CSA JPI HDHL 2.0

Evaluation of Joint Funding Actions

Nutrition and Cognitive Function (NutriCog)

Content

1 Introduction and aims

Monitoring and evaluating of JPI HDHL activities is highly important to measure the success, concrete outcomes and impact of the JPI HDHL and to allow for continuous improvement and development of this initiative. Therefore, these activities are an integral part of the work plan of the current Coordination and Support Action (JPI HDHL CSA 2.0).

The evaluation activities continuously performed by JPI HDHL include:

- Monitoring and evaluation of the processes and general performance of JPI HDHL → Report on the third and fourth Process evaluation of JPI HDHL (CSA Deliverable D6.1, D6.4)
- Evaluation of the funding activities of JPI HDHL → Report on the evaluation of JPI HDHL funding activities (CSA Deliverable D6.2, the present report)
- Monitoring and evaluation the activities of JPI HDHL not related to funding → Report on the evaluation on the progress of the alignment activities (CSA Deliverable D6.3)
- Overall evaluation of the impact of JPI HDHL → Report on the evaluation of the impact of JPI HDHL (CSA Deliverable D6.5)

These tailored activities focus on different aspects of JPI HDHL presented in the consecutive published Implementation Plans (IP) and will result in publicly available reports like this one.

The main aim of this report is to evaluate the monitoring data of the funded research in JPI HDHL in relation to the respective aim of the call and the IP and to analyse the output, outcomes and impact of JPI HDHL funding activities (both on call and project level). The results of the evaluations will allow the fine-tuning, refining and planning of new activities for the following IP to reach the expectations of all stakeholders and fulfill the JPI HDHL objectives. The evaluation will also assist in raising awareness for the activities performed under the umbrella of JPI HDHL and provides the basis for the communication and dissemination of JPI achievements.

2 Approach for the evaluation of the JFA

The evaluation is based on comparison of the objectives of the IPs and the outputs/outcomes of the different funding activities of the JPI HDHL. In addition, the Scientific Advisory Board (SAB) and Stakeholder Advisory Board (SHAB) of the JPI HDHL have been involved in the evaluation process. The evaluation of the Joint Funding Actions builds on the related work packages in the ERA-Net ERA-HDHL, in particular WP 7, dealing with monitoring and communication of the additional transnational JFAs and their results.

The present report includes evaluations of all JFAs implemented by the JPI HDHL in 2015 and earlier:

- Determinants of Diet and Physical Activity Knowledge Hub (DEDIPAC KH, 2013)
- European Nutritional Phenotype Assessment and Data Sharing Initiative (ENPADASI, 2014)
- Biomarkers for Nutrition and Health (BioNH, 2014)
- Food Processing for Health (FP4H, 2014)
- Malnutrition in the Elderly (MaNuEl, 2015)
- Intestinal Microbiomics (IM, 2015)
- Nutrition and Cognitive Function (NutriCog, 2015)

2.1 Methods

For this report a 'Framework for the evaluation of JPI HDHL joint funding activities' (see Annex) has been developed by the task leader and agreed with the other involved CSA partners.

In a first step, relevant indicators have been collected and defined (see chapter **2.2 Indicators** for details). Based on these indicators the required data from the funded projects have been collected systematically in form of project reports and oral presentations at the project symposia (see chapter **2.3 Monitoring** for details). If necessary, further questions were addressed to the coordinators of the research consortia. In parallel, other necessary data and information (call documents, call statistics, etc.) have been collected from the respective Call Secretariats. In addition, the success and impact of funded projects has been assessed by experts (previous or former SAB and SHAB members) based on final project reports and symposia. For the experts' assessment a specific short evaluation questionnaire, based on the elaborated indicators, has been developed. This template asked the respective expert for a short written assessment of the funded projects based on 3-4 leading questions after the attendance of the final symposium and/or reading of the final report.

The actual evaluation has then been performed by the task leader by analysing the different data available following the evaluation framework and afterwards agreed with the other involved CSA partners.

2.2 Indicators

The indicators used in this evaluation report have been developed in a designated task force by several CSA partners in a separate task (Subtask 6.1.1 Definition of performance indicators) within the CSA JPI HDHL 2.0. Two different types of indicators on have been defined, general and specific indicators, comprising outcome, output and impact level:

(1) General indicators for all JFAs

To enable the comparison between joint funding actions (at least with JFAs using the same funding instrument) a set of general indicators for all JPI HDHL JFAs has been developed. These general indicators can be grouped into six overarching categories comprising several more specific indicators: Alignment of national funding, Involvement of national scientific communities, Collaboration, Capacity Building, Data and Knowledge Sharing, and Impact.

