The Gut Brain Axis
ILSI Europe’s research from gut to brain

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Number of publications in PubMed on gut brain axis over the past 30 years

- 1382 publications in total
- 325 publications in 2017
- Exponential increase

→ Emerging topic
Current ILSI Europe Scientific Portfolio

**FOOD SAFETY**
- Microbiological Food Safety
  - Control Options for Viruses in Food Processing
  - Industrial Microbiological Risk Assessment – Completed
  - Process Validation Protocols
  - EU Project EFCONT
- Contaminants
  - Reactions & Potential Mitigation of Mycotoxins During Food Processing
  - Bio-Markers of Exposure to Process-Related Contaminants
  - Mineral Oil Risk Assessment
- Low Dose Effect
  - Cancer Potency Database
  - Carcinogenic Dose-Response Database for TTC
  - Uncertainty in TTC
- New Approaches for Food Safety
  - ToxCast Data on Food Chemicals
  - Microbial Food Matrix Interactions
  - Next-Generation Sequencing
  - Application of Advanced Outcome Pathways
  - Authenticity of Food
  - Enzyme-Programme SUIFOOD
- Packaging
  - 6th International Symposium on Food Packaging
  - In Vitro Bioassays for Food Contact Materials Safety
  - Adhesives for Food Packaging Applications
  - PET and PS for Food Packaging Applications

**NUTRITION, DEVELOPMENT & HEALTHY AGEING**
- Glycaemia & Inflammation
  - Reduction of Post-Prandial Glycaemia
- Nutrition and Inflammaging
  - Metabolic Syndrome Studies
- Nutritional & Glycaemic Response in Children
- Early Life Nutrition
  - Early Growth Velocity – Completed
  - Specialised Formulas – Fat
- Holistic Approaches to Develop Alternative Strategies
- Nutrient Status of Population Groups
  - Catecholamine-Based Recommendations for Dietary Guidelines
  - Health Effects of Saturated Fats
  - Nutrition Guidelines for Diabetes
  - Healthy Ageing
  - Nutrition for the Ageing Brain
  - Plant-Based Ingredients & Cognitive Performance
  - Effect of Food Component Interactions on Brain Functions
  - Energy Balance
  - Dietary Fibres & Satiation
  - Adaptation to Changes in Satiation
  - Role of Sweet Taste on Nutrition & Food Preference
  - NFD Project Satiation

**EXPOSURE & INTAKE ASSESSMENT**
- Food Intake Assessment Methodology
  - Uncertainties in Food Intake Assessments
  - Evaluation of New Methods for Dietary Intake Assessment
  - Preferred Approaches for Quantifying the Impact of Modifying Nutrient Intakes
  - Additive Occurrence & Loyalty
- Food Intake Data
  - Adequacy of Dietary Fibre Intake
  - Adequacies of Omega 3 & Omega 6 PUFA Intakes
  - Dietary Supplements, Nutrient-Dense Food & Food Fortification & the Elderly
  - Iodine Intakes in Europe

**GUT MICROBIOTA & HEALTH**
- Probiotics
  - Structure-Function Relationship for Probiotic Compounds
  - Probiotics: Interaction with the Intestinal Barrier Function
  - Mechanisms of Probiotic Action
- Oral & Gut Microbiota
  - Oral & Systemic Health Resilience
  - Exploring the Role of Major Gut Microbiota Clusters – Completed
  - Microbiome Human Study Research Guidance
  - Short Chain Fatty Acid Production for Health

**NUTRITION SECURITY & SOCIETAL ASPECTS**
- Nutrition Security & Societal Aspects
  - Nudging Towards Healthier Food Choices
  - EU Project SURFANS
  - EU Project FITFOOD2030

**BIOMARKERS & FUNCTIONAL EFFECT MEASUREMENTS**
- Biochemical and Immunological Markers of Nutrition
  - Marker Validation Initiative Part III – Completed
  - Glycaemic Exposure Markers in the Non-Diabetic Population
  - Efficacy Markers of Diabetes Risk
  - Quality of Life Measures
  - EU Project PATHWAY-37
Schematic representation of the gut brain axis

- Controller of basic homeostatic processes
- Coordinates the responses to internal and external threats
  → Ensures survival of the organism

