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Implementing the Proclamation of Stroke and Potentially Preventable Dementias

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Abstract

Brain health plays a central role in wellbeing and in the management of chronic diseases. Stroke and dementia pose the two greatest threats to brain health, but recent developments suggest the possibility that preventing stroke may also prevent some dementias: 1. A large population study showed a 32% decrease in the incidence of stroke and a concomitant 7% reduction in the incidence of dementia; 2. Treatment of atrial fibrillation resulted not only in stroke reduction, but a 48% decrease in dementia; 3. A hypothesis free analyses has shown that the first phase of Alzheimer disease involves vascular dysregulation, opening the door to new therapeutic approaches; 4. Cognitive impairment, often treatable and reversible, accompanies heart and kidney failure. These developments, combined with the knowledge that stroke, dementia and heart disease share the same major treatable risk factors, particularly hypertension, offers an opportunity for their joint prevention.

This aspiration is expressed by a Proclamation of the World Stroke Organization on Stroke and Potentially Preventable Dementias and endorsed by the World Heart Federation, the World Hypertension League, Alzheimer Disease International and 18 other international, regional and national organizations as a call for action.

Keywords

Stroke, dementia, prevention

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Introduction

Without a healthy brain little else is worthwhile, and without brain health there is no health. In the era of growing chronic non-communicable diseases (NCDs), cognitive competence plays a crucial overarching role in prevention, treatment and rehabilitation of almost all NCDs.

Background

Specialization has created two expanding and divergent fields: stroke and dementia; and yet, stroke and dementia often occur together, pose risks for each other¹ and vascular and neurodegenerative pathologists interact additionally and synergistically, even in asymptomatic individuals.²

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We are pleased to submit our commentary Implementing the Proclamation of Stroke and Potentially Treatable Preventable Dementias. As this has multidisciplinary implications for the World Stroke Organization, World Heart Federation, World Hypertension League and European Society of Hypertension, we are proposing publication in both International Journal of Stroke (World Stroke Organization) and Journal of Clinical Hypertension. Drs. Weber and Donnan are aware of this manuscript and have agreed to simultaneous publication

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In principle, 90% of strokes³ and about 35% of dementias⁴ are preventable. Stroke and dementia statistics are usually studied in isolation and the fact that stroke doubles the chances of developing dementia⁵ is frequently ignored when calculating the percentage of potentially preventable or even reversible dementias. If this fact is considered, the true number of potentially preventable dementias would be higher than the assumed, since stroke and dementia share the same risk factors⁶ and given that stroke is more common than dementia worldwide, at least half of dementias should be preventable in principle.

Other NCDs such as chronic heart failure, chronic kidney disease, diabetes and hypertension can be accompanied by cognitive decline and dementia, which again may be treatable and in some cases, with treatment of the underlying condition (e.g. kidney transplantation) even reversible. In this context diabetes and hypertension play a special role because they are on one hand important risk factors for the development of stroke, heart failure and chronic kidney disease, and on the other hand can be linked to cognitive impairment without having caused a stroke yet.⁷⁻¹¹

Challenges

Two common conditions remain below the threshold of awareness of many physicians.

Little strokes, big trouble

The commonest outcome of cerebrovascular disease is not clinical stroke, but cognitive impairment. Asymptomatic cerebral infarcts outnumber symptomatic one in a ratio about 5:1 and result in subtle neurological signs, cognitive impairment and a decrease in processing speed.¹²

Cerebral infarcts can cause not only damage by themselves, but can trigger inflammation and can kindle neurodegeneration.¹³ Similarly, asymptomatic cerebral hemorrhages may cause, contribute or trigger cognitive decline. The realization that multiple little asymptomatic strokes can amount to major cognitive impairment prompted the World Stroke Day warning theme for 2008 “Little Strokes, Big Trouble”.¹⁴

Organ failure and brain failure

All failures of major organs lead to different degrees of cognitive impairment. Heart failure constitutes the most prevalent.¹⁵⁻¹⁹ Kidney failure represents another common example, the cognitive status often fluctuating with the dates of dialysis.

