EngAge Ageing Symposium 2017
Physical exercise for optimizing brain health – a life course approach towards healthy ageing

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Points of Interests

• Brain health and lifestyles
• Towards Evidence Based Approaches
  – The Hong Kong Memory and Ageing Prospective Study
  – Physical activity interventions for people with neurocognitive disorders
• Physiological mechanisms
• Opportunities
Ageing World

World Alzheimer’s Report 2015
INFOGRAPHIC
The global impact of dementia

Around the world, there will be 9.0 million new cases of dementia in 2015, one every 3 seconds.

46.8 million people worldwide are living with dementia in 2015. This number will almost double every 20 years.

2015: 46.8 million
2030: 74.7 million
2050: 131.5 million

68% in 2050

Much of the increase will take place in low and middle income countries (LMICs). In 2015, 68% of all people with dementia live in LMICs, rising to 91% in 2030 and 99% in 2050.

This map shows the estimated number of people living with dementia in each world region in 2015.

Europe: 10.5 million
The Americas: 9.4 million
Asia: 22.9 million
Africa: 4.0 million

We must now involve more countries and regions in the global action on dementia.

World Alzheimer’s Report 2015
Ageing Brain

Hypothetical model from a life course approach

Muller M et al. Pediatrics 2014;134:761-770
Brain Health and Lifestyles

LONGTERM PROSPECTIVE STUDIES
Men and Women
Harvard Grant Study

• 75 years prospective study of factors that determines happy ageing (1939 – 1944)
  – 268 Harvard Men
  – 456 underprivileged non-delinquent men in Boston area
  – Longitudinal follow up
• Six factors measured by age 50 as excellent predictors of those who would be in the “happy-well” at age 80:
  – A stable marriage
  – A mature adaptive style
  – No smoking
  – Little use of alcohol
  – Regular exercise
  – Maintenance of normal weight

http://harvardmagazine.com/2001/03/the-talent-for-aging-wel-html
The Nun Study

• A longitudinal study on aging and disability using antemortem and postmortem data collected from 678 older School Sisters of Notre Dame since 1986.
  – The causes and prevention of Alzheimer's disease,
  – The mental and physical disability associated with old age.

• Healthy Aging versus dementia
  – AD pathology
  – Stroke
  – Early linguistic ability
  – Education

The Nun and the Harvard Men

- Early Life: Psychosocial factors, optimal environmental stimulation, physical health
- Midlife: Degenerative pathology
- Late life: Vascular lesions

Neuropathology

Healthy aging / Cognitive Decline
AGEING AND PHYSICAL EXERCISE
Exercise interventions for cognitive function in adults older than 50: a systematic review with meta-analysis

Joseph Michael Northey,¹,² Nicolas Cherbuin,³ Kate Louise Pumpa,¹,² Disa Jane Smee,² Ben Rattray¹,²

- 39 studies were included in the systematic review
- Physical exercise improved cognitive function (0.29; 95% CI 0.17 to 0.41; p<0.01)
- Interventions of aerobic exercise, resistance training, multicomponent training and tai chi, all had significant point estimates
- A duration of 45–60 min per session and at least moderate intensity, were associated with benefits to cognition
Physical activity delays hippocampal neurodegeneration and rescues memory deficits in an Alzheimer disease mouse model

M Hüttenrauch, A Brauß, A Kurdakova, H Borgers, F Klinker, D Liebetanz, G Salinas-Riester, J Wiltfang, HW Klafki and O Wirths

Transl Psychiatry, 2016. 6, e800
To explore the effects of long term physical activities on hippocampal neuronal loss and behavioral effects on Tg4-42 mouse models

Transl Psychiatry, 2016. 6, e800
Motor and balance skills were better in EE mice

- Long term physical activity attenuates hippocampal neuronal loss and reduce spatial memory deficits
- Changes in gene expressions versus standard cage

Transl Psychiatry, 2016. 6, e800
Lifestyle changes

TOWARDS EVIDENCE APPROACHES
Intellectual and physical activities, but not social activities, are associated with better global cognition: a multi-site evaluation of the cognition and lifestyle activity study for seniors in Asia (CLASSA)

Linda C. W. Lam¹, Paulus Anam Ong², Yustiani Dikot³, Yulia Soratin³, Huali Wang⁴, Mei Zhao⁴, Wenxiu Li⁵, Jacqueline Dominguez⁶, Boots Natividad⁶, Suraya Yusoff⁷, Jong-ling Fu⁸,⁹, Vorapun Senianarong¹⁰, Ada W. T. Fung¹, Ken Lai¹

Faculty of Medicine
The Chinese University of Hong Kong
Cognitive function and Lifestyles

- 2,404 participants across 9 East Asian cities
- Activities were categorized into
  - Physical
  - Intellectual
  - Recreational
  - Social
- Global Cognitive function was associated with intellectual and physical activities
  - Social activities were associated with lower cognitive function
- Same association in participants with activity for over 10 years

