Dementia and Physical exercise

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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**

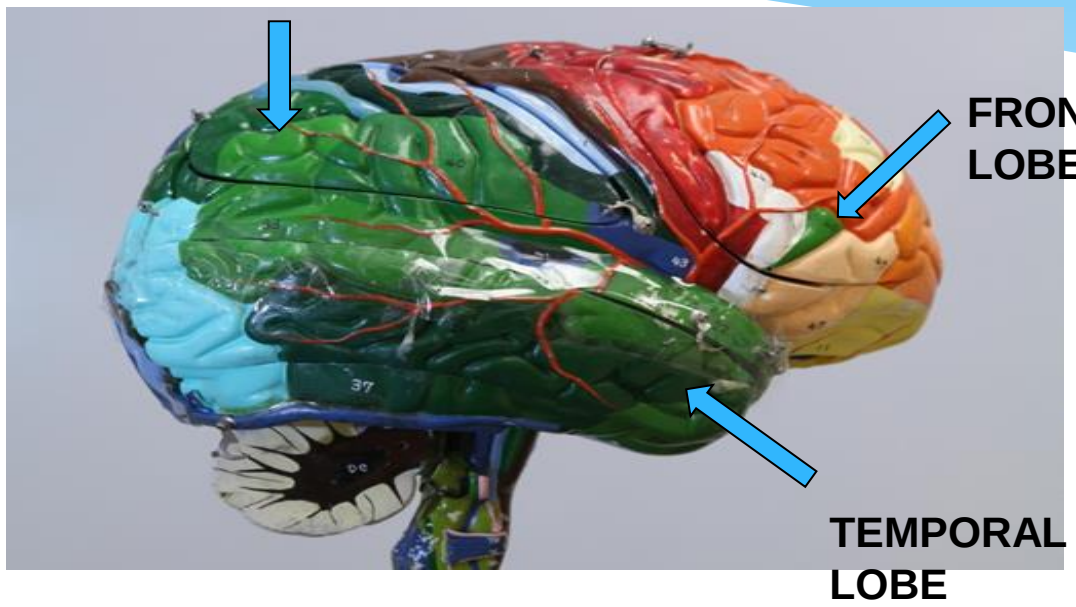
* **Alzheimer's disease is also the most *common* neurodegenerative disease (neurodegenerative diseases include Alzheimer's, Parkinson's and AmyotrophicLateral Sclerosis [ALS])**