(2) Specific indicators for each respective JFA

Since the aims and objectives differ greatly between the various JFAs, the definition of specific indicators was necessary to evaluate the success of a JFA in itself and not only in comparison to other JFAs. To evaluate the success of each JFA separately, specific indicators following from the corresponding Strategic Research Agenda and IP as well as the call text as of each JFA have been developed.

2.3 Project Monitoring

The comprehensive monitoring of the output and outcomes of the running and finished funded projects builds the basis for the performed evaluations. The systematic and structured collection of data from all funded projects has mainly been organized within a designated work package of the ERA-Net ERA-HDHL (WP7). The monitoring activities within ERA-HDHL comprised the monitoring of the

progress and the results of the research projects of the non cofunded JFAs implemented as part of ERA-HDHL, as well as the previous calls implemented through the IP 2014-2015.

Data from all funded projects have been collected in accordance to the indicators defined in WP6 of the CSA JPI HDHL 2.0. This comprises data both on call and project level:

(1) Call level:

For each Joint Funding Action, the funding organisation responsible for the Joint Call Secretariat (JCS) of a JFA was in charge of the statistical analysis of the call results based on the elaborated indicators (see 2.2). In particular the geographic distribution of the scientists applying to the call, the discipline and the type of organisation, the amount of funding requested per partner/consortium and the transnational cooperation has been analysed.

(2) Project level:

The follow-up of funded projects was taken care of by the respective JCS. For each funded project, annual scientific progress reports and one final report have been collected.[1] Project coordinators were asked to submit the respective scientific reports for the joint project, on behalf of the whole consortium to the respective JCS based on a pre-defined template including the specific indicators (see 2.2). Since 2019, these reports are collected using an online submission tool.

For the calls launched 2015 and later, the progress of ongoing JFAs has also been monitored by two status symposia organized by JPI HDHL. One status symposium has been held during the runtime of the projects (midterm symposium) and one just before the project is about to finish (final symposium). The main purpose of these symposia is to provide the JCS, the Call Steering Committee and members of the former Scientific Evaluation Committee (SEC) as well as representatives from SAB and SHAB with an update on the progress of the research projects. The presentations by the project coordinators and partners PIs are followed by a plenary discussion with questions from the audience.

For most of the earlier calls (DEDIPAC, ENPADASI, FoodBall/BioNH, MaNuEl) a final conference has been organized by the consortia itself without participation of SAB, SHAB or former reviewers.

[1] The data collection for the specific indicators as part of the final report was not possible for the first three JFAs (DEDIPAC, ENPADASI & MaNuEl) since the specific indicators have only be defined after the projects where finished. The project coordinators have been contacted retrospectively to answer those indicators.

3 JPI HDHL Joint Funding Action: Nutrition and Cognitive Function (NutriCog)

3.1 Aim of the call

In the Strategic Research Agenda (SRA) of the JPI HDHL the importance to understand the qualitative and quantitative links between diet, nutritional phenotype and risk factors for diet-related chronic diseases is described. The Implementation Plan 2014-2015 listed "nutrition and cognitive function" as one future priority topic. It was highlighted that "recent advances in non-invasive technologies like functional magnetic resonance imaging gives **new opportunities in assessing the effects of diet or diet components on processes in the brain** that are crucial for regulation of energy balance and metabolic homeostasis. **Determining how dietary factors affect brain, cognitive and metabolic function and performance in various life stages is a crucial element in defining the diet-disease relationship**. In particular related to chronic neurodegenerative diseases this is most important for understanding on how diet acts upon cognitive decline."

The Joint Action "Nutrition and Cognitive Function" (NutriCog) aimed to promote research activities that address the interrelation of diet and cognitive function. This knowledge should be used as the basis for dietary preventive strategies and recommendations to guide individuals and populations towards health promoting dietary habits.

The main objective of the NutriCog call was to support ambitious, innovative and transnational collaborative research projects addressing important questions relating to the interplay between nutrition and cognitive function, such as perception, reasoning, thinking, memory and/or cognitive processes. The influence of dietary patterns on cognitive functions and *vice versa* the effects of Central Nervous System nutrient signaling and cognitive processes on food intake, dietary patterns and eating behavior were relevant for this call, concentrating on prevention rather than progression of disease.

3.2 Peer-review Procedure and Results

The NutriCog Joint transnational call was launched on 30th of March, 2015 and was coordinated by the Call Secretariat DLR-PT (Project Management Agency in the German Aerospace Center). The implementation process was organized in a one-stage procedure consisting of the written evaluation and a peer review panel (PRP) meeting.

Deadline for submission of the full proposal was the 8th of June 2015. 39 full proposals were submitted of which 35 passed the eligibility check. Each full proposal was evaluated on a written basis by at least 3 international experts according to their expertise in the substantive area of the proposed research. Evaluation criteria were:

1. relevance to the aim(s) of the call,
2. scientific quality of the proposal (innovation potential, methodology),
3. feasibility of the project,
4. quality of the transnational collaboration (added value of the research consortium, on both scientific and transnational levels, multidisciplinary approach),
5. international competitiveness of participating research groups in the field(s) of the proposal and
6. translational impact of the expected results for future clinical and other health relevant applications.

