Intramuscular Botulinum Toxin-A Reduces Hemiplegic Shoulder Pain: A Randomized, Double-Blind, Comparative Study Versus Intraarticular Triamcinolone Acetonide

Jae-Young Lim, MD, PhD; Jae-Hyeon Koh, MD, MS; Nam-Jong Paik, MD, PhD

Background and Purpose—Shoulder pain is frequent after stroke and interferes with the rehabilitative process and outcome. However, treatments used for hemiplegic shoulder pain are limited and largely ineffective. This prospective, randomized, double-blind controlled study was conducted to compare the efficacies of botulinum toxin type A (BoNT-A) and triamcinolone acetonide (TA) on hemiplegic shoulder pain and their effects on arm function in patients with stroke.

Methods—Twenty-nine hemiplegic stroke patients with shoulder pain (duration ≤24 months, pain on numeric rating scale ≥6/10) were randomized into 2 groups. One group received intramuscular injections of BoNT-A (BOTOX 100 U total) during one session to the infraspinatus, pectoralis and subscapularis muscles in conjunction with an intraarticular injection of normal saline to painful shoulder joint, whereas the other group received an intraarticular injection of TA (40 mg) and an intramuscular injection of normal saline to the same muscles. Outcome measures were pain (measured using a numeric rating scale), physician’s global rating scale, shoulder range of motion (ROM) in 4 directions, arm function measured using Fugl-Meyer score, and spasticity measured using the modified Ashworth scale. Measurements were made at baseline and 2, 6, and 12 weeks after injection.

Results—At 12 weeks after treatment mean decrease in pain was 4.2 in the BoNT-A–treated group versus 2.5 in the TA-treated group (P=0.051), and improvements in overall ROM were 82.9° versus 51.8° in these groups (P=0.059), showing a strong trend toward there being less pain and better ROM among those treated with BoNT-A than with TA. However, no significant differences were observed between the 2 groups in terms of improvement in physician global rating, Fugl-Meyer score or modified Ashworth scales. No adverse effect was observed in either group.

Conclusions—Results from this study suggest that injection of BoNT-A into selected muscles of the shoulder girdle might provide more pain relief and ROM improvement than intraarticular steroid in patients with hemiplegic shoulder pain. A larger clinical trial needs to be undertaken to confirm the benefits of this approach. (Stroke. 2008;39:126-131.)

Key Words: botulinum toxin a ■ hemiplegia ■ shoulder painstroke

Shoulder pain is one of the most frequent complications of hemiplegia, and occurs in 20% to 70% of stroke patients. Moreover, it can interfere with the rehabilitative process and has been associated with poorer outcomes and prolonged hospital stays.1–9 A variety of factors may be responsible for shoulder pain after stroke, eg, joint pathology, adhesive capsulitis, subluxation of the head of the humerus, injury to rotator cuff tendons, spasticity of surrounding muscles, central poststroke pain, and complex regional pain syndrome.10–13 However, the etiology of hemiplegic shoulder pain (HSP) remains uncertain.

With regard to treatment, nothing has yet been proven effective, although different treatment methods such as physical therapy,12 functional electrical stimulation,14,15 and intraarticular steroid injection16–17 are being applied. In clinical practice, physicians frequently treat HSP using steroid injections,17 although their effects remain controversial.16–18

Botulinum toxin type A (BoNT-A) has been widely used to treat spasticity and other forms of muscle overactivity,19–24 and recently has been used to treat chronic pain, such as, myofascial pain, low back pain, lateral epicondylitis, various types of headaches, and neuropathic pain.25–34 The mechanism of pain reduction by BoNT-A may include a muscle relaxant effect35 and the inhibition of neurotransmitter release by sensory neurons.36–44

Given that the suggested pain relieving mechanisms of BoNT-A cover the possible etiologies of HSP, we considered that BoNT-A might be effective for treating HSP. In this

Received January 30, 2007; final revision received June 1, 2007; accepted June 13, 2007.
From the Department of Rehabilitation Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seoul, South Korea.
Correspondence to Nam-Jong Paik, MD, PhD, Department of Rehabilitation Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, 300 Gumi-dong, Bundang-gu, Seongnam-si, Gyeonggi-do, 463-707, South Korea. E-mail njpaik@snu.ac.kr
© 2007 American Heart Association, Inc.

