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GOED CLINICAL STUDY DATABASE

Examining the Science on Brain Health

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Defining Brain Health

The human brain is a powerful and complex body system, and there are multiple physiological features that contribute to its healthy operation and functioning. There are also hundreds of brain health effects and conditions, and these include both mental health and cognitive health. Brain development begins in utero, and the brain undergoes enormous changes during infancy and early childhood. Furthermore, maintaining and preserving cognitive health in older adulthood is also important for maintenance of quality of life. Apart from healthy structure and function of the brain, one in every eight people globally live with a mental disorder (WHO 2022) and important scientific research needs to be focused here as well.

In relation to brain health, DHA plays an important structural role in the brain, and EPA plays an important role in other metabolic processes including inflammation. Research to date suggests that increasing dietary intake of EPA and DHA through foods and/or supplements may contribute to improvements in brain health. The objective of this report is to provide an overview of the number of EPA and DHA omega-3 studies for specific brain health outcomes of potential interest and provide commentary on the current state of the science, notable research gaps and ideas for future directions.

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Brain Health: Quantitative Overview

This report provides a quantitative breakdown and commentary on brain health outcomes. However, it is important to note that a number of these brain health conditions can occur as comorbidities, which means that there is more than one health condition manifesting itself at the same time. Comorbid conditions can be difficult to diagnose and treat and can interfere with the interpretation of research results.

Results from the GOED Clinical Study Database

	Abstract Search	Advanced Search
Cognitive Health	377	62
Stress and/or Anxiety	407	123
Mood	501	160
Depression	343	180
Alzheimer's Disease and/or Dementia	155	115
Memory	131	73
Attention Deficit Hyperactivity Disorder (ADHD)	126	44
Traumatic Brain Injury	19	59

Table 1: Abstract and Advanced Search Quantitative Summary.
Data for the Abstract search includes the total of all study types. Data for the Advanced search is coming from Interventional studies, and both the Results (outcomes measured in a study) and the Participant Characteristics (measurements or descriptors of the participants). Abstracts are 93% complete to present, and Advanced search is 91% completed to 2021. Data collected May 18, 2023.

Brain Health: Cognitive Health

	Cognitive Health
Abstract Search: Total Studies (Interventional Studies)	377 (213)
Advanced Search: Results (Participant Characteristics)	32 (62)

Table 2: Number of Studies within the Abstract and Advanced Searches. Data collected May 18, 2023.

Commentary:

- There are multiple assessments and tools to evaluate cognitive health. The use of these various methods contributes to high heterogeneity between studies, making comparing results across studies especially challenging. This is one reason why it is difficult to report a succinct story about the effects of EPA+DHA on cognitive health throughout the lifespan.
- If investigating cognition, consider choosing a specific age group, severity or type of cognitive effect, duration of disease, duration of supplementation, reporting baseline EPA+DHA, dosage of EPA+DHA, and/or whether EPA+DHA are used independently or as an adjunctive therapy.

