**NeuroFAST: the Potential Impact**

In accordance with General Objective 8 of the NeuroFAST project – 'To disseminate our understanding to the broader scientific community, to policy makers across Europe, and to the lay public', the consortium has sought to maximise the impact of NeuroFAST research through a range of dissemination and exploitation activities targeted at a spectrum of end-users and stakeholders. In relation to the original call text, we report that NeuroFAST has provided added value by building up the necessary critical mass across diverse fields of research encompassing epidemiology, human nutrition, psychiatry, human brain imaging, psychology, obesity, metabolism, neuroendocrinology, neuroanatomy and neurophysiology. Collectively we have strengthened European research capacity, evidenced by the large number of publications and dissemination activities, thereby providing sound scientific support to European public health policies. The European dimension has been an important aspect of the overall success of this project in which there has been much added value in cross-fertilizing ideas, sharing technologies and providing early stage scientists with sufficient training for a future strength in this area. "Determinants of food addiction" has been a major activity (see below) and risk factors important for substance abuse disorders (including alcohol) and eating disorders" have been explored. We have therefore added to knowledge that is important for developing a better understanding of addiction patterns and their potential adverse effects.

**IMPACT**:

The NeuroFAST project has had impact, or has potential for impact, at a number of different inter-related levels – conceptual, in clinical practice, and in informing public health policy. Examples are given below.

A major impact of the NeuroFAST project has been at the conceptual level in redressing the imbalance that existed relating to the use of the term "food addiction", and in particular in the discussion of this term and its applicability in the popular media, where the real evidence base is frequently overlooked in the drive for a high profile news story. The role of the consortium in critically evaluating the food addiction concept has been recognised and applauded in a variety of fora and by a range of stakeholders from national regulators to the food and drink industry and nutritional scientists. We specifically propose that the term "food addiction" is a misnomer, because evidence in humans to justify this term is scant – single nutrients and/or particular foods including snacks have <u>not</u> been shown to result in the development of addiction. Instead, we suggest that susceptible individuals can develop a behavioural addiction to eating. It will be important to define criteria for the proposed diagnosis of "eating addiction" and to pinpoint the overlap with the criteria which have already been delineated for "food addiction". The diagnosis "eating addiction" would have repercussions at many levels – for health care, for the food industry and for those involved in policy, all of whom share the responsibility to help individuals that suffer from this currently undefined disorder.

Furthermore, on a practical level, we have extended the evidence base showing that normal weight and even underweight individuals can fulfil the criteria for "food addiction", thus clearly demonstrating that this 'diagnosis' is not specific to obese individuals. There appears to be substantial overlap between "food addicted" individuals and individuals with a disordered eating behaviour as illustrated by the high rate of "food addiction" in patients with

anorexia nervosa. However, using the YFAS questionnaire for the identification of individuals with "food addiction", work in NeuroFAST has shown that such individuals can also be characterised through brain imaging studies, thereby validating the use of this questionnaire for diagnosis. We assume that substantial overlap exists to constructs commonly used for eating disorders (e.g. restrained eating, disinhibition). Ongoing work additionally shows that subjects who fulfil the criteria for "food addiction" also show higher stress levels.

In light of the dire therapeutic situation for obesity, we are witnessing an unfolding discussion on the relevance of addiction in this condition. If substances in food lead to addiction, pressure would mount to pursue structural prevention: social, economic and policy strategies to curtail obesity rates. On the other hand, if eating addiction is best conceptualized as a behavioral addiction, the affected individual is seemingly at fault, reducing this pressure. Irrespective of whether scientific evidence will justify use of the term food and/or eating addiction, most obese individuals have neither a food nor an eating addiction. Obesity frequently develops slowly over many years; only a slight energy surplus is required to in the longer term develop overweight. Genetic, neuroendocrine, physiological and environmental research has taught us that obesity is a complex disorder with many risk factors, each of which have small individual effects and interact in a complex manner. The notion of addiction as a major cause of obesity potentially entails endless and fruitless debates, when it is clearly not relevant to the great majority of cases of overweight and obesity. The danger is that prevention efforts based on a single, minor cause of obesity risk undermining a holistic strategy that aims to reduce weight gain. We need strategies for preventing obesity that do not overly depend on any particular etiology of obesity. Lessons can be learned from previous successful public health programs such as the large-scale immunization programs which have all but wiped out specific contagious diseases, and programs aimed at preventing traffic accident casualties. The food industry must contribute to obesity prevention irrespective of whether, and to what extent, addiction is involved.