Stroke is available at http://stroke.ahajournals.org DOI: 10.1161/STROKEAHA.107.484048
study, we conducted a randomized clinical trial to compare the effects of intramuscular BoNT-A with those of intraarticular steroid on HSP and hemiplegic arm function in stroke patients. We hypothesized that BoNT-A injected into selected muscles in the region of the hemiplegic shoulder joint would elicit more significant pain reduction and range of motion (ROM) improvement of the shoulder than intraarticular steroid.

Methods

Subjects
Twenty-nine patients with hemiplegic shoulder pain aged 18 to 78 years were recruited for this study. The inclusion criteria were: (1) hemiplegia in an arm after stroke (maximum time interval between BoNT-A treatment and stroke ≤ 24 months and duration of pain ≤ 12 months), (2) a pain level in the hemiplegic shoulder of ≥ 6 (on a numeric scale of 0 to 10) as rated by the patient during passive ROM during at least 2 of 3 visits before enrollment, (3) limitation of passive external rotation of the hemiplegic shoulder of at least ≥ 20° compared with the unaffected side. Exclusion criteria were: (1) an intraarticular injection into the affected shoulder during the previous 6 months or use of systemic corticosteroids during the previous 4 months, (2) the presence of an other obvious explanation for the pain (eg, fracture, radiculopathy), (3) prior surgery to either the shoulder or neck region, (4) patient immobility involving confinement to bed for > 50% of daytime hours, (5) any medical condition that might increase the risk to the subject with exposure to BoNT-A (eg, diagnosed myasthenia gravis, Eaton-Lambert syndrome, amyotrophic lateral sclerosis, or any other disorder that might interfere with neuromuscular function), (6) a known allergy or sensitivity to any component of the medication, (7) evidence of recent alcohol or drug abuse or severe depression, (8) the presence of an unstable medical condition or a known uncontrolled systemic disease, (9) concurrent participation in another drug or device study or participation in such a study during the 30 days before enrollment, (10) prior treatment with BoNT-A, (11) the use of aminoglycoside antibiotics, curare-like agents, or any other agent that might interfere with neuromuscular function, and finally (12) any condition or situation that might place the subject at significant risk. Subjects were recruited from a single center, both from inpatients and outpatient clinic, between May 2004 and February 2006.

This study protocol was approved by the institutional review board, and all participants provided signed, written, informed consent. The study was conducted in accordance with regulatory standards of Good Clinical Practice and the Declaration of Helsinki.45

Interventions

The present study was a prospective randomized, double-blind, clinical trial which compared intramuscular BoNT-A and intraarticular triamcinolone acetonide (TA). Patients were randomized into 2 groups (the BoNT-A and TA groups) using a stratified randomization procedure with permuted block size of 4 using a computer that balances ages (≥ 65 or ≤ 110) and sex (male or female) with a minimum of 2 visits per week by a physical therapist blinded to group. In addition, all patients were given a standard brochure describing self-ROM exercise. Randomization codes were kept by one physician, and injection materials were prepared by this physician out of sight of patients. Syringes were sealed with plaster before injection to blind patients. Injection and evaluation were performed by separate physicians. One physician evaluated the outcome measures, and he was blinded to group allocation throughout the study. Therefore, the patients and all other people involved, except for the injecting physicians, were blinded for the type of treatment.

Outcome Measures

The primary outcome measures were pain measured using a numeric rating scale of 0–100 (NRS on a scale of 0–10; where 0=no pain and 100=highest pain level) during passive ROM of the shoulder in 4 planes (forward flexion, abduction, external, and internal rotation), a physician global rating scale (range 0–4; 0=no change; 1=slight improvement, but below the defined therapeutic goal; 2=attained the defined therapeutic goal; 3=improvement slightly exceeding the defined therapeutic goal; 4=improvement clearly exceeding the defined therapeutic goal), and the passive ROM of the shoulder in 4 planes using goniometry: forward flexion, abduction, external rotation, and internal rotation. All ROMs were measured in seated position.

