Realising the potential of MILK PHOSPHOLIPIDS as an ingredient to improve cognitive function

Professor Louise Dye
Human Appetite Research Unit, Institute of Psychological Sciences Leeds University
NUTRITION & MENTAL performance
– A clear but complex link

Nutrition impacts cognition

PROMOTION of optimal brain development

PREVENTION of neurodegeneration and cognitive decline
Phospholipids (PL) - bioactive and fundamental for life

- Phospholipids (PL) are bioactive lipids which play various important functions in ALL biological membranes – STRUCTURAL and FUNCTIONAL.

- There are five major PLs characterized by different head units (PC, PE, PI, PS PG).

- Dietary sources of PL include meat, egg, soy and MILK (bovine/human).

- Dietary PL has good oral bioavailability and readily crosses the blood brain barrier.
Phospholipids - from a BRAIN perspective

- Phosphatidyl choline (PC) [33-37% brain PL] key building block of membrane bilayers and provides choline for Acetycholine (Ach) synthesis
- Phosphatidyl ethanolamine (PE) [36% brain PL] key building block of membrane bilayers
- Phosphatidyl serine (PS) [10-20% brain PL] - plays a key role in biosynthesis and release of neurotransmitters. PS is neurotrophic, increasing total number and size of neurons
- Phosphatidyl Inositol (PI) [2-5% brain PL] key membrane constituent and as a participant in essential metabolic processes
- Sphingomyelin (SM) [11% brain PL] contributes to myelination of neurons, is required for the activity of a number of membrane-bound proteins and is also a source of choline. SM not found in plants.

Phospholipids constitute more than 60% of total brain lipid, most of which are incorporated in the membrane system.

The potential of MILK phospholipids to improve cognitive function

Bovine MILK PHOSPHOLIPIDS
A natural source of bioactive lipids with a SIMILAR profile as found in human BRAIN

* Cerebral cortex 16 year male from Svennerholm et al. 1968. Burling & Graverholt 2008
Brain development and cognitive functioning
- Lifelong process - from conception to adulthood

Infants experience the most rapid periods of postnatal brain growth and development

A vast range of nutrients are critically needed for optimal BRAIN development in this period

Composition of MILK has adapted to fulfill the needs

Recent research on brain neurogenesis and plasticity confirms that good nutrition is important for optimal brain function throughout our lifecycle

Recent research on brain neurogenesis and plasticity confirms that good nutrition is important for optimal brain function throughout our lifecycle

Infants experience the most rapid periods of postnatal brain growth and development

A vast range of nutrients are critically needed for optimal BRAIN development in this period

Composition of MILK has adapted to fulfill the needs

Recent research on brain neurogenesis and plasticity confirms that good nutrition is important for optimal brain function throughout our lifecycle

Brain development and cognitive functioning
- Lifelong process - from conception to adulthood

Infants experience the most rapid periods of postnatal brain growth and development

A vast range of nutrients are critically needed for optimal BRAIN development in this period

Composition of MILK has adapted to fulfill the needs

Recent research on brain neurogenesis and plasticity confirms that good nutrition is important for optimal brain function throughout our lifecycle

Brain development and cognitive functioning
- Lifelong process - from conception to adulthood

Infants experience the most rapid periods of postnatal brain growth and development

A vast range of nutrients are critically needed for optimal BRAIN development in this period

Composition of MILK has adapted to fulfill the needs

Recent research on brain neurogenesis and plasticity confirms that good nutrition is important for optimal brain function throughout our lifecycle

Brain development and cognitive functioning
- Lifelong process - from conception to adulthood

Infants experience the most rapid periods of postnatal brain growth and development

A vast range of nutrients are critically needed for optimal BRAIN development in this period

Composition of MILK has adapted to fulfill the needs

Recent research on brain neurogenesis and plasticity confirms that good nutrition is important for optimal brain function throughout our lifecycle
The potential of MILK phospholipids - as ingredients to improve cognitive function

BOVINE MILK phospholipids have been documented to IMPROVE BRAIN development & COGNITION in infants

POTENTIAL for PROMOTING optimal brain development during childhood?

POTENTIAL for PREVENTING neurodegeneration and cognitive decline?
Realising the potential for MILK PHOSPHOLIPIDS....
- Results from RECENT HUMAN clinical trials & PIGLET trials

- Functional milk drink enriched with bovine MILK phospholipids improved behavioral regulation in healthy pre-school CHILDREN (Vereman-Weuters et al. 2012)

- Supplementation to infant formulas of MILK derived PLs versus Egg-Yolk derived PLs was found positively associated with neurobehavioral development of pre-term infants and subscribed to its higher content of SPHINGOMYELIN (Tanaka et al. 2013)

- Supplementation of MILK derived complex lipids to infant formulas was associated with beneficial effects on cognitive development in healthy INFANTS (Gurnida et al. 2012, Timby et al. 2014)

- Supplementation of MILK derived phospholipids improved spatial learning and increased brain growth and composition in neonatal PIGLETS - (Liu et al. 2014)
Exploring the POTENTIAL for MILK phospholipids to IMPROVE cognitive performance in school children

AIM: To explore the effects of a daily supplement of MILK phospholipids on cognitive performance- & subjective state in school children.

