The convergence of stroke and dementia

A convergência do acidente vascular cerebral e da demência

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ABSTRACT
Neurological disorders account for the most Disability Adjusted Life Years (DALY’s) – of the Global Burden of Disease (10%). More than half of neurological DALY’s result from the combination of stroke (42%) and dementia (10%). The two pose risk for each other and share the same predisposing factors. A stroke doubles the risk of dementia. The close interactions call for convergent approaches. Stroke and dementia also converge at the microscopic level. The neurovascular unit has emerged as a key organizational structure of the brain. Involvement of any of its elements affects all the others. Thus, neurodegeneration impairs the microcirculation and disturbances of the microcirculation accelerate neurodegeneration. Evolving technologies allow “in vivo” imaging of the usual mixture of vascular and neurodegenerative pathology of the elderly that makes them prone to stroke and dementia. Since they occur together, they should be prevented together with a multimodal approach of lifestyle changes and mechanistic therapeutic targets. The two fields are also converging at the policy level. The World Stroke Organization has updated its Proclamation to include potentially preventable dementias that has been endorsed by Alzheimer Disease International, The World Federation of Neurology, the American Academy of Neurology and 20 international, regional and national organizations. Those interested in stroke and those dealing with dementia should work together where they can, differ where they must, with the common aim of preventing jointly, both stroke and dementia.

Keywords: stroke, dementia, prevention

THE CONVERGENCE OF STROKE AND DEMENTIA

Knowledge accrues in pieces but is understood in patterns. Specialization yields the pieces and integration reveals the patterns. The more the fields of stroke and dementia have advanced, the more it becomes obvious that they arise from common bases.

Epidemiology
Neurological disorders are the leading causes of disability adjusted life years (DALY’s) representing 10% of all causes. Among the neurological disorders, stroke accounts for 42% and dementia 10% of the DALY’s1. Stroke and dementia pose risk for each other. Over the age of 65 years, 64% of individuals suffering a stroke will have some cognitive impairment...
and among individuals who have some degree of cognitive impairment, a quarter of them have suffered a stroke. Part of the explanation may lie in the fact that stroke and dementia share the same preventable risk factors (Table). This may also explain in part why for each stroke or demented patient there are two with some cognitive impairment that puts them at risk of developing stroke, dementia or both. Further evidence for stroke and dementia arising from shared bases comes from the fact that a certain set of subjects is at risk of developing cognitive impairment before and after a stroke.

The incidence and prevalence of dementia is rising in the developing world and falling in the developed world. Although migrants escaping wars, dictatorships, or seeking a better life dominate the news, the number migrating remains too small to affect the fact that the genetics of the world’s population has not changed in the past few decades and hence, this divergence must be due to environmental, social and biological factors. One example of how some of these trends can be modified is provided by a study carried out in the Province of Ontario, Canada (population 14 million). In the year 2000, a stroke strategy involving the creation of stroke units, stroke prevention clinics and public campaigns to control risk factors resulted in better outcomes after stroke and transient ischemic attacks. Over a 12 year period, there was a concomitant decrease in the incidence of stroke by 32% and that of dementia by 7%. We have a study underway comparing the incidence of stroke and dementia in the provinces in Canada that have a stroke strategy and those provinces that do not, expecting to confirm the findings from Ontario.

Pathophysiology

Neurons and endothelial cells develop together, feed each other growth factors and eventually develop into a neurovascular unit with the addition of astrocytes, pericytes and macrophages. The neurovascular unit contains the blood brain barrier and is at the core of brain function and failure. Endothelial dysfunction can lead to malnourishment of the neurons and other brain cells and impaired clearance of toxic products from the brain, such as beta amyloid. Correspondingly, a sick neuron secreting beta amyloid oligomers can paralyze the capillaries. It is evident that neurogenerative processes that affect neurons will also have an impact on the microcirculation and vice versa and vascular disease involving the endothelial will affect healthy neurons. Consequently, although unexpected, the study showing that the first step leading to Alzheimer disease of old age is vascular dysregulation is not surprising.