In total 18 reviewers participated in the written review assessment. During the PRP meeting on the 9th and 10th of September 2015, the full proposals and the written assessments were discussed by 15 out of the 18 reviewers. The other three experts had been invited as external reviewers only, giving written evaluations on specific aspects in certain proposals. A ranking list was compiled and funding

recommendations were made to be considered for the final funding decision of the Call Steering Committee (CSC). 15 full-proposals were recommended for funding by the evaluation panel split into two categories of high (8 proposals) and medium (7 proposals) priority.

On the 3rd of November 2015, the CSC agreed on the final funding decision to fund 5 consortia:

1. **AMBROSIAC** – A menu for brain responses opposing stress-induced alterations in cognition
2. **iCASE** – Individualized cognitive, affective and social enhancement in nutritional interventions for longevity and well-being
3. **D-CogPlast** – Identification of dietary modulators of cognitive ageing and brain plasticity and proof of concept of efficacy for preventing/reversing cognitive decline
4. **MiTyrAge** –Targeting the mitochondria-tyr-kinase axis to prevent age-associated neuronal decline
5. **SELENIUS** – Selenium in early life to enhance neurodevelopment in unfavourable settings

The **AMBROSIAC** consortium aimed at the investigation of interrelations between diet, stress and cognition across the lifespan, using both preclinical and clinical approaches. The consortium was coordinated by John Cryan (Ireland). The consortium started in April 2016 and the runtime finished end of March 2020 after having received a 1-year runtime extension.

The partners of the **iCASE** consortium wanted to investigate the role of food supplements affecting serotonin levels and examine effects on cognitive ageing processes, in particular of social and affective cognition. The consortium was coordinated by Peter Kirsch (Germany). The consortium started in April 2016 and the runtime finished end of March 2020 after having received a 1-year runtime extension.

The aim of **D-CogPlast** was to examine the role of dietary bioactives affecting brain plasticity for cognitive ageing processes. Furthermore, different age groups were studied to investigate a sensitive population response to dietary interventions and exposure to stress and genetic predispositions were considered. The consortium was coordinated by Sandrine Thuret (UK). The consortium started in April 2016 and the last partner finished its subproject end of April 2021.

The **MiTyrAge** consortium aimed to investigate the role of dietary components for mitochondrial function and cognitive decline with age. The consortium was coordinated by Natascia Ventura (Germany). The consortium started in May 2016 and the runtime finished end of December 2019 after having received a 6 to 8-month runtime extension.

The partners of the **SELENIUS** consortium wanted to investigate the role of selenium for brain plasticity in relation to other trace elements and nutrients. Oxidative stress and inflammation were studied as key processes connecting diet, peripheral tissues and brain development. The consortium was coordinated by Luisa Minghetti (Italy). The consortium started in April 2016 and the runtime finished end of March 2020 after having received a 6 months runtime extension.

3.3 Evaluation Results

3.3.1 General Indicators

3.3.1.1 Alignment of national funding

12 funding organisations from 10 JPI HDHL partner countries participated in the call. The total *in cash* budget committed by the participating funding organisations for the NutriCog call was 9.2 Mio €.

3.3.1.2 Involvement of national scientific communities

3.3.1.2.1 Participation of national scientific communities

In response to the call, 39 full-proposals were submitted involving 177 PIs (principle investigators, leaders of subprojects). Based on the peer review process the decision was made to fund five consortia (**AMBROSIAC, iCASE, D-CogPlast, MiTyrAge and SELENIUS**) including 26 PIs from 10 JPI HDHL partner countries. 30.7 % of the PIs were female and 69.2 % male, while 60% of the project coordinators were female and 40% male. A list of all NutriCog partners in the funded projects can be found in Annex 1. The division of the PIs per country applying and accepted for funding respectively are depicted in fig.1. With the exception of Belgium, each country participating in the call had at least one PI in the funded consortia. Two funding organizations (FWO-Belgium and ISCIII-Spain), were not represented in the funded consortia.