In each case, the mechanisms vary, but typically the focus is on the primary organ affected with relatively

little research being done on the cognitive consequences and the role that brain itself may play.

Risk factors

Common risk factors

Stroke and dementias share almost the same risk factors. This holds true for dementias that would fall under the common term of vascular dementias, but also for degenerative dementia of the Alzheimer disease spectrum (Table 1) (Solomon 2014). The same applies to the common forms of heart, kidney and retinal disease.²⁰

Hypertension

Hypertension emerges as the most prevalent and treatable risk factor. The beneficial effects of treating hypertension in preventing heart disease and stroke are well established and empirical evidence suggests that treating hypertension benefits cognition.²¹ However, the optimal blood pressure for the brain remains to be determined. Part of the difficulty stems from the short duration of the clinical trials.²² Moreover, a number of blood pressure parameters relevant to the brain have not been addressed systematically. Pulse pressure relates to arterial brain stiffness^{23,24} which in turn correlates with brain perfusion, which itself may be heterogenous²⁵ requiring different blood pressure parameters. One of the strongest associations between hypertension and the brain relate to white matter changes (leukoaraiosis) that in turn represent harbingers of increased risk for stroke and dementia.²⁶ However, these white matter changes may have different origins. The brunt of hypertension associated infarcts, hemorrhages and white matter changes occur in the core of the brain, which one of us (VH) has called “the vascular centrecephalon”²⁷ and renamed “ancestral brain”, a high blood pressure system. In contrast, the “homo sapiens brain” (the enormous growth of the cerebral hemispheres, especially white matter) represents a low blood pressure system. By the time that the branches deriving from the Circle of Willis, round the hemisphere and the send branches to the depth of hemispheric white matter, the perfusion pressure is low. A group modeling the cerebral circulation has calculated that when the brachial blood pressure is 117/75, it is 113/73 in the ancestral brain and 59/38 in the sapiens brain.²⁸ In practical terms, it means that the optimal blood pressure for controlling the risk of infarcts, hemorrhages and leukoaraiosis may be too low for the homo sapiens brain resulting in subtle cumulative hypotensive damage. To determine the best level of blood pressure control for the individual may require determining cerebral blood flow autoregulation.

Diabetes

Along with the expanding statistics about obesity comes the increased risk of diabetes. The brain consequences of diabetes have been long established, but the mechanisms remain obscure.^{29,30}

Homocysteine

The association of high homocysteine levels and vascular risk leaves little doubt. Controversy still remains about treating high levels, however the evidence is slowly tipping the scales towards prevention.³¹

Other treatable and potentially preventable dementias

In addition to the above, a number of dementias of various etiologies are treatable and manageable to different degrees. These include toxic, metabolic, infectious, brain and systemic inflammatory, antibody, neoplastic and hydrocephalic disorders.³²

The important point is that cognitive disorders are more common than detected and more treatable and potentially preventable than realized.³³

Cerebrovascular disease as a trigger for neurodegeneration

Experimentally even a small cerebral infarct can produce extensive, mainly white matter inflammation and cognitive impairment and after a stroke, white matter inflammation correlates better with cognitive status at 6 months than the initial cognitive status.¹³

Longitudinal studies suggest that in the elderly one quarter have asymptomatic cerebrovascular disease, another quarter have symptomless Alzheimer pathology, but the combination double the chances that an individual will develop dementia.³⁴

A hypothesis free, data driven analysis of the Alzheimer Disease Neuroimaging Study (ADNI) identified the first pathological biomarkers in Late Onset Alzheimer Disease (LOAD) were vascular dysregulation, a surprising and promising finding.³⁵

Recent developments

Growing population, clinical and pathophysiological data compel new actions and approaches to the joint prevention of stroke and dementia.

