

Dementia and Physical exercise

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Outline

- * Definition
- * About dementia
- * Causes
- * Symptoms
- * Risk and Prevention
- * Diagnosis
- * Treatment
- * Exercise and dementia

Definition

- * Dementia is a general term for a decline in mental ability severe enough to interfere with daily life
- * Memory loss is an example

About dementia

- * Dementia is not a specific disease
- * It's an overall term that describes a group of symptoms associated with a decline in memory or other thinking skills severe enough to reduce a person's ability to perform everyday activities
- * Alzheimer's disease accounts for 60 to 80 percent of cases
- * Vascular dementia, which occurs after a stroke, is the second most common dementia type

About dementia

- * However, there are many other conditions that can cause symptoms of dementia, including some that are reversible, such as thyroid problems and vitamin deficiencies
- * Dementia is often incorrectly referred to as "senility" or "senile dementia," which reflects the formerly widespread but **incorrect belief that serious mental decline is a normal part of aging**

About dementia

- Alzheimer's disease is *one type* of dementia
- **Dementia** is a *general term* meaning “progressive mental decline” – can involve memory, language, judgment, intellect
- Dementia can be
 - **Primary (progressive and irreversible)**; examples include Lewy-Body dementia, fronto-temporal dementia, Alzheimer's disease, and other less common dementias
 - **Secondary (potentially reversible)**; for example, secondary to a brain tumor

ALZHEIMER'S DISEASE

- * Alzheimer's is the most common type of *primary* dementia
- * Alzheimer's disease is also the most common neurodegenerative disease (neurodegenerative diseases include Alzheimer's, Parkinson's and Amyotrophic Lateral Sclerosis [ALS])

ALZHEIMER'S DISEASE

- **Early onset familial Alzheimer's disease** (< 65 years of age); transmitted in an autosomal dominant manner (3 genes have been identified); accounts for only a very small percentage of individuals with the disorder (~5%, at most 10%)
- **Late onset (> 65 years of age); also known as *sporadic Alzheimer's disease*; cause unknown**
 - Sporadic non-familial Alzheimer's is now showing up in individuals <65 years of age as well

Causes of dementia

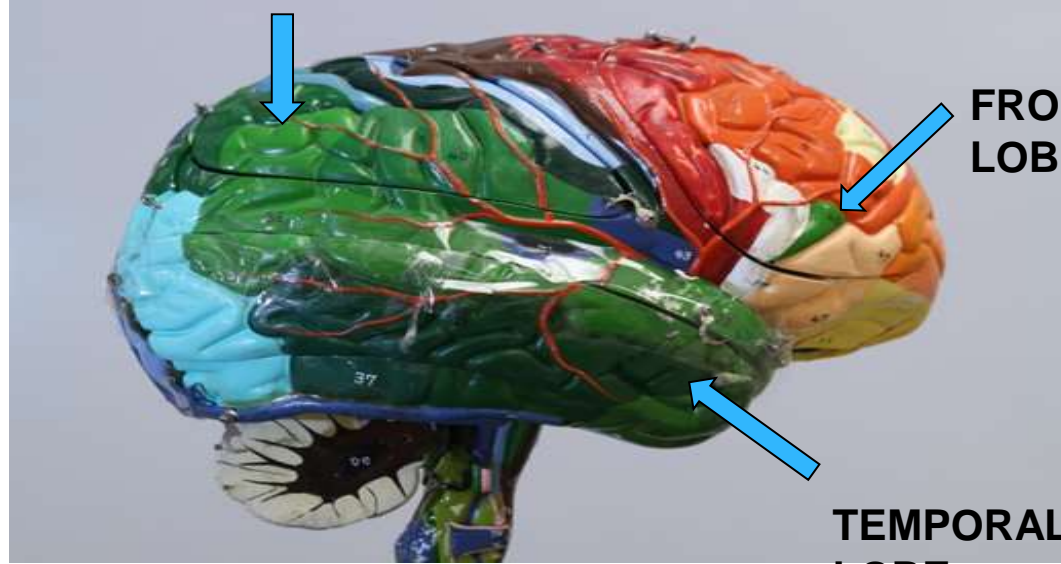
- * Dementia is caused by damage to brain cells
- * The brain has many distinct regions, each of which is responsible for different functions
- * Different types of dementia are associated with particular types of brain cell damage in particular regions of the brain

Causes cont..

