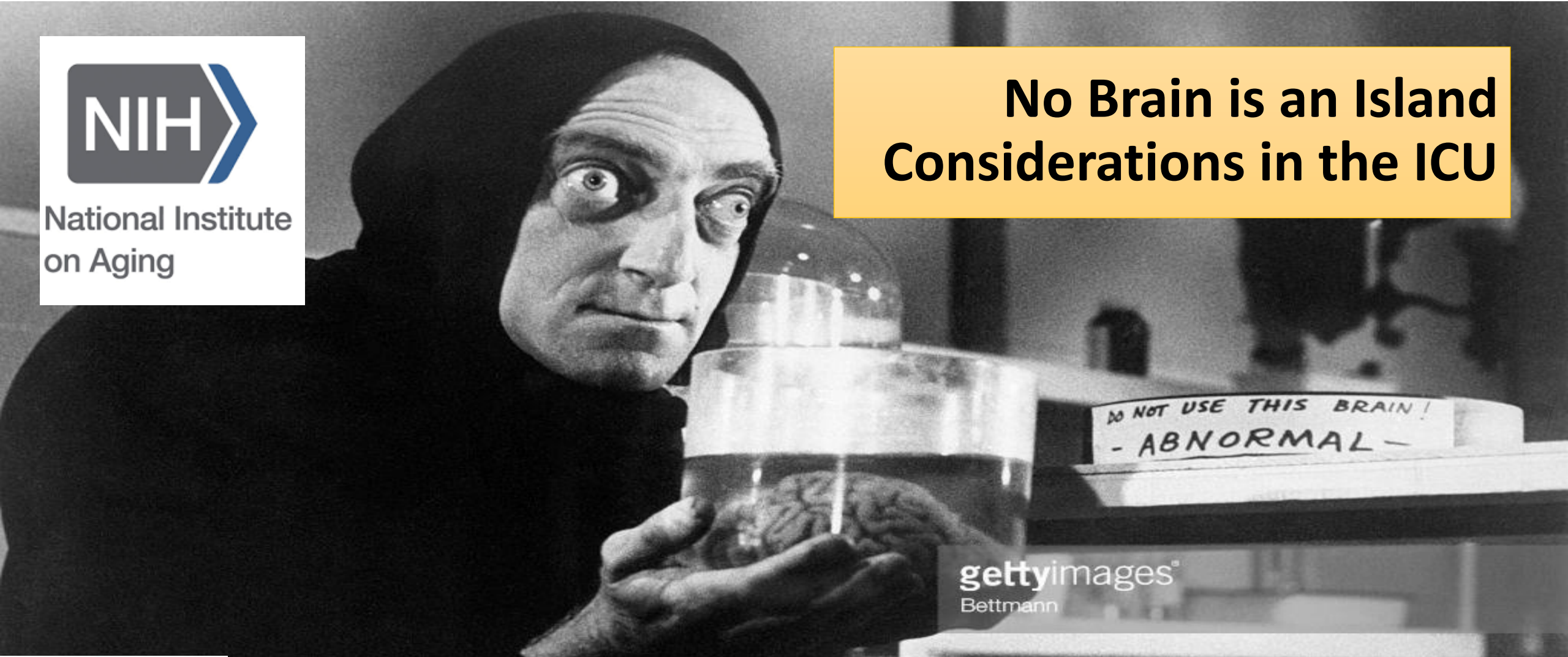




National Institute
on Aging

No Brain is an Island Considerations in the ICU



GEMSSTAR Meeting 2018

Michael Avidan, MBBCh, FCA(SA)
Dr. Seymour and Rose T Brown Professor of Anesthesiology

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on Aging**

Objectives of this Talk:

