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VASCULAR DEMENTIA 2018

10<sup>th</sup> International Conference on

# VASCULAR DEMENTIA

February 22-23, 2018 | Paris, France

## Scientific Tracks & Abstracts

### DAY 1

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## Evaluating nitric oxide and soluble guanylate cyclase signalling in vascular dementia

**Christopher J Winrow**

Ironwood Pharmaceuticals, USA

The nitric oxide (NO)-soluble guanylate cyclase (sGC)-cGMP signalling pathway plays a fundamental role in modulating diverse physiological processes including blood flow, inflammation, neuroprotection, fibrosis and metabolism. sGC is expressed throughout the CNS. sGC stimulators are small-molecule agonists of sGC that synergize with and enhance endogenous NO signalling. As such, sGC stimulators may provide therapeutic benefits in diseases either associated with loss of NO signalling or where stimulation of this pathway will restore homeostasis. Impaired endothelial cell function and reduced NO bioavailability have been observed across a variety of diseases affecting both micro- and macrovascular health, including vascular dementia where impaired blood flow, disrupted neurovascular coupling, inflammation and neuronal loss are thought to be core aspects of the disease. We are developing IW-1973 and IW-1701 as oral, once-daily sGC stimulators for both cardiovascular and non-cardiovascular indications. Phase 1 data in healthy human subjects demonstrate attractive pharmacokinetic properties and clear evidence of target engagement and expected hemodynamic effects, in a well-tolerated dose range. Phase 2 studies are currently ongoing. In addition, we are developing IW-6463, a novel, first-in-class CNS-penetrant, sGC stimulator with potential application to CNS disorders including vascular dementia and Alzheimer's Disease. Preclinical characterization of IW-6463 supports the broad therapeutic potential and multi-faceted pharmacology of this compound. We believe that sGC stimulation can afford therapeutic benefit for vascular dementia and other diseases, and that there are opportunities for multiple therapeutic products differing in their pharmacology, distribution and pharmacokinetics.

### Biography

Christopher Winrow completed his Ph.D. at the University of Alberta and post-doctoral fellowship at the Salk Institute. He has authored 70 publications and has over 15 years of neuroscience drug discovery and development experience, delivering five compounds from HTS through successful clinical proof of concept. He led the Belsomra® discovery team from screening to regulatory approval in less than 10 years, resulting in this first-in-class CNS therapeutic garnering approvals by U.S. and international regulatory agencies. Dr. Winrow is Senior Principal Investigator at Ironwood Pharmaceuticals in Cambridge, MA where he is responsible for leading multidisciplinary teams through proof of concept for clinical-stage compounds. Christopher Winrow and the Ironwood team are employees and shareholders of Ironwood Pharmaceuticals and are developing sGC stimulators for therapeutic applications.

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## Dealing with dementia as a terminal illness

**Molly Carlile**

The Deathtalker (Author), Australia

Western cultures are notoriously death denying and this applies equally to people in later life who are often living with multiple chronic illnesses, dementia being one. Dementia, though known to be a terminal illness is rarely discussed as such and the grief a person and their family experience on receipt of a diagnosis of dementia is often under explored by health professionals. Why is this? Health professionals often feel ill-equipped to undertake difficult conversations with patients and their families, and so their grief goes un-addressed and end of life issues remain unexplored until the person enters the active dying or imminent death phase, at which time both the person and their family are ill-prepared for the palliative nature of the care that is now appropriate. In order to provide the best level of care and quality of life for people living with dementia, it is essential for health professionals to assist them to explore their values, their fears and apprehensions and to understand what a good death and high level of quality of life looks like for each individual diagnosed with dementia. This presentation will explore the importance of advance care planning, holistic care and exemplary end of life care (including exploring the issues of grief and loss) for people and their families living with dementia and the road blocks that currently exist that prevent these conversations from happening early in the illness trajectory.

## Biography

Molly Carlile AM is a multi-award winning international speaker, author and specialist in the field of palliative care, grief and loss, education and community development. She has a significant clinical background and has held senior leadership roles in acute and community healthcare in addition to sitting on numerous health service boards, department of health advisory committees and academic committees in both nursing and palliative care. She has won local, national and international awards for her work in the field and was awarded a Member of the Order of Australia for her contribution to palliative care. She has presented her papers at national and international conferences for the past 10 years, is a regular media commentator and is currently working on her third book about *death and grief*.