Refinements in magnetic resonance imaging (MRI) techniques are allowing assessment not only of capillary function, but of capillary failure. It is becoming obvious that we cannot understand neurodegeneration without understanding the microcirculation or the microcirculation without understanding neurodegenerative processes.

Evidence is also accumulating in support of the concept that cerebral ischemia is an accelerated form of neurodegeneration. The hopeful part of this concept is that some of the so called neuroprotectants used in acute stroke may not have been powerful enough to overcome the massive disturbance of brain tissue of an acute brain infarct, but they may find a role in mitigating slower vascular pathophysiological processes.

Diagnosis

Appropriately, the urgency of a transient ischemic attack or the potential catastrophe of a stroke dominate the attention of stroke doctors. However, this has detracted from the realization that the most common consequence of cerebral vascular disease is not stroke, but cognitive impairment. For every clinical stroke there are about 5 so called “silent strokes” that are asymptomatic, but if the patients are examined, they often have mild neurological signs, decrease in processing speed and some cognitive impairment, particularly in executive function.

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

<table>
<thead>
<tr>
<th>Non-modifiable Risk factors</th>
<th>Risk factors</th>
<th>Modifiable Protective factors</th>
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<tbody>
<tr>
<td>Advanced age</td>
<td>Cerebrovascular disease/stroke</td>
<td>High education</td>
</tr>
<tr>
<td>Genetic factors (Apo E4)</td>
<td>Cardiovascular diseases</td>
<td>Physical activity</td>
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<td>Family history</td>
<td>Hypertension</td>
<td>Antihypertensives</td>
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<td></td>
<td>Hypercholesterolemia</td>
<td>Statins</td>
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<td></td>
<td>Obesity</td>
<td>Active lifestyle</td>
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<td></td>
<td>Diabetes</td>
<td>Mediterranean diet (added)</td>
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<td>Smoking</td>
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<td></td>
<td>Homocysteine</td>
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<td></td>
<td>Stress</td>
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<td>Depression</td>
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<td>Atrial fibrillation (added)</td>
<td>Anticoagulation (added)</td>
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Modified from Solomon A et al. JIM 2014."
Encouragingly, brain imaging has advanced enough not only to detect small cortical infarcts, but also microbleeds. Additionally we have come to realize that white matter changes to the brain are a prelude not only to stroke, but to dementia\(^{13}\). Although positron emission tomography (PET) techniques are too expensive and unavailable for daily practice, they do provide the tools whereby we can begin looking at interactive brain mechanisms, correlating structural and functional magnetic resonance imaging with the ability to detect amyloid, inflammation and now tau protein depositions paving the way to move from muddled diagnosis to treatable mechanisms\(^{14}\).

**Treatment**

Treating stroke patients in stroke units and providing for those that qualify for thrombolysis and thrombectomy is worthwhile in itself. It will not be long before it is shown that this also affects favorably the cognitive preservation in these patients, an important factor in rehabilitation and enjoyment of life.

**Prevention**

Since stroke and dementia occur together, it makes sense to try and prevent them together. The Proclamation of the World Stroke Organization updated in 2015 and endorsed by all the major organizations dealing with the brain, stroke and dementia\(^{15}\) (Figure).

The World Stroke Organization, the World Heart Federation, the World Hypertension League and European Society of Hypertension have agreed to work closely in implementing the joint prevention of stroke and potentially preventable dementia.\(^{16}\) Moreover, a session at the World Health Summit preceded by a one day satellite meeting reviewed, summarized and evaluated the scientific bases for considering stroke and dementia jointly. (https://www.worldhealthsummit.org) (https://www.worldhealthsummit.org/satellites/dementia-stroke-prevention.html) An article to be published in Alzheimer’s & Dementia will summarize the results, recommendations and serve as a guide for implementing policy.

**CONCLUSION**

Stroke and dementia share the same risk factors, pose risks for each other, tend to occur together, interact pathophysiological and preventing stroke might prevent some dementias.

Strength will arise from the union of the two fields. To paraphrase the motto of Acadia (a part of Canada) "L’union fait la force".

**References**


