

# Mindfulness and its Relevance to Cognitive Decline and Dementia

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- Could mindfulness meditation reduce dementia risk factors?
  - Existing Evidence
  - Medit-Ageing Project







# What are psychological risks for dementia? Depression Anxiety Neuroticism

Depression

Anxiety

Neuroticism

#### Meta-analysis of clinical depression and incident dementia

Author(s) and Year		F	Risk Ratio [95%CI]
Dal Forno et al. (m)	2005	<b>—</b> —-i	2.36 [ 1.05 , 5.31 ]
Dal Forno et al. (f)	2005	⊨-■	1.58 [ 0.61 , 4.10 ]
Fuhrer et al. (m)	2003	⊢■⊣	3.20 [ 1.72 , 5.96 ]
Fuhrer et al. (f)	2003	⊢∎∔	0.70 [ 0.39 , 1.26 ]
Gatz et al.	2005	<b>—</b> •—i	2.82 [ 0.98 , 8.12 ]
Goveas et al.	2011	⊨-₩	2.03 [ 1.15 , 3.59 ]
Irie et al.	2008	H	2.20 [ 1.30 , 3.71 ]
Kim et al.	2011	<b>}</b> ∎	2.07 [ 1.04 , 4.11 ]
Luppa et al.	2013	<b>—</b> —	2.75 [ 1.01 , 7.49 ]
Palsson et al.	1999	⊢■	1.70 [ 0.70 , 4.11 ]
Vilalta-Franch et al.	2012	<b>⊧</b> I	2.64 [ 1.15 , 6.02 ]
RE Model		•	1.98 [ 1.50 , 2.63 ]
	0.1	2 1.00 8.00	г )
	Relat	ive Risk (log so	cale)

Cherbuin et al BMJ Open 2015

• Positive association between depression diagnosis and risk of dementia

#### Meta-analysis looking at anxiety symptoms and incident dementia

community						
Author	Year				Relative Risk (95% CI)	% Weigh t
Palmer (2a, 2b)	2007				2.05 (1.22, 3.44)	23.8
Chan	2011		-		.58 (0.22, 1.53)	13.9
Brodaty (2a)	2012				2.34 (0.32, 17.04	) 4.87
Burton	2013				2.67 (2.01, 3.55)	29.74
De Bruijn	2014 -		+		0.99 (.33, 2.97)	11.94
Mah	2014				1.35 (0.57, 3.22)	15.69
Overall (I-squared =	59.4%, p = 0.031)		$\diamond$		1.61 (1.00, 2.58)	100.0
NOTE: Weights are analysis	from random effec	ts				
	.1		1	10		

Figure 2 Pox plot predictive value of envioty for incident demontie in the

Depression

Anxiety

Neuroticism

Gulpers et al Am J Ger Psychiatry 2015

• Symptoms of late-life anxiety are associated with incident dementia

#### Clinical anxiety diagnosed >10 years before dementia assessment

	Lead Author	Average follow-up / Look-back period	Size of Study (N)	Odds ratio or Hazard ratio
Depression	Boot et al	Lifelong diagnoses from medical records	441	OR 7.4
Anxiety	Gallacher et al	17.3 year follow-up	1160	OR 1.62
	Petkus et al	28 year follow-up	1082	HR 1.48
Neuroticism	Zilkens et al	~20 year look back	27,136	OR 1.61

- All studies (N > 28,000) showed association between anxiety and dementia
- Early to mid-life anxiety is associated with incident dementia

Gimson, et al. BMJ Open 2018

# Meta-analysis of proneness to distress (aka neuroticism) with dementia incidence



• Neuroticism associated with 13% increased risk of developing dementia

#### Personality scores by cognitive status in a large cohort (N = 13,882)



Terracciano et al. J Psychiatric Res. 2017

• Individuals with cognitive impairment or dementia have higher levels of neuroticism personality characteristics than any other personality trait and than cognitively intact older adults



- Transdiagnostic
- Encompasses worry & rumination
- Describes *process* rather than content
- Stable style of thinking
- Can be triggered by external or internal events
- Can be sustained outside of conscious awareness