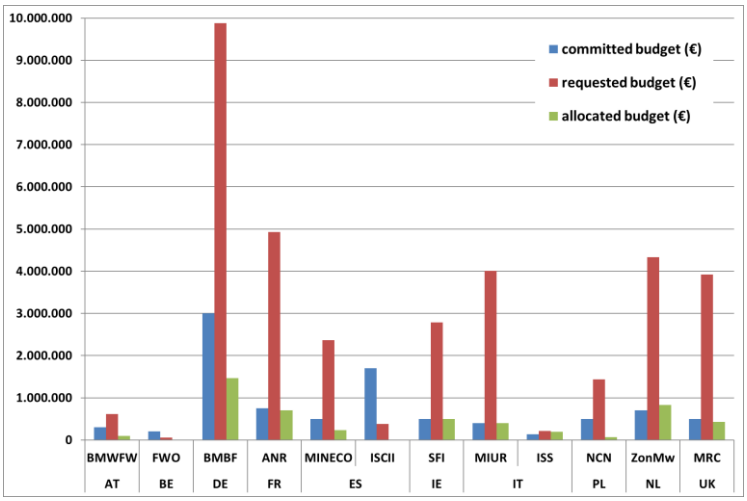

Figure 1: Numbers of PIs per country in the implementation of NutriCog

3.3.1.2.2 Distribution of national funding

Like all previous joint funding actions implemented by the JPI HDHL, the funding of NutriCog was organized as a „virtual common pot“ meaning that each country and/or funding organization finances the activities of their respective national scientists.

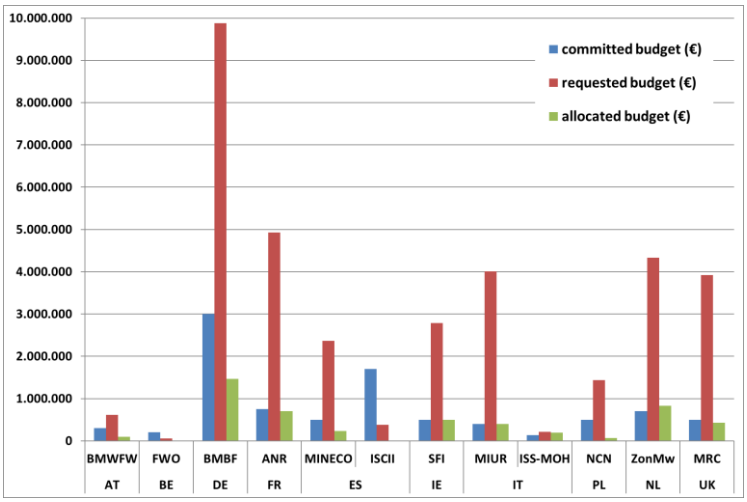

Figure 2: Committed, requested and allocated funding budget of NutriCog consortia, distributed by countries.

The total requested budget for all full proposals submitted for the NutriCog call was 34.9 Mio € *in cash* resulting in an oversubscription factor of 3.8. As shown in fig. 2 the requested budget of 8 countries was substantially higher compared to the committed budget reflecting the large interest of the

research community in the released call. For the five funded consortia, the allocated budget was 4.9 Mio € which is 53.6 % of the initially committed budget of 9.2 Mio €. The largest amount of allocated *in cash* money was available for applicants from Germany.

Table 1 gives an overview of the final composition of the funded consortia. 3 to 6 countries are involved in the research and the budget differed between 0.8 to 1.9 Mio € depending mostly on the size of the consortium.

Table 1: Composition of funded consortia and received budget

Name of consortium	Number of PIs	Involved countries	Budget
AMBROSIAC	6	6 (Ireland, France, Germany, Italy, The Netherlands, United Kingdom)	1.9 Mio. €
iCASE	4	3 (Germany, Spain, The Netherlands)	1.0 Mio €
D-CogPlast	6	5 (United Kingdom, Austria, France, The Netherlands, Spain)	1.0 Mio €
MiTyrAge	4	3 (Germany, Italy, Spain)	0.8 Mio €
SELENIUS	6	5 (Italy, France, Germany, Poland, United Kingdom)	1.0 Mio €

In total, 24 academic research institutions, 4 small and medium sized enterprises (from Spain and the Netherlands) and 1 large industry partner (from Germany) were involved in the five funded consortia.

3.3.1.3 Success of implementing collaboration

The consortia worked under the umbrella of the NutriCog call; however, the studies were conducted independently from each other with no planned collaboration between them. The consortia, with the exception of **iCASE,** collaborated either with industrial partners or other JPI HDHL or European projects.

AMBROSIAC initiated right from the beginning of their runtime the collaboration with Nutricia Danone (The Netherlands) to look at dietary interventions for improving health. Furthermore, the consortium collaborated with the JPI HDHL projects DEDIPAC, ENPADASI, the ERA-HDHL project HEALTHMARK as well as the Irish projects INFANTMET, SMARTFOOD, and TODDLERFOOD funded by DAFM (Department of Agriculture, Food & Marine, Ireland) and the German Rhineland Study. The consortium collaborated also with the EC funded projects FibeBiotics and MyNewGut project (FP7 Knowledge Based Bio-Economy European Union).