Secondary outcome measures were arm function measured using Fugl-Meyer scores51 (range 0–66; 0=no function; 66=normal function), and spasticity measured at the external rotator muscles of the shoulder using the modified Ashworth scale52 (range 0–5; 0=no spasticity; 5=joint is rigid in flexion or extension). Adverse effects were monitored throughout the study. Measurements were made at baseline and 2, 6, and 12 weeks after injection by a blind evaluator.

Statistical Analysis

We estimated that a sample size of 12.3 per group (14.5 considering a 15% follow-up loss) were needed to achieve 80% statistical power to detect a 2.0 difference in pain scores between the treatment groups at a statistical significance level of 0.05.

In this study, subjects that provided baseline and at least 1 posttreatment measurement constituted the Intention-to-Treat (ITT) population, whereas those completed all tests from baseline to the 12-week follow-up constituted the Per Protocol (PP) population. For the ITT population, outcome measurements were analyzed using the last observation carried forward (LOCF) method.55

After normal distributions were assessed using the Kolmogorov-Smirnov test, we used repeated measures ANOVA (ANOVA$_{0.98}$) with “GROUP” (BoNT-A versus TA) as the between-subject factor and “TIME” (baseline and 2, 6, and 12 weeks postinjection) as the within-subject factor to compare the effects of GROUP and TIME on HSP. Conditioned on significant F-values ($P<0.05$), post hoc analyses were conducted and corrected for multiple comparisons with Tukey tests.

Results

Four of the initial 29 participants (2 from the BoNT-A group, 2 from the TA group) were lost to follow-up because of admission to other hospitals (n=3) or poor general condition (n=1). After first follow-up (2 weeks after the injection), 3 other patients also dropped out (1 patient in week 6 and 2 during week 12, Figure 1). No side effects were observed in either group over the 12-week follow-up period. At baseline, no significant differences were detected between each muscle was injected at 2 points at least and no one injection point received more than 25 U. The maximum total dose in any one muscle was 50 U and a maximum total dose per patient was 100 U. The control group received intraarticular injections of TA (40 mg) and 4.0 mL injections of intramuscular saline to the infraspinatus, subscapularis and pectoralis muscles. All patients received a standard course of physiotherapy during the 6-week period after injection with a minimum of 2 visits per week by a physical therapist blinded to group. In addition, all patients were given a standard brochure describing self-ROM exercise. Randomization codes were kept by one physician, and injection materials were prepared by this physician out of sight of patients. Syringes were sealed with plaster before injection to blind patients. Injection and evaluation were performed by separate physicians. One physician evaluated the outcome measures, and he was blinded to group allocation throughout the study. Therefore, the patients and all other people involved, except for the injecting physicians, were blinded for the type of treatment.
the two groups in terms of age, sex, etiology, or pain duration (Table 1).

Intention-To-Treatment Analysis Using the LOCF Method

Twenty-five patients who were followed-up at least once were included in the ITT analysis (Table 2).

At baseline, pain intensity was comparable in the 2 groups (7.9±0.3, Mean±SE in the BoNT-A group and 7.6±0.5 in the TA group, P=0.690 by t test). ANOVA_RM showed a significant effect of TIMEbaseline, LOCF [F(1,23)=61.1; P<0.001], but not of GROUPBoNT-A, TA [F(1,23)=1.2; P=0.287] without a significant interaction TIMEbaseline, LOCF X GROUPBoNT-A, TA [F(1,23)=4.3; P=0.051]. We performed post hoc testing because the interaction approached a statistical significance, and it showed no differences in pain reduction at LOCF (P=0.100). However, there was a strong tendency toward mean decrease in pain intensity being more prominent in the BoNT-A group (4.2±0.4) than the TA group (2.5±0.8) with independent samples t test (P=0.051).

However ANOVA_RM revealed no significant effect of TIMEbaseline, LOCF [F(1,23)=1.2; P=0.278] and GROUPBoNT-A, TA [F(1,23)=0.3; P=0.573] without a interaction [F(1,23)=0.1; P=0.928] in physician global rating scale, indicating there was no detectable differential effect of BoNT-A versus TA on the physician’s rating.