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## Vascular dementia in traumatic brain injury and stroke

Hans Von Holst  
Karolinska Institute, Sweden

Vascular dementia is the second most common dementia type after Alzheimer's disease. Although the epidemiology of vascular dementia is somewhat difficult to estimate exactly, it is substantial nationwide as stroke is one of the major causes. It may also be defined as cerebrovascular dementia as the etiology results in reduced blood flow to parts of the brain tissue. A majority of the cases are elderly people over 70 years. The causes to vascular dementia include high blood pressure, lipids, obesity and diabetes as well as external traumatic brain injury. The clinical picture presents different symptoms depending on injury location and includes, among others, memory problems, reduced thinking and impaired linguistic abilities, slow motoric motion, depression, aggressiveness and impaired judgment. Also, temporary confusion caused by different stress situation is not uncommon. With the introduction of advanced imaging technology such as computerized tomography, magnetic resonance tomography and positron emission tomography, the anatomical location of the defect tissue area can better be identified. The treatment of vascular dementia varies depending on its cause as well as on anatomical location. With the introduction of more advanced laboratory and imaging technology, it is possible to better understand the consequences to vascular dementia on a molecular level including the protein metabolism. With better knowledge from medical and technical development, the primary prevention of vascular dementia will be highlighted such as reducing metabolic disorders but also by the primary prevention in avoiding traumatic brain injuries following fall, traffic accidents and due to different leisure activities.

### Biography

Hans Von Holst received his Medical Doctor's degree in 1976 and specialist in Neurosurgery in 1982 at Karolinska University Hospital. In 1985, he earned his PhD and Associate Professorship in Neurosurgery, Clinical Neuroscience at Karolinska Institute. During 1991-1996, he was appointed as Chairman of the Department of Neurosurgery and Division Manager of the Neuro-clinics at Karolinska University Hospital, respectively. He has been appointed as Senior Neurosurgeon from 1974 to 2015. From 1995-2015, he was appointed as Professor in Neuro-engineering at Royal Institute of Technology. He has published around 140 original papers in reputed journals, reviews and books and has been serving as an Editorial Board Member in several journals.

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## Cerebral arteriovenous malformations, hemodynamics, risk of hemorrhage and its relationship with dementia

**Felipe Padilla Vazquez**

Instituto Nacional de Neurología y Neurocirugía, Mexico

**Background & Aim:** Cerebral arteriovenous malformations (AVM) are hemodynamic lesions which must be studied as such, to determine the cerebral blood flow, average velocity, the Reynolds number to determine turbulent or laminar flows, to calculate in each one their risk of hemorrhage and their anatomical characteristics in this way make therapeutic decisions. In some lesions with venous hypertension or fistulous nests, they generate a high degree of hyper flow, which can cause perilesional vasculopathy to the AVMs nidus, areas of hypoperfusion that can generate dementia.

**Method:** We did a retrospective study that included 639 patients with ruptured and un-ruptured AVMs. We proposed a new classification score (1-4 points) for AVM rupture risk using three factors; feeding artery mean velocity (Vm), nidus size and type of venous drainage. We employed descriptive statistics and logistic regression analysis. We analyzed the different type of nidus in each AVM (plexiform, mixto and fistulous), angiopathy data were determined by recruitment in some lesions and their perinidal repercussion. The patient's clinic was determined as well as the study of superior mental functions with a mini-mental test.

**Results:** A total of 639 patients with cerebral AVMs, 388 (60%) had un-ruptured AVMs and 251 (40%) had ruptured AVMs. Logistic regression analysis revealed a significant effect of Vm (mean velocity), nidus size and venous drainage type in accounting for the variability of rupture odds ( $P=0.0001$ ,  $R^2=0.437$ ), for patients with AVMs. Based in the odds ratios, grades 1 and 2 of the proposed classification were corresponded to low risk of hemorrhage, while grades 3 and 4 were associated with hemorrhage: 1 point OR=0.10795% CI; 0.061-0.188, 2 point OR=0.227 95%, CI; 0.153-0.338, 3 point OR=3.292 95%, CI; 2.325-4.661, and 4 point OR=23.304 95%, CI; 11.077-49.027. We catalog different types of venous drainage, type 1, the anterograde (downstream or normal flow); type 2 the retrograde (upstream or reverse flow) and type 3, retrograde (upstream or reverse flow)+facial venous drainage. We observed that patients who had retrograde flow associated with large AVMs with a fistulous nidus were those that presented dementia data.

