J Neurol Neurophysiol 2017, 8:1 (Suppl)
http://dx.doi.org/10.4172/2155-9562.C1.044

Reducing risk of vascular dementia and increasing healthspan: Integrated biopsychosocial systems of care for population health

Michael Changaris
John F Kennedy University, California, USA

Vascular dementia (VaD) is a highly complex disease process characterized by multiple pathogenic processes and disease pathways, heterogeneous symptom presentation and bidirectional interactions with other forms of dementia. Addressing population-based impacts of vascular disease can increase life span and overall wellbeing, while improving community health and reducing the financial and resource burden on care delivery systems. An effective population-based response to the impact of VaD and its role in other forms of cognitive decline should incorporate assessment, interventions and treatment pathways adapted for key primary, secondary and tertiary prevention targets for vascular disease and its comorbidities. VaD is associated with pathogenic processes that can lead to the classical symptoms characterized by the classic step-wise decline in functioning (e.g., multi-infarct dementia), as well as pathology that enhances a steady decline of cognitive, affective and behavioral functioning, in line with the symptomology of other forms of dementia (e.g., microbleeds and microinfarcts). Vascular disease also exhibits direct neuroplastic impacts that can lead to reduced neurogenesis, degradation in or poor repair of myelin sheaths, decline in synaptogenesis, apoptotic cascades and impacts of the neuro-immune regulators on brain plasticity. While incidents of isolated VaD are less common then Alzheimer's dementia, prevalence of vascular disease is high, increasing the risk for cognitive impairment in other progressive dementing processes. It is likely that vascular disease exacerbates the symptoms and risk of transition between mild cognitive impairment and other forms of dementia. VaD has a profound effect on health care costs, communities, individual health, family health and systems of care. This presentation will explore the development of an integrated biopsychosocial systems-based approach to population health improvement, achieved by developing key assessments, treatments and pathways of care aimed at primary, secondary and tertiary prevention of vascular dementia and its impacts on other forms of cognitive decline.

drchangaris@gmail.com

A role for vascular inflammation and neutrophil trafficking in the pathogenesis of Alzheimer's disease

Gabriela Constantin
University of Verona, Italy

A dysfunctional blood-brain-barrier and vascular inflammation have been implicated in the pathogenesis of Alzheimer's disease (AD). However, the role of leukocyte trafficking mechanisms in AD is unclear. Using mice with five familial AD (5xFAD) mutations presenting amyloid pathology, and 3xTg-AD mice with both amyloid and tau pathology, we found increased expression of vascular adhesion molecules in areas with amyloid deposits. Surprisingly, we found an increased accumulation of neutrophils in the brain of AD mice with an infiltration peak at the onset of cognitive deficit. Migrating neutrophils released IL-17 and neutrophil extracellular traps (NETs) and established contacts with glial cells. Two-photon microscopy experiments also showed that integrins and selectins control neutrophil extravasation and intraparenchymal motility. Neutrophil depletion or the inhibition of neutrophil trafficking improved memory function, reduced microglial activation, amyloid deposition, tau phosphorylation and synaptic dysfunction compared to control animals. Notably, restoration of cognitive function in mice with temporary inhibition of neutrophil function during early disease was maintained at later time points in aged animals. To understand the relevance of our data in humans, we analyzed human cortical brain samples from subjects with AD. In Alzheimer's patients, neutrophils adhered and spread inside brain venules or migrated into the parenchyma and released NETs in larger numbers than in control subjects. Current Alzheimer's disease therapies provide only temporary improvement and marginally reduce the rate of cognitive decline. Therefore, we propose that targeting vascular inflammation and leukocyte trafficking may represent a new therapeutic strategy in AD.

gabriela.constantin@univr.it