



## Review

## Physical activity in the prevention of ischemic stroke and improvement of outcomes: A narrative review

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## ABSTRACT

Physical activity is an integral component of stroke prevention. Although approximately 80% of strokes are due to cerebral ischemia, the mechanisms linking physical activity to the incidence of and recovery from ischemic stroke are not completely understood. This review summarizes evidence from human and animal studies regarding physical activity in the prevention of overt and covert ischemic stroke and associated injury. In cohort studies, people who are physically active have reduced rates of overt ischemic stroke and ischemic stroke mortality. However, few human studies have examined physical activity and the incidence of covert stroke. Evidence from animal models of ischemic stroke indicates that physical activity reduces injury after ischemic stroke by reducing infarct size and apoptotic cell death. Accordingly, physical activity may reduce the magnitude of injury from ischemic stroke so that there are fewer or less severe symptoms. Future research should investigate physical activity and incidence of covert stroke prospectively, ascertain the optimal dose and type of exercise to prevent ischemic injury, and identify the underlying neuroprotective mechanisms.

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## 1. Introduction

Despite significant advances in the treatment and rehabilitation of stroke, most people continue to experience enough cognitive and motor impairment after stroke to interfere with everyday function. Approximately 80% of overt strokes (strokes with overt symptoms) are of ischemic origin. Symptoms of ischemic stroke may also be covert (silent). Of concern, covert strokes may outnumber overt strokes by five to one and are associated with high rates of dementia, depression, and abnormal gait (Vermeer et al., 2007). Accordingly, prevention of overt and covert ischemic stroke is of the utmost importance.

Considerable evidence supports the inclusion of physical activity as an integral component of ischemic stroke prevention. Many observational studies have confirmed that people who are physically active have lower rates of ischemic stroke than those who are sedentary (Reimers et al., 2009). However, observational studies offer little insight into the mechanisms of stroke prevention. One scenario could be that physical activity improves vascular function and reduces the likelihood of vascular risk factors that contribute to ischemic stroke risk (Leung et al., 2012; Yung et al., 2009). Another scenario could be that exercise improves the response to an ischemic event and so reduces infarct size after stroke and thereby minimizes the frequency or severity of overt symptoms (Fig. 1). Knowledge of rates of covert ischemic stroke in relation to physical activity could provide insight into the mechanisms of prevention. Despite high prevalence of covert strokes among older adults (Vermeer et al., 2007), few studies have examined rates of covert stroke and physical activity levels (Dubbart et al., 2009; Willey et al., 2011). Indeed, in comparison to overt stroke, covert stroke has been poorly studied, mainly due to low clinical diagnostic rates. As a result, studies of covert stroke primarily rely on diagnosis using magnetic resonance imaging (MRI) rather than clinical diagnoses.

Results from animal studies complement evidence from human exercise studies. Whereas human studies can detail real-world occurrence of overt and covert ischemic stroke rates over years and decades, animal studies provide controlled experiments to probe the effects of physical activity on ischemic stroke outcomes. Consequently, the objective of this paper is to review and integrate human and animal research regarding the role of physical activity in the prevention of ischemic stroke and resulting functional outcomes. This review addresses the potential influence of physical activity on ischemic stroke by discussing the incidence of ischemic stroke and the neuronal injury and symptom severity after stroke. Those studies that examined physical activity during stroke recovery and those studies that focused on physical activity in the modification of vascular risk without capturing ischemic stroke incidence were beyond the scope of this review.

## 2. Physical activity and incidence of ischemic stroke

Stroke prevention guidelines suggest adherence to general physical activity recommendations (at least 30 min of moderate intensity exercise per day) in order to reduce the risk of stroke (Goldstein et al., 2006). Much of the evidence supporting this recommendation arises from observational studies. In a recent meta-analysis that included studies using a variety of populations, ages, study designs, and definitions of physical activity, men and women who were most physically active had 25% lower risk of incident ischemic stroke than those who were least physically active (odds ratio (OR), 95 percent confidence interval (95% CI): 0.75, 0.67–0.84) (Reimers et al., 2009). This reduction of ischemic stroke risk associated with physical activity appears to be approximately the same in men and in women (Reimers et al., 2009; Wendel-Vos

et al., 2004). People who were moderately physically active also had lower risk of ischemic stroke compared to those who were sedentary. Recent studies generally confirmed these results, though the difference between physical activity groups was not always statistically significant (Sattelmair et al., 2010; Willey et al., 2009).

### 2.1. Evidence for a dose of physical activity

Evidence from cohort studies generally suggest a dose effect (Reimers et al., 2009) – that is, those people who were more physically active had a greater reduction in stroke risk – but the dose of physical activity that maximizes the reduction in ischemic stroke risk is less clear. Most studies of physical activity and ischemic stroke considered the overall volume of physical activity (hours per week) or volume of physical activity weighted by activity intensity (measured by kilocalories or metabolic equivalents (MET) per week) (Reimers et al., 2009). Studies that measured volume of physical activity as a continuous variable or in two levels (high versus low) generally found that people who were more physically active had reduced ischemic stroke risk compared to those who were less physically active. However, when three or more levels of physical activity volume were considered, people with moderate physical activity volumes often had lower risk of ischemic stroke compared to those with the highest physical activity levels.

Fewer studies investigated whether the intensity or duration of each bout of physical activity was important to the reduction in ischemic stroke risk (Hu et al., 2005; Nakayama et al., 1997; Willey et al., 2009). Some (Hu et al., 2005; Willey et al., 2009), but not all (Nakayama et al., 1997), studies concluded that more intense physical activity was associated with a greater reduction in stroke risk. For example, in a recent study (Willey et al., 2009), people who participated in physical activity at an intensity of at least 5.5 METs (equivalent to light stationary cycling) had a 35% lower incidence of ischemic stroke compared to those who participated only in less intense physical activity, regardless of duration (Willey et al., 2009). This study indicated that intensity of physical activity was more strongly associated with stroke risk than total volume of physical activity (kcal/week). In contrast, a recent cross-sectional study that examined only minor stroke found that light and moderate but not heavy exercise was associated with reduced risk (Deplanque et al., 2012). We found no studies that investigated whether the duration of each session of physical activity was associated with stroke risk. A summary of modification of the physical activity–ischemic stroke relationship by exercise and individual characteristics is provided in Table 1.

### 2.2. Evidence for type of physical activity

An older meta-analysis suggested that occupational physical activity confers more protection than leisure physical activity (Wendel-Vos et al., 2004). People in the highest level of occupational physical activity had a 43% reduction in ischemic stroke risk (OR, 95% CI: 0.57, 0.43–0.77) compared to those with inactive occupations whereas those in the highest level of leisure physical activity only had a 21% reduction in ischemic stroke risk (OR, 95% CI: 0.79, 0.69–0.91) (Wendel-Vos et al., 2004). Why this is so is unclear but may be due to a larger differential in physical activity volumes between groups segmented by occupational activity versus leisure activity. That is, since more time is spent in work than in leisure, there may have been more difference in physical activity volume between the highest and lowest levels of occupational physical activity than between the highest and lowest levels of leisure physical activity.

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