(antiplatelet 1% and anticoagulation 0.8%) in patients with cervical arterial dissection.

The CADISS trial was the first prospective, randomized trial of anticoagulation versus antiplatelet therapy in patients with cervical arterial dissection (1). Two-hundred and fifty patients were randomized, the majority of whom presented with stroke or transient ischemic attacks ($n = 224$, 90%); the remainder presented with headache, neck pain, or Horner syndrome. One-hundred twenty-six patients were assigned to antiplatelet treatment versus 124 to anticoagulation. There was no significant difference in the subsequent rate of stroke or death in the two groups—3/126 in the antiplatelet group (2%) versus 1/124 in the anticoagulation group (1%) ($P = 0.63$). All recurrent strokes occurred in patients who presented with an initial stroke; there were no deaths. There was one case of subsequent significant subarachnoid hemorrhage in the anticoagulation group; there were no significant hemorrhagic events in the antiplatelet group (1).

Although this trial demonstrated no significant difference in the rate of stroke or death between patients receiving antiplatelet medication and those receiving anticoagulation, it also importantly highlighted the relatively low rate of subsequent stroke in patients with symptomatic dissections (90% TIAs or stroke on presentation). However, some patients presenting with dissection, and perhaps particularly with early, severe, recurrent stroke, might not have been included in either the observational or the randomized part of the study because they could not provide consent. In addition, antiplatelet therapy was variable across this study with 28 (22%) of 126 patients receiving aspirin alone, 42 (33%) receiving clopidogrel alone, one (1%) receiving dipyridamole alone, 35 (28%) receiving aspirin and clopidogrel, and 20 (16%) receiving aspirin and dipyridamole. It is thus difficult to make conclusions about a particular type of antiplatelet therapy as compared with warfarin anticoagulation (used in the anticoagulation arm) for cervical arterial dissection. Nevertheless, as a result of the extremely low rates of stroke or death in this study, the authors calculated that a phase 3 trial with adequate power to detect a potential difference between the two treatment approaches would require 4876 patients in each group. The impracticality of such a study and the relative similarity of rates of stroke in patients receiving antiplatelet or anticoagulation therapy in class IV studies (2, 4), systematic reviews (5, 7) and now a class I study (1) reinforces an overall lack of difference in efficacy between the two treatment modalities.

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1878-8750/$ - see front matter
http://dx.doi.org/10.1016/j.wneu.2015.05.003

Acute Brain Injury after Subarachnoid Hemorrhage

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BACKGROUND

Spontaneous subarachnoid hemorrhage (SAH) caused by the rupture of cerebral aneurysms is a subtype of stroke that carries particularly high mortality and morbidity (7). Immediately after aneurysmal rupture, many physiological derangements, such as elevated intracranial pressure, decreased cerebral blood flow, and global cerebral ischemia, may occur (4). These immediate responses trigger various cascades of events resulting in pathologic changes in the affected brain within the acute phase of SAH. Moreover, excessive amount of extravasated blood and its degradation products are known as the major contributors to brain injury after hemorrhagic stroke (1). As yet, the few clinically available treatments for SAH mainly focus on prevention of aneurysmal rebleeding and prophylaxis of delayed cerebral ischemia caused by vasospasm; however, no effective treatments against SAH-induced acute brain injury are available.