Ruscio et al Behav Res Ther 2011 Just & Alloy J Abnorm Psychol 1997 Brosschot Neurosci Biobehav Rev 2010



Self-relevant, persistent thoughts that elaborate on negative themes Harvey et al 2004

# Cognitive Debt Hypothesis



Marchant & Howard J Alzheimer's Disease 2015

# Cognitive Debt Hypothesis



Marchant & Howard J Alzheimer's Disease 2015





- Evidence for psychological risk factors for dementia
- Repetitive Negative Thinking may be the 'active ingredient' driving risk
- Helpful to use cognition and biological markers as proxy outcomes for dementia
- Indicates a need to explore psychological interventions to reduce dementia risk

Research starting to explore *potentially* protective psychological factors:

• Purpose in Life

Bartrez-Faz et al. 2018

• Psychological therapies offered in the UK National Health Service



• Meditation/Mindfulness?....

Klimecki et al. 2019

#### **Protective Factors?**

#### Protective factors promote resistance and/or resilience to pathology



Arenaza-Urquijo & Vermuri *Neurology* 2018 Arenaza-Urquijo et al. Frontiers in Aging Neuroscience 2015





What are psychological risks for dementia?



- Could mindfulness meditation reduce dementia risk factors?
  - Existing Evidence
  - Medit-Ageing Project









- Promotes non-judgmental awareness and attention to experiences of the present moment
- Can be employed as a secular form of cognitive/emotional training
- Majority of research focuses on 2 types of interventions:
  - Mindfulness-based stress reduction (MBSR)
  - Mindfulness-based cognitive therapy (MBCT)



# **Mindfulness-Based Interventions**

Designed to promote non-judgmental awareness and attention to experiences of the present moment





# **Mindfulness-Based Interventions**

Designed to promote non-judgmental awareness and attention to experiences of the present moment





Khoury et al Clin Psychol Rev 2013

Mean Hedge's g

<b>Exiety</b> Pre-Post Studies targeting	Depression $(n = 6)$
Pre-Post Studies targeting Anxiety ( Pre-Post Studies targeting Psychological disorders ( Pre-Post Studies targeting Pain Pre-Post Studies targeting Cancer ( Pre-Post Studies targeting Physical/Medical condition ( Pre-Post Studies using MM Pre-Post Studies using MBCT ( Pre-Post Studies using MBCT ( Pre-Post Studies using MBCT (	$ \begin{array}{c} a=26) \\ (n=2) \\ a=26) \\ (n=1) \\ a=19 \\ (n=4) \\ a=44) \\ a=44) \end{array} $
Waitlist Controlled Studies targeting <b>[</b>	<u>Depression</u> $(n = 8)$
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Mean Hedge's g

Khoury et al Clin Psychol Rev 2013





Mean Hedge's g

Khoury et al Clin Psychol Rev 2013





• Mindfulness intervention significantly reduced levels of neuroticism compared with the control group

# **Mindfulness-Based Interventions**

Designed to promote non-judgmental awareness and attention to experiences of the present moment



Caveats: Good evidence but few studies with active control conditions, and generally not focused on older adults or in relation to dementia





Mindfulness-based intervention effects on mental health (e.g. anxiety and depression) partially act via changing repetitive negative thinking. Gu et al. Clinical Psychology Review 2015

# **Mindfulness-Based Interventions**

Designed to promote non-judgmental awareness and attention to experiences of the present moment



Caveat: Promising findings but few studies



Marciniak et al. Frontiers in Behavi Neuroscience 2014



# Effect of meditation on cognitive functions in context of aging and neurodegenerative diseases

Study	Participants	Significant effect on cognitive functions	Memory	Attention	Executive functions <sup>a</sup>
Alexander et al. (1989)	Elderly		Yes	Yes	Yes
Pagnoni and Cekic (2007)	Elderly		_	Yes	_
van Leeuwen et al. (2009)	Elderly		_	Yes	_
Newberg et al. (2010a)	Elderly, MCI, Alzl	heimer's disease	Yes	Yes	Yes
Newberg et al. (2013)	Elderly, MCI, Alzl	heimer's disease	No	No	No
Grant et al. (2010)	MCI, Alzheimer's	s disease, caregivers	Yes	-	_

