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# Reserve and Resilience

*an epidemiologic approach using longitudinal cognitive testing and brain autopsy data*

Data from the Honolulu-Asia Aging Study (HAAS, n=331) and the Nun Study (NS, n=288)

- Repeated testing with the Cognitive Assessment and Screening Instrument (CASI) or the CERAD battery.
- Neuropathology -- comprehensive brain autopsy, defining distributions and severities of dementia-associated lesions to define the *total neuropathology burden*:
  - Alzheimer lesions: neocortical neuritic and diffuse *amyloid plaques*, neocortical neurofibrillary *tangles*.
  - *Lewy bodies* (alpha synuclein) neocortex, brain stem, limbic.
  - vascular ischemic injury: *infarcts* – large, lacunar and micro.
  - hippocampal sclerosis, TDP-43 (*LATE*).
  - *brain weight*, generalized brain atrophy.

# *definitions applicable to epidemiologic analyses*

**Reserve** → structural and functional **resources existing prior to a pathologic assault or injury**, and that define a “starting point” for decline, erosion, or degeneration due to the pathology.

*Measurements of cognitive reserve are based on pre-morbid neuropsychologic testing or imputed cognitive competence attributable to primary intelligence, or to **learned or cultivated abilities** that provide more efficient, more redundant, or alternative (default) systems to support or augment accomplishment of cognitive tasks.*

*Measurements of brain reserve are based on pre-morbid brain structure or function, normal brain **anatomy, including gray and white volumes, bicameral functions, corpus colosum thickness, reaction time, etc.***

**Resilience** → cognitive resilience is recognizable only with demonstrable neurologic injury or assault; it becomes apparent when the individual’s **observed** cognitive performance is (or was) less distorted or impaired than **expected**, given the type and severity of the neuropathology.

*We view cognitive resilience as a dynamic phenomenon distinct from cognitive or brain reserves.*

# *Epidemiologic and neuropathologic data measuring resilience*

- **Concept:** resilience
- **Measure:** observed vs expected final cognitive score ratio
- **Operational definition:** A resilience index = observed final test score / expected final score, from a statistical model taking age at death, baseline test score (pre-morbid), interval last observed score to death, and the total neuropathologic burden based on 5 lesion types assessed at brain autopsy.