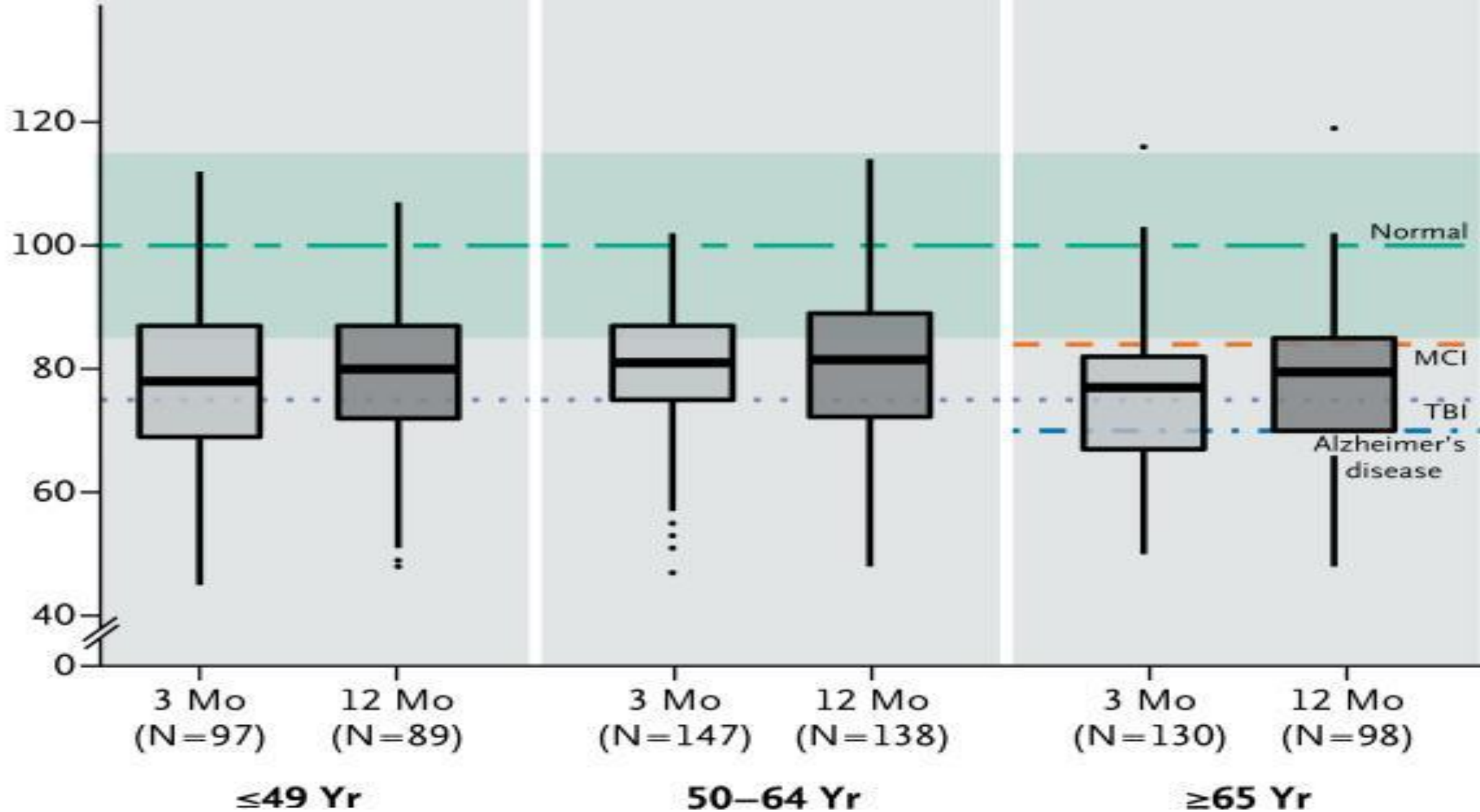
Considerations for research into ICU and Cognition

1. Choose projects that are important and about which you are passionate.
2. Make it as simple as possible, but not simpler.
3. Focus on potentially modifiable targets.
4. Consider where your work fits on the translational continuum.
5. Pick projects in areas where you have local expertise.
6. Try to construct a narrative arc.

1. An Important Public Health Challenge

Up to 9 out of 10 intensive care unit (ICU) survivors will suffer some degree of cognitive impairment at hospital discharge and approximately half will have decrements that persist for years.

RBANS Global Cognition Score



Which domains are impaired?

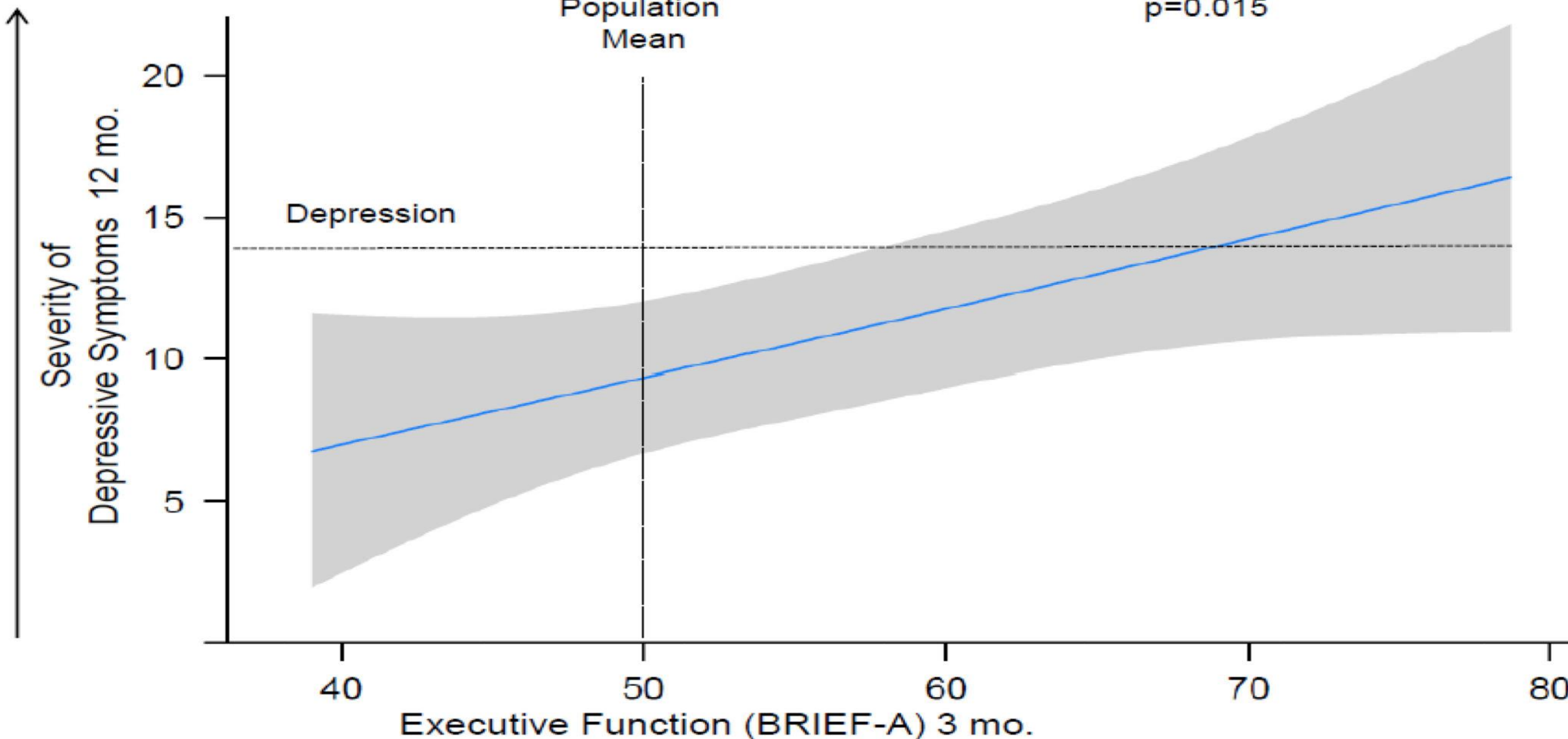
ICU-related neurocognitive impairments occurred in many cognitive domains and are particularly pronounced with regard to memory, executive functions, attentional functions, and processing speed.

