Depression is a highly prevalent chronic illness that is more frequent in women than in men. It is also one of the most widespread causes of years lost due to disability, which by some projections will take the leading place among the most important diseases in developing countries and third place in developed countries by the year 2020. Depression has a strong impact on society due to the severe burden of disease, and therefore it is one of the foremost public health issues facing physicians today. The rapid growth of the elderly population worldwide further intensifies the problem of depression, because its prevalence among people older than 65 years is estimated to be at least 15%. Depressive symptoms frequently occur among patients with atherosclerosis and coronary artery disease. While it is well known that depression is one of many sequelae of stroke, some recent studies have shown that depressive symptoms and psychological distress might also predict ischemic stroke.

In an attempt to explain the relationship between cardiovascular disease and depression, some studies have suggested pathophysiological mechanisms including altered autonomic nervous system activity, increased tendency of blood coagulation, and elevated low-grade inflammation. In addition to these pathophysiological pathways, increased platelet aggregability in depression may play a role in the process, leading to poststroke depression. According to Cohen et al., depression may double the risk of heart attack in hypertensive patients, particularly among women. Despite the large number of studies aiming to clarify various aspects and triggering events of this disorder, many controversies about its incidence, main determinants, consequences, and treatment still persist.

Selective serotonin reuptake inhibitors (SSRIs) are a relatively new class of drugs, and they have proven to be effective in the treatment of depression. In comparison with other antidepressants, SSRIs seem to have fewer side effects and therefore have become more frequently recommended and widely prescribed in primary care. Despite good tolerability and safety, some reports have nevertheless described an association between SSRIs and risk of bleeding disorders, particularly in the elderly. This effect of SSRIs has been linked with serotonin depletion in platelets, which potentially leads to abnormal aggregation and prolonged bleeding time. A recent English cohort study suggested weak evidence to support the hypothesis or the link between SSRIs and the precipitation of bleeding events at a population level. The nested case-control study from Denmark reported in this issue of Stroke, however, showed that current use of SSRIs was not associated with an increased risk of hemorrhagic and ischemic stroke. Previous publications have suggested associations between the use of SSRIs and a decreased risk of acute myocardial infarction and stroke. The study by Bak et al did not reconfirm that the current use of SSRIs was associated with a decreased risk of stroke, but interestingly noted that previous use of SSRIs was associated with an increased risk of ischemic stroke. Whether the current use of SSRIs has some protective effect or not is still unclear, and further research is in demand. The findings from the study by Bak et al warrant further studies that should distinguish whether the increased risk for stroke is clearly attributed to previous use of SSRIs or simply because of premature withdrawal of SSRIs in the treatment of depression. In addition, the findings suggested that the current use of anticoagulation therapy or antihypertensive drugs was associated with an increased risk of hemorrhagic stroke. Furthermore, the current or previous use of low-dose acetylsalicylic acid was associated with increased risk of hemorrhagic stroke compared with risk in nonusers. It may be that, in combination, the effect of aspirin platelet-related properties of SSRIs may increase the risk of bleeding, but this should be carefully investigated in controlled trials since both drugs are widely used in the population. Therefore, clinicians should be vigilant of potential drug-drug interactions between the use of SSRIs in combination with aspirin, even at low doses or in the presence of hypertension, which could result in an unwanted effect in the patient.

Despite these potential problems, it is commonly agreed that SSRIs are the drugs of choice in the treatment of depression. Further investigation of the role of antidepressants, particularly in the treatment of poststroke depression, is warranted.

**References**


Key Words: antidepressive agents ─ serotonin ─ stroke ─ stroke, hemorrhagic
Use of Selective Serotonin Reuptake Inhibitors and the Risk of Stroke: Is There Reason for Concern?

Dimitrije Jakovljevic and Jaakko Tuomilehto

Stroke. 2002;33:1448-1449
doi: 10.1161/01.STR.0000018582.96060.3E

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2002 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/33/6/1448

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/