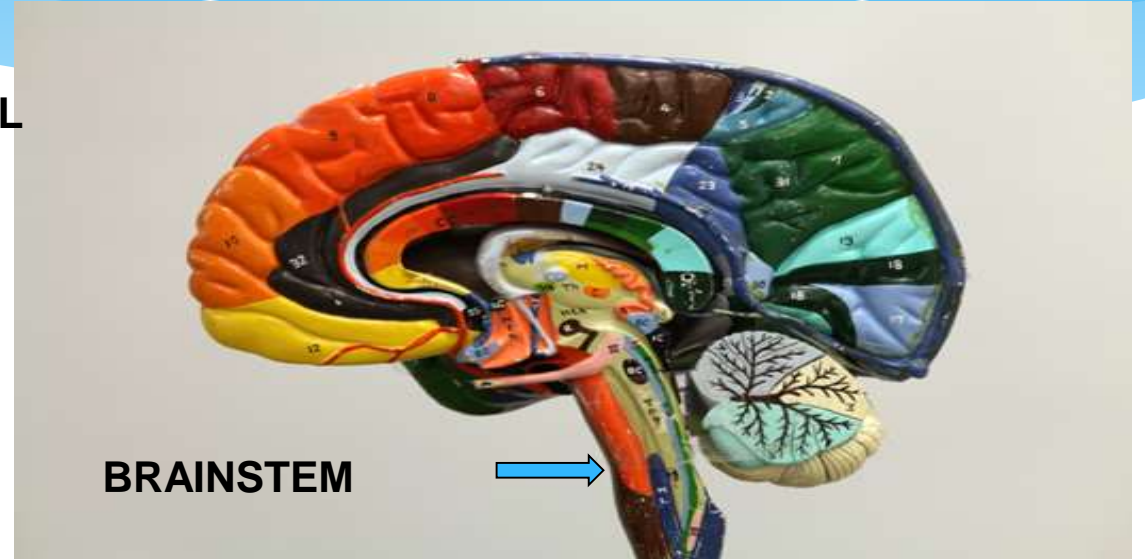
- * While most changes in the brain that cause dementia are permanent and worsen over time, thinking and memory problems caused by the other conditions and may improve when the condition is treated or addressed:
- * Depression
- * Medication side effects
- * Excess use of alcohol
- * Thyroid problems
- * Vitamin deficiencies

ALZHEIMER'S DISEASE IS A NEURODEGENERATIVE DISEASE – MEANING THAT SPECIFIC GROUPS OF NEURONS DIE

PARIETAL LOBE



TEMPORAL LOBE



BRAINSTEM

Higher-order” cortical areas, especially of the frontal, parietal and temporal lobes, and a few brainstem/deep hemispheric structures preferentially degenerate

MAJOR BRAIN AREAS AFFECTED

Cortical/Subcortical

- **Neo-cortex** (higher-order sensory areas; thought and reasoning; working, short-term and long-term memory), **Hippocampus** (explicit, episodic and spatial memory), and **Amygdala** (emotional memory)

*Brainstem/Deep hemispheric***

- **Locus coeruleus** (norepinephrine; attention, regulation of blood flow, sleep/wake cycles)
- **Raphe nuclei** (serotonin; mood regulation)
- **Nucleus basalis of Meynert** (acetylcholine; reward?)

***These areas “regulate or modulate” the activity of neurons in other areas of the brain, especially the cortex*

DEFAULT MODE NETWORK

- Parts of the **medial frontal and temporal lobe** (including hippocampus) and **cingulate gyrus** that are active when we are not attending to external stimuli
- Plays a critical role in our **internal dialogue and reflection of our life, memories, autobiography**
- A major system which is lost in Alzheimer's disease

Cingulate gyrus

**Medial areas of Frontal and
Temporal Lobes**



Medial brain

ALZHEIMER'S DISEASE IS A DISORDER OF *DYSREGULATION*

- *Dysregulation of cortical neurons*
- *Dysregulation of the brain's immune response*
- *Dysregulation of the brain's metabolism*
- *Dysregulation of the normal removal of toxic substances from the brain*