Marciniak et al. Frontiers Behav Neuroscience 2014

- Six studies, all but one showed improvements in cognitive domains that were assessed.
- Different forms of meditation used in each study (e.g. zen, kirtan kirya, MBSR)



# Reviews of mindfulness-based interventions influence on cognitive functioning in older adults

Six studies, all but one showed improvements in cognitive domains that were assessed. Different studies investigated different forms of meditation (e.g. zen, kirtan kirya, MBSR) Marciniak et al. *Frontiers Behav Neuroscience* 2014

Review included six mindfulness-based studies, 3 RCTs, with older adults. Positive effects reported on memory, executive function and processing speed. However, there was high risk of bias and small sample sizes. Berk et al. *Aging & Mental Health* 2017

# **Mindfulness-Based Interventions**

Designed to promote non-judgmental awareness and attention to experiences of the present moment



Caveats: Promising findings but limited by heterogenous interventions, no follow-up, and restricted cognitive test batteries.

# Biological Markers of Alzheimer's Disease



#### Palmqvist et al Nature Communications 2017



Brain structure involved in learning & memory

# Vemuri & Jack Alzheimer's Research Therapy 2010

# Hippocampal Atrophy:

# Brain Amyloid:

**Regions associated with meditation** 

**Review of effects of mindfulness-based interventions on brain function and structure** 



Gotink et al. Brain & Cognition 2016

#### **Regions affected early in Alzheimer's disease**

#### **Brain Amyloid:**



#### **Hippocampal Atrophy:**



Brain regions associated with mindfulness are also implicated early in Alzheimer's disease

#### **Regions associated with meditation**

#### **Review of effects of mindfulness-based interventions on brain function and structure**



#### Gotink et al. Brain & Cognition 2016

#### **Regions affected early in Alzheimer's disease**

#### **Brain Amyloid:**



#### **Hippocampal Atrophy:**



Brain regions associated with mindfulness are also implicated early in Alzheimer's disease

# **Mindfulness-Based Interventions**

Designed to promote non-judgmental awareness and attention to experiences of the present moment



Caveats: Generally promising findings but limited because information is not from older adults, and is not specific to Alzheimer's disease biological markers (e.g. amyloid).



Could mindfulness meditation reduce dementia risk factors?

# **Existing Evidence**

# **Promising findings:**

- Reduces psychological risk factors via repetitive negative thinking
- Positive effects on cognition (attention & memory)
- Affects same brain regions that show early amyloid aggregation and atrophy

# **BUT few studies and often:**

- Small sample sizes
- Heterogeneous groups (ie not older adults)
- Heterogenous meditation practices
- No active control condition
- No follow-up



Could mindfulness meditation reduce dementia risk factors?

**Existing Evidence** 

# What is Needed:

- Clinical trials with large samples of older adults
- Manualised intervention designed for this population
- Well-matched active control condition
- Longitudinal follow-up
- Multiple measures to understand mechanisms of action





What are psychological risks for dementia?



- Could mindfulness meditation reduce dementia risk factors?
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  - Medit-Ageing Project

#### HORIZON 2020 WORK PROGRAMME 2014 – 2015 8. Health, demographic change and wellbeing Personalising health and care

PHC 22 – 2015: Promoting mental wellbeing in the ageing population



PI: Dr Gaël Chételat

# SILVER SANTÉ STUDY MEDIT-AGEING

Investigating the impact of meditation training on mental health and wellbeing in the ageing population

www.silversantestudy.fr

www.silversantestudy.eu

#### **MEDIT-AGEING PROJECT**

11 partners in 6 European countries (France, UK, Spain, Switzerland, Belgium & Germany)





# **MEDIT-AGEING Includes 2 Randomized Controlled Trials**



- Clinical study
- 8-week intervention offered to patients at high risk of developing dementia
- 147 patients included across 4 countries
- If successful could be adopted by healthcare systems
- Primary outcome = anxiety