Population studies

Concomitant with a successful stroke strategy, the age-specific incidence of stroke and of dementia in Ontario (population 14 million) dropped by 32% and 7%,

respectively, over a 12 year period.³⁶ Based on this and other evidence a Proclamation calling for the joint prevention of stroke and dementia was launched in 2015, sponsored by the World Stroke Organization and endorsed by Alzheimer Disease International, the World Heart Federation, the World Hypertension League and all the major international, regional and some national organizations dealing with the brain, stroke and dementia.³⁷

Clinical studies

The FINGER Study showed for the first time that multiple lifestyle interventions can result in cognitive improvement among individuals at risk of developing dementia, even when they are APOe4 positive.³⁸

A Swedish study involving 444,106 patients with atrial fibrillation showed that anticoagulation decreases the risk of dementia by 48%.³⁹

Opportunities

The World Health Summit

The World Health Summit is sponsored by Angela Merkel, Emmanuel Macron and Jean-Claude Juncker of the European Commission. The aim is to improve health all over the planet, catalyzing that process through collaboration and open dialogue, and steering tomorrow's agenda to improve research, education, healthcare, and policy outcomes.

It brings together researchers, physicians, key government officials, and representatives from industry as well as from non-government organizations (NGOs) and healthcare systems all over the world to address the most pressing issues facing every facet of healthcare and medicine in the upcoming decade and beyond.

The World Health Summit is built on the stable foundation of academic freedom and excellence provided by the M8 Alliance and has strong political support from a variety of partners at global, national and state levels.

The prevention of cardiovascular disease requires an interdisciplinary approach. The World Stroke Organization, World Heart Federation and the World Hypertension League, together with other stakeholders, have established an innovative partnership approach focused on collective advocacy towards Ministries of Health to implement evidence based interventions in secondary, primary and primordial prevention of circulatory disease.⁴⁰ All these organizations are uniquely positioned to address the various components that determine circulatory health, and this strong collaboration will produce synergistic results to benefit all our patients.^{41,42,43} This united effort in the joint prevention