BEHAVIORAL CHANGES IN ALZHEIMER'S DISEASE

- * **Memory loss**
- * **Decreased initiative**
- * **Depression; emotional instability**
- * **Inability to inhibit behavior**
- * **Faulty judgment, loss of insight**
- * **Severe language deficits**
- * **LOSS OF “SELF” and ABILITY TO “ENGAGE” INTERNALLY**

*Factors that **Increase Risk** for Late-onset Alzheimer's Disease*

- **Age**

*Factors that **Increase Risk** for Late-onset Alzheimer's Disease*

- **Age**
- **Inheritance of E4 alleles for Apolipoprotein E (Apo E)**

Factors that **Increase Risk** for Late-onset Alzheimer's Disease

- * **Age**
- * **INHERITANCE OF E4 ALLELES FOR ApoE**
- * **Head injury**

Factors that **Increase Risk** for Late-onset Alzheimer's Disease

- Age
- Inheritance of E4 alleles for ApoE
- Head injury
- **Obesity**

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- **High fat diet; elevated cholesterol**

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- * Obesity
- * High fat diet; elevated cholesterol
- * **Atherosclerosis, diabetes, hypertension**

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- **Hormone replacement therapy**

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- Hormone replacement therapy
- **Chronic stress (leads to high blood cortisol)**

Factors that **Increase Risk** for Late-onset Alzheimer's Disease

- Age
- Inheritance of E4 alleles for ApoE
- Head injury
- Obesity
- High fat diet; elevated cholesterol
- Atherosclerosis, diabetes, hypertension
- History of untreated depression
- Hormone replacement therapy
- Chronic stress (leads to high blood cortisol)
- **Diagnosis of MCI (Mild Cognitive Impairment)**

*Factors that **Decrease Risk** for Late-onset Alzheimer's Disease*

- * **GOOD GENES!** (Inheritance of E2 alleles for Apo E)

*Factors that **Decrease Risk** for Late-onset Alzheimer's Disease*

- * **Good genes!** (Inheritance of E2 alleles for apo E)
- * **Healthy diet**

Factors that **Decrease Risk** for Late-onset Alzheimer's Disease

- * Good genes! (Inheritance of E2 alleles for Apo E)
- * Healthy diet
- * **Restful sleep**

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- * **Continuing mental challenge**

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- * Good genes! (Inheritance of E2 alleles for apo E)
- * Healthy diet
- * Restful sleep
- * Continuing mental *challenge*
- * **Maintaining strong social connections**

Factors that **Decrease Risk** for Late-onset Alzheimer's Disease

- * Good genes! (Inheritance of E2 alleles for apo E)
- * Healthy diet
- * Restful sleep
- * Continuing mental *challenge*
- * Maintaining strong social connections
- * ****Exercise****

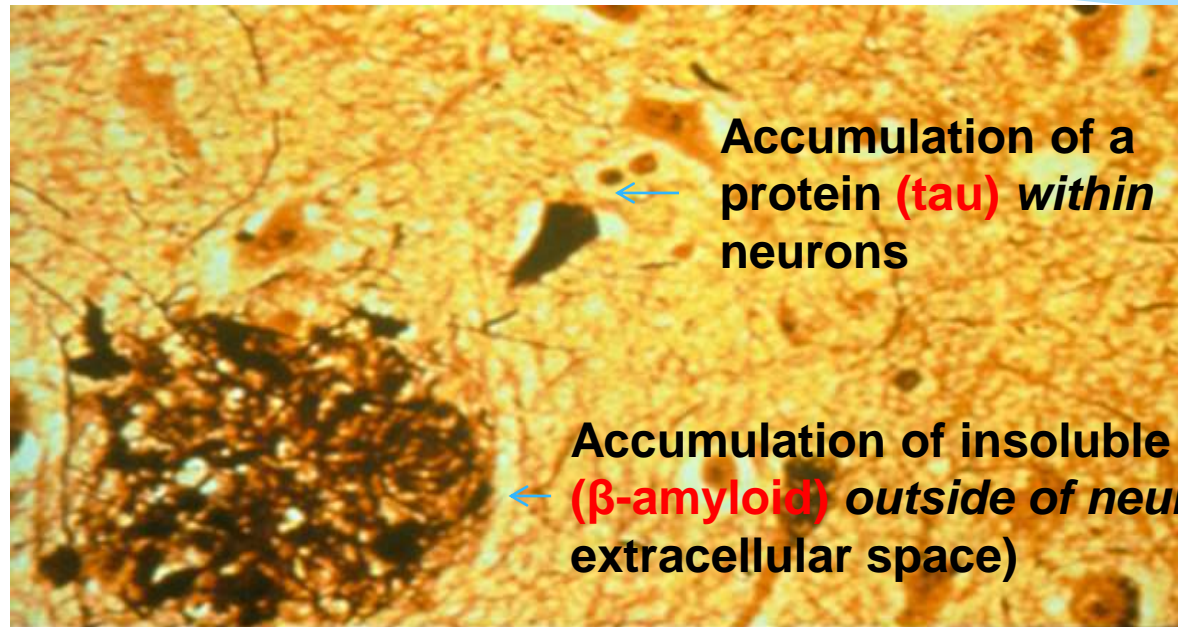
Alzheimer's Disease causes death of neurons