- Defence machinery to fight pathogens
- Key role in regulating homeostasis
  → part of fundamental physiological processes and a close crosstalk with other body systems

- An unhealthy gut contributes to a wide range of diseases
- The gut microbiota plays a major role in gastrointestinal health
Gut related activities

- 12 Activities
- 3 Workshops
- 9 Publications

- An unhealthy gut contributes to a wide range of diseases
- The gut microbiota plays a major role in gastrointestinal health
Beneficial health effects have been reported on consumption of specific prebiotic or probiotic food products/ingredients/supplements. Evaluation of the evidence for prebiotics and probiotics’ functionality in several areas of application like inflammatory conditions or metabolism and energy homeostasis.
Intestinal Barrier

Health Benefits of Prebiotics and Probiotics

Mechanistic Insights into Functions of Prebiotics and Probiotics

Gut Microbial Composition and Metabolism

Gut related activities

Prebiotic effects: metabolic and health benefits

Human Intestinal Barrier Function in Health and Disease
Gut related activities

Intestinal Barrier

Health Benefits of Prebiotics and Probiotics

Mechanistic Insights into Functions of Prebiotics and Probiotics

Gut Microbial Composition and Metabolism

Prebiotic effects: metabolic and health benefits

Human Intestinal Barrier Function and Disease

Systematic review of the effects of the intestinal microbiota on selected nutrients and non-nutrients
Gut Microbial Composition and Metabolism

Stakeholder Workshop, on 3-4 December 2015

• Gut microbiota metabolism extends metabolic flexibility of host to process a wide range of substrates

• Microbial metabolites of nutrients and non-nutrients can be important cell signaling molecules (SCFA, bile acids) and have impacts on health (SCFA, TMA, phenolics)

• Large inter-individual variation in microbiota → potential consequences for metabolism of dietary compounds and health
Mechanistic Insights into Functions of Prebiotics and Probiotics

Mechanisms of Probiotic Action

• Investigate and evaluate current knowledge about the mechanisms of probiotic action
• Link health benefit, physiological function and probiotic mechanism;

Structure-Function Relation of Prebiotics

• Prediction how a specific core structure of a carbohydrate compound impacts the gut microbiota, and subsequently the host

→ This activity is a first step in defining structure-function relations

Molecular mechanism of cross-talk at mucosal level

Cellular responses in the mucosa (local)

Cellular / physiology effect in host (mucosal and systemic)

Clinical benefit (meta-analysis)

Rastall, 2017 Designing next generation prebiotics for lifelong health? Presentation at IPC2017
Immune system related activities

- 10 Activities
- 2 Workshops
- 9 Publications

- Defence machinery to fight pathogens
- **Key role in regulating homeostasis**
  → part of fundamental physiological processes and a close crosstalk with other body systems
Immune system related activities

- Understanding the complexity of the immune system and its role in maintaining health
- Understanding the health relevance of immune modulation and the role of nutrition
- Understanding the impact of nutrition on immune functions

Monitoring immune modulation by nutrition in the general population: identifying and substantiating effects on human health

Inflammatory Disease Processes and Interactions with Nutrition

Markers to measure immunomodulation in human nutrition intervention studies?
Low-grade inflammation

• Characterised by raised concentrations of inflammatory markers in the systemic circulation

• Pathological feature of a wide range of chronic disease conditions:
  → Metabolic syndrome (MetS);
  → Non-alcoholic fatty liver disease (NAFLD);
  → Type 2 diabetes mellitus (T2DM);
  → Chronic kidney disease (CKD);
  → Cardiovascular disease (CVD);
  → Cognitive decline.
• Highlighted the **importance of low-grade inflammation** in health and disease;
• Reviewed and interpreted the extensive literature on the **dietary modulation of low-grade inflammation** by macronutrients, micronutrients and non-nutrients (such as fibre and other plant bio-actives);
• Provided a comprehensive overview of the hierarchy of **inflammatory markers as biomarkers of risk** of the metabolic syndrome, diabetes, cardiovascular disease, cognitive and gut health;
• Focused on issues relevant to the **translation of research findings into health claims**.

→ Controlling inflammation a key future preventative and therapeutic target
Explains the nature of chronic low-grade inflammation in the context of overweight and obesity;

Describes the factors that might influence it, in particular those related to diet.