ANOVA_RM applied to total ROM revealed a significant effect of TIMEbaseline, LOCF [F(1,23)=74.2; P<0.001], but not of GROUPBoNT-A, TA [F(1,23)=2.8; P=0.106] without a significant interaction [F(1,23)=4.0; P=0.059], indicating that ROM was improved in both groups. However, total ROM was more reduced in the BoNT-A group (82.9±9.4°) than the TA group (51.8±12.9°) with t test (P=0.059), although baseline values were not comparable at baseline (270.7±9.9° in the BoNT-A group versus 313.2±13.6° in the TA group, P=0.016 by t test).

ANOVA_RM applied to each 4 planes (forward flexion, abduction, external rotation, and internal rotation) showed similar effects but internal rotation, which showed a significant GROUPBoNT-A, TA effect (Table 2).

Arm function as determined using Fugl-Meyer scores was comparable in the 2 groups at baseline (33.7±4.8 in the BoNT-A group and 23.8±7.5 in the TA group, P=0.260 by t test). ANOVA_RM showed a significant effect of TIMEbaseline, LOCF [F(1,23)=14.2; P=0.001], but not of GROUPBoNT-A, TA [F(1,23)=2.1; P=0.164] without a significant interaction [F(1,23)=1.7; P=0.210], reflecting both groups improved in arm function.

Regarding Modified Ashworth scale, ANOVA_RM revealed no significant effect of TIMEbaseline, LOCF [F(1,23)=1.5; P=0.227], GROUPBoNT-A, TA [F(1,23)=3.4; P=0.079] or interaction [F(1,23)=0.2; P=0.702].

Per Protocol Analysis

Twenty-two patients (11 from the BoNT-A group and 11 from the TA group) who completed final follow-up evaluations were included in the PP analysis.

Although pain intensity was comparable in the 2 groups at baseline (P=0.737 by t test), mean decrease in pain intensity was greater in the BoNT-A group (7.5±0.3 at baseline to 3.2±0.5 at 12 weeks postinjection) than in the TA group (from 7.6±0.5 to 5.2±0.8, P=0.064 by t test). ANOVA_RM applied to pain scales showed a significant effect of TIMEbaseline, 2, 6, and 12 weeks [F(3,60)=29.8; P<0.001], but not of GROUPBoNT-A, TA [F(1,20)=1.3; P=0.256], without a significant interaction [F(3,60)=2.8; P=0.050]. Post hoc testing showed no statistical differences between the two groups over time (P>0.05, Figure 2).

For the net changes in physician global rating scales, ANOVA_RM revealed no TIME effect, 2, 6, 12 weeks [F(2,40)=1.8; P=0.171], GROUPBoNT-A, TA [F(1,20)=1.0; P=0.334], or interaction effect [F(2,40)=0.4; P=0.662].

The improvement in shoulder ROM (sum of 4 directions) was greater in the BoNT-A group than in the TA group (91.0±8.7° versus 51.8±12.9°, P=0.021 by t test).

ANOVA_RM applied to total ROM revealed a significant effect of TIMEbaseline, 2, 6, 12 weeks [F(3,60)=54.8; P<0.001], but not of GROUPBoNT-A, TA [F(3,60)=0.9; P=0.348], with a significant interaction [F(3,60)=4.2; P=0.009]. However, post hoc testing did not show any statistical differences between the 2 groups over time (P>0.05, Figure 3), suggesting that the greater improvement in shoulder ROM in the BoNT-A group than in the TA group might be caused by differences in baseline value between 2 groups (279.1±10.4° in the BoNT-A group versus 313.2±13.6° in the TA group, P=0.060 by t test).

ANOVA_RM applied to Fugl-Meyer score showed a significant effect of TIMEbaseline, 2, 6, 12 weeks [F(3,60)=10.7; P=0.000],

Table 1. Patient Characteristics at Baseline

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>BoNT-A (n=16)</th>
<th>Triamcinolone (n=13)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64.8±2.1</td>
<td>57.1±3.6</td>
<td>0.079</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>8/8</td>
<td>7/6</td>
<td>0.837</td>
</tr>
<tr>
<td>Lesion type, infarction/ hemorrhage</td>
<td>12/4</td>
<td>8/5</td>
<td>0.436</td>
</tr>
<tr>
<td>Involved side, right/left</td>
<td>6/10</td>
<td>3/10</td>
<td>0.404</td>
</tr>
<tr>
<td>Time since onset, days</td>
<td>230.4±53.8</td>
<td>299.5±73.9</td>
<td>0.446</td>
</tr>
</tbody>
</table>