Age and Ageing, 2015; 44: 835-840
Types of PE and Dementia Risks

JADMA, 2015;16:899e1-e7
Types of PE and Dementia Risks

• 15,589 participants assessed at Elderly Health Centres in the first 6 months in Hong Kong
• Followed at 6 years for cognitive outcome
• Controlled for sociodemographic and physical health factors,
• Aerobic exercise (OR 0.81, 95% CI 0.68-0.95, p=0.01) and
• Mind-body exercise (OR 0.76, 95% CI 0.63-0.92, p=0.004) were associated lower risks of dementia at 6 years

JADMA, 2015;16:899e1-e7
Original Study

Physical Exercise Helped to Maintain and Restore Functioning in Chinese Older Adults With Mild Cognitive Impairment: A 5-Year Prospective Study of the Hong Kong Memory and Ageing Prospective Study (HK-MAPS)

Duan Yang Ma BSocSc, MPhil a,*, Candy H.Y. Wong MBChB a, Grace T.Y. Leung MBChB, FHKCPsych, FHKAM (Psy) b, Ada W.T. Fung BA, MSc, PhD a, Wai Chi Chan MBChB, MRCPsych, FHKCPsych c, Linda C.W. Lam MD, FRCPsych, FHKCPsych a

JAMDA, 2017;18:306-311
Hong Kong Memory and Ageing Prospective Study - HKMAPS

- A prospective cohort study of determinant of cognitive decline in 787 randomly selected community living Chinese non-demented older adults in Hong Kong.
- Baseline 2005-6, 5 year follow up at 2011
- At follow up = 454
  - Cognitive normal = 327
  - Mild Cognitive Impairment = 127

PE and Daily Function

- Association between physical exercise habits, cognitive and functional outcome at 5 years
- Regular physical exercise habits (at least once a week)
  - Persistent practice
  - Pick Up
  - No practice
- Cognitive function
  - MMSE
  - Delayed recall
  - Category verbal fluency
- Everyday function
  - Disability Assessment for Dementia

JAMDA, 2017;18:306-311
PE and Daily Function

- At baseline, the persistent exercise group had higher cognitive function than non-exercise group.
- At follow up,
  - Persist group had least cognitive and functional decline.
  - Pick Up group did not show significantly better preserved cognitive function.
  - Pick up group had better ADL scores than no exercise.

JAMDA, 2017;18: 306-311
INTERVENTIONS FOR MILD COGNITIVE IMPAIRMENT
Original Study

A 1-Year Randomized Controlled Trial Comparing Mind Body Exercise (Tai Chi) With Stretching and Toning Exercise on Cognitive Function in Older Chinese Adults at Risk of Cognitive Decline

Linda C.W. Lam MD, Rachel C.M. Chau MSc, Billy M.L. Wong MSc, Ada W.T. Fung MSc, Cindy W.C. Tam MRCPsych, Grace T.Y. Leung MRCPsych, Timothy C.Y. Kwok FRCP, Tony Y.S. Leung MSc, Sammy P. Ng MPH, Wai M. Chan MPH

JADMA, 2012;13:568e15-20
Tai Chi versus Stretching & Toning Exercise

- A one year single blind cluster randomized controlled trial.
- Intervention
  - Intervention – 171 (24 forms Simplified Tai Chi)
  - Control - 218 stretching and toning exercise
- Subjects over 65 years old
- At risk of Cognitive decline
  - Mild Cognitive Impairment / Clinical Dementia Rating 0.5
  - No regular mind body exercise before

JADMA, 2012;13:568e15-20
Why Tai Chi?

- **Assumptions**
  - A culturally friendly intervention is important for lifestyle modification
  - Mind Body exercise is dual modality training (Physical + cognitive)
At one year

- 389 subjects with mild cognitive impairment
- Cluster RCT
  - 3 times/week
  - Tai Chi (T) versus stretching exercise (C)
- Both I (n=171) & C (n=218) groups demonstrated improvements in cognitive test performance.
- For completers-only analyses, I group had
  - Lower risk of developing dementia at 1 year (odds ratio 0.21, 95% CI 0.05-0.92, P = 0.04)
  - Greater improvement in delayed recall (p=0.05)
  - Better postural balance.
  - More significant drop in depressive symptoms.