Relationship to neuropsych disorders

- Depression
- PTSD
- Pain
- Anxiety
- Mental health related QOL

Worse

worse



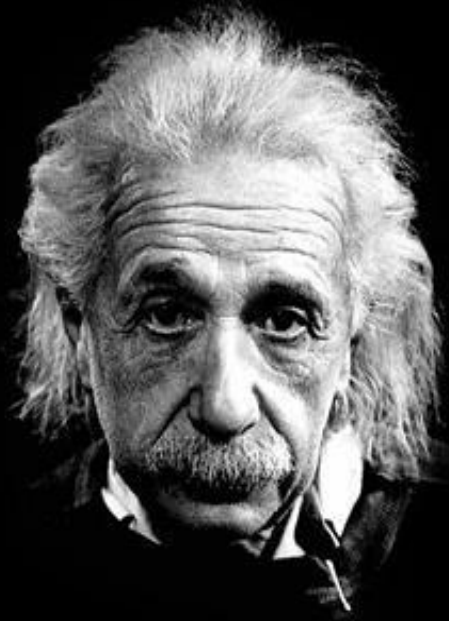
Population Mean

p=0.015

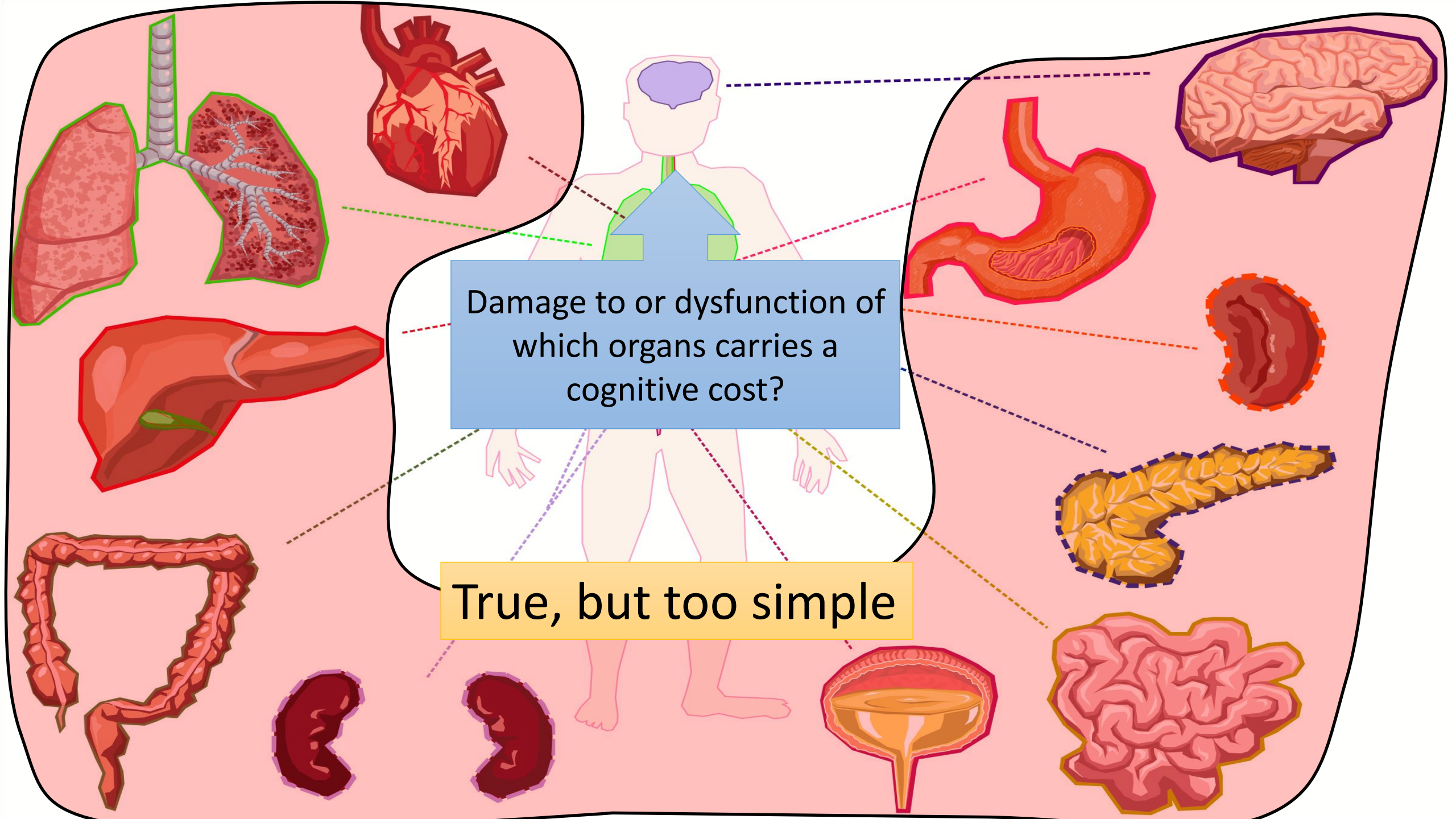
Depression

Executive Function (BRIEF-A) 3 mo.

worse

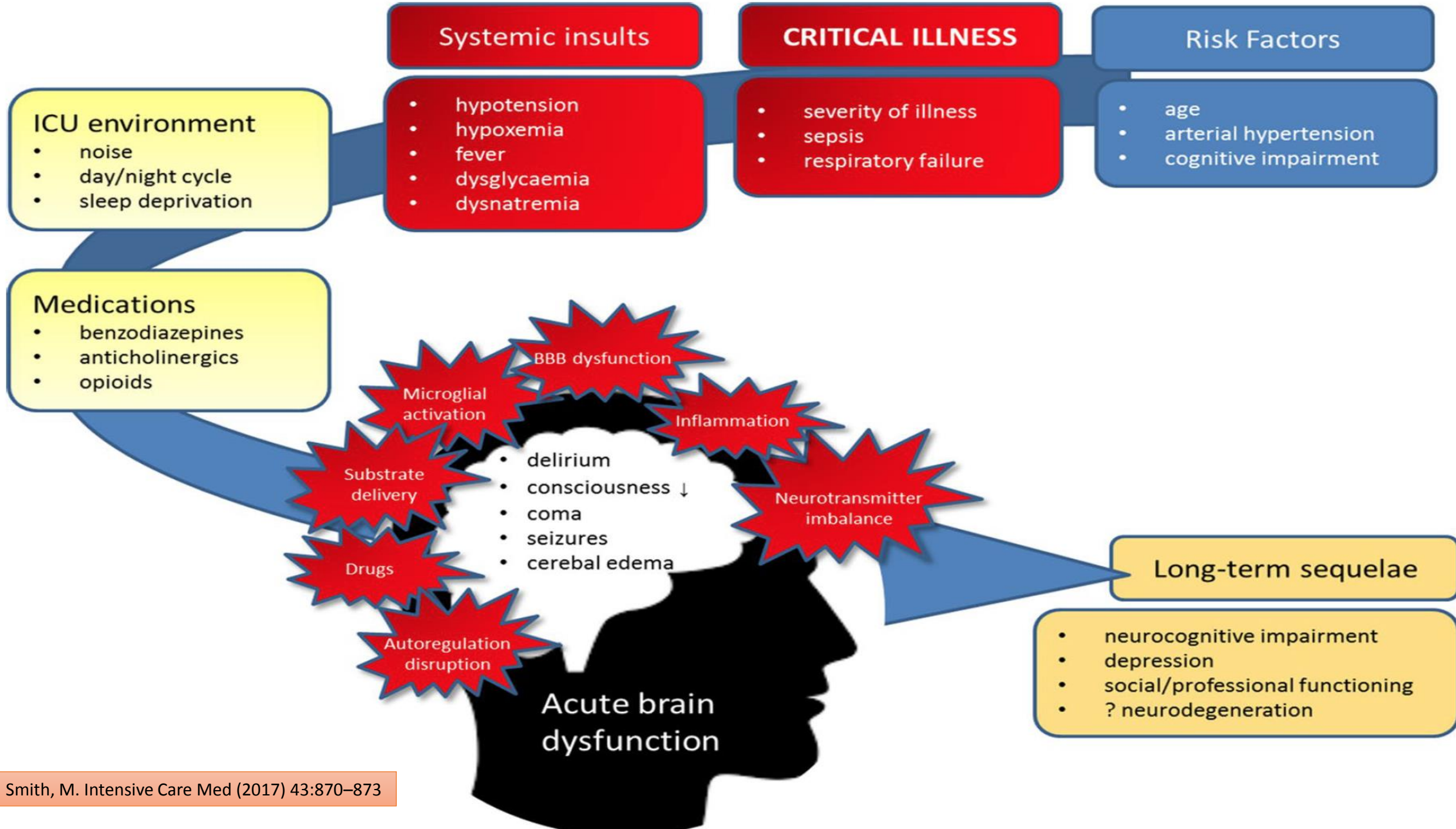


2. “Make things as simple as possible, but not simpler.”

An anatomical diagram of the human body with various organs highlighted in different colors. A central blue box contains the text "Damage to or dysfunction of which organs carries a cognitive cost?". Dotted lines connect this box to various organs: the brain (purple), heart (red), lungs (green), liver (red), stomach (orange), kidney (red), and large intestine (yellow). A yellow box at the bottom contains the text "True, but too simple".

