

# Dietary treatments of dementia

**LIPIDIET** is a research project in which crucial studies have been undertaken to develop effective means of mitigating cognitive degeneration, Alzheimer's disease and dementia

'**DEMENTIA**' IS THE collective term which denotes a group of degenerative diseases which affect the cognitive abilities of individuals. Although Alzheimer's is often thought to be synonymous with dementia, it is more accurately described as the most common attributive cause of formal dementia. Dementia is typically manifest among the elderly population, and while a number of therapeutic treatments have been developed to reduce symptoms, a cure to eliminate the disease is not available; thus, the disease is prolonged in patients and is eventually fatal.

Over the course of the next two decades, the relative proportion of elderly people living in developed and industrialised nations worldwide is set to soar, signalling the increasingly pressing need for funding in dementia-based research.

## THE LIPIDIET PROJECT

LipiDiDiet is an innovative programme whose remit revolves around dementia-related research. The initiative benefits from funding provided by the 7th Framework Programme (FP7) of the European Commission, and follows on from previous projects in the field of dementia. The project's predecessor, LipiDiet, was incorporated within the 5th EU research programme in 2002. During its years of activity, evidence was accumulated to support the hypothesis that certain lipids were beneficial in reducing disease progression in Alzheimer's. This stimulated further research, and in 2007, the follow-up LIPIDIET project was implemented.

The European LIPIDIET project addresses the therapeutic and preventative impact of nutritional lipids on neuronal and cognitive performance in Alzheimer's disease and Vascular dementia. Despite the findings which suggested that certain lipids are useful

in preventing cognitive degeneration from enveloping further in cases of Alzheimer's, their beneficial effects appear to be limited to patients who are at a very early stage of the disease. As such, the principal aim of LIPIDIET is to complement current medical therapy of Alzheimer's disease

with nutrition, with particular emphasis on disease prevention and treatment of the very first stages of Alzheimer's disease. The development of a lipid-based diet, it is proposed, will reduce the risks associated with Alzheimer's, and bear a stabilising effect on cognitive performance in aging.

## Mitigating cognitive decline in the elderly

Could you begin by offering an insight into the background of the project and its overall aims and objectives?



The overall objective of LIPIDIET is to provide a suitable and easily accessible prevention to cognitive decline for the elderly. With aging, cognitive performance is at risk and decreases due to dementia related diseases, especially Alzheimer's disease. Diet-related approaches typically offer a very low risk of unwanted side effects, are cost efficient and accessible. Certain aspects of the human brain biology are also receptive to such treatments, rendering them safe and viable.

Vascular dementia and Alzheimer's disease demonstrate a number of similarities; what are the greatest challenges in studying these two diseases simultaneously? How do you propose to make dietary supplements that are beneficial to both conditions?

Aging is the main risk factor for both Vascular dementia and Alzheimer's disease, and the two often occur together. For these conditions, as well as for normal aging which can cause a loss in cognitive performance, we are targeting neuronal and, in particular, synaptic function. It therefore makes perfect sense to evaluate the effectiveness of our interventions on all three. Risk factors also overlap, and because we can test whether the addition of substances to the formulation decreases overall effectiveness, we can generate complex formulations that target several conditions at once. Obviously, we can do this only because of the diet-derived approach, so typically we don't need to worry too much about negative side effects.

However, the LIPIDIET initiative does not concentrate exclusively on Alzheimer's disease; its members and partners also work to implement dietary products which maintain and support the normal cognitive function in healthy ageing more generally, and endeavour to reduce cerebrovascular risks.

Furthermore, as part of the LIPIDIET remit, the team also collate, prepare and disseminate diet- and lifestyle-based healthcare advice for the elderly. This communicative arm of the project is fundamental in providing support and guidance to both vulnerable and less vulnerable members of the aging population across the EU. As an indication, the project has created a 'healthy brain' index – a service which enables individuals to calculate their personal risk of developing dementia, and suggests recommendations on how to maintain cognitive performance.

#### PREVIOUS STUDIES INVOLVING DHA

Studies carried out by LipiDiet, LIPIDIET and other consortia indicate that omega-3 fatty acids, and docosahexaenoic acid (DHA) in particular, have a significant role in neuronal function and normal development of cognitive functions.

In terms of quantity, it has been established that the human brain has a much greater demand for DHA than other omega-3 fatty acids. As such,

under normal circumstances, vast amounts of DHA are found in the brain. Dr Tobias Hartmann, project coordinator of LIPIDIET, outlines the reasons why DHA is integral to regulating processes within the human brain. He comments: "DHA is needed to allow optimal function of neuronal membranes, and some DHA is also used as an antioxidant or converted to highly neuroprotective substances".

In Alzheimer's disease, the presence of DHA in the brain is noticeably lacking. Hartmann explains the implications derived from the paucity of DHA: "In the absence of DHA, alternative molecules are formed, which cannot provide optimal performance but increase the risk of neuroinflammation," he states.

In the first series of clinical studies conducted under the project banner, supplementation of DHA in patients was found to help mitigate the onset of Alzheimer's disease, especially when used alongside additional diet-derived therapies that help to prevent neurodegeneration and assist in synaptic function.