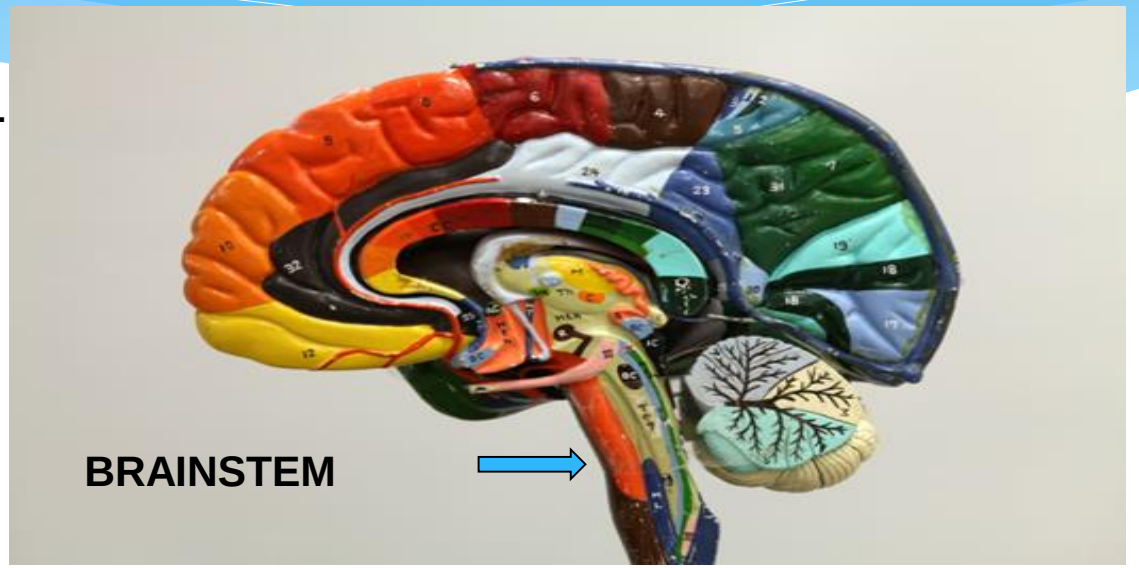
ALZHEIMER'S DISEASE

- **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

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





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***

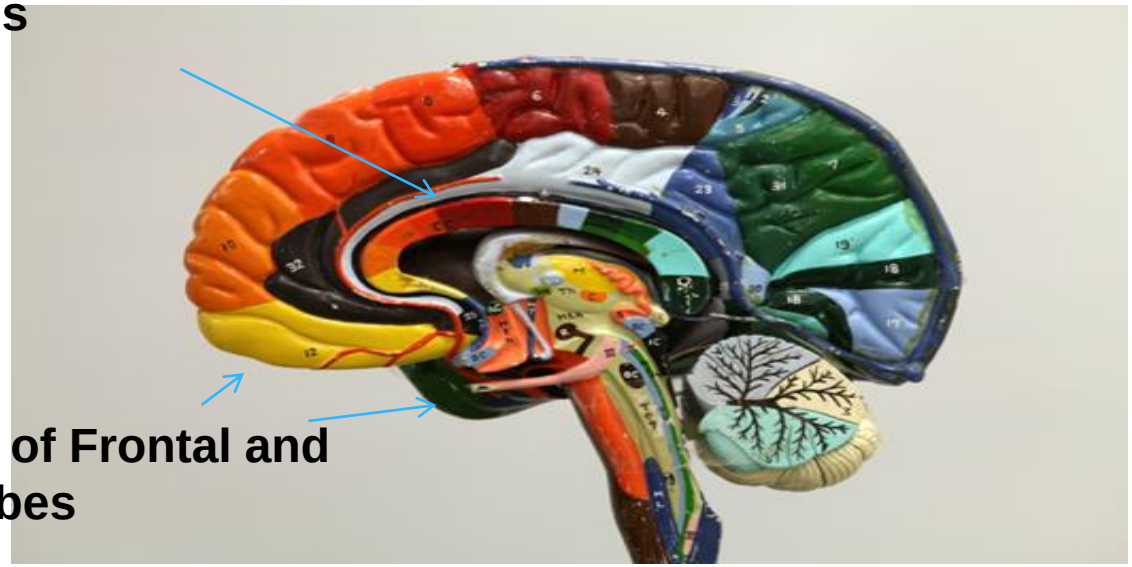
- **Locus coeruleus** (norepinephrine; attention, regulation of blood flow, sleep/wake cycles)
- **Raphe nuclei** (serotonin; mood regulation)
- **Nucleus basalis of Meynert** (acetylcholine; reward?)