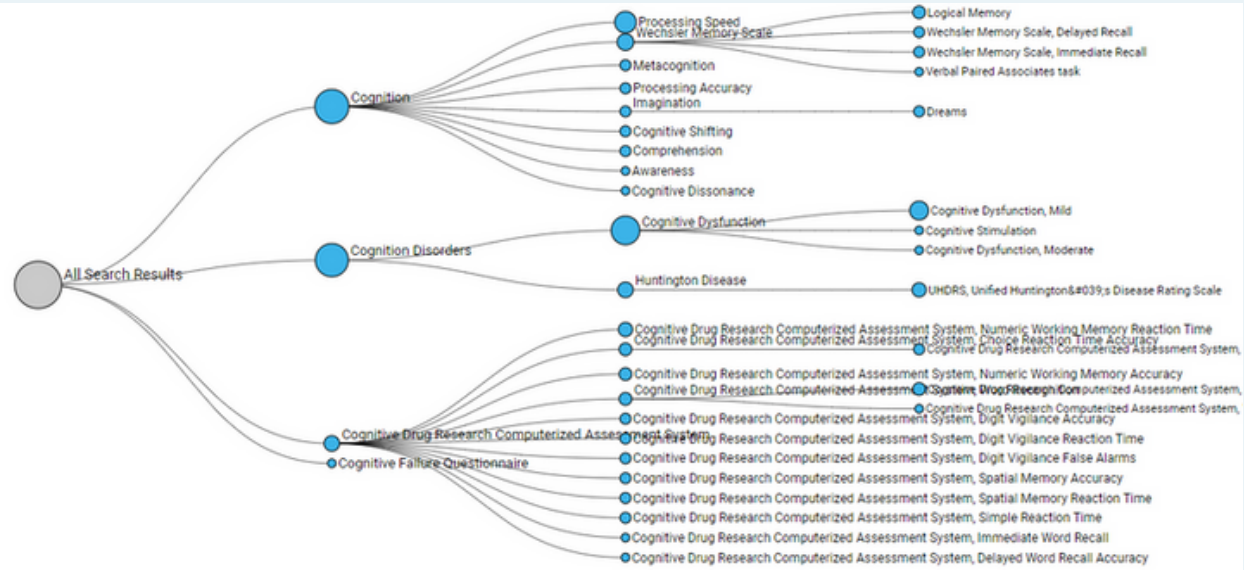

Figure 1: Advanced search results and participant characteristics for cognition and associated terms.

Brain Health: Stress and/or Anxiety

	Stress	Anxiety
Abstract Search: Total Studies (Interventional Studies)	356 (281)	67 (44)
Advanced Search: Results (Participant Characteristics)	52 (49)	41 (81)

Table 3: Number of Studies within the Abstract and Advanced Searches. Data collected May 18, 2023.

Commentary:

- Inconclusive evidence exists to date on the effect of EPA+DHA on stress and anxiety. Some studies reported that people with specific clinical diagnoses of anxiety had significant benefits with higher dosages (>2,000mg/day EPA+DHA), compared to people taking lower doses, and compared to people without a clinical diagnosis of anxiety.
- If investigating stress and anxiety, careful selection of studies under this umbrella term is important to assess impacts of EPA+DHA on stress related to the brain compared to stress at a cellular level. Many of the studies related to “stress” included studies on oxidative and cellular stress.

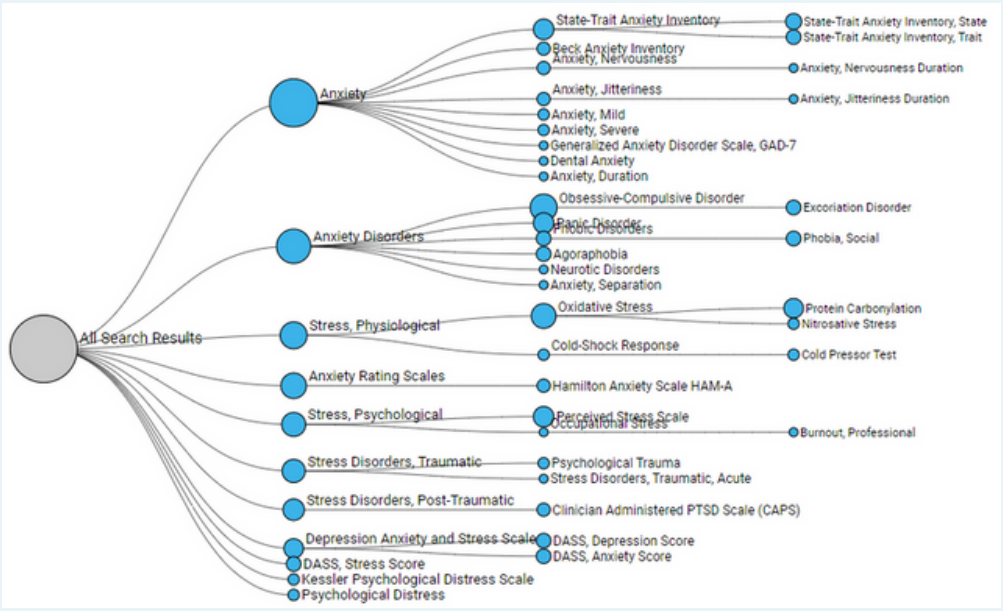

Figure 2: Advanced search results and participant characteristics for terms associated with stress and anxiety.

Brain Health: Mood

	Mood	Emotions
Abstract Search: Total Studies (Interventional Studies)	501 (354)	162 (99)
Advanced Search: Results (Participant Characteristics)	20 (85)	79 (113)

Table 4: Number of Studies within the Abstract and Advanced Searches. Data collected May 18, 2023.