The **D-CogPlast** consortium collaborated with the JPI HDHL projects FoodBall (Food Biomarker Alliance) from the JPI HDHL Biomarker 2014 call, with MaPLE (Gut and blood microbiomics for studying the effect of a polyphenol-rich dietary pattern on intestinal permeability in the elderly) from the JPI HDHL Intestinal Microbiomics 2015 call and with DiGuMet (Diet x gut microbiome-based metabotypes to determine cardio-metabolic risk and tailor intervention strategies for improved health) from the JPI HDHL INTIMIC cofunded call “Interrelation of the Intestinal Microbiome, Diet and Health” (IM 2017). A further collaboration with COST POSITIVe action (FA 1403) about “Interindividual variation in response to consumption of plant food bioactives and determinants involved” was initiated during the runtime of the consortium.

A new collaboration with the industrial partner Magnitude Bioscience was initiated by the **MiTyrAge** consortium working on automated *C. elegans* neurobehavioral recording throughout the lifespan.

Furthermore, **SELENIUS** started collaborating with the HDHL-INTIMIC Knowledge Platform on Food, Diet, Intestinal Microbiomics and Human Health towards the end of their project runtime.

The success of the established collaborations on transnational and scientific level is assessed in the following subchapters.

3.3.1.3.1 Interdisciplinary collaboration

The 5 funded consortia covered various scientific disciplines like neuroscience, biochemistry, nutrition, cell and molecular biology, neuropathology and some more. The expertise of each consortium is listed in table 2.

Table 2: List of disciplines of NutriCog funded consortia

Name of consortium	List of disciplines
AMBROSIAC	animal science, biochemistry, food metabolomics, food science, microbiology, microbiomics, molecular biology, neurosciences, nutriceutics, nutritional sciences
iCASE	genetics, neurosciences, nutritional sciences, psychology
D-CogPlast	nutrition, cognition, ageing, brain plasticity, metabolomics, lipidomics, *in vitro* parabiosis
MiTyrAge	cell biology, neuroscience, physiology, biogerontology, geriatrics, molecular and cellular neurology, neuropathology, nutritional sciences
SELENIUS	biochemistry, cell biology, molecular biology, neurosciences, nutritional sciences

3.3.1.3.2 Transnational collaboration

The collaboration within the single work packages (WP) differed between the 5 funded consortia, which is depicted in Figures 3 to 7. **AMBROSIAC**, **D-CogPlast** and **SELENIUS** divided the tasks in their work packages between the partners of the consortium. In contrast to this, the each partner in the **iCASE** and **MiTyrAge** consortium coordinated one WP alone. Reasons for this could be the size of the consortia since both consisted of 4 partners and the very specific expertise of each partner.

Ireland as the coordinator of **AMBROSIAC** was involved in all three work packages as well as the French partner. The German partner took over WP 1 (human studies investigating the nutrition-dependent increased susceptibility for stress-induced cognitive deficits in memory and executive functioning from adulthood to old age) and WP 2 (human nutritional intervention studies), while the Dutch partner was only involved in WP2. The UK partner worked in WP3 (preclinical studies aiming at deciphering the molecular mechanisms by which targeted nutritional interventions improve stress-induced vulnerabilities in cognition) together with 3 additional partners of the consortium (Fig. 3).

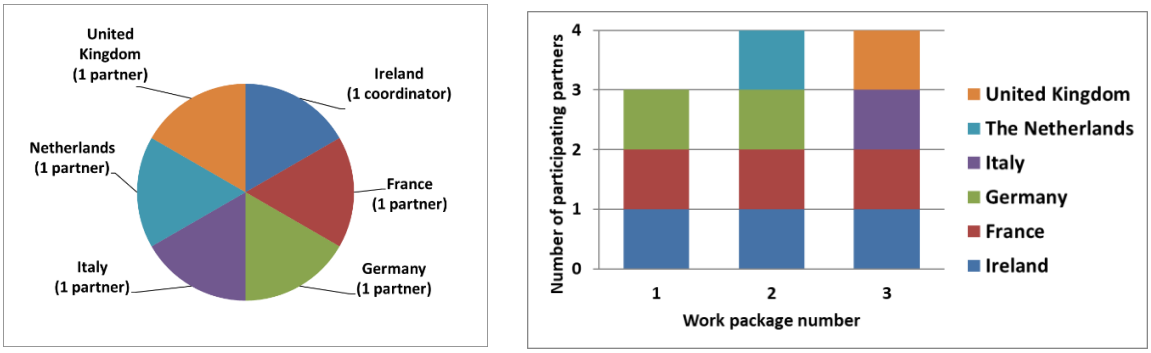

Figure 3: Transnational composition and number of participating partners per work package in the consortium AMBROSIAC