***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



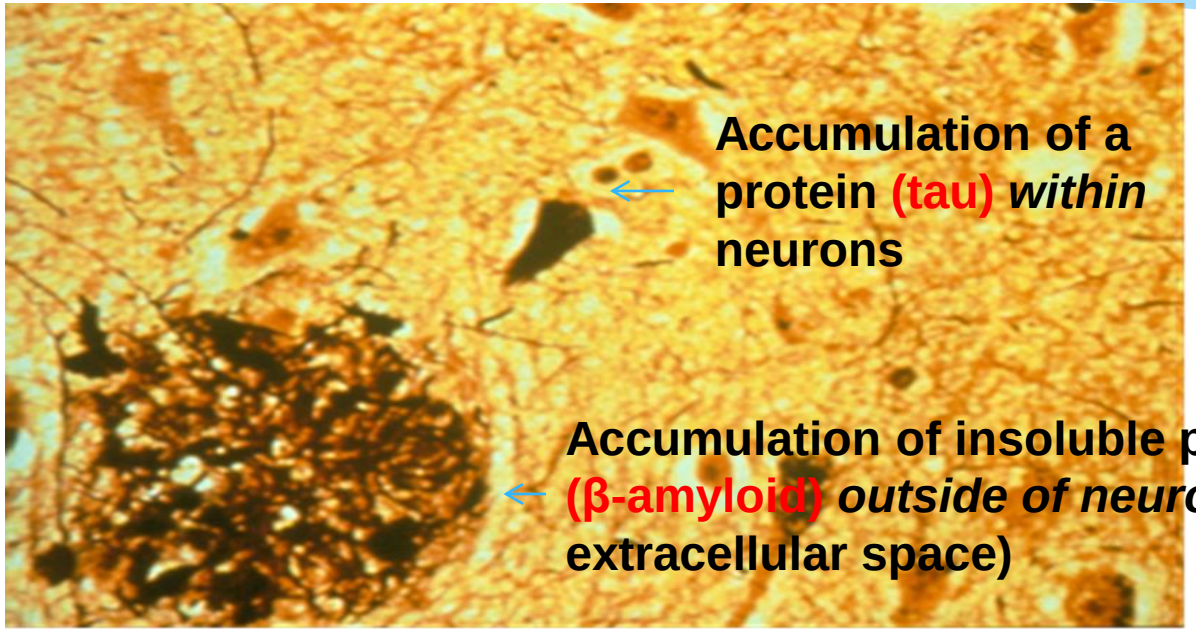
Medial areas of Frontal and Temporal Lobes

Medial brain

Alzheimer's Disease causes death of neurons

Alzheimer's disease **Normal (age-matched)**

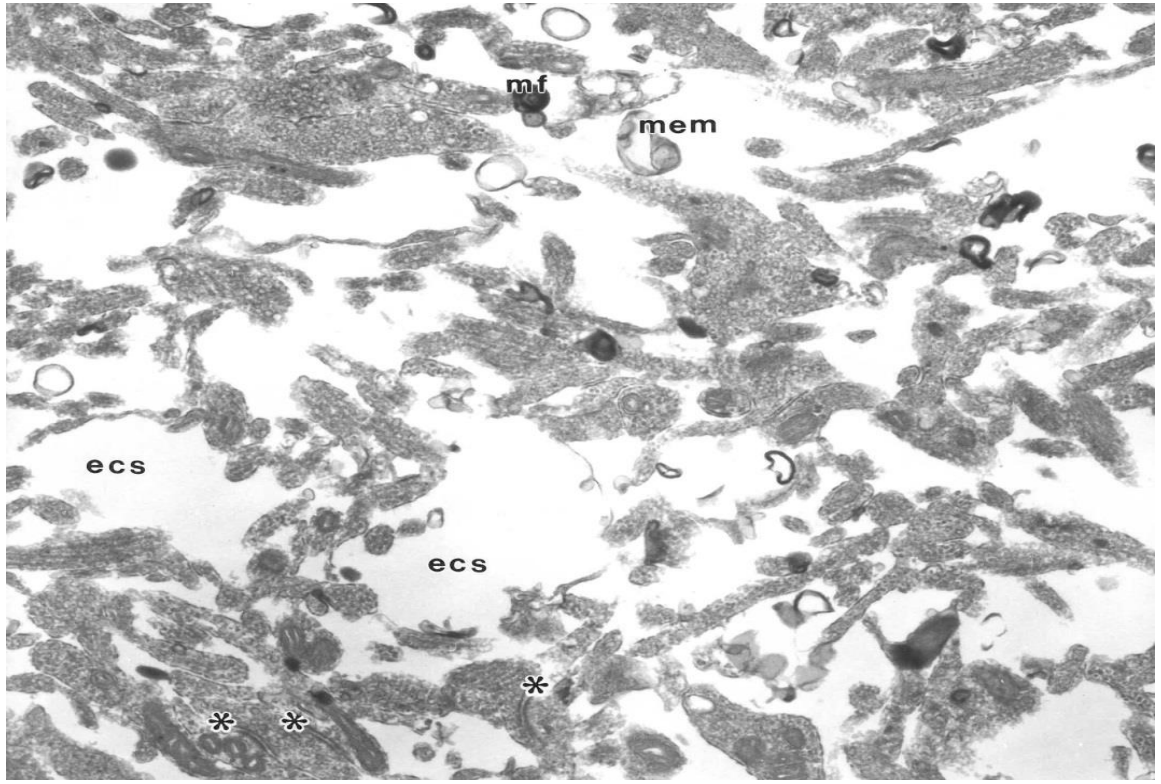
At Autopsy, Abnormal Cellular and Extracellular Accumulation of "Altered" Proteins (β-amyloid and tau) can be Identified within neurons and in the "extracellular" space