Commentary:

- Most studies evaluate depression, anxiety and mood disorders rather than emotion and mood in a general sense. Therefore, if a search for "mood" is conducted, it is important to evaluate what brain health conditions are being examined to evaluate potential effects. Greater benefits for EPA+DHA intake were reported for people with a clinical diagnosis of anxiety or depression, and people taking a higher dose of EPA+DHA. Extreme study heterogeneity is reported in studies within this topic, making an overall conclusion or generalization impossible.

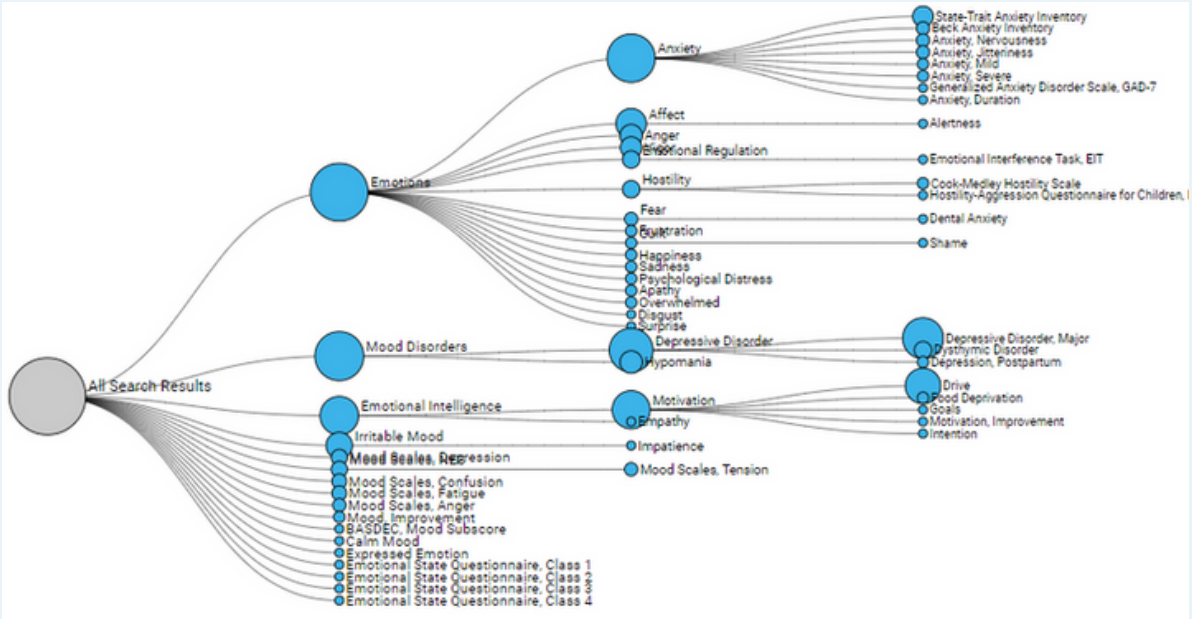

Figure 3: Advanced search results and participant characteristics for terms associated with mood and emotions.

Brain Health: Depression

	Depression
Abstract Search: Total Studies (Interventional Studies)	343 (179)
Advanced Search: Results (Participant Characteristics)	117 (178)

Table 5: Number of Studies within the Abstract and Advanced Searches. Data collected May 18, 2023.

Commentary:

- If investigating depression, consider examining whether EPA+DHA are part of an adjunctive treatment or independent treatment, what dosage of EPA+DHA was used, baseline EPA+DHA levels, differences in the clinical evaluation of the type and severity of depression (i.e. major depressive disorder, perinatal depression, etc.), age of the participants, occurrence of other health conditions, compliance, etc.
- A helpful first step (although large in scope) might be to categorize the available studies to date based on one of the above parameters to address the significant study heterogeneity within this topic area.