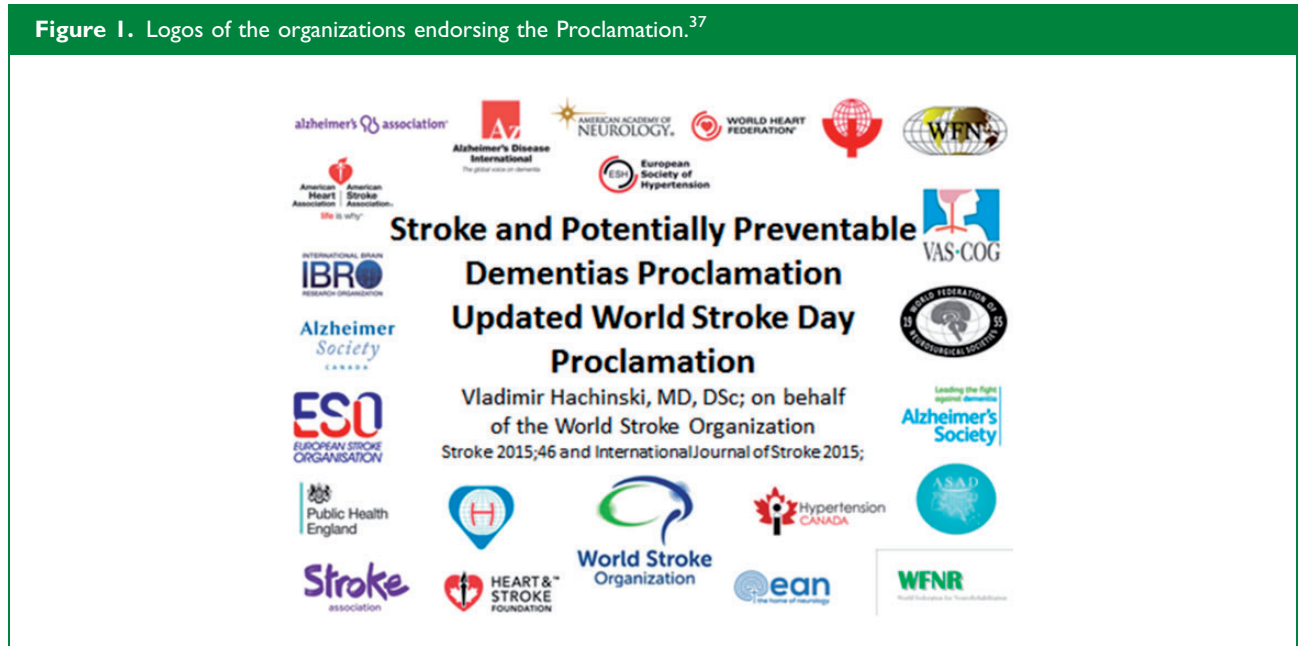


Table 1. Main proposed common risk and protective factors for stroke and dementia

Non- Modifiable	Modifiable	
Risk factors	Risk factors	Protective factors
Advanced age	Cerebrovascular disease/Stroke	High education
Genetic factors (Apo E4)	Cardiovascular diseases	Physical activity
Family history	Hypertension	Antihypertensives
	Hypercholesterolemia	Statins
	Obesity	Active lifestyle
	Diabetes	Healthy diet*
	Atrial fibrillation	Anticoagulant medications*
	Smoking	Cessation*
	Homocysteinemia	Vitamin Bs* & folate*
	Stress	Psychotherapy and
	Depression	Medication*

*Added.

Modified from Solomon A.Kivipelto M. et al.⁶

of stroke and dementia, building on the larger framework and achievements of better blood pressure control⁴³ and continued advances in cardiovascular disease prevention^{44,45,46} would finally also affect prevention of vascular dementias.

The pessimism arising from the growing list of failed trials in cognitive impairment and dementia pursuing the amyloid/tau hypothesis is countervailed by the increasing evidence that by preventing stroke, we can begin preventing some dementias now.

The number of individuals trying to understand the interaction of stroke and dementia and try and prevent them together is still small enough that most of them will be able to gather in Berlin in October 13-14, 2018 to highlight what is known and what needs to be done next. A one day Satellite meeting scheduled for Saturday, October 13th has been organized that will also be the background for the main conclusions at the World Health Summit itself. <https://www.registration-whs.com/Program/WHS2018>. Following the meeting, a manuscript summarizing the main findings will be published. It covers pathophysiology, epidemiology, clinical aspects with an emphasis on dementia prevention by stroke prevention.

A workshop has also been organized for Sunday, October 14th at the World Health Summit on the theme of “Preventing dementia by preventing stroke” that summarizes the main findings and recommendations. <https://www.worldhealthsummit.org/satellites/dementia-stroke-prevention.html>.

All of the organizations endorsing the Proclamation have been asked to publicize the meetings, to send delegates and to participate in developing an action agenda.

Conclusions

The new opportunities becoming evident by investigating the broader picture of health and disease including comorbidities such as stroke and dementia confirm the philosophy of the M8 Alliance and the World Health Summit that health is much more than increasingly specialized medicine. We need a holistic view on health and disease. Comorbidities need to be looked at closely with respect to their interdependence. Stroke and dementia are thus an important example for this comprehensive holistic approach, ever more needed in the aging societies in all countries around the world.

If we want to make progress, improve health and prevent disease on a global level, the example of hypertension, cardiovascular disease, stroke and dementia teaches us an important lesson also in other areas of medicine. The aims of the coalition for vascular health and the program of the World Health Summit therefore includes cutting edge science and the translation to clinics, public and global health and the aim is to discuss problems and solutions with stakeholders from academia, the private sector politics and civil society. We believe that the possibilities of preventing and treating widespread diseases such as hypertension, stroke and dementia provide an important example on what can be achieved based on already existing evidence. We have to take responsibility and call for action.

Author Contributions

All authors contributed equally to the concept. VH wrote the first and final drafts. GD, DL, RK, KT, WH contributed to individual sections and had overall intellectual input.


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