Elsewhere in the project, the outcomes achieved prospectively in a large community sample of adolescents are in accordance with several important findings of cross-sectional studies and of studies with clinical samples. Female participants suffered from an eating disorder (ED) about ten times as often as male participants; furthermore, our data confirmed the period of adolescence as the time period associated with the highest risk for developing an ED. These findings imply the importance of targeted preventive interventions focussing specifically on this age group and gender. We also found life-time comorbidities of around 50% with substance use disorders (SUDs) in individuals with EDs and significant cross-sectional associations between bulimia nervosa and SUDs, which is again similar to findings obtained from studies with clinical samples. These outcomes emphasize that comorbid SUDs should receive special attention in the treatment of EDs, since they are highly prevalent comorbid conditions. Additionally, the high prevalence rates of core ED-symptoms further emphasize the need for prevention and early detection programmes. Our results considering stability rates of EDs further add to this point; in light of greater chronicity of threshold EDs and given that only about half of the individuals with EDs in our sample fully remit from the disorder, these programmes should receive greater societal attention and financial resources. The observed differential cross-sectional comorbidity patterns for anorexia nervosa and bulimia nervosa may also highlight the need for the development of specific interventions for different diagnostic groups of EDs. The obtained outcomes regarding temporal associations between EDs and SUDs moreover indicate a necessity to prevent incident depressive and anxiety disorders in individuals that have remitted from an ED or SUD, respectively.

The analysis for common and specific risk factors of EDs and SUDs identified a range of variable risk factors and fixed markers including the most potent risk factors for ED, SUD and comorbid ED+SUD. Compared with previous risk factor studies, the current analysis in a sample of adolescents and young adults therefore demonstrates complex pathways to onset of individual disorders (ED, SUD) as well as comorbid ED+SUD. It provides important information for factors to be targeted by universal, selective and indicated preventive interventions thus informing the development of future preventive approaches for these disorders. As for the comparison between community samples and clinical samples, studies addressing different comorbidities of eating disorders yielded highly inconsistent results due to major methodological differences. By using the same assessment instrument and applying the same case definitions for the most prevalent comorbid mental disorders in the comparison of a community-based sample and a clinical sample we tried to overcome some of the previous limitations. Overall, based on our comparison of a large, representative community sample and a clinical sample the pattern of results found demonstrates the large differences in both prevalence and comorbidity rates between the samples. Only some of the findings of this comparison are in accordance with previous results. The comparison demonstrates impressively that prevalence and comorbidity rates reported on the basis of clinical samples should therefore generally be considered with caution since they may reflect treatment specifications and referral practice rather than "true" epidemiological associations.

Workplace health initiatives around the world are growing in number and scope, as employers come to realize that addressing employee health & wellness is linked to increased productivity and reduced absenteeism, and that the returns on this strategic investment and overall health cost savings are high. Since many adults spend a substantial amount of their time at work and consume at least one meal at work each day, a healthy workplace environment is important, particularly as jobs become more sedentary. An increased prevalence of obesity among employees can have indirect economic consequences for employers, in terms of productivity through illness and absenteeism. The research in the workplace as part of NeuroFAST sought to provide an evidence base to influence health interventions aiming to promote work wellness. Influences on eating behaviour are complex, and particularly the role of stress on food intake and food choice is a challenging research area. However, the approach adopted in the NeuroFAST project has addressed both psychological and physiological aspects and has the potential to make recommendations about the management of stress for public health and policy practitioners.

We compared workplaces with and without the Healthy Working Lives (HWL) award, to identify whether this UK initiative at work is effectively (positively) influencing staff behaviour (eating and physical activity) and stress levels. Comparing workplaces with and without the award did not reveal any notable differences in eating behaviour or nutritional profile in the employees. Thus, the HWL initiative does not appear to influence energy intake, energy expenditure, energy balance or stress in the employees who participated in the NeuroFAST study. Indeed, employees in the workplace with a public health initiative had higher levels of stress than those working in alternative environment. If obesity and unhealthy behaviours are to be addressed in the workplace, evidence based intervention and robust evaluation will be required. Compared to individuals who work during the day, shift workers have been identified to be at greater risk of metabolic related disorders. Other factors such as protected break time for shift workers could be targeted to ensure better nutrition profile and less reliance on snack foods that are often nutrient poor.