Alzheimer's disease

Normal (age-matched)

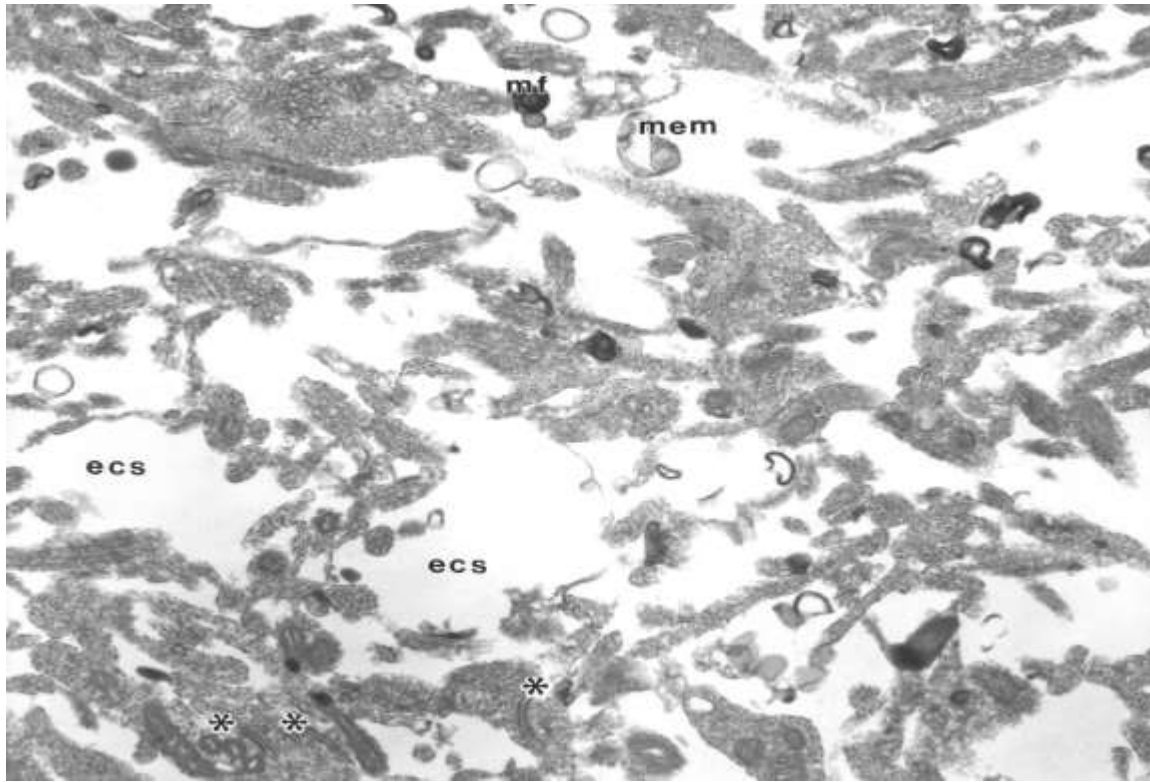
At Autopsy, Abnormal Cellular and Extracellular Accumulation of “Altered” Proteins (**β -amyloid and tau**) can be Identified within neurons and in the “extracellular” space