- Experimental study
- 18-month intervention to examine longer-term impact on behavioural and biological outcomes
- 137 older adults included from France
- If successful, would support meditation effects and could be adopted by general public
- Primary outcome = brain imaging measure of anterior cingulate (region implicated in Alzheimer's disease and meditation)

# **Participants**



# **Subjective Cognitive Decline – Definition**

- Self-experienced persistent decline in cognitive capacity
- Normal performance on standardized cognitive tests
- No diagnosis of MCI or dementia
- Not explained by a psychiatric or neurological disease

# **Participants**



# **Subjective Cognitive Decline**

- Increased risk of developing dementia
- Frequently experience symptoms of anxiety
- No therapy offered as part of standard clinical care

Hill et al *Gerontologist 2016* Jessen et al *Alzheimers Dement* 2014

# **Participants**



- 4 European Sites
- Recruited from memory clinics
- Age  $\geq 60$
- Normal cognitive performance
- Expressed memory concern/worry
- No interfering medication or disorder
- No clinical dx of anxiety or depression

Jessen et al. *Alzheimers Dement* 2014 Jak et al *Am J Geriatr Psychiatry* 2009 Bondi et al. *JAD* 2014

# Interventions

# Caring Mindfulness-Based Approach for Seniors (CMBAS)

- Adapted from standard mindfulness-based stress reduction programme & Zellner Keller et al. *Mindfulness* 2014
- Mindfulness & compassion training
- Psychoeducation to help manage ageing-related cognitive & health concerns

# Health Education Programme (HE)

- Adapted from a published manual & intervention
- Educational sessions include problem-solving & planning, managing medicines, memory, sleep, stress, exercise, communication, diet
- Group activities and discussions about topics

Lorig et al *Living a Healthy Life with Chronic Conditions* 2012

Caring Mindfulness-Based Approach for Seniors (CMBAS) Barnhofer et al *in preparation*  Structure: Adapted for SCD & manualised
Length: 8 weeks (plus a half-day session)
Duration: 2-2.5 hours per week
Type: Facilitator-led, Group-based (7-12 attendees)
Homework: 6 days/week ~1hr/day



# **Participant Flow**



# Measures



# Visit 2







#### **Assessments Administered**

# Criteria for Assessment Selection

Domain	Name	Acronym
Anxiety	State-Trait Anxiety Inventory (trait subscale)	Trait- STAI
Psycho-social		
Sleep		
Cognition		
Personality		
Lifestyle		

# Gold Standard

- Validated in 4 languages
- Suitable for older adults
- Brief
- Easy to administer

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Could mindfulness meditation reduce dementia risk factors?

# **Medit-Ageing Project**

#### What is Needed:







# Summary

What are psychological risks for dementia?

- Evidence for psychological risk factors for dementia Repetitive Negative Thinking may be the 'active ingredient' driving risk
- Helpful to use cognition and biological markers as proxy outcomes for dementia
- Indicates a need to explore psychological interventions to reduce dementia risk
- Could mindfulness meditation reduce dementia risk factors?
- Emerging evidence supports mindfulness meditation as a promising intervention to reduce dementia risk factors but there are significant limitations (e.g. sample sizes, heterogeneous methodology)
- Medit-Ageing study underway to rigorously examine mindfulness meditation effects and mechanisms of action on behavioural and biological dementia-related outcomes in older adults.

# Acknowledgements

#### Medit-Ageing Scientific Team & Research Sites Gaël Chételat Frank Jessen

Eider Arenaza-Urquijo Julie Gonneaud Antoine Lutz Thorsten Barnhofer **Fabienne** Collette Olga Klimecki Géraldine Poisnel Miranka Wirth

#### Statisticians & **Methodologists:** Eric Frison **Roxane** Coueron Julien Asselineau



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This project has received funding from the European Union's Horizon 2020 research and innovation programme Project No: 667696 under call H2020-PHC-22 www.silversantestudy.eu

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