## DISSEMINATION

Project concepts and outputs have been disseminated to a wide range of stakeholder groups using a range of contemporary media and strategies appropriate to the subject matter and the intended audience.

### *Website*

The NeuroFAST website was established in the first months of the project and incorporated materials related to the project aims and objectives and the consortium partners that were appropriate to visitors from all different stakeholder communities who might visit the site looking for scientific information and news in a digestible form. The intention was to maintain an active vibrant website conveying the breadth and scope of activity within the NeuroFAST project. The website was relaunched halfway through the duration of the project. Since then the focus has been on incorporating a steady flow of news-type material highlighting the dissemination activity of scientists within the consortium, and thereby drawing attention to the science behind the project and the research being performed. The focus has remained on material that will be accessible to a wide range of stakeholders from policy, the media, the industrial sector and the interested public, as well as members of the scientific community, with news items, web-links and podcasts designed to draw visitors into other parts of the site. News items were uploaded reporting project activities and dissemination events, mainly focussed on the publication of the consensus review, supporting its message to the scientific community (who might access the article from a conventional science database) with materials (published paper, video, podcast, press coverage etc) appropriate to a wide range of stakeholders in the wider community.

### *Briefing notes/reviews*

Briefing notes have been prepared and made available for download from the NeuroFAST website. An introductory briefing document outlining the project was backed up by four Research Briefs, all available for reading and download from the website. Three of these covered areas of major scientific interest within the project and were intended as scientific summaries and position statements representing the position of the NeuroFAST consortium on key areas of scientific debate that were particularly relevant to the project. These documents were entitled ‘The biology behind “food addiction”’, ‘Food addiction and the psychiatric classification of addiction’, and ‘Can stress make you fat?’. A fourth briefing document presented an overview of a public engagement event developed by the NeuroFAST consortium and was entitled ‘Public engagement with science’. These documents were written to be accessible to policy colleagues, the media, interested members of the public, and other stakeholders.

### *Conference presentations*

Consortium scientists have presented research findings at a wide range of scientific congresses in the topic areas of physiology, psychology, psychiatry, obesity, feeding behaviour and public health, amongst others. Many of these presentations, oral and poster, have been accompanied by press releases, review articles and podcasts, thereby expanding the reach of the project and its research beyond the immediate audience. The consensus position of the consortium on ‘food addiction’ has also been the topic of a number of presentations to diverse audiences.

***Public engagement***
A wide range of public engagement activities have been undertaken by the consortium throughout the lifetime of the project, including participation in major 'set piece' events such as the International Science Festivals in Gothenburg and Edinburgh, the Annual British Science Festival, and the European Researcher Nights. Project scientists have been interviewed for the print, broadcast and online media, with material carried in the popular press (including a detailed report on `food addiction´ in the prestigious German newspaper *Frankfurter Allgemeine Zeitung*) and in the Spanish Newspaper "El Pais", on radio and television, and in online for a such as CommNet, MedicalXpress and EC 'top news'. Other examples include an article on stress and obesity in Sceptic magazine (UK), and a MOOCs (Massive Open Online Course) run by the University of Edinburgh and the University of Aberdeen that use food addiction as a debating point for course learners.

***Policy engagement***
High level engagement with policy makers and advisors and key stakeholder groups was achieved when the first consensus statements of the consortium related to food addiction were presented to the EU Platform for Action on Diet, Physical Activity and Health and the High Level Group of Member States on Nutrition and Physical Activity in February 2013. It is hoped that the NeuroFAST project, along with the FP7 projects Full4Health, SATIN and Nudge-it, will be invited back to these meetings to continue the engagement with these important fora. The first step in the process of re-engagement will be the production of a 'highlights' briefing document communicating key outputs and concepts to gauge interest amongst the programmers of these meetings.