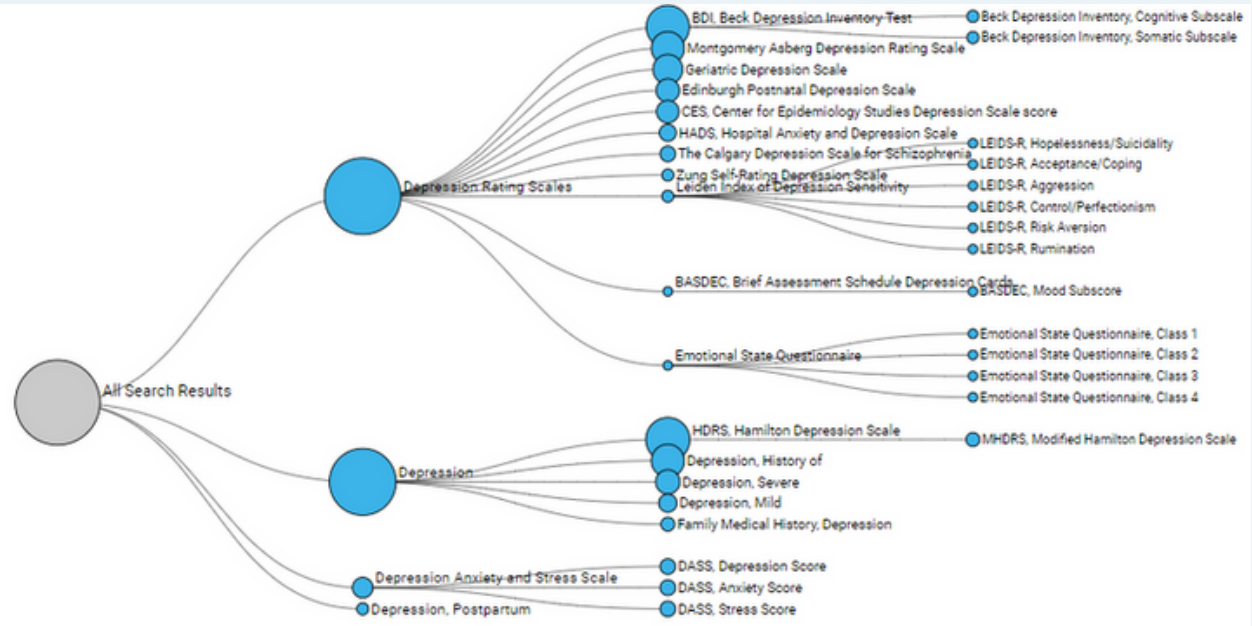

Figure 4: Advanced search results and participant characteristics for Depression associated terms.

Brain Health: Alzheimer's and Dementia

	Alzheimer's Disease	Dementia
Abstract Search: Total Studies (Interventional Studies)	117 (53)	136 (62)
Advanced Search: Results (Participant Characteristics)	29 (50)	54 (115)

Table 6: Number of Studies within the Abstract and Advanced Searches. Data collected May 18, 2023.

Commentary:

- If investigating this topic, supplementation timelines (when during the disease diagnosis), length of supplementation, follow up timepoints, patients' health status, severity of disease, and baseline EPA+DHA levels need to be considered.
- Based on the overall Abstract conclusions, the older studies (<2015) tended to be positive, while newer studies (>2016) tended to be neutral.
- An evaluation of the animal studies may be relevant to determine a possible physiological linkage between EPA+DHA and brain changes during dementia.