**Conclusion:** This classification is useful and easy to use, and it may allow for the individualization of each cerebral AVM and the assessment of rupture risk based on a model of categorization. The retrograde flow and the fistulous nidus of the AVMs have a high risk of dementia.

### Biography

Felipe Padilla Vazquez is a specialist in neurointervention, neuropathic endovascular therapy, cerebrovascular diseases, column surgery, CNS oncological surgery, headaches, neuropathic pain and presently he is a Member of the Mexican Society of Neurological Surgery AC.

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## Management of challenging behaviors in dementia: A geriatrician's perspective

**Si Ching Lim**

National University of Singapore, Singapore

Dementia is becoming an expensive disease worldwide and its prevalence is on the rise, particularly in the developing countries. The non-cognitive symptoms of dementia, also known as neuropsychiatric symptoms or behavioral and psychological symptoms of dementia (BPSD) is particularly challenging for the caregivers resulting in significant caregiver stress, leading to burnout and institutionalization. BPSD occurs in >90% of people with dementia at some point during the course of their illness. An overview of BPSD-types of behavioral problems encountered etiology of BPSD, approach to treatment of BPSD focusing on Person Centered Care (PCC) and treatment options. For healthcare workers, particularly the ones not trained in geriatric and gerontology, BPSD is challenging and stressful. The majority of caregivers will end up restraining-either physically or chemically, the patients for their safety. Restraining the elderly comes with complications like physical deconditioning, DVT, UTI, urinary retention, constipation, pneumonia, pressure sore, etc. The aim of this presentation is to introduce to the audience the causes of challenging behavior and how to manage the agitated patients non-pharmacologically, with restraints as a later alternative. The presentation will include two-three cases for discussion.

### Biography

Si Ching Lim has a special interest in dementia care particularly in patients with behavioral and psychological symptoms of dementia. She is currently working as an In-charge of a 20 bedded dementia ward in a teaching hospital in Singapore and is responsible in developing the ward and training the staff in managing elderly with delirium and dementia with challenging behavior. She is also an Adjunct Assistant Professor at National University of Singapore and Dukes Graduate Medical School.

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## Workshop

### DAY 1



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*David Truswell*

Culture Dementia, UK

## Raising awareness about vascular dementia in the African-Caribbean community in London

London, the UK capital is home to 58% of all those who identified themselves as African-Caribbean in the UK 2011 National Census. It is demographically the oldest of the Black populations in the Census categories and proportionally has a higher rate of dementia than the White UK majority. With research indicating that vascular dementia and early onset dementia is growing issues for Caribbean men under the age of 65 strong cultural beliefs lead many of those most at risk to dismiss any mainstream efforts at preventative health education. Denial of problems and refusal to seek help or diagnosis can often lead to a major crisis before there is any engagement with professional support services and frustrate efforts to develop ongoing links with services. Culture dementia UK a voluntary organization has been working on awareness raising and providing support in the African-Caribbean community in London. The presentation explores how the African-Caribbean cultural narrative of independence and resilience mitigates against help-seeking in dementia and some of the approaches adopted by Culture Dementia UK to raise awareness and encourage people to look for support.

## Biography

David Truswell has worked in community based mental health services in the UK for over thirty years developing services for people with complex care needs and enduring mental health problems in a career spanning the voluntary sector, local authority services, and the NHS. From 2009-2011, he was the Dementia Implementation Lead for Commissioning Support for London, working with commissioners across London to improve dementia services. He is the Chair of the Dementia Alliance for Culture and Ethnicity and an independent writer and researcher on dementia support and services for black and minority ethnic communities, working with a number of projects and initiatives.