Damage to or dysfunction of
which organs carries a
cognitive cost?

True, but too simple



Factors conspiring to damage the brain

Predisposing Factors

- Advanced age
- Multiple medical comorbidities
- Pre-existing cognitive impairments

Factors Associated with Critical Illness

- Hypoxemia
- Hypotension
- Sepsis
- Blood glucose dysregulation

Other ICU Factors

- Medications
- Mechanical ventilation
- Inflammatory mediators
- Metabolic disturbances
- Neurotransmitter imbalances
- Cholinergic deficiency

Mechanical Ventilation - Epidemiology

Experimental studies have served to explore the possible mechanisms or pathways involved in this lung to brain interaction.

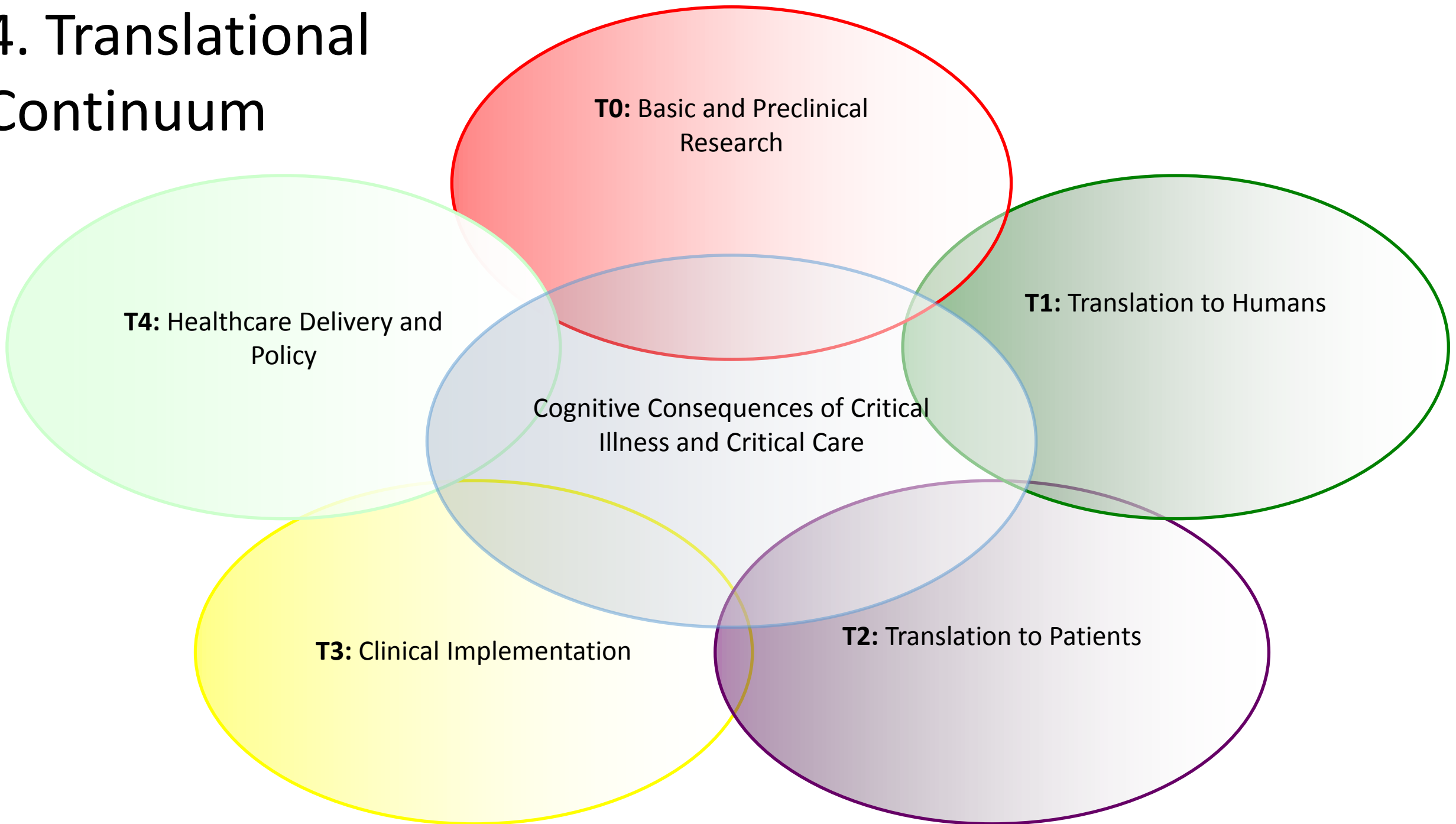
Mechanism

This communication can be mediated via a complex web of signaling events involving neural, inflammatory, immunologic and neuroendocrine pathways.

Prevention

MV can affect respiratory networks and the application of protective ventilation strategies is mandatory in order to prevent adverse effects. Therefore, strategies focused to minimize lung stretch may improve outcomes, avoiding failure of distal organ, including the brain.