All partners of **iCASE** were involved in WP 1 (management and coordination), while the other work packages were each handled by only one partner of the consortium. The German coordinator took over WP2 (neural effects of acute and prolonged tryptophan intake on social cognition and emotional processing), while the other German partner was involved in WP 5 (prediction of social cognition by

nutrition habits and genetics/epigenetics of the 5-HT system in a demographic sample). The Dutch partner worked in WP3 (promoting social cognition in the elderly through tryptophan and probiotics: a tailored approach) and WP6 (dissemination). However, the Dutch partner withdrew his participation during the first year and the work was distributed between the other partners of the consortium. The Spanish partner took over WP4 (Tryptophan and probiotic supplements ingest and its effects on cognition and mood in young and elderly populations) (Fig. 4). WP3 and WP4 wanted to identify the effects of a tryptophan-supplement diet on social cognitive and emotional parameters in older and younger participants by combining an experimental and a proof of concept approach. Since both work packages were very similar regarding their scientific goals and the methodology applied, the consortium addressed all scientific questions of both work packages only in WP4 while WP3 could not be realized because of the withdrawal of the Dutch partner. The remaining partners of the consortium shared the work of WP6.

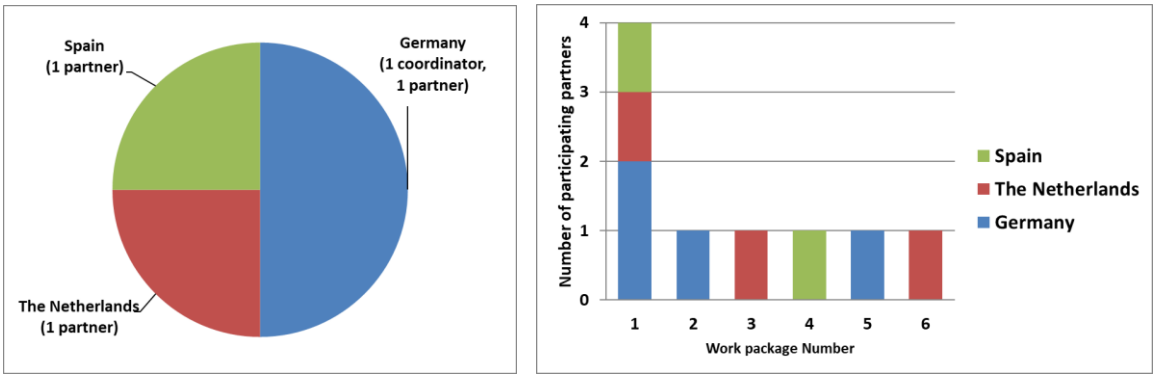

Figure 4: Transnational composition and number of participating partners per work package in the consortium iCASE

D-CogPlast consisted of 3 work packages in which always several partners were involved. WP1 (identification dietary/bioactive compounds associated with cognitive decline in French human cohort) was led by both French partners together with the Spanish partner. WP2 (investigate ability of identified dietary/bioactive compounds to modulate brain plasticity and neuronal integrity) was managed by 4 partners of the consortium (UK, France, The Netherlands, Austria), while WP3 (test efficacy of identified dietary bioactive compounds to prevent and/or reverse cognitive decline in a mouse model) were handled by the partners from Austria, The Netherlands and UK (Fig. 5).

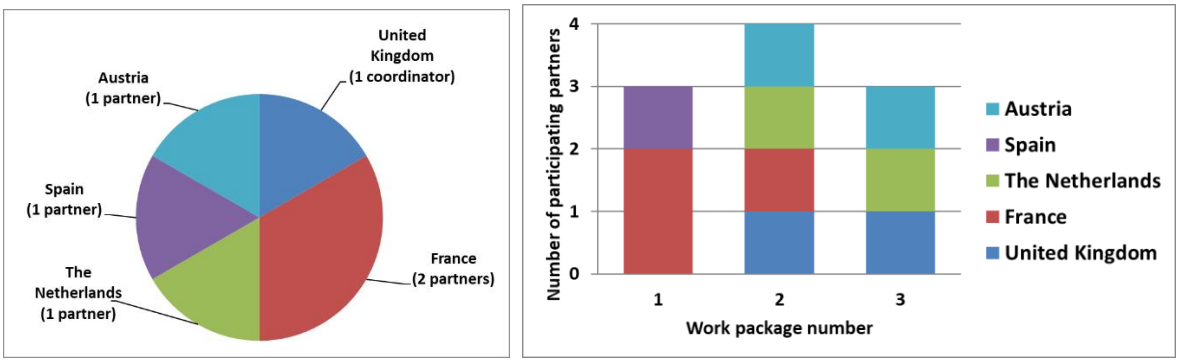

Figure 5: Transnational composition and number of participating partners per work package in the consortium D-CogPlast

Each partner in the **MiTyrAge** consortium took over the one work package on its own. No cooperation between the partners within the work packages was organized, however the formulated aims of the consortium pointed to a close collaboration between the single work packages. One German partner took over WP1 (human studies and in vitro analysis in primary neurons) while the German coordinator

worked on WP2 (C. elegans studies). The Italian partner took over WP3 (kinase studies) and the Spanish partner WP 4 (mice studies) (Fig. 6).