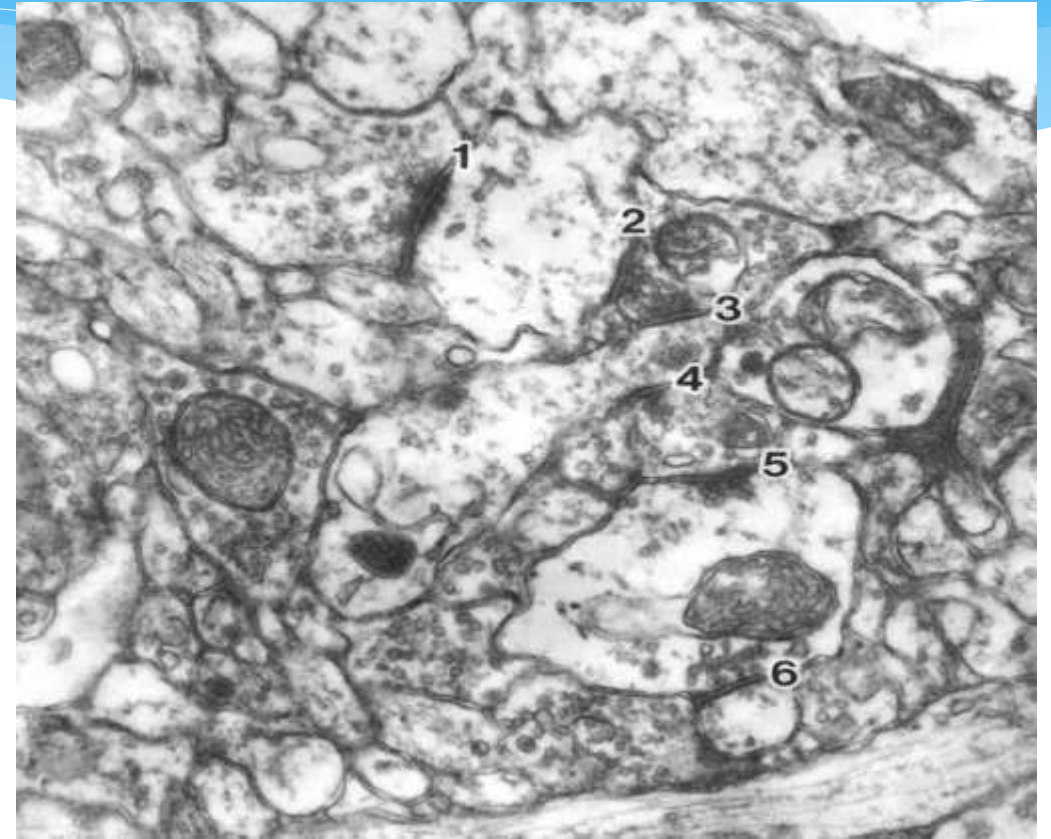
Accumulation of a protein (**tau**) *within* neurons

Accumulation of insoluble protein (**β -amyloid**) *outside of neurons* (in extracellular space)

β -Amyloid Protein is Normally removed from the Brain during Restful Sleep



Extracellular (ecs or interstitial) space is abundant in the developing brain



In the adult brain, there is much less extracellular space; this *increases* by 60% at night – and toxic waste products are removed across the blood-brain barrier

Treatment

- * Treatment of dementia depends on its cause
- * There is no cure and no treatment that slows or stops its progression
- * Need to develop an inclusive care plan

Physical Benefits of Exercise

■ Increases

**Endurance
Strength (muscle & bone)
Flexibility
Balance & posture
Restful sleep
Resistance to stress
Overall cardiovascular fitness
Weight control**

■ Decreases

**Hypertension
Heart disease
Type II diabetes
Osteoporosis
Falls**

Cognitive Benefits of Exercise

■ *Increases*

- ❖ Generation of new neurons in hippocampus and prefrontal cortex
- ❖ Survival of neurons (by ↑ neurotrophic factors and ↑ blood supply)
- ❖ Synaptic Plasticity (modifiability of synapses through multiple mechanisms)
- ❖ Restful sleep (promotes memory consolidation and ↑↑ amyloid clearance from the brain)
- ❖ Production of Neurotransmitters/Substances that play a role in Attention, Arousal, Mood & Well-Being