Although these trials involved the allocation of DHA – that is, an omega-3 fatty acid – Hartmann provides a tantalising glimpse at the possibility of non-lipid based treatments

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## Dr Tobias Hartmann, project coordinator of LIPIDIET, outlines the current focus of the initiative in aiming to develop diet-related approaches to prevent the onset of dementia and other cognitive diseases in the elderly

**Could you shed light on the *in vivo* animal models that you use to assess age related cognitive decline and genetic risk factors? Will these animal models have direct relevance to human trials?**

These animals model Alzheimer's disease and cerebrovascular pathology and we carry out long-term studies to reflect age-related changes. They enable us to study key parameters of these diseases to see how effective our treatments are. Importantly, we can also study the molecular mechanisms, which guide us to better interventions. Whatever enters a clinical trial has been extensively studied with these animals. This is absolutely essential for safety, but also in terms of effectiveness. The clinical trials – which are run no differently to any other clinical trials used to evaluate the effectiveness of a pharmaceutical drug – take a very long time to conduct and are very expensive. Therefore one has to make absolutely sure that the intervention is safe

and represents the best possible combination to achieve a cognitive benefit.

**The current economic climate has had a considerable impact on research funding. How is the project funded and have you received any interest from industrial partners?**

The project is part-funded by the European Union through FP7; this covers the bigger part of the costs. The current economic climate has not yet had an impact on the project because the funding scheme on which this project runs had been devised before that situation appeared. Irrespective of this, the project had sufficient foresight to focus on an intervention that is to be affordable to the EC population and does not represent a burden to the healthcare systems. The project is always open to add additional partners if this would benefit the project. Since the project started, we have added five more partners.

**How do you see your research evolving in the future? Are there any particular areas that you would like to focus on?**

A major issue is to increase effectiveness. Prevention suffers most from late application; however, most people would shift to prevention only once they learn about their high individual risk. When this happens, a lot of valuable time has often been lost. Therefore it is desirable to develop interventions that are more effective in the way that they can stop the progression of the disease sooner.

Another aspect relates to the treatment of age-related diseases in a more general approach. It is not very practical for the consumer to use many products in parallel to treat, or prevent, the typical spectrum of age-related diseases. Although this may sound very optimistic, this is a goal which – for many of the main health issues connected with aging – comes increasingly into scientific reach, especially in using a combinatory approach based on low risk molecules derived from diet.

## INTELLIGENCE

# LIPIDIET

THERAPEUTIC AND PREVENTIVE IMPACT OF NUTRITIONAL LIPIDS ON NEURONAL AND COGNITIVE PERFORMANCE IN AGING, ALZHEIMER'S DISEASE AND VASCULAR DEMENTIA

### OBJECTIVES

- To develop a lipid based diet that reduces the risk of Alzheimer's disease and related diseases and has a stabilising effect on cognitive performance in aging.
- To provide diet and life-style based health care advice for the elderly.

### KEY COLLABORATORS

Saarland University (USAAR), Germany

University of Kuopio (UKU), Finland

University of Szeged (USZEG), Hungary

Tel Aviv University (TAU), Israel

Radboud University Nijmegen Medical Center (RUNMC), The Netherlands

Göteborgs Universitet (UGOT), Sweden

VU University Medical Center (VUMC), The Netherlands

Karolinska Institutet (KAU), Sweden

University of Bonn (UKB), Germany

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**TOBIAS HARTMANN's** main research interest is in dementia prevention and combining basic science with translational aspects. He is a neuroscientist by training, and is the coordinator of several past and current large research projects. Before LIPIDIET he coordinated LIPIDIET (2000 – 2005). He chairs the institute for neurodegeneration and Neurobiology at Saarland University and is also Director of the German Institute for Dementia Prevention (DIDP).

being viable in dietary therapy. He remarks: "Not all diet derived molecules we are currently working on are related to omega-3 or lipids; there are several other molecules which apparently help to assist neuronal function in the desired way". This identification, it is hoped, will prove elemental in harnessing further research into ways of developing effective dietary-based means of nullifying the progression of Alzheimer's disease.

### EARLY INTERVENTION: CRUCIAL

Dementia is not 'contracted' as such; rather, it is diagnosed only after a long preclinical prodromal phase in which cognitive processes gradually deteriorate. Within this prodromal phase, the first identifiable stage – in clinical terms – is that of mild cognitive impairment, as Hartmann elucidates: "At the first clinical stage, individuals have not yet developed dementia, but are already noticing the first signs of cognitive decline". He continues: "It is believed that, at this stage, treatment might still be very effective".

As the disease progresses further – for instance, to Alzheimer's disease – patients experience neurodegeneration and synapse loss on a sizeable scale. As yet, a cure has not been successfully developed to reverse this process; consequently, it is held that the earlier a neuroprotective intervention is applied, the more likely it is that cognitive performance can be restored or increased. Hartman elaborates on the benefits of early intervention: "Even if the intervention would not cure the disease, it would be sufficient to stop the progressive process. Because cognitive decline is so little before actual dementia has developed, the affected

individual can continue to live his/her life without any major problems". Treatments which successfully mobilise an increase in cognitive performance are very rare, and the increases are generally very small. Thus, the focus of LIPIDIET research involves preserving rather than improving levels of cognitive performance.

### EXPERTISE AND A MULTIDISCIPLINARY APPROACH

LIPIDIET is comprised of 18 research partners whose work and investigative studies span a diverse range of areas from basic neuroscience and chemistry to food production. In addition, the project draws on the expertise and experience of researchers entrenched in studies of applied science, dementia and health-orientated food science. Indeed, the multidisciplinary approach which the project implements and endorses is a key factor in its development of dietary-based means of mitigating dementia and dementia-related diseases. Recently, LIPIDIET secured Numico – now a subsidiary of Danone – as a primary industrial partner under whose auspices diet-based products can be handled commercially.

The multidisciplinary approach – coupled with the fact that the project is part-funded through the 7th Framework of the European Commission – enables research to be problem-orientated: studies are not merely focused on the development of one product; instead, the project takes its place in a pool of other programmes and projects associated with identifying the molecular mechanisms that lead to cognitive decline. It is such sustainable approaches that underpin the future of dementia research.