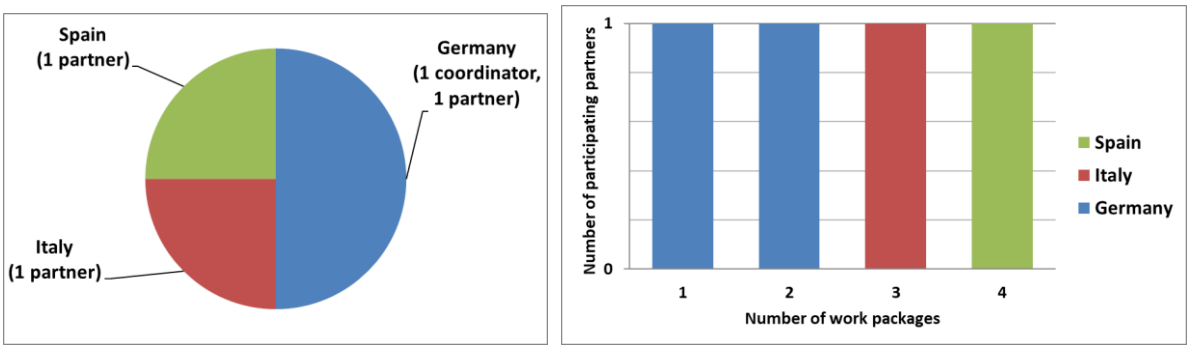

Figure 6: Transnational composition and number of participating partners per work package in the consortium MiTyrAge

The Italian coordinator was involved in all 5 work packages of the **SELENIUS** project while the other Italian partner was involved in 4 work packages with the exception of WP4. The French partner was involved in 4 work packages with the exception of WP3 (Assessment of molecular mechanisms involved in essential metal (Se and Zinc) and micronutrient effects by using in vitro models). The UK partner was involved in WP1 (Characterization of the behavioural phenotype of rats fed with a Se-deficient diet, with and without Pb exposure) and WP5 (Data integration) in which all partners of the consortium participated. Furthermore, the German partner worked in WP2 (Ex vivo characterization of multiple Se effects in rat models, focusing on synaptic plasticity and inflammation/oxidative stress in brain and adipose tissue), while the Polish partner was involved in WP4 (Epidemiological study: using data collected in a pre-existing EU mother-child cohort study to verify the relation among micronutrients, Pb exposure and cognitive development in children) (Fig. 7).

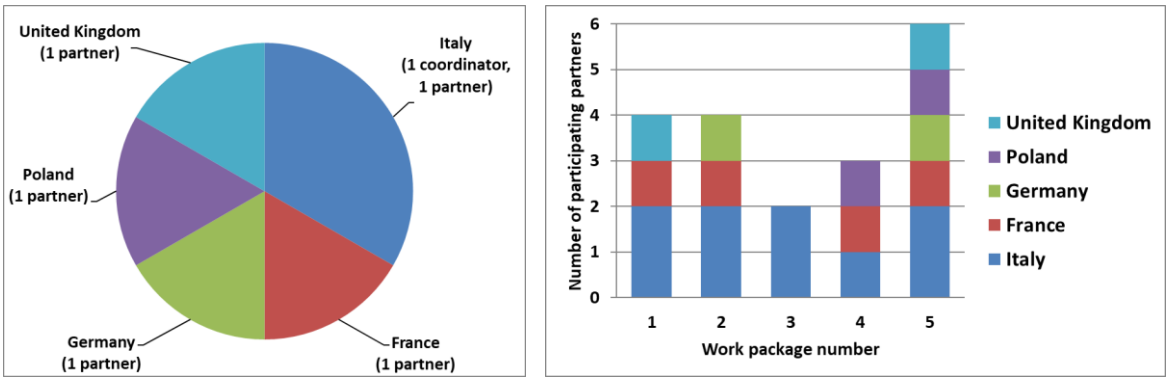

Figure 7: Transnational composition and number of participating partners per work package in the consortium SELENIUS

3.3.1.3.3 Intensity of Collaboration

The intensity of collaboration varied between the different consortia. The partners of **AMBROSIAC** met one time in Florence and once in Bordeaux. Additionally, 3 PhD students got the chance of a lab exchange between 1 week up to 1 year.

The **iCASE** consortium organized monthly (sometimes bimonthly) telephone meetings, about 10 online meetings regarding exchange and discussion of methods and met 4 times physically in Mannheim, Badajoz, Bonn and Brussels. A lab exchange was organized for 1 master student for 3 months and for 2 Postdocs for 3 and 9 months, respectively.