Values are Mean±SE. BoNT-A indicates botulinum toxin type A; TA, Triamcinolone acetonide.
but not of GROUP<sub>BoNT-A, TA</sub> [F(1,20)=2.5; \( P=0.133 \)], in the absence of a significant interaction [F(3,60)=1.9; \( P=0.138 \)] (Figure 4), and spasticity scores were comparable over TIME<sub>baseline, 2, 6, 12 weeks</sub> [F(3,60)=0.9, \( P=0.469 \)] and GROUP<sub>BoNT-A, TA</sub> [F(1,20)=1.7, \( P=0.203 \)] without a significant interaction [F(3,60)=0.2; \( P=0.906 \)].

**Discussion**

The main finding of this double-blind randomized study was that injections of BoNT-A into shoulder girdle muscles showed a strong trend to reduce HSP and improve shoulder ROM more so than intraarticular steroid injections. Furthermore, this positive effect of BoNT-A treatment over steroid was more evident at 12 weeks postinjection, which suggests that BoNT-A might have a longer lasting effect than steroid. Treatments were well tolerated and no adverse event was observed in any subject.

Recently, Yelnik et al<sup>48</sup> reported that intramuscular injections of BoNT-A into subscapularis muscles elicited more significant pain relief and ROM improvement than a placebo at 4 weeks postinjection in a double-blind, randomized, placebo-controlled study, which concurs with the results of the present study. In our study we used an active drug rather than placebo as a control and followed the outcome measures longer than Yelnik et al’s study, which provided more evident effect of BoNT-A on HSP. We think that it is possible that even better or longer results could have been achieved using a higher dose because the beneficial effects of BoNT-A over steroid were prominent after 12 weeks postinjection in the present study, which needs further exploration.

Given the fact that the causes of HSP are uncertain and that an effective treatment has yet to be established, we decided to treat HSP using BoNT-A injections. In this study, we selected intraarticular steroid injection as a control therapy, because this therapy is frequently applied in the clinical setting and one survey showed that clinicians believed in its effectiveness.<sup>56</sup>

We believe that the possible mechanisms of improved hemiplegic shoulder pain after BoNT-A injection could be associated with the antinoceptive effect of BoNT-A. Although no direct association between BoNT-A and spasticity was found during the present study, the muscle relaxing or tone reducing effects of BoNT-A might also have contributed to pain reduction. We believe that the limited observed effect of BoNT-A on spasticity was probably because of the fact that we recruited patients with mild to moderate degrees of spasticity, which concurs with the findings that BoNT-A did not elicit more significant arm functional improvement than

### Table 2. Improvement in Outcome Measures at Follow-Up (ITT Analysis with LOCF Method)

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>BoNT-A (n=14)</th>
<th>Triamcinolone (n=11)</th>
<th>Time</th>
<th>Group</th>
<th>Time X Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain, numeric rating scale</td>
<td>4.2±0.4</td>
<td>2.5±0.8</td>
<td>&lt;0.001</td>
<td>0.287</td>
<td>0.051</td>
</tr>
<tr>
<td>Physician global rating scale</td>
<td>0.2±0.2</td>
<td>0.2±0.3</td>
<td>0.278</td>
<td>0.573</td>
<td>0.928</td>
</tr>
<tr>
<td>Passive ROM of shoulder&lt;sup&gt;5&lt;/sup&gt;</td>
<td>82.9±9.4</td>
<td>51.8±12.9</td>
<td>&lt;0.001</td>
<td>0.106</td>
<td>0.059</td>
</tr>
<tr>
<td>Flexion</td>
<td>21.5±4.3</td>
<td>13.2±4.6</td>
<td>&lt;0.001</td>
<td>0.150</td>
<td>0.204</td>
</tr>
<tr>
<td>Abduction</td>
<td>22.9±4.1</td>
<td>17.3±4.3</td>
<td>&lt;0.001</td>
<td>0.569</td>
<td>0.362</td>
</tr>
<tr>
<td>External rotation</td>
<td>21.1±3.4</td>
<td>13.2±5.8</td>
<td>&lt;0.001</td>
<td>0.334</td>
<td>0.231</td>
</tr>
<tr>
<td>Internal rotation</td>
<td>17.5±2.6</td>
<td>8.2±4.2</td>
<td>&lt;0.001</td>
<td>0.010</td>
<td>0.062</td>
</tr>
<tr>
<td>Fugl-Meyer score</td>
<td>10.0±2.2</td>
<td>4.9±3.5</td>
<td>0.001</td>
<td>0.164</td>
<td>0.210</td>
</tr>
<tr>
<td>Modified Ashworth scale</td>
<td>0.1±0.1</td>
<td>0.3±0.4</td>
<td>0.227</td>
<td>0.079</td>
<td>0.702</td>
</tr>
</tbody>
</table>