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## Serum levels of high molecular weight adiponectin and leptin in elderly patients with dementia

Marwa Ahmed Mohamed Saad  
Alexandria University, Egypt

Dementia is a progressive impairment of cognitive function sufficient to cause functional decline. It may affect up to 28 million individuals worldwide; 30% of those older than 85 years. Adiponectin is a cytokine released by the adipose tissue, and presents in the cerebrospinal fluid of human. It has important functions in the central nervous system. Leptin is another cytokine was implicated in cognitive decline and dementia processes. We aimed in the present study to determine the serum levels of adiponectin and leptin in elderly patient with dementia. 60 subjects aged 65 years and older were involved, divided into two groups; group-1: 40 demented patients and group-2: 20 age and sex matched healthy subjects as a control group. Participants with dyslipidemia, hypertension, diabetes mellitus, chronic liver diseases, chronic kidney diseases, thyroid disorders, or morbid obesity were excluded from the study. All participants were subjected to MMSE and MOCA tests, serum adiponectin and leptin were measured. Serum adiponectin was higher, while leptin levels were lower in demented patients. A significant negative correlation between serum levels of adiponectin and both MMSE and MOCA scores, while a high positive correlation was noted between serum levels of leptin and both MMSE and MOCA scores. We concluded that serum adiponectin and leptin were strongly associated with dementia in elderly patients, which may help in understanding of its pathogenesis and emergence of new drugs for better outcome of this devastated disease.

### Biography

Marwa Ahmed Mohamed Saad has completed her Master's degree in Internal Medicine and Doctorate degree in Internal and Geriatric Medicine at Alexandria University, Egypt. She is currently working as an Assistant Professor of Geriatric Medicine, Consultant of Internal and Geriatric Medicine and Fellow of Egyptian Society of Geriatrics and Gerontology.

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## Type III diabetes: A misnomer for dementia

Aanchal Sareen, Rishabh Parihar and Ravinder Kumar  
Uzhhorod National University, Ukraine

Diabetes mellitus (DM) is a disease of the peripheral organs while diabetes insipidus (DI) is a disease of the brain. Both forms of diabetes are characterized by excess levels of blood sugar or glucose. Whereas the former is due to insulin resistance or insufficiency the latter is due to insufficiency of hypophyseal anti-diuretic hormone (ADH). But the causes underlying the accumulation of glucose in circulation are different for DM and DI. While type-1 diabetes (T1D) is due to autoimmune destruction of insulin-producing pancreatic islets of Langerhans (IL), type-2 diabetes (T2D) is a lifestyle disease due to exhaustion of IL to produce insulin in response to hyperglycemia. Whereas glucose fuel unavailability in the mitochondria leads to deficit of energy production in the form of ATP, its accumulation in blood leads to complications due to inflammatory damage to blood vessels. The brain uses glucose as a primary source of energy. Cognitive function becomes impaired when blood glucose drops to low levels, and severe hypoglycemia may cause neuronal damage. Recently, Alzheimer's disease (AD) has been hypothesized to be type-3 Diabetes (T3D), presumably caused by insulin resistance in the brain, an organ absolutely dependent upon glucose as fuel for ATP biosynthesis. This can create a dangerous spiral, in which a hypoglycemic event caused by T2D can lead to mental deterioration and vice versa. If the brain is starved of energy, it is possible that neurological problems like dementia and Alzheimer's disease are more likely to develop. It is found that clinically significant hypoglycemia is associated with a two-fold increased risk for developing dementia and likewise patients with dementia were more likely to experience a severe hypoglycemic event with brain damage in the cerebral cortex and hippocampus.

## Biography

Aanchal Sareen has completed her higher education from India in 2014 and presently pursuing MD in General Medicine from Ukraine. Her research was published in International Medical Student's Conference 2017 Krakow, Poland (pharmacy and internal medicine fields). She also has been an active Member at Uzhhorod Medical Students Conference, Ukraine 2017.

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## Characteristics of different type of dementia in neurosonology: What we know?

**Babak Zamani**

Iran University of Medical Sciences, Iran

Neurosonology of brain parenchyma is a new growing field in different type of brain disorders. There is some data about usefulness of this noninvasive technique in some degenerative disorders like Parkinson's disease and dystopia. During last few years in our department we studied different neurosonological landmarks in different types of dementias including substantia nigra echogenicity, raphe nuclei echogenicity, midbrain width, 3th ventricular diameter and lenticular nucleus echogenicity.