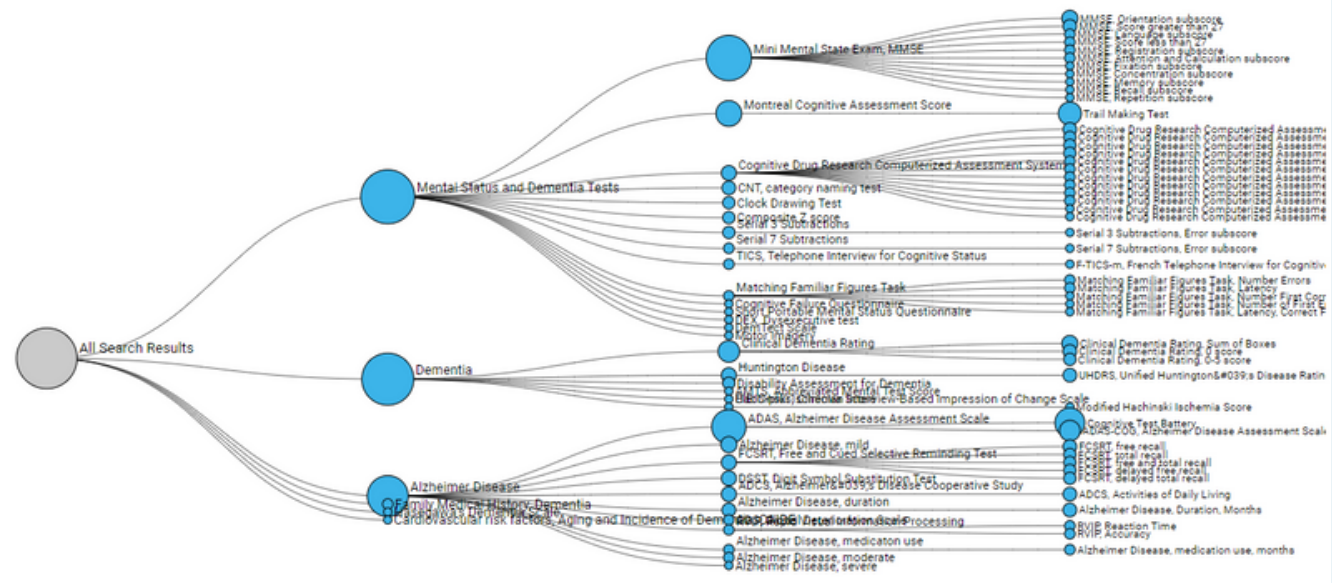

Figure 5: Advanced search results and participant characteristics for Alzheimer's Disease and Dementia associated terms.

Brain Health: Memory

	Memory	Memory and Learning Tests
Abstract Search: Total Studies (Interventional Studies)	131 (93)	15 (15)
Advanced Search: Results (Participant Characteristics)	26 (31)	56 (61)

Table 7: Number of Studies within the Abstract and Advanced Searches. Data collected May 18, 2023.

Commentary:

- If investigating memory, most studies linked to this term investigated cognitive decline, which is briefly covered in the cognitive health topic. Consideration for the severity of the memory loss, and for the types of assessments used, is important in defining the scope for a project related to memory or impacts on EPA+DHA on memory and learning tests.

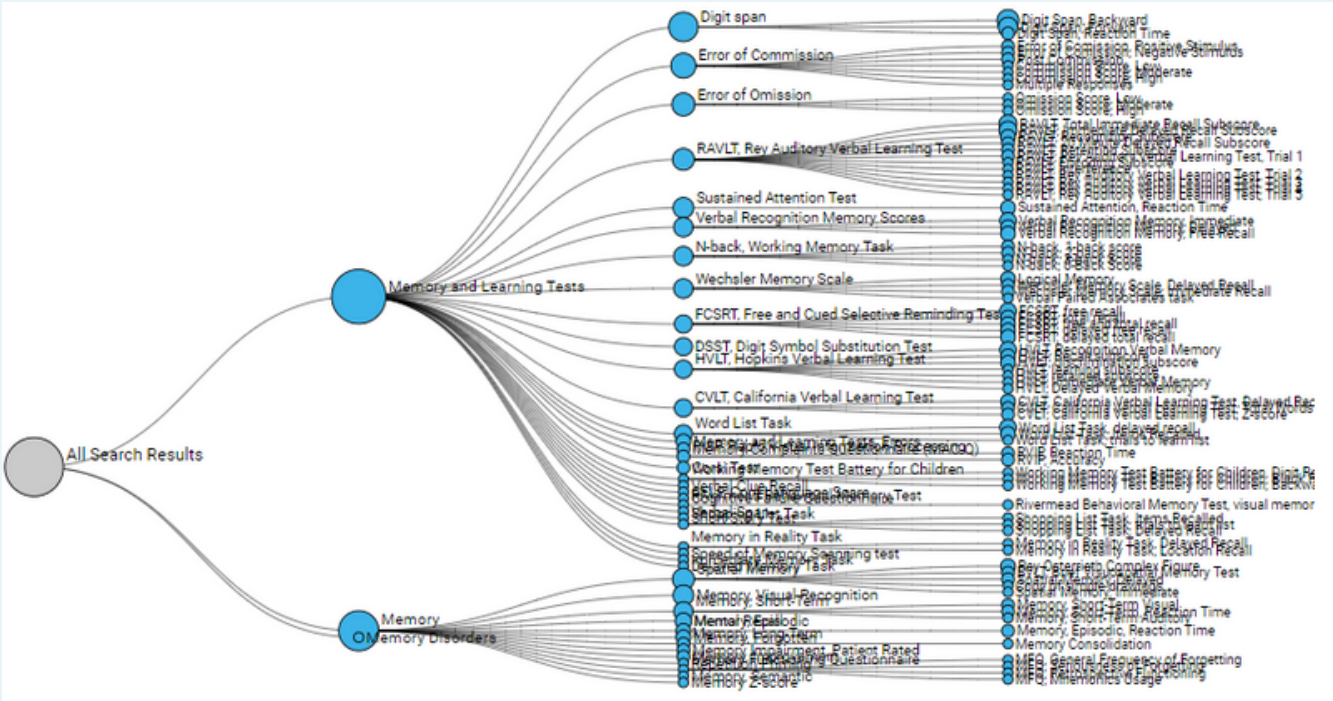

Figure 6: Advanced search results and participant characteristics for memory and associated terms.