4. Translational Continuum



5. Local Expertise

- Delirium
- Sleep medicine
- Genomics
- Dementia
- Imaging
- Neurophysiology
- Specific organ systems (e.g., heart, liver, kidney)
- Specific diseases (e.g. sepsis, ARDS)
- Microbiome

First Steps

Identifying objective risk factors and risk markers are first steps towards developing and effectively targeting interventions to prevent post-ICU cognitive impairment.

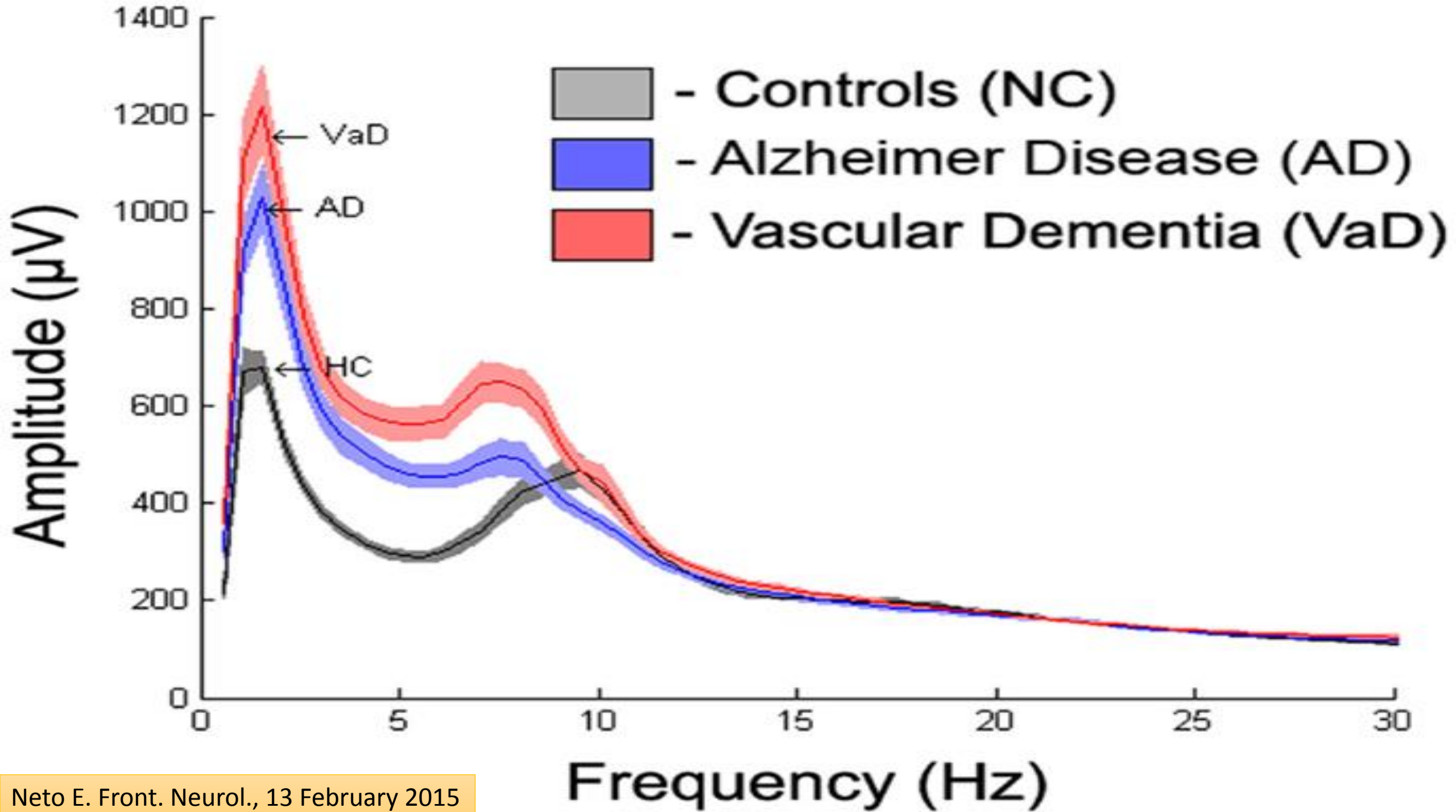
Sleep and circadian dysfunction

Potential neurobiological mechanisms including accumulation of beta amyloid pathology, abnormalities of tau, synaptic abnormalities, changes in hippocampal long-term potentiation, impaired hippocampal neurogenesis and gene expression changes.

A study demonstrating the prevalence of sleep abnormalities after critical illness and their longitudinal association with cognitive impairment would yield potential targets for therapy and novel endpoints for ICU-based studies.

Neurophysiology

Although it is an imperfect tool, EEG may be able to provide prognostic information. If quantitative EEG is linked with long-term cognitive outcomes, it may serve as a good intermediate endpoint in therapeutic trials assessing interventions to decrease the risk of post-ICU cognitive impairment.



Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour

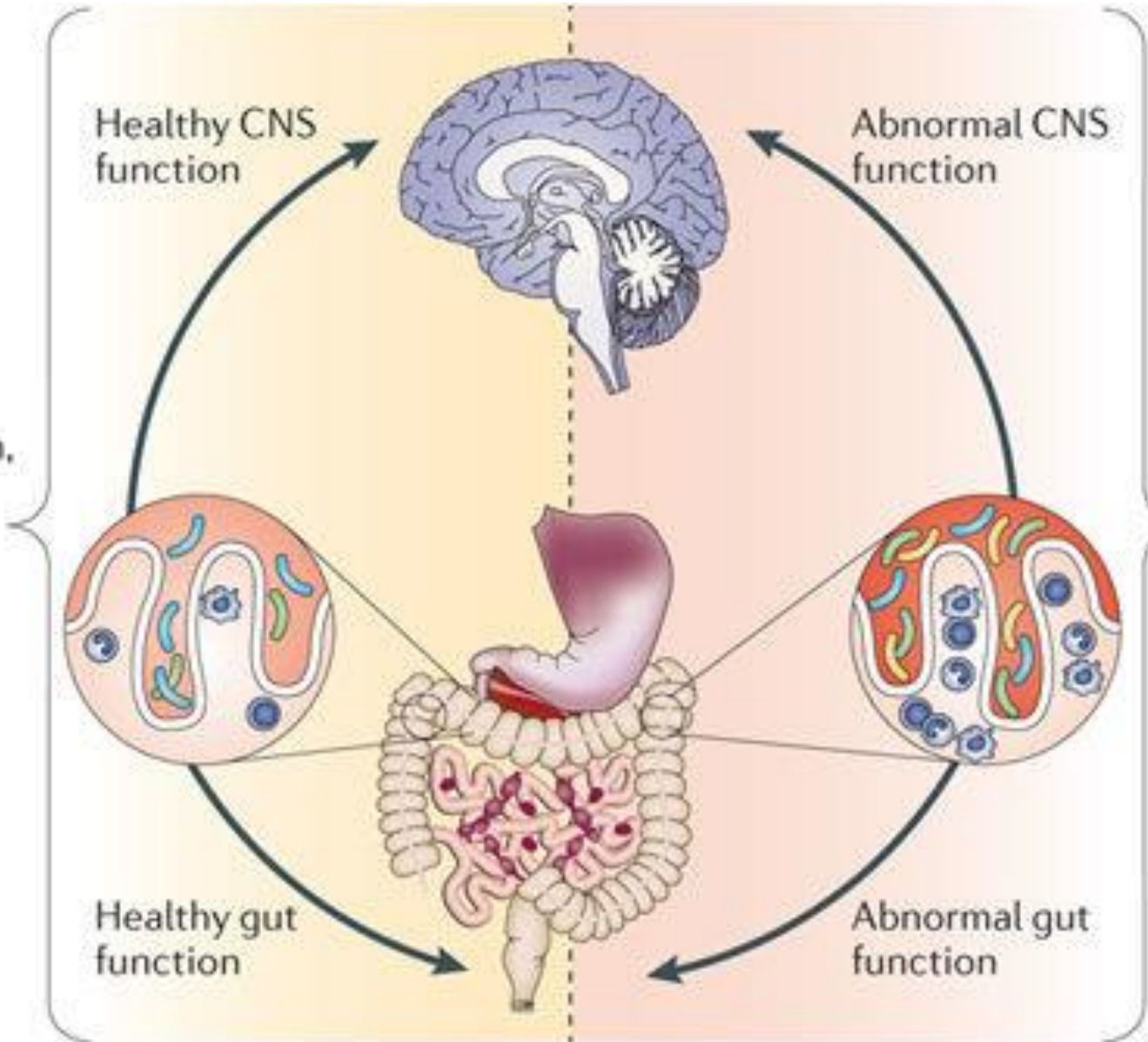
The (Other) Forgotten Organ

The gut microbiota

The human gastrointestinal tract is inhabited by 1×10^{13} to 1×10^{14} microorganisms — more than 10 times that of the number of human cells in our bodies and containing 150 times as many genes as our genome — and the gut microbiota is therefore often referred to as the forgotten organ.

Neural, Endocrine and Immune Pathways

- Healthy status**
- Normal behaviour, cognition, emotion, nociception
 - Healthy levels of inflammatory cells and/or mediators
 - Normal gut microbiota