***Consensus review on food addiction and eating addiction***
In the final year of the project a consensus review on food addiction was authored by consortium members and published in a prestigious review journal with the specific intention of engaging with a wide range of stakeholders from scientific, healthcare, policy, and industry communities, and with the wider public throughout Europe and internationally. The review was intended to disseminate key messages originating from the NeuroFAST project, and was promoted through a range of print and broadcast media, online resources, and face-to-face interactions with relevant groups and individuals. A wide range of promotional activities were planned around the release of the review article on-line, with the article itself and supporting material (video, podcast etc) available for download on the NeuroFAST website. There were co-ordinated press releases across Europe, which spawned interviews with print media, radio and television, resulting in widespread coverage. The review paper generated invitations to talk at a number of meetings across Europe including The European Food Information Council Scientific Advisory Board, the European Federation of the Associations of Dieticians (DIETS-EFAD), and a public meeting of the Food Safety Authority of Ireland. This consensus paper was only possible due to prior efforts of the group to address the implications of research in their fields; the respective articles were published within a special issue of *Obesity Facts* titled "NeuroFAST – the Integrated Neurobiology of Food Intake, Addiction and Stress".

**EXPLOITATION**

It is still early to fully realise the extent to which the results from our project will be exploited. Much of our "product" is new knowledge, and exploitation of this knowledge will be likely to inform policy and practice, public understanding of science, and, in the longer

term, design and composition of foods, drinks and diets, and drug development and target rationalisation. Examples of some of these routes to exploitation are detailed below.

***Concepts***

As already mentioned, we believe that the NeuroFAST consensus on "Food Addiction" has the potential to be the catalyst for an important shift in the way that the concept is considered and discussed. Our dissemination effort in this direction has gone some way to countering the sensationalist headlines that are all too frequently generated from the 'food addiction' concepts, with a more rational, balanced perspective being picked up on by the popular media. Thus, output from NeuroFAST has already been exploited for the benefit of public understanding of science, countering the unhelpful message that could take hold that food addiction somehow explains the obesity epidemic, thereby rendering the individual powerless to influence their own condition. Further opportunities to promote this more balanced perspective and the concept of 'eating addiction' as opposed to 'food addiction' are likely to emerge over the coming months and years. The NeuroFAST consortium will continue to actively engage with these opportunities to deliver a more balanced assessment of the evidence base in this area, whilst also pursuing opportunities for further research to convert the 'eating addiction' concept into a diagnosable condition of clinical relevance.

***Clinical practice***

Our epidemiological studies identified both common and specific risk factors of EDs, SUDs and comorbid ED+SUD. Outputs suggest that interventions should be more targeted in terms of age group and gender, and that comorbid SUDs and EDs should receive special attention. These results provide important information for factors to be targeted by universal, selective and indicated preventive interventions thus informing the development of future preventive approaches to be developed by both scientists and policy makers for these disorders.

***Public health policy***

Our "stress in the workplace" studies have shown that different individuals respond differently to the same stressful situation in terms of their dietary habits and body weight. We have only just completed this study but expect the work to receive considerable attention by relevant stakeholders including employers and those involved in policy. Public health policies such as those applied to the workplace need to be effective, based on an evidence foundation, and need to be evaluated for effect. If current initiatives do not produce any measurable benefit, we need to understand why this is, and what we should do instead. Consequently, studies such as those conducted in the NeuroFAST project have a real potential to inform the debate surrounding public health policy.

***Drug targets and patenting***

The outcomes achieved in relation to Objectives 11.1 'To determine whether the opioid receptors are required for the rewarding properties of food' and 11.2. 'To investigate the biochemical basis of the interaction between the ghrelin system with the different opioid-receptor subtypes and the relationship of the later to food preference and the motivation to eat' led to two important findings:

1) that kappa opioid receptor subtype is a suitable drug target for the treatment of obesity and some associated co-morbidities such as NAFLD and NASH

2) that the ghrelin system influences energy homeostasis at central level via an energy sensor driven pathway involving p53/sirt-1/AMPK.

These findings attracted the interest of the Technology Transfer Division at Beneficiary 9 and led to the development of two patents. One is already filed ('*p53 as drug target for the*

*treatment of obesity and its comorbidities*'/ REF P201130250-SPAIN). As follow up of this patent we conducted preclinical studies showing that this was a feasible approach and have a partner (INNOPHARMA) which is carrying out studies related to the development of more selective compounds and oral formulations before translation/transference to the clinic. In addition we have another patent '*KOR-antagonists in the treatment of obesity and its comorbidities*' whose draft is currently under consultation with the Legal Office of Beneficiary 9, and where there is optimism from data generated during NeuroFAST showing that the KOR are involved in the effects exerted at central level by several relevant signals (ghrelin, MCH, nicotine) involved in energy homeostasis as well as by our unpublished observations (see fourth period report) showing that it prevents diet-induced NAFLD/NASH.