiratory cough flow of voluntary cough (74 L/min; \(P=0.0002\)) between baseline and 28 days in all groups. Peak expiratory cough flow of capsaicin-induced reflex cough was unchanged. There were no between-group differences that could be attributed to respiratory muscle training. There were also no differences in the 90-day incidence of pneumonia between the groups (\(P=0.65\)).

Conclusions—Respiratory muscle function and cough flow improve with time after acute stroke. Additional inspiratory or expiratory respiratory muscle training does not augment or expedite this improvement.


(Stroke. 2015;46:447-453. DOI: 10.1161/STROKEAHA.114.007110.)

Key Words: breathing exercises ■ cough ■ pneumonia ■ prevention and control ■ rehabilitation ■ stroke

Poststroke pneumonia (PSP) is a well-known complication during the first few weeks after stroke.\(^1\) PSP incidence ranges from 2% to 57% in different studies, with a median of 10%.\(^2\) Patients who develop PSP have higher mortality, longer hospitalization, worse functional outcomes, and higher care needs.\(^2,3\) Impaired swallow and increased risk of aspiration are major risk factors for PSP.\(^2\) Cough (voluntary or reflex) is the most immediate protective mechanism from aspiration\(^4\) and requires coordinated activation of inspiratory, expiratory, and intrinsic laryngeal muscles.\(^4\) Stroke impairs respiratory muscle strength and cough flow by ≈50% compared with nonstroke controls.\(^5,6\) Respiratory muscle weakness is attributable to the disruption of central motor output, as opposed to intrinsic loss of peripheral muscle function.\(^3\) However, whether respiratory muscle strength and cough flow improve with stroke recovery is not known.

Respiratory muscle training (RMT) loads respiratory muscles beyond the usual level of functioning, resulting in strengthening of these muscles.\(^7\) Inspiratory muscle training leads to greater precough inspiratory volume, which increases expiratory cough flow. Expiratory muscle training increases intrathoracic driving pressure during the expulsive phase of cough. A meta-analysis of RMT in neurological diseases suggested that RMT improves inspiratory but not expiratory muscle strength, but was limited by small numbers and heterogeneity in patients, design, and outcome measurement.\(^8\) The effects of RMT on improving cough in patients with acute stroke, who have a higher risk of aspiration, remain unknown.

We hypothesized that RMT may facilitate recovery of respiratory muscle and cough function in patients with acute stroke, and thus reduce the risk of PSP. The objectives of this study were to investigate the following: (1) the extent of respiratory muscle recovery after acute stroke; (2) the effectiveness of RMT in improving respiratory muscle strength and cough generation; and (3) safety and concordance with RMT in patients with acute stroke.

Methods

Design
The study was a single-blind randomized controlled trial with 3 study groups; reporting followed Consolidated Standards of Reporting Trials (CONSORT) guidelines.\(^9\) Subjects were allocated using a...
computer-generated block-randomization sequence concealed in numbered sealed envelopes. Consequent eligible patients were allocated strictly in sequence. Participants were blinded to allocation, and end-point assessments were undertaken by an observer blinded to allocation. Good Clinical Practice guidelines were followed in the collection, storage, and handling of data conforming to institutional and United Kingdom (UK) Stroke Research Network governance guidelines. Data analysis was masked to allocation and supported by the King’s Clinical Trials Unit.

Participants
Participants were recruited at King’s College Hospital, London, United Kingdom, and received UK guidelines–recommended stroke rehabilitation on accredited units or at home. Patients with acute hemorrhagic or ischemic stroke were included, if they met the following criteria: age >18 years within 2 weeks of stroke onset; National Institutes of Health Stroke Scale10 score 5 to 25 with motor impairment; ability to give informed consent and follow study procedures. Exclusion criteria were as follows: blood pressure >180/100 mmHg more than twice in 24 hours; angina, myocardial infarction, or acute heart failure within 3 months; significant pulmonary disease; and neurological conditions other than stroke. All participants gave written informed consent. The study was approved by the UK National Research Ethics Service.

Intervention
RMT was undertaken daily for 4 weeks using the threshold load training method11 supervised by a qualified trainer. Training was provided in hospital initially and at home after discharge. Participants were required to breathe in (inspiratory training) or breathe out (expiratory training) against the resistance using commercially available devices (Threshold IMT; Threshold PEP; Respironics, Parsippany, NJ). Training consisted of 5 sets of 10 breaths each with 1-minute rests between sets. Resistance was set at 50% of maximal inspiratory (PImax) or expiratory (PEmax) mouth pressure for inspiratory or expiratory training, respectively. Maximal mouth pressures were reassessed and resistance readjusted weekly by the trainer. Resistance was set at 10% of maximal mouth pressure in the sham training regimen.