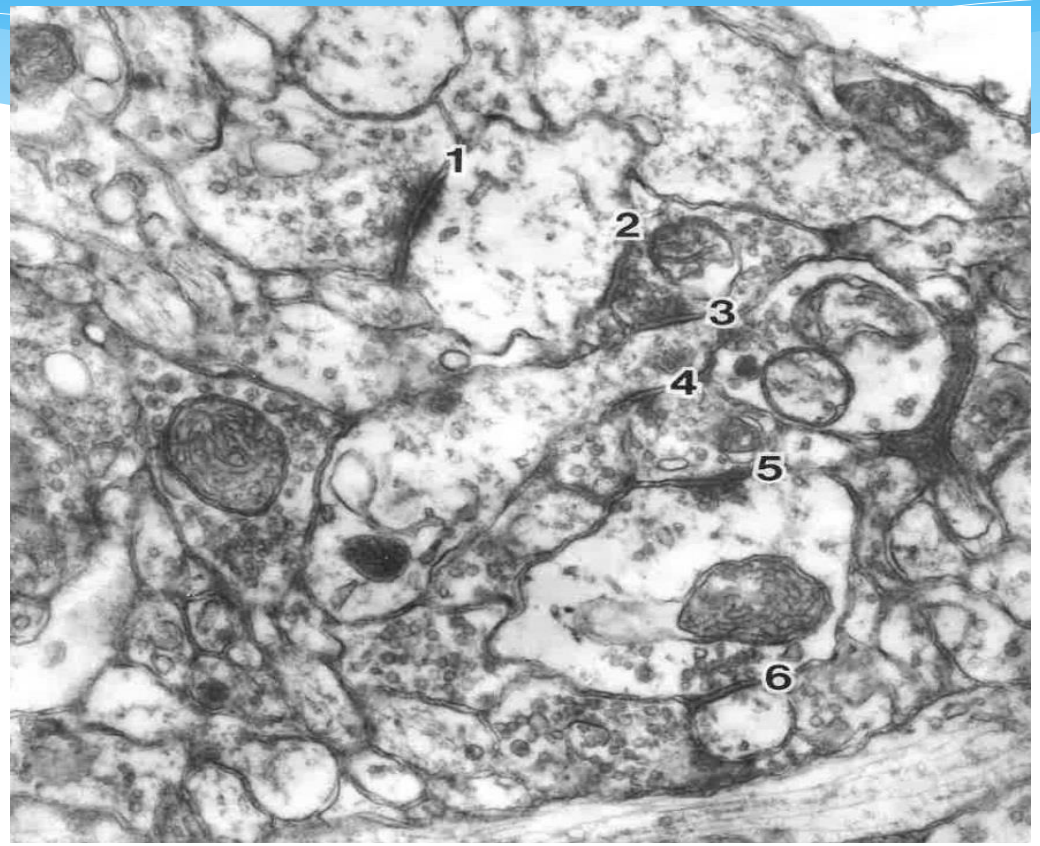
ALZHEIMER'S DISEASE IS A DISORDER OF *DYSREGULATION*

- ***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***

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

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**

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

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* Head injury

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- Chronic stress (leads to high blood cortisol)

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- 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