Brain Health: Attention Deficit Hyperactivity Disorder (ADHD)

	ADHD
Abstract Search: Total Studies (Interventional Studies)	126 (73)
Advanced Search: Results (Participant Characteristics)	20 (44)

Table 8: Number of Studies within the Abstract and Advanced Searches. Data collected April 6, 2023.

Commentary:

- If investigating this topic, consider baseline levels of EPA+DHA, severity of ADHD symptoms, dosage of EPA+DHA plus other dietary or supplemented nutrients, etc.

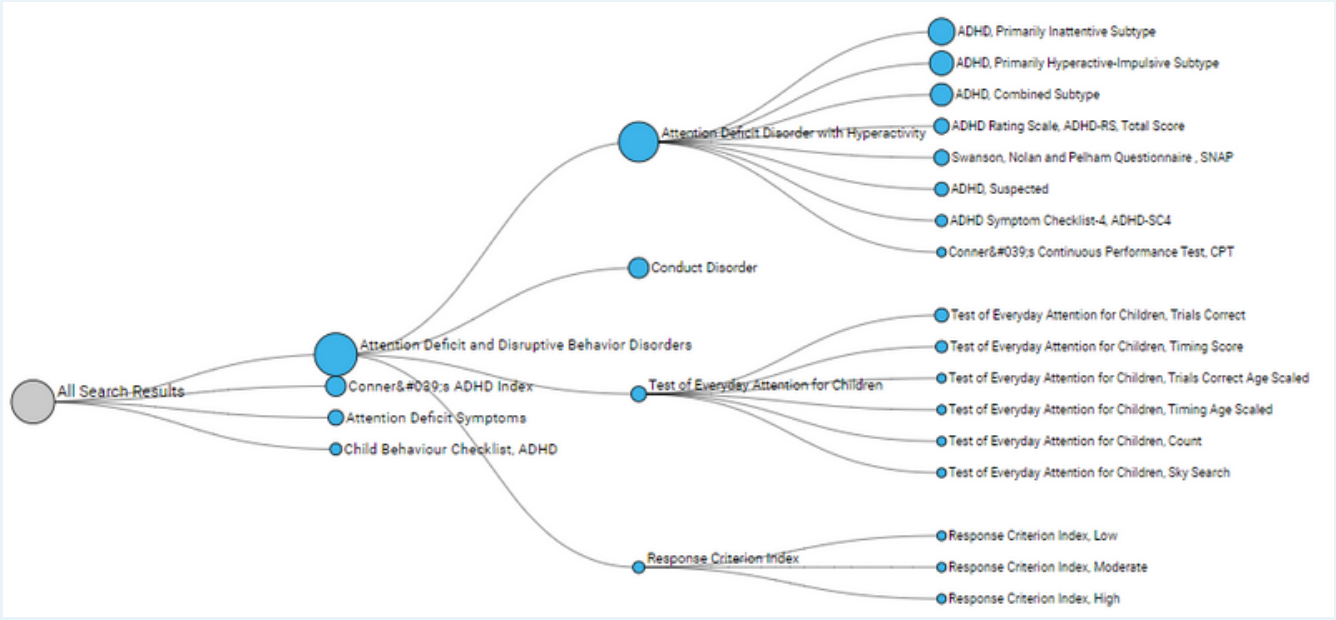

Figure 7: Advanced search results and participant characteristics for ADHD and associated terms.

Brain Health: Traumatic Brain Injury

	Traumatic Brain Injury
Abstract Search: Total Studies (Interventional Studies)	19 (13)
Advanced Search: Results (Participant Characteristics)	18 (59)

Table 9: Number of Studies within the Abstract and Advanced Searches. Data collected April 27, 2023.

