The dementia impact and scientific conundrum: two challenges in search of a public health solution

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WHY?
WHY?

17:15 – 18:15
WEDNESDAY
19 FEB TO 27 MAY 2020
ETH Zürich HG D16.2

THIS IS PUBLIC HEALTH

LECTURE AND DISCUSSION SERIES ON PRIME TOPICS OF PUBLIC HEALTH

Happy 15th Birthday

SSPH+ SWISS SCHOOL OF PUBLIC HEALTH

ETH Zürich
Let’s start with a definition: PUBLIC HEALTH

Great diversity: cool!

The common ingredient is a viewpoint, a world view...

Public Health is the discipline that addresses health at the population level.
WHY am I here?

SEE

PAST

CHANGE

FUTURE

THIS IS PUBLIC HEALTH
Alzheimer

Frankfurt, 1901/1906
Prof. Alois Alzheimer describes a NEW DISEASE in a 51-year-old woman, August D.

August D’s brain histopathological lesions
Really?

It’s a common, disease of late-life.

Sir Martin Roth

Newcastle, 1965
First epidemiological study on dementia

Old Age Mental Disorders in Newcastle upon Tyne
Part I: A Study of Prevalence
By D. W. K. KAY, P. BRAMISH and MARTIN ROTH
Viewpoints and world views
Where are patients with dementia seen?

Illustration: Hans Moller, mollers.dk
How much does it COST?

- 1.3 trillion USD in 2019
- = Apple market value

Forecasted global costs of dementia 2015-2030

Global costs of dementia (US$ millions)

Year


1.3 Trillion USD
Are we doomed?

The Global Action Plan on the Public Health Response to Dementia 2017 - 2025

**Vision**
A world in which dementia is prevented and people with dementia and their carers live well and receive the care and support they need to fulfil their potential with dignity, respect, autonomy and equality.

**Goal**
To improve the lives of people with dementia, their carers and families, while decreasing the impact of dementia on them as well as on communities and countries.

Geneva, in 2017
The WHO launched the dementia global action plan
What's the plan?

7 action areas
A public health approach

Dementia as a public health priority
Dementia awareness and friendliness
Dementia risk reduction
Dementia diagnosis, treatment & care
Support for dementia carers
Information systems for dementia
Dementia research and innovation

Risk reduction
Research
The problem

What are the causes of dementia?

WE DO NOT KNOW
Problem: we do not know the causes

1. **Primary prevention is impossible**
2. **Secondary prevention is difficult**

A 2 year **multidomain intervention** of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial


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Risk reduction

**World Wide Fingers**

Alzheimer's Association
Problem: we do not know the causes
1. Primary prevention is impossible
2. Secondary prevention is difficult
3. Research is crucial!

Research priorities to reduce the global burden of dementia by 2025

- Prevention, identification, and reduction of risk (e.g., genetic, lifestyle, or environmental)
- Diagnosis, biomarker development, and disease monitoring
- Pharmacological and non-pharmacological clinical-translational research
- Quality of care for people with dementia and their carers
- Delivery of care and services for people with dementia and their carers
- Physiology and progression of normal ageing and disease pathogenesis
- Public awareness and understanding

Hiral Shah, Emiliano Alberese, Cynthia Dugan, Igor Rudan, Kenneth M. Langa, Maria C. Carrillo, Kui Yee Chan, Yves Joanette, Martin Prince, Martin Rossor, Sheikha Seccane, Heather M. Seyler, Reisa Sperling, Mathew Varghese, Huilai Wang, Marc Wortmann, Tarun Dua


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Problem: **we do not know the causes**

1. **Primary** prevention is **impossible**
2. **Secondary** prevention is **difficult**
3. **Research** is crucial!
4. **Treatment** is... “a prescription to **failure**”
The problem

What are the *causes* of dementia?

...we do have some clues
Neuropathological hallmarks
Disease pathways

1. Synaptic disruption
2. Immune response
Disease pathways

1. Amyloid angiopathy
2. (cerebral) Micro-bleeds
β-Amyloid plaques
SPREADING

1. Cortex
2. Hippocampus
3. Whole brain \textit{centripetal}
TAU-Neurofibrillary tangles

SPREADING

1. Hippocampus
2. Whole brain centrifugal
3. Brain atrophy
Cognitive impairment
Only TAU diffusion correlates with cognitive deficits

- Memory
- Language
- Agnosia
- Apraxya
Amyloid cascade hypothesis

1. Amyloid triggers tau phosphorylation (kinase)
2. Neurofibrillary tangles form
3. Neuronal death (apoptosis) > brain atrophy
Amyloid cascade hypothesis
John Hard posited this HP to explain AD

Perspective

Alzheimer’s Disease: The Amyloid Cascade Hypothesis

John A. Hardy and Gerald A. Higgins


John Hardy, 1992
The amyloid cascade HP
Drug development pipeline

- 28% Neuropsychiatric Symptoms
- 11% Symptomatic Cognitive Enhancers
- 61% Disease-Modifying Therapies
  - 32% Anti-Amyloid
    - Immunotherapy (n=6)
    - BACE inhibition (n=2)
    - Anti-aggregation (n=1)
  - 4% Anti-Tau
    - ↓ Tau phosphorylation and ↓ Amyloid (n=1)
  - 4% Anti-Amyloid & Anti-Tau
- 21% Other MOAs

28 Agents in Phase 3

*One main idea*

*Hypothesis

Cummings J 2019
Fig. (1). The amyloidocentric theory of AD. The amyloid cascade hypothesis represented as the geocentric Ptolemy’s theory of the solar system, which placed the Earth at the center and was accepted for many centuries.

Roberta Ricciarelli\textsuperscript{1,*} and Ernesto Fedele\textsuperscript{2,3,*}
Public health approach (viewpoint)
A NEW discipline is born: Population Neuroscience

Population Neuroscience
Dementia Epidemiology Serving Precision Medicine and Population Health

Mary Ganguli, MD, MPH,* Emiliano Albanese, MD,† Sudha Seshadri, MD,‡
David A. Bennett, MD,§ Constantine Lyketsos, MD, MHS,¶
Walter A. Kukull, PhD,¶ Ingmar Skoog, MD, PhD,#
and Hugh C. Hendrie, MB, ChB, DSc**

Epidemiology  Neuroscience  ‘Omics’

T. Paus
M. Ganguli
E. Albanese

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The challenge
Population Neuroscience blends:
1. METHODOLOGIES rationale for choosing methods
2. METHODS techniques to conduct research

Population Neuroscience should shake the assumptions
The solution

A scientific revolution

- Scientific **progress** is NOT about ‘development by accumulation’.
- **Assumptions** must change, not the HP:
- A **paradigm shift** is a mix of enthusiasm and promise, not a logically determined procedure
- **Inspiration** is crucial...

Thoma Kuhn, 1962
The structures of Scientific Revolutions
Back to the past
Seeking inspiration from literature

Odyssey, Book XI
Odysseus meets the dead and his mother Anticlea, who does not recognize him...

The dead in classical mythology are forgetful
Take home message
The SSPH+ is our ‘School of Athens’, where several disciplines concur
Pop Neuroscience aspires to cause a paradigm shift in dementia research

WHY am I here?

The school of Athens, Raphael 1510, symbolizes the marriage of art, philosophy, and science

The combination of Plato’s gesture towards the sky with Aristotle’s empiricist ‘hand’
SSPH+ Lugano Summer School in Public Health Policy, Economics, and Management

Course 1, Aug 24 – 26, 2020: Policy Options on Mental Health in the SDGs era


www.ssphe-lugano-summerschool.ch