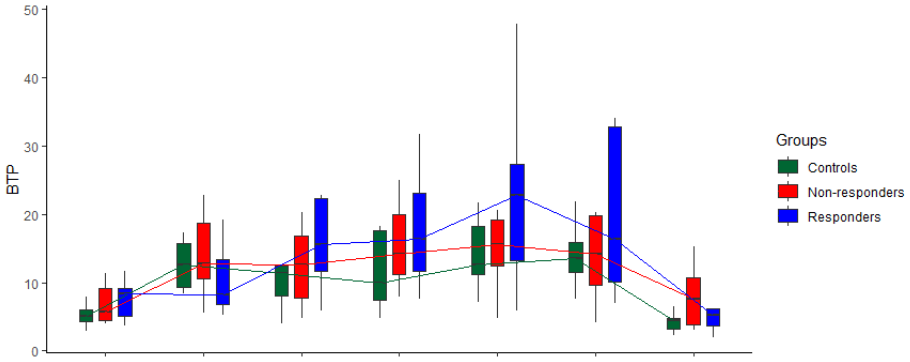
**Figure 1** – Changes Brain Tissue Pulsations as assessed with brain ultrasound during N2O exposure




# FC34: Cognitive reserve and depressive burden in older adults: variation according to reserve measurement

**Authors**: Federico Triolo (Aging Research Center, Karolinska Institute, Stockholm Sweden) and Serhiy Dekhtyar (Aging Research Center, Karolinska Institute, Stockholm Sweden).

**Objective:** Individual differences in the timing of dementia have been attributed to cognitive reserve (CR), thought to reflect lifelong engagement in stimulating experiences, which provide resilience against brain pathology. In older adults, dementia and depression are closely related, and some studies have linked CR with depression risk in old age. It is unclear if different ways of operationalizing CR exhibit similar association with old-age depression. We examined the association of two measures of CR with depressive burden in older adults: *activity-based CR*, capturing engagement in stimulating activities using proxy variables, and *residual-based* CR, indicating residual variance in cognition, not explained by the brain status.

**Methods:** We used data on 354 adults aged 60+ from the Swedish National Study on Aging and Care in Kungsholmen, followed for 15 years. Residual-based reserve was computed from a regression predicting episodic memory with a brain-integrity index incorporating six structural neuroimaging markers (white- matter hyperintensities volume, whole-brain gray matter volume, hippocampal volume, lateral ventricular volume, lacunes, and perivascular spaces), age, and sex. Activity-based reserve incorporated education, work complexity, social network, and leisure activities. Depressive burden was captured over the follow- up with the Montgomery-Åsberg Depression Rating Scale and time until clinically relevant level of symptoms (>6) was modelled using Cox proportional hazard models.

**Results:** Preliminary results indicate that, upon minimal adjustment (age, sex, brain integrity status), top tertiles (ref: bottom tertile) of both *activity-based* (HR: 0.77; 95% CI: 0.61-0.98) and *residual-based* CR (HR: 0.62; 95% CI: 0.44-0.98) were associated with a lower risk of depressive burden onset over 15 years. Upon further adjustment for anthropometrics, health behaviors, and chronic disease burden, the association of activity-based CR was



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attenuated, whereas residual-based CR preserved its effect on depressive burden (HR [fully adjusted model]: 0.59; 95% CI: 0.40-0.88). Next steps include evaluating the ability of reserve measures to attenuate the association of brain integrity with depressive burden using interaction analysis.

**Conclusion:** Preliminary findings suggest that CR may be linked with depression development in older adults, although the association may vary depending on measurement of reserve. Association of activity- based reserve may be attributed to somatic disease pathways.

## FC35: Depressive symptom transitions in older adults: effects of psychosocial, behavioral, and clinical factors

**Authors:** Federico Triolo (Aging Research Center, Karolinska Institute, Stockholm Sweden) and Serhiy Dekhtyar (Aging Research Center, Karolinska Institute, Stockholm Sweden).

**Objective:** Depression evolves dynamically in old age. Studies of natural history of major depression in older adults suggest that 19–34% recover, 27%–32% remain chronically ill, and approximately 40% experience a fluctuating course. Another way of approaching depression from a longitudinal point of view is by adopting a symptom-based approach, that in addition to the evolution of clinically manifested diagnostic entities, also focuses on transitions involving subclinical/subsyndromal states, although few studies have attempted it. We examined psychosocial, behavioral, and clinical determinants of transitions across states that include no depression, subsyndromal-, and clinical depression.

**Methods:** We used data on 3086 adults aged 60+ from the Swedish National Study on Aging and Care in Kungsholmen, followed for 15 years. Markov-state transition models were used to capture transition patterns, as well as their associated determinants. Death and dropout constituted absorbing states. Depression was diagnosed in accordance with DSM-5; SSD was based on having at least 2 symptoms in the absence of DSM diagnosis. Determinants of transition patterns included index of social connections and support (i.e., psychosocial determinants); smoking, alcohol consumption, and physical activity (behavioral determinants); somatic disease burden and history of depression (clinical determinants).

**Results:** At baseline, 10% of the study population exhibited clinically relevant levels of depressive symptoms. Over a 15-year period, a total of 11,489 transitions were observed. Preliminary results indicate that behavioral factors (primarily smoking) were mostly associated with transitions from no depression to clinical depression, as well as from clinical depression to death. Mostly the same pattern was seen for clinical determinants, although higher burden of chronic diseases and previous depression also increased the likelihood of transition from no depression to SSD. Notably, of high baseline values of social connection and support were found to: 1) lower the likelihood of transitioning from no depression to either SSD or clinical depression; 2) lower the likelihood of transitioning from SSD to clinical depression; and 3) increase the likelihood of transitioning from clinical depression to no depression.



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