



Tests of cognitive function: Criteria for validation and considerations for investigating the effects of foods and nutrients in ageing¹

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Background and Objectives:

There is increasing interest in the effects of particular foods and/or nutrients on age-associated cognitive decline. This requires tests that can be used in experimental trials which are valid, reliable and sensitive measures of cognitive function and ideally can also act as valid surrogates or (bio)markers of the neural processes underlying major domains of cognition. The ILSI Europe Nutrition & Mental Performance Task Force Expert Group (EG) aimed to evaluate tests specific to various cognitive domains and suitability of these for nutrition intervention studies, particularly in the elderly where cognitive abilities decline. The EG proposed guidance to select the most suitable tests for nutritional intervention studies using cognitive outcomes.

Methods:

- Tests in the domains of memory (verbal, visual, spatial, and articulated working memory), selective and sustained attention, executive function, information processing speed, and global cognitive function were reviewed;
- Tests were evaluated for applicability of the validation criteria developed by ILSI Europe (see column headers of Table 1);²
- Examples of findings with cognitive tests used in intervention trials with specific nutrients is documented.

Results:

Table 1. Application of essential criteria for validation of cognitive function tests

Cognitive domain	Everyday functional or behavioral relevance	Neural mechanisms	Appropriate target populations	Established testing paradigms	Utility, validity, and reliability	Established sensitivity to nutraceuticals	
						Acute or subchronic effects	Long-term studies or changes in disease state
Memory							
Verbal, visual, spatial	Learning, retention, recall, spatial information, pairing of object/verbal with spatial information, mapping Short or long term	Hippocampal, medial temporal lobes, dentate gyrus, amygdala	Healthy individuals of all ages, individuals with MCI or mild-moderate Alzheimer's disease, and other severe forms of memory impairment	Word list learning, immediate and delayed verbal recall, verbal and object recognition, paragraph recall	Widely established to be practical and reliable, excellent face, criterion, and construct validation	Enhancements with carbohydrates, glucose, protein, breakfast, low GI versus high GI breakfast, soy isoflavones,	3 months: berry polyphenols in MCI, 6 months: high dairy diet in habitual low dairy consumers; DHA
Attention (sustained, selective)	Sustained performance on attention-requiring tasks over an extended period of time in a low-arousal context, selective attention for some aspects of information while ignoring others	Sensory systems, superior colliculus and thalamus, frontal eye fields, lateral intraparietal areas, prefrontal cortex, reward and motor systems	Healthy children and adults, ADHD	Single letters, digits, or shapes presented serially where predefined stimuli must be responded to or ignored; also simulated driving tests, simulated shift work	Sustained attention overlaps with "vigilance," and arousal; selective attention overlaps with "divided attention"; other related concepts are tonic and phasic alertness	Consistent improvements following caffeine, inconsistent results with carbohydrates; children and adults with ADHD perform worse on attention tests	Not commonly used in long-term studies
Executive function							
Inhibition, planning, judgement, task switching, verbal fluency	Trip planning, handling finances, fixing things, using equipment, following recipes, making judgements, multi-tasking, using strategies	Frontal lobes and neural pathways connecting memory centers, cortex and subcortical connectivity, dorso-lateral prefrontal cortex	Healthy young adults, older women and men, cognitively impaired elderly	Executive function tests cover a broad range of abilities, some speed related including interference, task switching, digit symbol matching, tracking tasks requiring working memory, problem solving and mental organisational tasks	Can include or overlap with working memory and information processing abilities. As these higher order executive functions are complex not all executive tests are assessing the same aspect of executive function, however many do have good correlations	N3-fatty acids: improvement for cognitively impaired elderly; flavonoids: improvement in older men and women	2yrs: B vitamins benefit elderly with MCI
Information processing							
Simple reaction times, choice reaction time, tracking, neglect	Response times, comparisons, seeing differences, picking up detail, keeping track, left right response accuracy	Ascending reticular formation projections to the cortex, posterior lateral prefrontal cortex, superior medial frontal cortex	Healthy individuals of all ages; participants with ADHD, stroke, Parkinson's disease, MCI, mild or moderate Alzheimer's disease, and other dementias	Simple and choice reaction time paradigms, tracking tasks, tasks requiring stimulus discrimination and processing	Tests widely established for utility, practicality and reliability; extensive validation	Breakfast consumption: low GI breakfast cereals, energy drinks, drinks containing fat and glucose, caffeine,	3yrs: healthy elderly with high homocysteine levels, folic acid supplementation gave significant benefit
Global cognition							
Not domain specific	General intelligence-crystallized and fluid, overall mental functioning	Total brain volume	Older adults, MCI, Mild or moderate Alzheimer's disease and other dementias Diabetics	Multi-domain tests, either brief screening tests or in-depth batteries	Tests widely established for utility, practicality and reliability; extensive validation for targeted age groups and conditions	Cognitively healthy young and older adults have not shown improvement	DHA-phospholipids improved cognition in MCI

Abbreviations: MCI, mild cognitive impairment; ADHD, attention-deficit hyperactivity disorder; GI, glycemic index

Conclusions:

When selecting tests of cognitive function for nutrition intervention studies, the following questions should be asked:

- ❖ Which cognitive domain(s) is the nutrition intervention expected to affect?
- ❖ Is it a well standardized cognitive test?
- ❖ Is its sensitivity to the nutrient known, or its ability to discriminate between the groups under test?
- ❖ Are the underlying neural correlates of the cognitive domain understood and how does the biological mechanism of action of the nutrient on cognition relate to these?
- ❖ Which everyday functional activities does the nutrient enhance or deplete?

Overall, the field of cognitive function assessment is in need of further alignment of measures in each domain to enable valid comparisons of study outcomes, particularly for nutrition intervention studies.

References:

1. de Jager et al. Cognitive function: Criteria for validation and selection of cognitive tests for investigating the effects of foods and nutrients. *Nutrition Reviews*. Accepted.
2. de Vries et al. Markers for nutrition studies: review of criteria for the evaluation of markers. *European Journal of Nutrition*. Accepted.