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* **Exercise**

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 (!)**

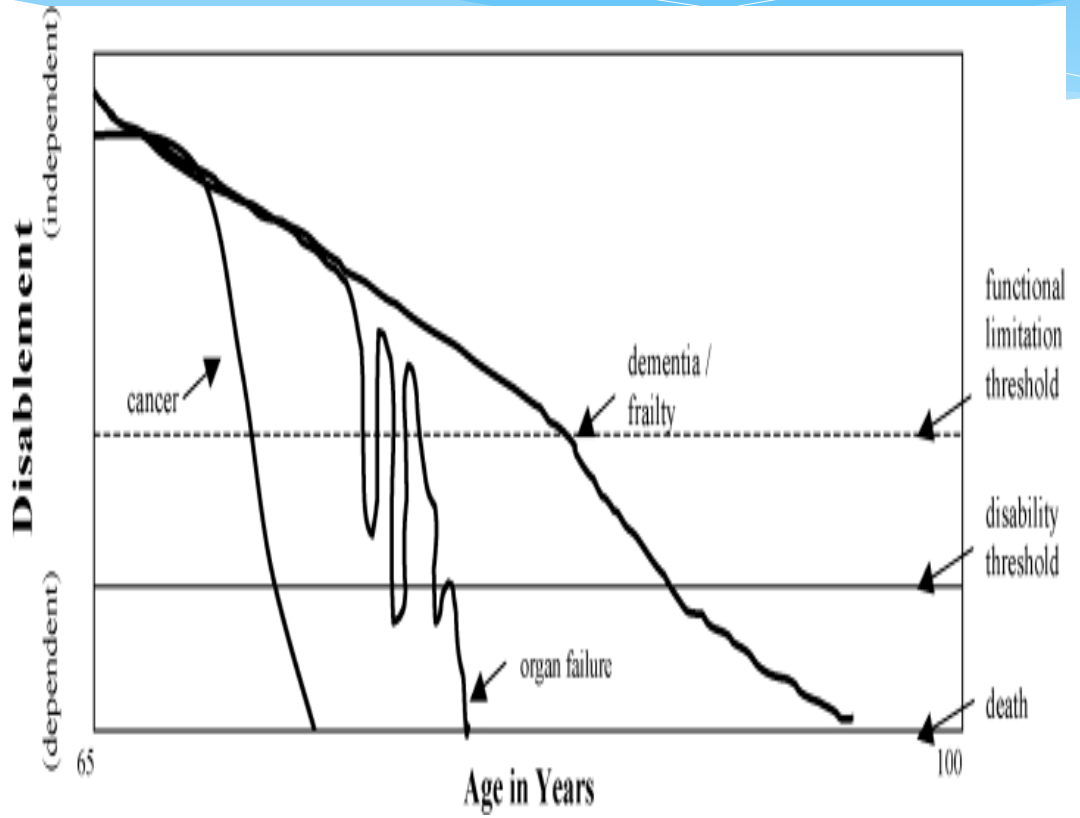
- ***Under your control***
  - **Keeping safe**
  - **Eating a healthy diet (stay close to the earth and sea; fruits, veggies, nuts, whole grains, fish high in omega 3 oils)**
  - **Maintaining a healthy weight**
  - **Restful sleep**
  - **Continuing mental challenge**
  - **Maintaining strong social & 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