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram.
group. Participants kept a diary of training and adverse events, which was reviewed in weekly training visits.

**Outcomes**
Assessments were performed at baseline, 28±2 days (postintervention), and 90±5 days (sustainability of training effect). The primary outcome was peak expiratory cough flow (PECF) of voluntary cough at 28 days. Secondary outcomes were PECF of capsaicin-induced involuntary cough and maximal mouth pressures. Incidence of pneumonia was observed. Pneumonia was defined as temperature >37.5°C on 2 consecutive measurements or a single measurement of >38.0°C with chest symptoms, and ≥1 of the following: white cell count >11,000/mL, pulmonary infiltrate on chest radiograph, positive microbiology cultures.

**Assessment of Respiratory Function**
Baseline spirometry (SpiroUSB; CareFusion, San Diego, CA) and maximal mouth pressure assessments (MicroRPM; CareFusion Ltd, Rainham, England). Voluntary cough was assessed by asking participants to make repeated maximal cough efforts into a tight-fitting face mask. Involuntary coughs were induced by the nebulization of escalat-

**Sample Size**
Sample size calculation was based on an estimated group SD of 50 L/min for the primary outcome (voluntary cough PECF). A sample size of 16 subjects per group would give the study 80% power to detect 50 L/min difference between groups at the 5% significance level. Blinded data from the first 40 participants not divided by allocation showed higher than expected variation in baseline PECF, and the sample size calculations were revised so that the study retained 80% power at the 5% significance level. This required 20 subjects in each group, and assuming an attrition rate of 25%, sample size was increased to 78 subjects.

**Statistical Analysis**
Data were analyzed using statistical software (Stata v11.2; StataCorp, College Station, TX). Intention-to-treat analyses were conducted using ANCOVA. Intervention groups were compared against the sham training group at the primary end point (day 28), adjusting for baseline level of the outcome variable, sex, age, admission National Institutes of Health Stroke Scale score, baseline peak expiratory flow (as per spirometry), and training intensity. Predictive model-based multiple imputation was used to impute missing data. Logarithmic transformations of data were conducted to meet model assumptions. Subanalyses were undertaken to compare participants who completed the study with those who discontinued; and with participants with good and poor training completion. Training safety data (adverse effects; vital parameters before and after training) were summarized descriptively.

**Results**
Between March 2011 and April 2014, 1827 patients with acute stroke were screened, of whom 191 (10%) were eligible and 82 (4.5%) consented to participate. Main reasons for exclusion were admission National Institutes of Health Stroke Scale score ≤5 (n=725, 40%), unable to give consent or follow

