

Energy Availability, Metabolic Flexibility, and Cognitive Aging: Extending the EPK Framework Toward Neuroenergetic Health

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Abstract

This paper evaluates an EPK hypothesis linking dietary energy, activity, sleep and stress with cognitive function across ageing. It distinguishes whole-body energy expenditure from cerebral fuel utilisation and short-term test performance from dementia prevention. Human null findings and alternative brain fuels are retained alongside mitochondrial and stress mechanisms. Animal mood, cellular senescence and sleep-pressure experiments provide research leads but do not establish dietary treatment for neurodegenerative disease. A longitudinal design with direct cognitive outcomes is proposed.

Scope and evidence selection

This is a targeted narrative synthesis and hypothesis paper, updated through 2 October 2026. Sources were selected from the existing EPK evidence library, primary publications and the recent companion reviews. Selection was question-led and not systematic; no pooled effect, formal risk-of-bias score or new participant dataset is reported. Bibliographic records and available abstracts/full texts were used. Abstract-only access limits appraisal of allocation, missing data, confounding and adverse events. Supporting, contrary and null findings are retained.

1. From whole-body intake to brain function

EPK is defined as mean dietary energy intake in kcal/day divided by body mass in kg. It is an intake-to-total-mass ratio, not a direct measure of energy balance, ATP production or nutritional sufficiency. Sports energy availability instead subtracts exercise expenditure from intake and divides by fat-free mass. Those quantities must be recorded separately; sports thresholds cannot be transferred numerically to EPK. [1]

Cerebral energy metabolism is central to neural function, but dietary carbohydrate, circulating glucose and regional brain glucose utilisation are different quantities. The brain can use substrates other than glucose under relevant conditions; a review of brain energy rescue discusses several candidate approaches, not a single dietary solution. [2]

Human lactate research demonstrates another usable cerebral substrate. Therefore, an EPK account should not equate every reduction in glucose oxidation with a complete loss of neuronal energy supply. Nor does eating more glucose establish increased uptake in an affected brain region. [3]

2. Direct human evidence and its limits

In a short crossover investigation in women, diet-induced low availability did not alter the measured cognitive outcomes, while exercise-induced low availability affected one outcome. This mixed result constrains the prediction that low intake broadly impairs cognition in all settings. [4]

Acute mental-work studies examine eating behaviour and expenditure under specific tasks. They do not show that subjective mental effort produces large calorie requirements or that increased intake improves subsequent cognitive performance. [5]

Age-associated differences in body composition and activity complicate associations between intake, metabolism and cognition. Whole-life expenditure data require adjustment for body size and composition; cross-sectional centenarian observations cannot establish a protective RMR target. [6] [7]

3. Stress and mitochondrial context

Sapolsky's account of glucocorticoid actions emphasises timing and context. This provides a basis for measuring stress exposure, not for asserting that every rise in cortisol damages the brain. [8]

Picard et al. associated blood-cell mitochondrial features with mood and caregiving stress, while experimental mitochondrial perturbations changed stress responses in mice. Neither study establishes an EPK intervention effect or measures a person's brain energy availability from their diet. [9] [10]

Cellular allostatic-load and mitochondrial-disease research show that higher expenditure can coexist with dysfunction. An intervention should therefore not target a higher metabolic rate as proof of healthier cognition. [11] [12]

4. Sleep, mood and cellular ageing

Fruit-fly work on mitochondrial sleep pressure and experimental work on fatty-acid oxidation in senescence identify separate mechanisms. They do not demonstrate that low EPK causes insomnia, that fibroblast senescence describes mature neurons, or that a high-carbohydrate diet prevents dementia. [13] [14]

A high-fat-diet mouse experiment implicates arachidonic-acid-related inflammatory signalling in depressive-like behaviour. Behavioural tests in male mice should not be translated into a human diagnosis or a recommendation to use aspirin. [15]

The small RiaGev trial studied a combination of nicotinamide and D-ribose and NAD-related measures. It does not isolate niacinamide or demonstrate prevention of cognitive decline. Biomarker changes require a separate link to meaningful function. [16]

The mitochondrial quantum preprint remains a preliminary mechanistic lead. It supplies no EPK clinical validation, and the cognitive proposal here does not depend on a quantum mechanism. [17]

5. Dietary fat and cautious translation

Experimental lipid-membrane findings depend on molecular species and model conditions. The presence of oxidisable lipids is not itself evidence that dietary PUFA causes dementia. Cell experiments should inform precise hypotheses, not an indiscriminate dietary prohibition. [18]

An EPK cognitive study should record fat quality, carbohydrate quality, total intake and medication, but avoid turning exploratory associations into treatment advice. A favourable mood change and a durable

cognitive change are separate outcomes, and neither establishes prevention of neurodegenerative disease.

6. A longitudinal cognitive evaluation

Choose one validated primary cognitive endpoint, allow for practice effects, and follow participants long enough to assess durable change. Record baseline cognition, education, vascular risk, mood, sleep, medication, physical activity, food access and body composition. Early disease can reduce intake, creating reverse causation.

Because the ratio is determined entirely by intake and mass, it cannot contain information absent from those inputs. Its usefulness is a question of practical summarisation and predictive performance. Compare a prespecified EPK model with flexible models of intake, mass, fat-free mass and activity, including nonlinear terms where justified. Use the same held-out validation procedure, report calibration and uncertainty, and prefer the simpler model if performance is similar. A favourable comparison with a deliberately weak linear model would not establish a new biological quantity.

Repeated observations should establish temporal ordering. Whole-body calorimetry cannot substitute for cerebral imaging or neuronal measurements; a brain-specific substudy would need its own protocol and interpretation. Do not infer mediation because intake, a peripheral biomarker and cognition correlate at one visit.

The framework would be weakened if any association disappeared after appropriate adjustment or if an intervention changed intake without improving the prespecified outcome. A short feasibility trial can establish measurement acceptability; it cannot demonstrate dementia prevention.

Conclusion

EPK offers a way to organise questions about fuelling, stress, sleep and cognition. Current evidence supports measuring these domains separately and retaining alternative mechanisms. Claims about cognitive ageing require direct longitudinal or interventional evidence.

Version and disclosure

Version 1.2 corrects unsupported citation groupings, integrates direct human null findings and stress evidence, separates mood from cognition, and limits mechanistic and supplement extrapolation. This version supersedes v1.1.1 for the current text; the earlier PDF and DOI remain an archive of that release. Reference numbering has been rebuilt for this version and must not be transferred from earlier editions.

The author develops EPK and has an intellectual and potential commercial interest in its evaluation. AI-assisted editorial drafting and source checking were used. This independent working paper has not undergone external peer review. No new human intervention or participant analysis is reported. Copyright 2026 Billy Craig. Author-owned text is licensed CC BY-ND 4.0; third-party material retains its own rights.

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Version history

v1.2 - 2 October 2026: scientific and editorial revision, refreshed reference mapping and integrated recent evidence. Unverified MSc quantitative claims are excluded from the evidential basis.

v1.1.1 - 11 September 2026: earlier licensing release. Archived DOI: [10.5281/zenodo.22710073](https://doi.org/10.5281/zenodo.22710073). Earlier versions remain available through Zenodo.

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