■ *Decreases*

- ❖ Age-related loss of neurons in cortex
- ❖ Age-related decline in cognitive performance
- ❖ Risk for Alzheimer's Disease

Factors that **Decrease Risk** for Alzheimer's Disease

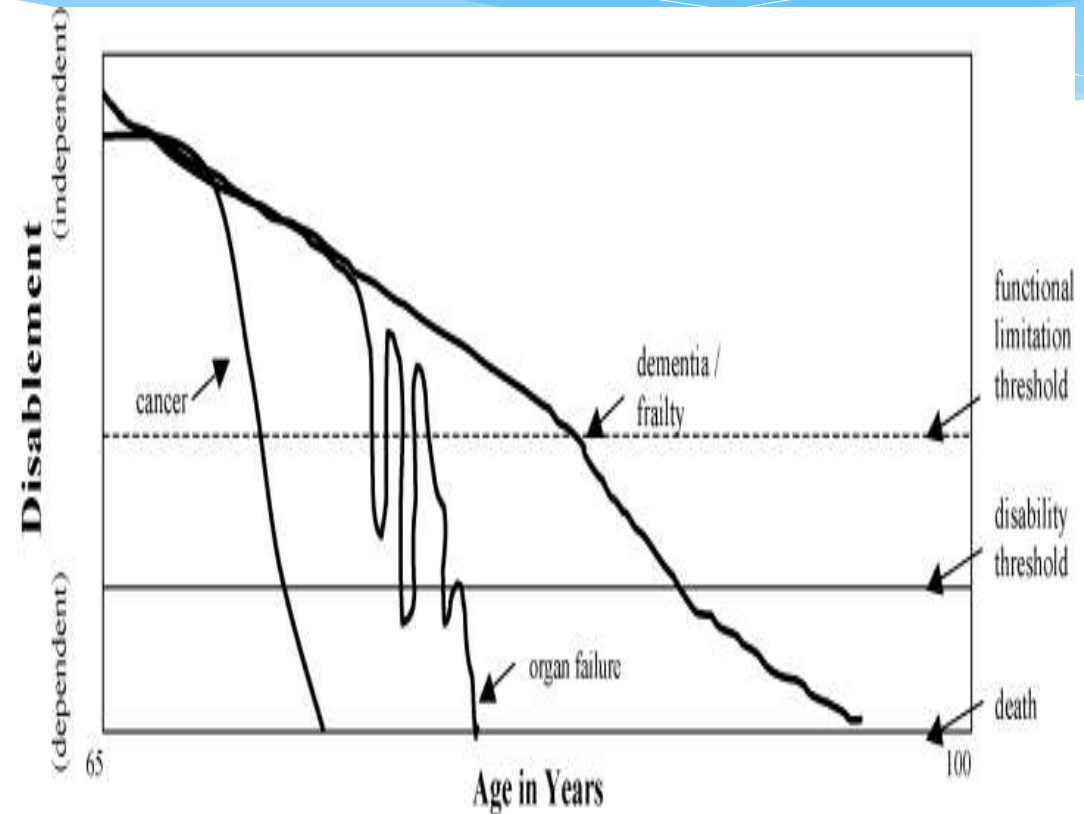
- **Not under your control**
 - Choosing good parents 😊
 - Not aging (!)
- **Under your control**
 - Keeping safe
 - Eating a healthy diet (stay close to the earth and sea; fruits, veggies, nuts, whole grains, fish high in omega 3 oils)
 - Maintaining a healthy weight
 - Restful sleep
 - Continuing mental challenge
 - Maintaining strong social & personal connections
 - **PHYSICAL EXERCISE!**

After a diagnosis of dementia staying fit may not be supported by our social context

- * Many people (including older people themselves) view older age as a time of inactivity
- * Dementia is a feared condition and hence kept hidden and avoided
- * Australian hospitals and private health fund programs are not very dementia friendly.
- * Community gyms often aren't suitable

Biological perspectives

- * Dementia is a disease that makes disengagement easy
 - * Insight and self awareness of deficits
 - * Executive dysfunction and behavioural inertia
- * Dementia gets worse and leads to disability and death
- * Long disease trajectory with variable rates of deterioration



Promoting functional independence

- ◆ Encourage “dyadic” interventions including environmental assessment and modification, problem solving and carer training
- ◆ Encourage exercise