ITT indicates intention to treat; LOCF, last observation carried forward. Values are differences from baseline (Mean±SE).

![Figure 2](image-url) **Figure 2.** Improvement in numeric pain rating scale during the study (PP analysis). ANOVA<sub>PP</sub> revealed a significant effect of TIME [F(3,60)=29.8; \( P<0.001 \)], but not of GROUP [F(1,20)=1.3; \( P=0.256 \)], without a significant interaction [F(3,60)=2.8; \( P=0.050 \)]. Post hoc testing showed no statistical differences between the 2 groups over time (\( P>0.05 \)).

![Figure 3](image-url) **Figure 3.** Improvement in shoulder passive range of motion (ROM) during the study (PP analysis). ANOVA<sub>PP</sub> revealed a significant effect of TIME [F(3,60)=54.8; \( P<0.001 \)], but not of GROUP [F(3,20)=0.9; \( P=0.348 \)], with a significant interaction [F(3,60)=4.2; \( P=0.009 \)]. Post hoc testing did not show any statistical differences between the 2 groups over time (\( P>0.05 \)).

Given the fact that the causes of HSP are uncertain and that an effective treatment has yet to be established, we decided to treat HSP using BoNT-A injections. In this study, we selected intraarticular steroid injection as a control therapy, because this therapy is frequently applied in the clinical setting and one survey showed that clinicians believed in its effectiveness.<sup>56</sup> We believe that the possible mechanisms of improved hemiplegic shoulder pain after BoNT-A injection could be associated with the antinoceptive effect of BoNT-A. Although no direct association between BoNT-A and spasticity was found during the present study, the muscle relaxing or tone reducing effects of BoNT-A might also have contributed to pain reduction. We believe that the limited observed effect of BoNT-A on spasticity was probably because of the fact that we recruited patients with mild to moderate degrees of spasticity, which concurs with the findings that BoNT-A did not elicit more significant arm functional improvement than...
TA. It is also possible that the small population size may have contributed to this negative effect. Our sample size estimation was based on pain improvement rather than spasticity or arm function, and the sample size required to detect significant spasticity or arm functional improvement changes would have been larger.

The main limitation of the present study is its limited sample size and follow-up loss. We think more than expected follow-up loss (24.1% not 15% as estimated before trial) might resulted in insufficient statistical power for ANOVA_BRM in the present study.

In conclusion, injections of BoNT-A into selected muscles of the shoulder girdle provided more significant shoulder pain relief and improved ROM of the shoulder but not arm function versus the intraarticular injection of steroid. This finding supports the idea that BoNT-A could be used as an alternative treatment for hemiplegic shoulder pains that are otherwise difficult to treat. A larger trial needs to be commenced to confirm the benefits of BoNT-A in HSP.

Acknowledgments
The authors thank Dr John D. Rogers, at Allergan, for his valuable comments on the study design and the manuscript.

Sources of Funding
An unrestricted educational grant to cover the cost of the BOTOX in this study was provided by Allergan Korea.

Disclosures
None.

References
Intramuscular Botulinum Toxin-A Reduces Hemiplegic Shoulder Pain: A Randomized, Double-Blind, Comparative Study Versus Intraarticular Triamcinolone Acetonide
Jae-Young Lim, Jae-Hyeon Koh and Nam-Jong Paik

Stroke. 2008;39:126-131; originally published online November 29, 2007;
doi: 10.1161/STROKEAHA.107.484048

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/39/1/126

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/