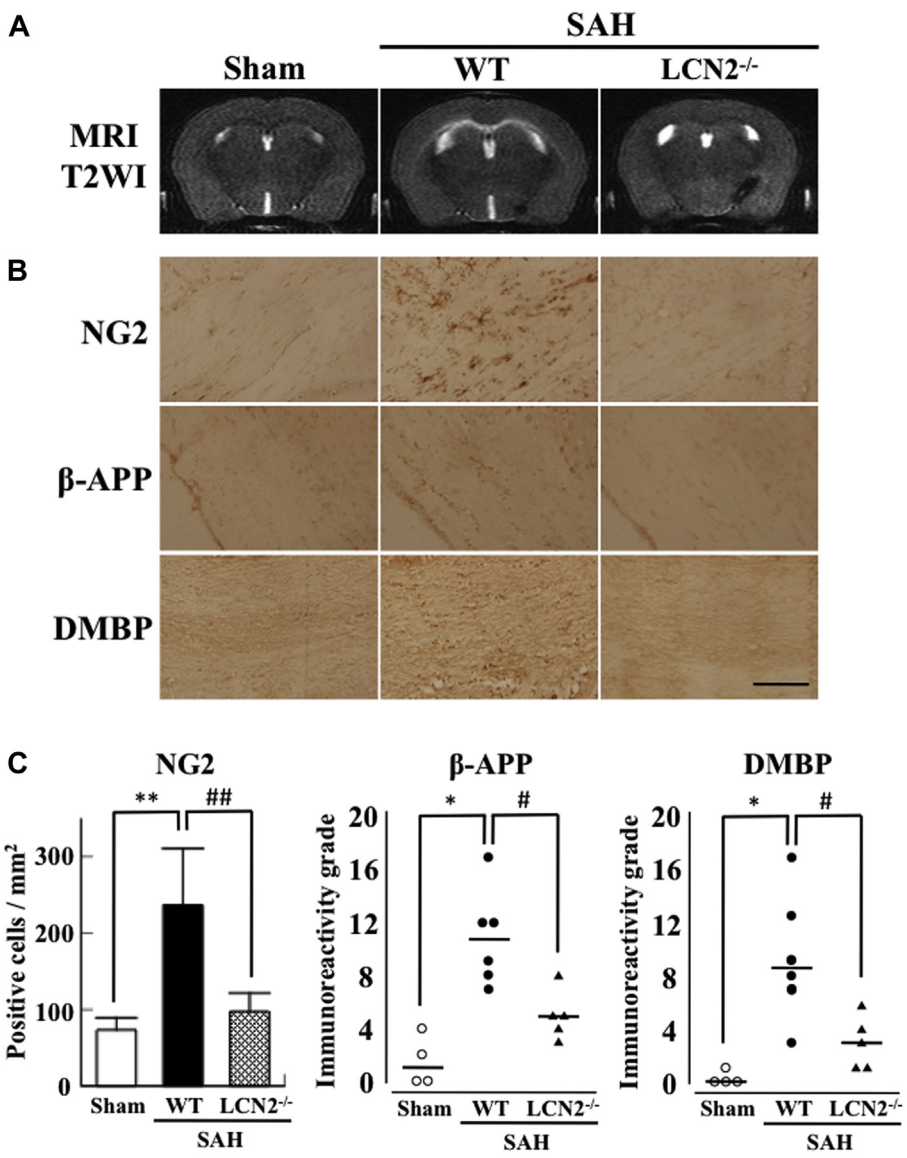

Figure 1. Representative coronal T2-weighted images (T2WI; **A**) and NG2 (marker for oligodendrocyte precursors), β-amyloid precursor protein (β-APP; marker for damaged axon), and degraded myelin basic protein (DMBP; marker for degraded myelin) immunohistochemistry in white matter of sham and WT and LCN2$^{-/-}$ animals 24 hours after subarachnoid hemorrhage (**B**). Quantification of each result (**C**). $^{**}P < 0.01$; $^{*}P < 0.05$ versus WT; $^{\#\#}P < 0.01$; $^{\#}P < 0.05$ versus LCN2$^{-/-}$ animals. Scale bar = 100 μm. Reproduced with permission from Egashira Y, Hua Y, Keep RF, Xi G: Acute white matter injury after experimental subarachnoid hemorrhage: potential role of lipocalin 2. Stroke 45:2141-2143, 2014.

We briefly describe the recent advances and future direction in the research for SAH-induced acute brain injury.

NEURONAL DEATH

The leading cause of neuronal death after SAH is transient global ischemia induced by elevation of intracranial pressure. Global ischemia seems to initiate disruption of the blood-brain barrier, as well initiating inflammation, which contributes to additional neuronal death (4). In addition, excessive iron, the major degradation product of hemoglobin, has been determined as a key factor that causes neuronal death post SAH (6). In a rat arterial perforation model, there was excessive accumulation of nonheme iron and iron-handling proteins in tissue adjacent to SAH. High iron content in neurons leads to oxidative deoxyribonucleic acid injury and results in neuronal death. The iron chelator deferoxamine effectively reduced these elevations of iron and iron-handling proteins in