### Biography

Babak Zamani has worked in Iranian Board of Neurology in 1993. He has also worked as a President of Iranian Stroke Society and Vice President of Iranian Neurological Society.

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## A new direction for Alzheimer's research

**James D Weinstein**  
Marshall University, USA

Although billions of dollars have been spent for research on Alzheimer's disease (AD), little progress has been made in finding a therapy which stops the progressive dementia characteristic of the disease. Numerous drugs, having failed over years of research suggests the need for re-evaluation of how the research is now being done. To that end, three changes in current AD research methodology are offered and these changes are absolutely necessary to provide the means to find an effective treatment for the disease. First, AD is a disease of four etiologies rather than from a single primary cause. These four should be treated simultaneously for an effective therapy. Second, AD drug testing is wasting much time effort and money by aiming for a statistical verification of the slowing of dementia. The end point should be the complete cessation of progressive dementia, and testing should begin with small cohorts. Third, combination therapies with drugs currently available, used off label, ought to be tried. One example of such a combination is reviewed.

## Biography

James D Weinstein has completed his MD in 1964 from University of Pennsylvania and his Internship from New England Center Hospital in Boston in 1965. He has worked as a Neurosurgeon for more than 40 years in New Jersey and West Virginia. He has published more than 25 papers in reputed journals.

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*P Giannakopoulos*

University of Geneva, Switzerland

## Multimodal prediction of subtle cognitive decline in elderly controls: An update

**Introduction & Aim:** The presence of apolipoprotein E4 (APOE\*E4) is the strongest currently known genetic risk factor for Alzheimer's disease and is associated with brain gray matter loss, notably in areas involved in Alzheimer's disease pathology. Our objective was to assess the effect of APOE\*E4 on brain structures in healthy elderly controls who subsequently developed subtle cognitive decline.

**Materials & Method:** This prospective study included 382 community dwelling elderly controls. At baseline, participants underwent MR imaging at 3T, extensive neuropsychological testing and genotyping. After neuropsychological follow-up at 18 months, participants were classified into cognitively stable controls and cognitively deteriorating controls. Data analysis included whole-brain voxel-based morphometry and ROI analysis of GM.

**Results:** APOE\*E4 related GM loss at baseline was found only in the cognitively deteriorating controls in the posterior cingulate cortex. There was no APOE\*E4-related effect in the hippocampus, mesial temporal lobe, or brain areas not involved in Alzheimer disease pathology. Controls in the cognitively deteriorating group had slightly lower GM concentration in the hippocampus at baseline. Higher GM densities in the hippocampus, middle temporal lobe, and amygdala were associated with a decreased risk for cognitively deteriorating group status at follow-up.

**Conclusions:** APOE\*E4 related GM loss in the posterior cingulate cortex (an area involved in Alzheimer disease pathology) was found only in those elderly controls who subsequently developed subtle cognitive decline but not in cognitively stable controls. This finding might explain the partially conflicting results of previous studies that typically did not include detailed neuropsychological assessment and follow-up. Most important, APOE\*E4 status had no impact on GM density in areas affected early by neurofibrillary tangle formation such as the hippocampus and mesial temporal lobe.

## Biography

P Giannakopoulos has obtained his MD at University of Athens in 1989 before completing a full training on Psychiatry and Psychotherapy in London at Maudsley Hospital and Geneva as well as Post-doctorate training in Paris at La Pitié-Salpêtrière Hospital, Federation of Neurology. In 1998, he has been appointed as an Associate Professor and Medical Head of the Division of Geriatric Psychiatry of the University Hospitals of Geneva. Later on he obtained the position of full tenured Professor of Psychiatry at University of Geneva. From 2003 to 2011, he also assumed a parallel position of Full Professor of Old Age Psychiatry at University of Lausanne in order to promote the academic careers of junior staff locally. He has been the Chairman of the Department of Mental Health and Psychiatry in Geneva for 10 years (2005-2015); Vice Dean of the Faculty of Medicine at University of Geneva and; In-charge of postgraduate and continuous education (2003-2011). From December 1st 2015, he is the Medical Head of the Forensic Psychiatry Development in Geneva County. He has published more than 220 peer reviewed articles in the field of neurobiology of aging with particular focus on predictive biomarkers of cognitive decline.

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