Strategic collaboration between The University of Leeds, UK and Arla Foods Ingredients, Denmark

Randomized, 6 week, parallel groups, double blind, placebo controlled trial

Participants: n= 84, 6-8 year old school children – 3 cohorts from 2 primary schools in UK

Supplement: MILK phospholipid (Lacprodan® PL20) enriched milk or non-enriched milk.

Delivered as a school-based intervention (Monday – Friday)

3 Assessments – baseline (Week 0), mid-intervention (Week 3) & post-intervention (Week 6)

Measures of cognitive performance, related to learning (CANTAB) i.e. improvement in performance from baseline to week 6

Subjective state measures (Visual Analogue Scales ratings)
CANTAB Cognitive Tests and Brain Regions

- Delayed Matching to Sample
- Reaction Time
- Rapid Visual Information Processing
- Emotion Recognition Test
- Attention Switching Task
- Stop Signal Task
- Spatial Working Memory
- Stockings of Cambridge
- Paired Associates Learning
- Verbal Recall / Recognition Memory
- Pattern or Spatial Recognition Memory
Phospholipid Intervention for Cognitive Ageing Reversal (PLICAR)
CLINICAL TRIAL exploring the POTENTIAL for MILK phospholipids in seniors

AIM: To investigate neurocognitive effects of daily supplementation with MILK phospholipids, in elderly participants with age-associated memory impairment.

- Jointly funded by Arla Foods Ingredient, Denmark and Swinburne University of Technology
- The trial protocol has been published: Scholey et al. 2013. Trials, 14:404
- Is registered on the Australia and New Zealand Clinical Trials Registry as ACTRN12613000347763
- Is currently recruiting

Human clinical trial to evaluate whether chronic (daily) supplementation with MILK phospholipid over a 6-month period improves cognitive functioning and mood in healthy older adults (>55 years) with age-associated memory impairment (AAMI).
Brain composition and functioning alters as we age - decline in cognitive and mental functioning

- Concentration of most lipids in the human DECREASE after age of 20
- PL decreases 18-31% and the volume of the brain declines with age at a rate of around 5% per decade after the age of 40

To date Nutritional supplements with PL´s like PC and PS in ISOLATION have shown beneficial effects for treating or slowing the progression of mental decline/AAMI


Estimated prevalence of AAMI diagnosis
- 40 % of people age 50-59
- > 50 % of people age 60-69
- Up to 80 % of people age >80

AAMI, Age associated memory impairment, i.e., normal decline in mental functioning
MCI, mild cognitive impairment
AD, Alzheimers disease
Phospholipid Intervention for Cognitive Ageing Reversal (PLICAR)
CLINICAL TRIAL exploring the POTENTIAL for MILK phospholipids in seniors

- Randomized, double-blind, placebo-controlled parallel groups
- N= 150 (N = 50/group) AAMI participants aged > 55 years randomized to receive daily supplement of MILK phospholipids (Lacprodan® PL-20) or one of two placebos (phospholipid-free milk protein concentrate or inert rice starch)
- 6-month intervention with testing at baseline, 90 days and 180 days

Neuroimaging – MRI, fMRI (subset of participants)

PRIMARY outcome: composite memory score from the Rey Auditory Verbal Learning Test
SECONDARY outcome: include cognitive, cardiovascular, gastrointestinal, brain imaging and biochemical measures

Scholey et al. 2013
Conclusions

- Good & growing evidence for role of Milk PL in cognition early in development & later in life
- Challenging to measure the effects of nutrition on cognitive function

- Effects - subtle
- Nutritional interventions with enduring effects on cognition may take months or even years to manifest
- Cognitive tests need to be carefully selected
- Appropriate samples – children, middle aged (40-65yrs -pre AAMI)
- Consider additive/synergistic effects of other behaviour e.g. physical activity, body weight change
Future Directions

- Changing nature of diet, health & population
  - Understand effects of altered eating patterns
  - Effects of under & over-nutrition
- Cognitive benefits could be conferred directly – specific nutrients or overall intake
- Or via other effects on health e.g. better gluco-regulation, reduced triglycerides or other markers
- Important to preserve cognitive capacity in ageing
- Need functional foods to help maintain brain function
THANK YOU for your ATTENTION!
References

• Andersen. 2003. Trajectories of brain development: point of vulnerability or window of opportunity? Neuroscience and Biobehavioral Reviews 27;3-18
• Svennerholm 1968. Distribution and fatty acid composition of phosphoglycerides in normal human brain J Lip Res 9, 570-579
• Tau et al. 2010 Normal Development of Brain Circuits. Neuropsychopharmacology REVIEWS 35, 147-186
• Scholey et al. (2013). Trials , 14:404
• Liu et al. 2014. J. nutr. 00xx-xx
• Gurnida et al. 2012. Association of complex lipids containing gangliosides with cognitive development of 6-month-old infants. Early Hum Dev
• Timby et al 2014 Neurodevelopment, nutrititon, and growth until 12 mo of age in infants fed a low-energy, low-protein formula supplemented with bovine milk fat globule membranes: a randomized controlled trial. Am J Clin Nutr
• Tanaka et al. 2012. Sphingomyelin-fortifiedmilk has a positive association with neurobehavioural development of very low birth weight infants during infancy, randomized control trial. Brain Dev 35;45-52