---

**Table 1. Baseline Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Expiratory Training (n=27)</th>
<th>Inspiratory Training (n=26)</th>
<th>Sham Training (n=25)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>65.7 (15.4)</td>
<td>62.5 (14.6)</td>
<td>65.1 (13.9)</td>
<td>0.702</td>
</tr>
<tr>
<td>Men</td>
<td>14 (52%)</td>
<td>17 (65%)</td>
<td>16 (64%)</td>
<td>0.541</td>
</tr>
<tr>
<td>NIHSS score (median, IQR)</td>
<td>7 (5, 12)</td>
<td>8 (6, 11)</td>
<td>8 (6, 12)</td>
<td>0.645</td>
</tr>
<tr>
<td>Premorbid NADL score (median, IQR)</td>
<td>61 (45, 63)</td>
<td>59 (48, 63)</td>
<td>57 (46, 63)</td>
<td>0.875</td>
</tr>
<tr>
<td>Stroke type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>22 (82%)</td>
<td>23 (88%)</td>
<td>24 (96%)</td>
<td>0.308</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>5 (18%)</td>
<td>3 (12%)</td>
<td>1 (4%)</td>
<td>0.308</td>
</tr>
<tr>
<td>Stroke side</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>10 (37%)</td>
<td>8 (31%)</td>
<td>11 (44%)</td>
<td>0.689</td>
</tr>
<tr>
<td>Right</td>
<td>17 (63%)</td>
<td>17 (65%)</td>
<td>14 (56%)</td>
<td>0.689</td>
</tr>
<tr>
<td>Bilateral</td>
<td>…</td>
<td>1 (4%)</td>
<td>…</td>
<td>0.689</td>
</tr>
<tr>
<td>Stroke site</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical</td>
<td>12 (44%)</td>
<td>10 (38%)</td>
<td>11 (44%)</td>
<td>0.273</td>
</tr>
<tr>
<td>Subcortical</td>
<td>14 (52%)</td>
<td>12 (46%)</td>
<td>8 (32%)</td>
<td>0.273</td>
</tr>
<tr>
<td>Brain stem/cerebellar</td>
<td>1 (4%)</td>
<td>4 (15%)</td>
<td>6 (24%)</td>
<td>0.273</td>
</tr>
<tr>
<td>Current smoker</td>
<td>6 (22%)</td>
<td>5 (19%)</td>
<td>9 (36%)</td>
<td>0.344</td>
</tr>
<tr>
<td>Unsafe swallow on BSA*</td>
<td>13 (48%)</td>
<td>10 (38%)</td>
<td>12 (48%)</td>
<td>0.723</td>
</tr>
<tr>
<td>Forced spirometry</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FVC, L</td>
<td>2.2 (1.0)</td>
<td>2.1 (0.8)</td>
<td>2.4 (1.0)</td>
<td>0.437</td>
</tr>
<tr>
<td>FEV1, L</td>
<td>1.7 (0.9)</td>
<td>1.8 (0.7)</td>
<td>2.0 (0.9)</td>
<td>0.394</td>
</tr>
<tr>
<td>PEF, L/min</td>
<td>246 (145)</td>
<td>238 (130)</td>
<td>276 (149)</td>
<td>0.596</td>
</tr>
<tr>
<td>Maximal voluntary cough</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PICF, L/min</td>
<td>123 (59)</td>
<td>125 (66)</td>
<td>149 (85)</td>
<td>0.272</td>
</tr>
<tr>
<td>PECF, L/min</td>
<td>471 (218)</td>
<td>465 (307)</td>
<td>516 (278)</td>
<td>0.644</td>
</tr>
<tr>
<td>VI, L</td>
<td>1.7 (0.9)</td>
<td>1.4 (0.7)</td>
<td>1.6 (0.6)</td>
<td>0.455</td>
</tr>
<tr>
<td>VE, L</td>
<td>1.3 (0.8)</td>
<td>1.3 (0.7)</td>
<td>1.5 (0.7)</td>
<td>0.560</td>
</tr>
<tr>
<td>CVAC, L/s²</td>
<td>160 (92)</td>
<td>171 (132)</td>
<td>189 (128)</td>
<td>0.694</td>
</tr>
<tr>
<td>GCT, s</td>
<td>0.24 (0.1)</td>
<td>0.28 (0.2)</td>
<td>0.22 (0.1)</td>
<td>0.289</td>
</tr>
<tr>
<td>Capsaicin-induced involuntary cough</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PICF, L/min</td>
<td>91 (46)</td>
<td>88 (49)</td>
<td>83 (35)</td>
<td>0.884</td>
</tr>
<tr>
<td>PECF, L/min</td>
<td>273 (112)</td>
<td>313 (143)</td>
<td>272 (103)</td>
<td>0.823</td>
</tr>
<tr>
<td>VI, L</td>
<td>1.3 (0.6)</td>
<td>1.1 (0.6)</td>
<td>1.1 (0.5)</td>
<td>0.428</td>
</tr>
<tr>
<td>VE, L</td>
<td>0.7 (0.3)</td>
<td>0.7 (0.4)</td>
<td>0.6 (0.3)</td>
<td>0.994</td>
</tr>
<tr>
<td>CVAC, L/s²</td>
<td>105 (50)</td>
<td>127 (62)</td>
<td>117 (42)</td>
<td>0.358</td>
</tr>
<tr>
<td>GCT, s</td>
<td>0.18 (0.1)</td>
<td>0.24 (0.14)</td>
<td>0.21 (0.1)</td>
<td>0.341</td>
</tr>
<tr>
<td>Maximal mouth pressures, cmH₂O</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEmax</td>
<td>62 (34)</td>
<td>56 (34)</td>
<td>64 (34)</td>
<td>0.636</td>
</tr>
<tr>
<td>PImax</td>
<td>39 (32)</td>
<td>42 (27)</td>
<td>45 (27)</td>
<td>0.690</td>
</tr>
</tbody>
</table>

Data are mean (SD) and frequency (%), unless stated otherwise. BSA indicates bedside swallowing assessment; CVAC, cough volume acceleration; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 sec; GCT, glottis compression time; IQR, interquartile range; NADL, Nottingham Activities of Daily Living questionnaire; NIHSS, National Institutes of Health Stroke Scale; PEF, peak expiratory flow; PECF, peak expiratory cough flow; PEmax, maximal expiratory mouth pressure; PICF, peak inspiratory cough flow; PImax, maximal inspiratory mouth pressure; VE, expired cough volume; and VI, inspired cough volume.