Commentary:

- There have been extensive animal studies showing intake of EPA+DHA reduces cellular injury and adverse outcomes associated with traumatic brain injury.
- Given the severity and sensitivity of brain injuries, interventional studies are limited to date, and most evidence comes from case studies and individual reports. The case studies that have been published report significant improvements with a large dose of EPA+DHA intake after a head injury. Overall summarized trial data reports that there is no evidence to support or disprove the effectiveness of EPA+DHA intervention in older adults with a history of head trauma.

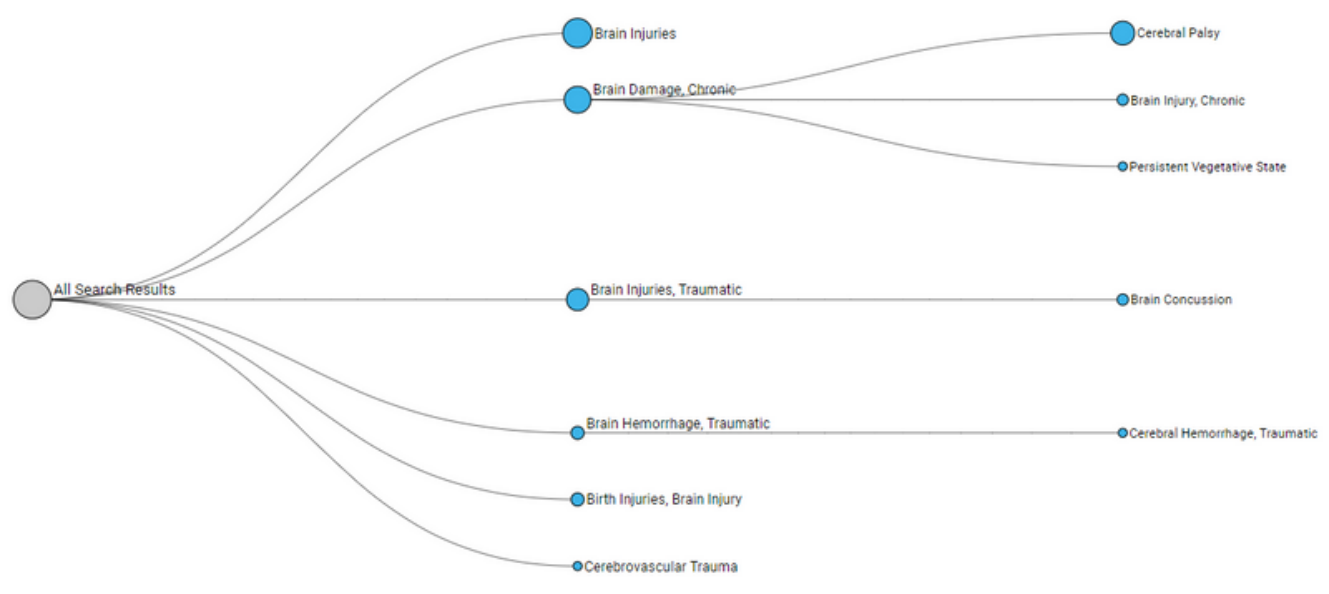

Figure 8: Advanced search results and participant characteristics for traumatic brain injury and associated terms.

Terms and Definitions

- Abstract Search study types include Case-Control, Cohort (Prospective), Cohort (Retrospective), Cross-sectional, Interventional, Meta-analysis, Systematic Review, and Non-Systematic Review.

- Results - outcomes assessed or measures taken throughout or at the end of a study.

- Participant Characteristics - descriptors of people who were part of the study.

- Heterogeneity - This word is mentioned multiple times across some brain health outcomes, and it defines difference between related items. For the purposes of reviewing the data across a health outcome in a metanalysis, heterogeneity is often a statistical test used to determine how similar (or comparable) or how different (not comparable) the studies are to each other. For example, a meta analysis reporting significant heterogeneity means that the studies were significantly different from each other – making their comparisons and grouping of data difficult if not impossible. A score or rating of high heterogeneity may be attributable to differences in participants (age, other health conditions, life stage, supplement dosage) or tests conducted (assessments or tests or other outcomes), or study design, or the number of people in the study.