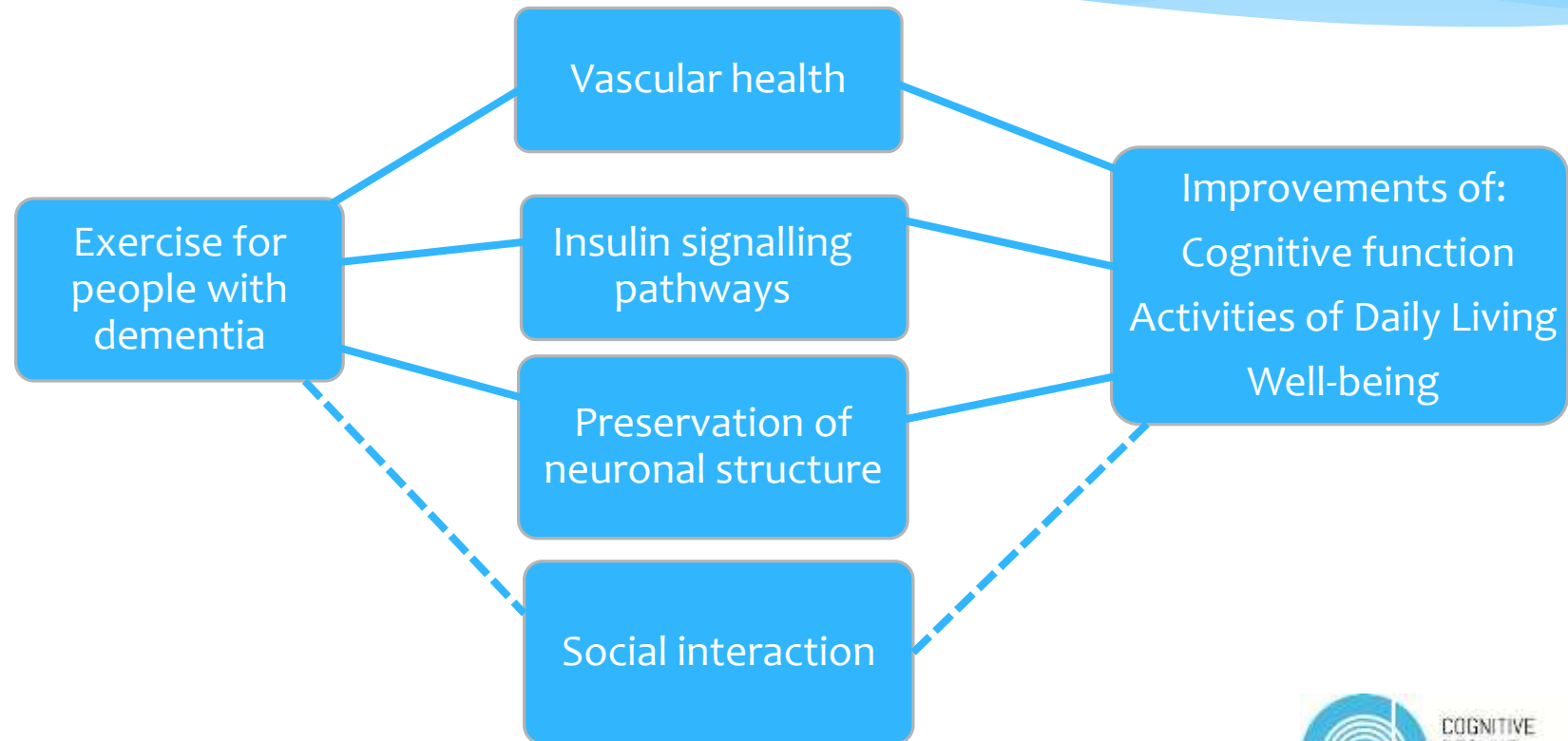
Exercise and Dementia



Exercise

- * **Exercise** is a subcategory of physical activity that is *planned, structured, repetitive and purposeful* whose main objective is to improve one or more components of physical fitness
- * **Physical activity** is any bodily movement produced by skeletal muscles that requires energy expenditure