*BSA by trained nursing staff, according to algorithm and including evaluation of level of consciousness, oromotor function, and trials of water/food; concerns trigger review by speech and language therapist.
study procedures (n=342, 19%), transfer to local hospitals in the first 72 hours (n=207, 11%), and cardiac, pulmonary, or neurological conditions other than stroke (n=194, 11%). Of 191 eligible patients, 41 (21%) declined giving no reason, 37 (19%) considered study procedures onerous, 29 (15%) were not interested in research, and 2 (1%) had safety concerns. Of 82 consented participants, 63 (77%) completed the primary end point (day 28), and 46 (56%) completed assessments at 90 days. Figure 1 shows the CONSORT flow diagram.

Primary and Secondary Outcomes
There were no differences in baseline characteristics between groups (Table 1). Respiratory muscle strength (PEmax, PImax) increased from baseline to day 28 and day 90 in all groups regardless of training allocation (Table 2). PECF of voluntary cough increased at 28 days in all groups, but was significant only for inspiratory and sham training (Table 2). There was no change in the PECF of involuntary cough from baseline to day 28 or to day 90 in any group. There were no between-group differences in voluntary cough, involuntary cough, and inspiratory or expiratory mouth pressures at any time-point in patients receiving inspiratory, expiratory, or sham training. Intention-to-treat analyses adjusted for missing values and multiple testing failed to show any significant differences between the sham and the inspiratory or expiratory training groups for the primary or any of the secondary outcome measures.

Within-group comparison of change (day 28–baseline) in cough flow and respiratory muscle strength from baseline to primary end point. Data are mean (SD). PECF indicates peak expiratory cough flow; PEmax, maximal expiratory mouth pressure; and PImax, maximal inspiratory mouth pressure.

Table 3. On-Treatment Analysis

Table 4. On-Treatment Analysis

Parent and secondary outcomes at the study time points. Data are mean (SD) and frequency (%). Pneumonia incidence is cumulative during entire study period. PECF indicates peak expiratory cough flow; PEmax, maximal expiratory mouth pressure; and PImax, maximal inspiratory mouth pressure.
expiratory training resulted in earlier achievement compared with sham training.

On-treatment analyses were conducted in 63 participants (21 per group) who remained in the study from baseline to day 28. There were no significant differences in baseline characteristics between the 3 groups or between the 63 complete cases and the 19 subjects who discontinued after randomization. On-treatment analyses showed an improvement over time in voluntary cough PECF, PEmax, and PImax in each study group (Table 3). There were no changes from baseline in involuntary PECF in any group. Between-group comparison showed no significant intervention effect (Table 4).

There were no differences in the 90-day incidence of pneumonia between the groups ($P=0.65$; Table 2). Sensitivity analyses were undertaken for the assumptions that all participants who discontinued training or were missing in any group developed pneumonia (worst case) or alternately did not develop pneumonia (best case). There were no differences between the sham and the training groups under any of these assumptions.

Concordance With Intervention

Training participation varied widely from the prescribed regimen of 28 days and 140 sets for each of the groups. The actual training (median and IQR) undertaken by the participants was 17 (6, 24) days and 80 (25, 115) sets. There were no differences in training concordance between the groups. One patient reported subjective discomfort and transient rise in blood pressure during expiratory muscle training, which resolved within minutes of discontinuing training. Minor adverse events included headache, fatigue, and light-headedness which were transient and did not affect participation.

The mean changes in cough flow and respiratory muscle strength outcomes were compared in participants who trained half (700 breaths) or more of the prescribed repetitions ($n=54$) with participants who trained less than half ($n=28$). There were no significant differences between the higher and lesser trained groups for voluntary cough PECF (92 versus 28 L/min; $P=0.08$), involuntary cough PECF (26 versus −14 L/min; $P=0.185$), PEmax (18 versus 9 cmH2O; $P=0.102$), and PImax (15 versus 12 cmH2O; $P=0.732$).

Discussion

This study showed that peak expiratory flow of voluntary cough and maximal inspiratory and expiratory mouth pressures improved in the first 4 weeks after stroke onset, but there were no changes in involuntary cough. A standardized program of inspiratory or expiratory RMT delivered for 4 weeks did not significantly add to the extent or speed of natural recovery of respiratory muscle strength or cough flow. Although RMT was safe, it had low eligibility (10% of patients screened), participation (43% of eligible patients consented), and concordance (52% of patients completed ≥70% of training).