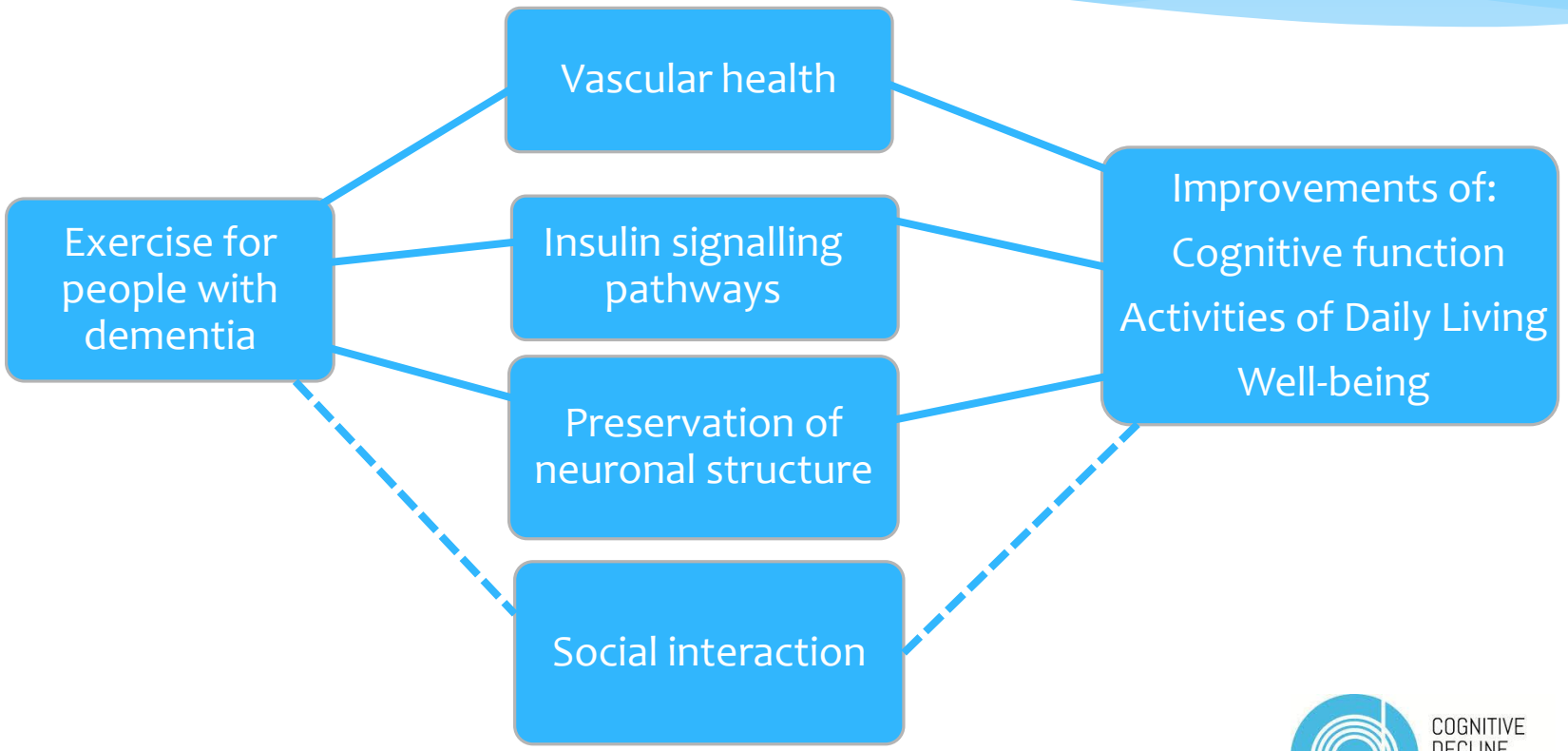
Exercise and Dementia

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



COGNITIVE DECLINE PARTNERSHIP CENTRE

Prevention of Dementia

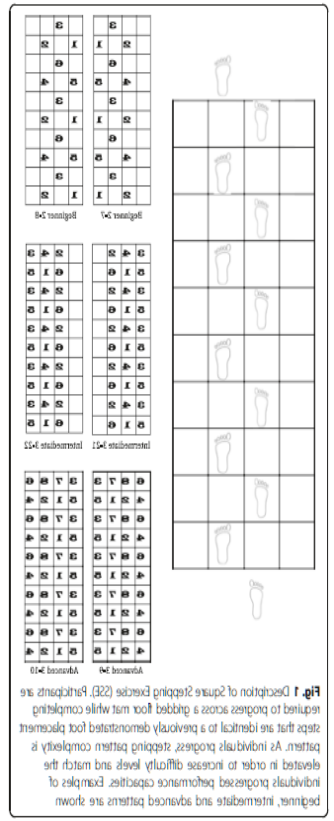
- Lots of observational evidence that ongoing physical activity from mid life reduces the risk of dementia
- In normal older adults cognition improves with exercise
- Some RCT evidence once you have Mild Cognitive impairment that the rate of cognitive loss slows but trials are inconsistent

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

Raji 2010; Watson 2010; Zuliani 2007

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)

Cassilhas 2007; Littbrand 2006; Venturelli 2011

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”