Focus on the latest research findings in the areas of inflammation and cardio-metabolic, cognitive and gut health,

Reviews how early-life nutrition as well as the macronutrient and plant bioactive composition of the adult diet influence inflammatory processes.
Immune system related activities

Understanding the complexity of the immune system and its role in maintaining health

Understanding immune modulation across lifespan

Understanding the health relevance of immune modulation and the role of nutrition

Understanding the impact of nutrition on immune functions

Immune disorders
- Infections
  - Diarrhea
  - Common cold
- Gastritis
- Allergy
- Inflammation
- Obesity
- Metabolic Disorders
- Ageing
- Alzheimer's
- Cardiovascular Disease
- Inflammatory Bowel Disease
- Joint inflammation
- Arthritis
- Skin
- Cancer
- Microbiota
- Antimicrobials
- Permeability
- Nutrition

Monitoring immune modulation by nutrition in the general population: identifying and substantiating effects on human health

Inflammatory Disease Processes and Interactions with Nutrition

Markers to measure immunomodulation in human nutrition intervention studies

A Consideration of Biomarkers to be used for Evaluation of Inflammation in Human Nutritional Studies

Understanding the impact of nutrition on immune functions

Monitoring immune modulation by nutrition in the general population: identifying and substantiating effects on human health

Inflammatory Disease Processes and Interactions with Nutrition

Markers to measure immunomodulation in human nutrition intervention studies

A Consideration of Biomarkers to be used for Evaluation of Inflammation in Human Nutritional Studies
Low Grade Inflammation mediated alteration of brain functions

- Pro-inflammatory cytokines potently modulate the activity of the neuro-endocrine system → chronic inflammation could result into dysregulation of the HPA axis.
- Pro-inflammatory cytokines significantly modulate neural plasticity and neurogenesis.
- Pro-inflammatory cytokines have potent effects on neurotransmitter metabolism and function.

Calder et al., 2017 Ageing Research Reviews 40: 95–119
Brain related activities

• 7 Activities
• 4 Workshops
• 10 Publications

Brain

• Controller of basic homeostatic processes
• Coordinates the responses to internal and external threats

⇒ Ensures survival of the organism

Nutrition

Immune system

Gut

91 Experts
14 Countries

Controller of basic homeostatic processes
Coordinates the responses to internal and external threats
⇒ Ensures survival of the organism
Impact of nutrition on cognition and behaviour in childhood

Examination of measures, techniques and tests for assessing effects of food and nutrients.

Workshop Series ‘Nutrition for the Ageing Brain’

Plant-Based ingredients and cognitive performance

Food Component Interactions and Brain Functions

Impact of nutrition on cognition and behaviour in childhood

Brain related activities

Nutrition and cognition: assessing cognitive abilities in children and young people

The influence of children’s diet on their cognition and behavior

Micronutrient status, cognition and behavioral problems in childhood

Nutrition for the ageing brain: Towards evidence for an optimal diet

Brain imaging and human nutrition: which measures to use in intervention studies?
Nutrition for the Ageing Brain Workshops

- Neurogenesis
- Oxidative Stress
- miRNAs
- N-3 PUFAs
- Amino Acids
- Polyphenols
- Multinutrients

Nutrition for the Ageing Brain Workshops

Upcoming 3rd Workshop
‘Nutrition for the Ageing Brain: Moving Towards Clinical Applications’
30 – 31 August 2018, Madrid, ES

Objectives
1. Debate the potential for maintaining cognitive function through dietary intake.
2. **Focus on clinical aspects and novel strategies** developed to determine whether diet and nutrients have efficacy in individuals affected by cognitive decline.

Main themes
- Impact of nutrition on brain functions using neuroimaging technologies;
- **Microbiome and immune status: impact on brain function**;
- Biomarkers of food intake and cognitive health;
- Sleep deprivation: effects on diet and cognitive performance;
- New methodologies applied to dementia and how nutrition could play a role.
In brief: Research from gut to brain
In brief: Research from gut to brain

- **415 experts**
- **21 countries**
- **29 activities**
- **28 publications**

- **9 workshops**
- **4.37 median impact factor**
- **4,058 citations**
- **48 median citations**
In brief: Research from gut to brain
Outlook: The Ageing Gut

Derived from ILSI Europe’s Emerging Issue Process


Start in Q3/4 2018