In this exploratory study, PECF was used as a surrogate marker for effective cough, which is an important defense against aspiration and PSP. The weakness in cough seen in
patients with stroke has been shown to be related to down-regulation of cortical influences that modulate cough production, rather than peripheral muscle weakness. Although a mean PImax of ≈60 cmH2O at day 90 in all groups may suggest a persistent and clinically meaningful weakness, the SD of 30 cmH2O implied high variability and many participants achieved PImax values of >80 cmH2O. In addition, PImax has a wide range in normal subjects, with many having PImax values of <80 cmH2O.

Previous studies have shown that RMT can improve inspiratory but not expiratory muscle strength. Most of these studies were undertaken in patients with multiple sclerosis, Parkinson disease, amyotrophic lateral sclerosis, or myasthenia gravis; and group difference in PImax was not significant in individual studies but only became significant when data were pooled in meta-analysis. In addition, fewer studies included an expiratory muscle training element and the numbers of patients in whom PEmax was measured was smaller, which may have contributed to a lack of effect in meta-analysis.

The present study differed from previous research in stroke and other neurological diseases in several respects; RMT was started early when the potential for spontaneous recovery was still present and delivered at high intensity but low training frequency. Training concordance was higher in the inpatient setting and was lower once patients had been discharged home. It is possible that optimal training completion with greater supervision, or a different protocol with higher training frequency, may have been more successful; but this needs to be balanced against resources available to support RMT delivery and the time detracted from participation in other therapies. To increase the power of analysis, we pooled our data with 2 previous randomized controlled trials of RMT in patients with subacute and chronic stroke using similar outcomes. The larger sample of 132 patients in the pooled analysis still failed to show any significant increases in either inspiratory or expiratory pressures with RMT (Figure 2).

The major objective of RMT in patients with stroke is to reduce PSP. This exploratory study was not powered to show, and did not show, an effect on PSP incidence ≈90 days post-stroke. A randomized controlled trial to show a 5% decrease in PSP would require 828 patients to have 80% power at the 5% significance level based on data from this study and using pairwise comparisons. Taking into account an attrition rate of 25% and a participation rate of <5%, >22,000 patients would need to be screened for eligibility, which may not be feasible, even as a multicenter study. Given the lack of effectiveness of RMT to alter the physiological variables on which the assumption of PSP prevention is based, undertaking such a study would be futile.

The small study sample is a limitation, but the power of analysis was increased by applying strict inclusion criteria, increasing the sample size after interim analysis and undertaking pooled analysis. Variable training concordance is a potential source of bias, but neither comparison based on training intensity nor sensitivity analysis showed significant differences in outcomes. Missing data, confounding because of nonsignificant differences in baseline prognostic variables and multiple testing, are sources of potential statistical bias, but these were minimized by using regression with predictive model-based multiple imputation for analysis and correcting for multiple testing. Although the randomized controlled design ensured that there were no between-group differences in baseline variables (Table 1), analysis with ANCOVA was undertaken to improve statistical power by adjusting for wide within-group variation in baseline factors (inherent to small samples), training concordance, and loss to follow-up.

To conclude, this study shows that although RMT is safe in patients with acute stroke, only a small number of patients with incident stroke are eligible and will participate and be concordant with RMT protocols. Because these have no significant effect on increasing muscle strength or cough effectiveness, RMT is unlikely to make a clinically meaningful difference in reducing PSP in patients with acute stroke. Hence, further trials of RMT with the clinical end point of PSP prevention are not warranted.

Acknowledgments

We thank Dr John Hodson, Biostatistics Department, Institute of Psychiatry, Psychology and Neuroscience, King’s College London, United Kingdom for statistical support; Dr Ross Pollock for contributing to data collection and trial administration; and Dr Mehool Patel for overseeing the study at the collaborating site.

Sources of Funding

This article presents independent research funded by the National Institute of Health Research (NIHR) for Patient Benefit Programme (Grant Reference Number PB-PG-0408-16096). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

Disclosures

None.

References


Does Respiratory Muscle Training Improve Cough Flow in Acute Stroke? Pilot Randomized Controlled Trial
Stefan Tino Kulnik, Surinder Singh Birring, John Moxham, Gerrard Francis Rafferty and Lalit Kalra

Stroke. 2015;46:447-453; originally published online December 11, 2014; doi: 10.1161/STROKEAHA.114.007110
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/46/2/447

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/