JADMA, 2012;13:568e15-20
At one year

CDR sum of boxes

- Baseline
- 2 months after induction
- 6 months after induction
- At one year

Intervention vs. Control
Cognitive function

Delayed recall

- Baseline
- 2 months after induction
- 6 months after induction
- At one year

10 minute delayed recall

- Intervention
- Control
Postural balance

Berg Balance Scale

Baseline 5th month 9th month 12th month

Intervention

Control
Adherence and benefits

COGNITIVE AND PHYSICAL ACTIVITIES IN MILD COGNITIVE IMPAIRMENT
Lifestyle leisure activity intervention in Chinese older adults

- One year study cluster randomized control trial on structured lifestyle activities
- Participants (n=555)
  - 60 year or above
  - Mild Cognitive Impairment
- 4 lifestyle leisure activity schedules
  - Cognitive (C)
  - Physical (P)
  - Integrated Cognitive-Physical (CP)
  - Social (S) activity programs
- Baseline, 4th, 8th and 12th months

Lam et al., pone 2015 March 31.0118173
# Activity schedule

<table>
<thead>
<tr>
<th>Group</th>
<th>Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Social group</td>
<td>1 social</td>
</tr>
<tr>
<td>2. Cognitive Group</td>
<td>1 cognitive</td>
</tr>
<tr>
<td>3. Physical</td>
<td>1 stretching &amp; toning exercise</td>
</tr>
<tr>
<td>4. Cognitive Physical</td>
<td>1 cognitive</td>
</tr>
</tbody>
</table>
At one year

- **Improvements** in ADAS-Cog, delayed recall and verbal fluency (p<0.05)
- **Stable Clinical Dementia Rating or functioning scores**
- No group differences in multi-domain MCIs
- In the single domain MCI group, the combined CP group
  - had a trend of lower ADAS-Cog (p=0.0005),
  - better delayed recall (P<0.0005) and verbal fluency scores (p<0.0001)
ADAS-Cog Scores

Baseline 4th month 8th month 12th month

- mdMCI cognitive
- mdMCI cognitive physical
- mdMCI physical
- mdMCI social
- sdMCI cognitive
- sdMCI cognitive physical
- sdMCI physical
- sdMCI social

CP intervention in sdMCI group
P=0.0005
Delayed recall

CP intervention in sdMCI group
P<0.0005
Adherence and cognitive improvement

- Cognitive Improvements
  - Higher program adherence
  - Younger age
  - Better Baseline cognitive function

Lam et al., pone 2015 March 31.0118173
What happens in the brain?

PHYSIOLOGICAL MECHANISMS
Physical & cognitive exercise – are they the same?
Physical exercise versus cognitive training

• 100 older adults randomized to
  – Progressive Resistance training + Computer cognitive training (PRT+CCT)
  – PRT + Sham
  – CCT + Sham
  – Double Sham

• Structural versus connectivity modifications…

Suo et al, Mol Psy, 2016
• Resistance training x Time interaction in Post Cingulate gyrus, p< 0.05
• Enhancement of PC cortical thickness is correlated with ADAS improvement, p< 0.05

Suo et al, Mol Psy, 2016
Cognitive training improved hippocampal - superior frontal lobe connectivity, and affected overall memory performance $p<0.05$

Suo et al, Mol Psy, 2016
Determinants of telomere attrition over one year in healthy older women: Stress and health behaviors matter

Eli Puterman1,*, Jue Lin2, Jeffrey Krauss3, Elizabeth H. Blackburn2, and Elissa S. Epel1,*
Health behaviors, Stress Coping and Cellular response

- 239 post menopausal disease free non-smoking women
- 1 year observation
- Life event stressors
- Health behaviors
  - Leisure time physical activity
  - Dietary pattern
  - Self report sleep quality
  - Cumulative health behaviors

At one year

- Life event stressors associated with telomere attrition
- Low scores for health behaviors, stressors had greatest telomere attrition
- High health behavior scores, stressful life events not apparently related to telomere attrition

Baseline Telomere Length and Effects of a Multi-domain Lifestyle Intervention on Cognition

- Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)
- 2 year RCT
  - 1,260 people at risk of cognitive decline
  - aged 60–77 year
  - lifestyle intervention (diet, exercise, cognitive training, and vascular risk management) versus control (general health advice) groups
- Shorter LTL was related to less healthy baseline lifestyles
- Intervention benefits on executive functioning were more pronounced among those with shorter baseline LTL

Sindi et al., Journal of Alzheimer’s disease, 2017 July
Opportunities

• Physical exercise, an important lifestyle factor at later life, plays an important role in healthy brain ageing
• Supported by epidemiologic studies, clinical interventions, and translational research
• Ready for Health Promotion
  – Guidelines on practical advice and tips
  – Benefits with no age limits
• Adherence
  – Technology guided
  – Safe devices with efficacy
  – Public education
WHAT WOULD YOU WANT TO DO WHEN YOU ARE 100 YEAR OLD?
Tao Porchon Lynch, 98

Cheung Suet Ling, 93
Cure or Care

An intervention that could delay the onset of dementia by 2 years in 2020, 13% reduction of people with dementia from 2012 and 2050. An intervention that could delay onset by 5 years, the reduction would be 35%.

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Declaration

• The content of this presentation has no potential conflicts of interests with pharmaceutical or related industries.
• Personal passion for practice of mind body exercise and mindfulness meditation
THANK YOU