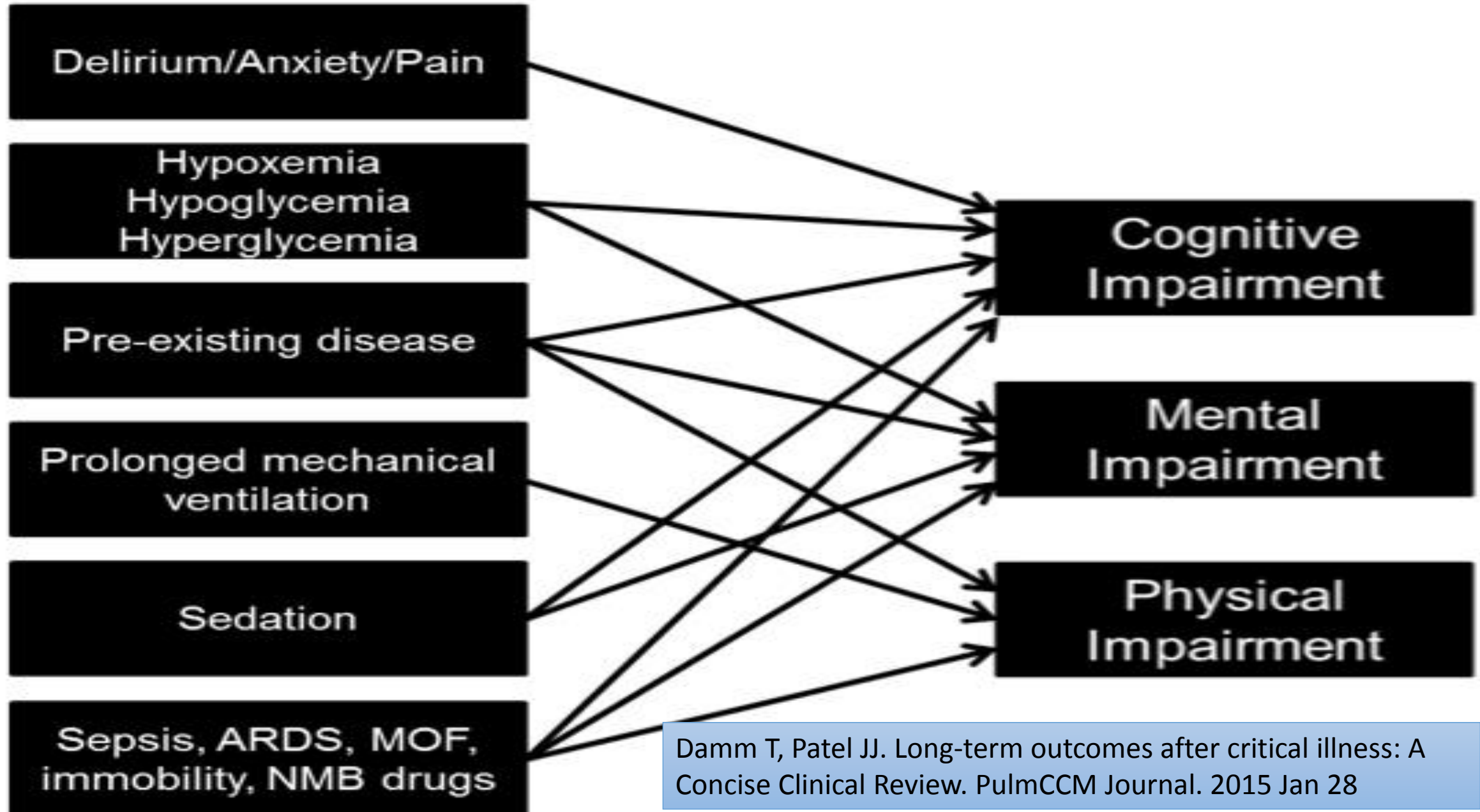
- Stress/disease**
- Alterations in behaviour, cognition, emotion, nociception
 - Altered levels of inflammatory cells and/or mediators
 - Intestinal dysbiosis

Cryan JF, Dinan TG. Nat Rev Neurosci. 2012 Oct;13(10):701-12.

6. The PICS Narrative

RISK FACTOR

PICS DOMAIN



Damm T, Patel JJ. Long-term outcomes after critical illness: A Concise Clinical Review. PulmCCM Journal. 2015 Jan 28



From: Intensive Care Unit Delirium: A Review of Diagnosis, Prevention, and Treatment

Anesthes. 2016;125(6):1229-1241. doi:10.1097/ALN.0000000000001378

Bundle to Prevent PICs



Assess, prevent & manage pain

- CPOT or BPS to assess pain, insure adequate pain control
- Use of regional anesthesia and nonopioid adjuncts
- Analgesia-based sedation techniques with fentanyl



Both SAT & SBT

- Daily linked SAT and SBT
- Multidisciplinary coordination of care
- Faster liberation from MV



Choice of sedation

- Targeted light sedation when sedation necessary
- Avoidance of benzodiazepines
- Dexmedetomidine if high delirium risk, cardiac surgery, MV weaning



Delirium monitoring & management

- Routine CAM-ICU or ICDSC assessments
- Nonpharmacologic intervention, including sleep hygiene
- Dexmedetomidine or antipsychotic if hyperactive symptoms



Early mobility & exercise

- Physical and occupational therapy assessment
- Coordinate activity with SAT or periods of no sedation
- Progress through range of motion, sitting, standing, walking, ADLs



Family engagement & empowerment

- Reorientation, provision of emotional and verbal support
- Cognitive stimulation, participation in mobilization
- Participation in multidisciplinary rounds

Mitigation

Long-term neurocognitive impairments experienced by critically ill survivors may be mitigated by early interventions, combining cognitive and physical therapies.

Psychological and neurocognitive management options available for critically ill patients

Preventative strategies

Adherence to PAD guidelines²⁶

Use of the 'ABCDE' bundle³⁶

Music therapy⁴⁶

Early psychological intervention⁴²

Neurorehabilitative strategies

Patient diaries⁴⁹

Follow-up clinics⁵⁶

Follow-up visit⁶¹

Focus/Support groups⁶²

Cognitive rehabilitation in combination with physical rehabilitation⁶⁵

PAD: Pain, Agitation and Delirium; ABCDE: awakening and breathing, choice of sedation with fewer adverse effects, daily delirium monitoring and early mobility exercise.

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No Brain is an Island

No brain is an island entire of itself;
every brain is a piece of the corpus, a part of the human;
if a clot be washed away to the lungs, your grip is the less, as well as if a
prominent artery were clogged, as well as any manner of thy
peripherals or of thine vitals were;
any organ's distress diminishes me, because I am involved from heart
to mind.
And therefore never send to know for whom the bell tolls; it tolls for
thee.

With apologies to John Donne