How exercise may benefit people with dementia

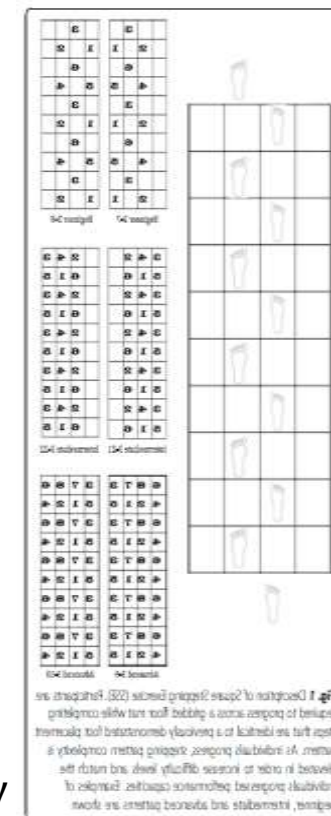


Prevention of Dementia

- ◆ Lots of observational evidence that ongoing physical activity from mid life reduces the risk of dementia
- ◆ In normal older adults cognition improves with exercise
- ◆ Some RCT evidence once you have Mild Cognitive impairment that the rate of cognitive loss slows but trials are inconsistent

Evidence on exercise after diagnosis isn't as clear

- * The vascular effects of aerobically based exercise training are well documented however the impact of aerobic exercise on cognition after diagnosis has not been unequivocally established
- * Multimodality exercise programs with mind motor training are now a focus – visuospatial outcomes
- * Holistic frailty approaches have growing evidence
Gregory M. Group based exercise and cognitive physical training in older adults with self reported cognitive complaints: the multiple-modality, Min-Motor (M4) study protocol. BMC Geriatrics 2016



Frailty and dementia

- * Postulated that frailty and dementia share common underlying mechanisms:
 - * Cardiovascular and cerebrovascular disease are risk factors for both frailty and AD
 - * Raised levels of pro-inflammatory cytokines eg. interleukins, CRP, TNF- α common to both, indicating possible state of **low grade chronic inflammation**
 - * Mitochondrial malfunction
 - * Oxidative stress

Recommendations for management of frailty in dementia

* Aerobic exercise:

- * Some suggestion increases hippocampal size
- * Slows cognitive decline and improves function in people with mod-severe dementia
- * Is feasible in nursing home residents with dementia

* Resistance/strength training:

- * Lowers interleukins and TNF- α
- * Improves cognitive function (in older people without cognitive impairment)

Exercise prescription

- * F- frequency (how often)
- * I- Intensity (How much)
- * T- Time (How long)
- * T – Type (What)
- * V- Volume (FIT)
- * P- Progression

Components of an exercise training session

Warm-up: at least 5–10 min of light-to-moderate intensity cardiorespiratory and muscular endurance activities

Conditioning: at least 20–60 min of aerobic, resistance, neuromotor, and/or sports activities (exercise bouts of 10 min are acceptable if the individual accumulates at least 20–60 min · d⁻¹ of daily aerobic exercise)

Cool-down: at least 5–10 min of light-to-moderate intensity cardiorespiratory and muscular endurance activities

Stretching: at least 10 min of stretching exercises performed after the warm-up or cool-down phase

Ex P_x Vigorous

Name:
Age

Type of activity	Aerobic (walking)	Strength	Flexibility
Number of days per week	3 days	2-3 days 48 hours apart	2-3 time per week to daily
Minutes per day	20-60 minutes	2-4 set of 8-10 repetitions with 2-3 rest intervals between the sets	Hold stretch for 10-30 secs per joint
Intensity	77-95% HR _{max}	7-10 RPE	Stretch to the point of feeling slight tightness or discomfort

Ex P_x

Name:

Age:

Exercise prescription

1. Walking, 30-60 minutes/day ,@ RPE 5-6/ 64-77% HR_{max}, 3 days/ week for X/7
2. Strength training, 2-4 set of 8-10 repetitions with 2-3 minutes rest intervals@ RPE 5-6, 2 days/ week, 48 hours apart for X/7
3. Flexibility 20 minutes/day, 2-4 days/week, stretch to the point of feeling a slight tightness or discomfort for X/7

Conclusion

- * Rehabilitation Models for Dementia are emerging but lots of gaps
- * Different populations so different delivery models at various time points
- * Ripe for “disruptive innovation”