Search Terms

Cognitive Health:

- Abstract Search terms: cognitive health or cognitive decline or cognition.
- Advanced Search terms: cognition; cognition disorders; cognitive dissonance; cognitive dysfunction; cognitive dysfunction: mild, moderate, advanced, severe; cognitive failure questionnaire; cognitive drug research computerized assessment system: choice reaction time, choice reaction time accuracy, delayed word recall accuracy, digit vigilance false alarms, digit vigilance reaction time, immediate word recall, numeric working memory accuracy, working memory reaction time, simple reaction time, spatial memory accuracy, spatial memory reaction time, word recognition accuracy, and word recognition reaction time.

Stress and/or Anxiety:

- Abstract Search terms: stress or anxiety.
- Advanced Search terms for stress: stress, physiological; stress, psychological; DASS, Depression and Anxiety Stress Scale; DASS, stress score; Kessler Psychological Distress Scale; perceived stress scale; psychological distress; stress disorders, post-traumatic; stress disorders, traumatic; stress disorders, traumatic, acute.
- Advanced Search terms for anxiety: anxiety, jitteriness; anxiety; anxiety disorders; anxiety rating scales; anxiety, duration; anxiety, jitteriness duration; anxiety, mild; anxiety, nervousness; anxiety, nervousness duration; anxiety, separation; anxiety, severe.

Mood:

- Abstract Search terms: mood or emotions.
- Advanced Search terms: mood disorder; mood scales (anger, confusion, depression, fatigue, NES, Tension), mood, improvement; BASDEC, mood subscore; calm mood; irritable mood; emotions: excluding anxiety and psychological distress. Emotions; expressed emotion; emotional regulation, emotional state questionnaire (class 1, class 2, class 3, class 4); emotional intelligence.

Depression:

- Abstract Search terms: depression.
- Advanced Search terms: depression, depression anxiety and stress scale; depression rating scales; depression, history of; depression, mild; depression, postpartum; depression, severe; BDI, Beck Depression Inventory (test, cognitive subscale; somatic subscale); CES, Center for Epidemiological Studies Depression Scale Score; DASS, depression score.

Search Terms

Alzheimer's Disease and/or Dementia:

- Abstract Search terms: Alzheimer or Alzheimers or Alzheimer's or Dementia.
- Advanced Search terms: Alzheimer Disease; Alzheimer Disease, mild; Alzheimer Disease, moderate; Alzheimer Disease, severe; Alzheimer Disease, duration, months; Alzheimer Disease, medication use, months; ADAS-COG (Alzheimer Disease Assessment Scale, Cognitive Subscale) Cooperative Study and commands, comprehension of spoken language, concentration or distractibility, constructional praxis, and delayed word recall. Dementia; clinical dementia rating (0 score, 0-5 score, sum of boxes); disability assessment for dementia; family medical history, dementia; Hasegwa's dementia scale; mental status and dementia tests; AMTS abbreviated mental test score; cardiovascular risk factors, aging and incidence of dementia, CADE.

Memory:

- Abstract Search terms: memory.
- Advanced Search terms: memory; memory consolidation; memory disorders; memory functioning questionnaire; memory impairment, patient rated; memory Z-score; memory, episodic; memory, episodic, reaction time; memory, forgotten; memory, improvement; memory, long-term; memory, semantic; memory, short-term; memory, short-term auditory. Memory and Learning Tests: memory functioning questionnaire; memory and learning tests (errors); memory complaints questionnaire (MAC-Q); memory in reality task, delayed recall; memory in reality task, location recall.

ADHD:

- Abstract Search terms: ADHD or ADD or attention deficit hyperactivity disorder.
- Advanced Search terms: attention deficit disorder with hyperactivity; attention deficit and disruptive behavior disorders; attention deficit symptoms; ADHD rating scale; ADHD symptom checklist; ADHD, combined subtype; ADHD, primary hyperactive-impulsive subtype; ADHD, primary inattentive subtype; child behavior checklist, ADHD; Conner's ADHD index; ADHD, suspected ADHD.

Traumatic Brain Injury:

- Abstract Search terms: traumatic brain injury or brain concussion or brain damage or brain injury.
- Advanced Search terms: brain hemorrhage, traumatic; cerebral hemorrhage; cerebral hemorrhage, traumatic; brain injuries, traumatic; brain stem hemorrhage, traumatic; brain injuries, brain injury; brain injury, chronic; brain concussion; post-concussion syndrome; brain damage, chronic; cerebrovascular trauma; brain injuries, diffuse.

For questions and comments, please contact csd@goedomega3.com.