The **D-CogPlast** consortium organized its kick-off meeting in London, one meeting in Clermont-Ferrand as well as one meeting in Bordeaux and one in Barcelona during their runtime. Furthermore, 19 online meetings according to the work packages were organized additionally to one full consortium meeting

(online). One master student got the chance to work in another lab for 3 months and one master student for 1 year. Furthermore, 2 PhD students visited other labs for 6 month or 1 year, respectively.

The **MiTyrAge** consortium organized online meetings as often as necessary to coordinate experiments as well as material and data sharing. In addition, the last consortium meeting was organized as online event.

During the runtime of **SELENIUS** several meetings were organized including 3 meetings in Rome as well as 5 online meetings to discuss the results and preliminary results of the single work packages. A lab exchange was organized for one master student.

3.3.1.4 Success of scientific collaboration

3.3.1.4.1 Scientific Output

All consortia published their results during the runtime and afterwards; however, the published number per consortium differed between 3 up to 25 publications. Furthermore, the consortia presented their results orally or by posters to different targets groups like scientists, clinicians, general public, industry, policy makers and some more. The number of publications and presentations per consortium are depicted in table 3.

Table 3: Publication, oral and poster presentations of NutriCog funded consortia

Name of consortium	No. of publications	No. of oral presentations	No. of poster presentations	Target groups
AMBROSIAC	18	53	25	scientists, clinicians, general public,
iCASE	3 + 2 in preparation	3	4	scientists, general public
D-CogPlast	25 + 3 under review	23	15	scientists, policymakers, opinion-leaders, health care professionals, the food and beverage industry, consumer organizations, non-government organizations
MiTyrAge	6	4	2	scientists, policy makers, industry in the food chain market
SELENIUS	6	10	17	scientists, policy makers, clinicians, students

3.3.1.4.2 New funding obtained

AMBROSIAC, D-Cog-Plast and **MiTyrAge** obtained additional funding, while **iCase** and **SELENIUS** have not received further funding so far. Partners of the **AMBROSIAC** consortium received funding from European Horizon 2020 grant “Understanding causative mechanisms in co- and multimorbidities combining mental and non-mental disorders” (SC1-BHC-01-2019). **D-CogPlast** requested funding from ANR in France for the collaboration with the University Heart and Vascular Center Hamburg (Germany) to replicate the lipidomics signature of cognitive decline evidenced in a large German cohort of adults from the general population, the Hamburg City Health Study. Furthermore, the Dutch partner acquired funding from Alzheimer Nederland and has a JPND project proposal pending. The Spanish Partner is involved in the JPI Knowledge platform INTIMIC as well as EIT-Health Initiatives on Educational programs. Partner of the **MiTyrAge** consortium submitted a DFG grant to investigate molecular mechanisms underlying the protective effect of Lutein in a neurodevelopmental pathology which is

currently under revision. Furthermore, they received a 3 years FIRC (Future Institute Research Center) fellowship to investigate the significance of SRC-NRF2 connection in cancer.

3.3.1.5 Involvement in other JPI HDHL activities

The 5 consortia participated into different activities organized by the JPI HDHL. The amount of participation differed between 1 (**AMBROSIAC, MiTyrAge**) up to 7 activities (**D-CogPlast**). A detailed overview about the attendance of the JPI HDHL activities is listed in table 4.

Table 4: Participation of the NutriCog funded consortia on JPI HDHL activities

JPI HDHL activities	AMBROSIAC	iCASE	D-CogPlast	MiTyrAge	SELENIUS
ILSI workshop on "Nutrition for the ageing brain: functional aspects and mechanism"			x		
Intermediate JPI HDHL NutriCog symposium, September 2017	x	x	x	x	x
"Speech like Obama" workshop, 4th JPI HDHL conference Brussels, December 2017	x				
Final symposium 4th JPI HDHL conference Brussels, December 2017			x		
Networking meeting Knowledge Platform on Food, Diet, Intestinal Microbiomics and Human Health - November 2018 - Brussels					x
Fifth International JPI HDHL Conference, Brussels, 20th February 2019			x		
JPI HDHL Kick-Off meeting Knowlegde Plattform Intestinal Microbiomics -November 2019 - virtual meeting					x
Final JPI HDHL NutriCog symposium, Brussels, Belgium, 21st February 2019	x	x	x	x	x
JPI HDHL workshop on nutrition and Covid-19			x		
JPI HDHL training "Exploring pathways to impact training"			x		

3.3.1.6 Capacity Building

AMBROSIAC consortium generated 1 master student position, 4 PhD positions as well as 4 Postdoc positions and 10 research assistant positions. Furthermore, a one-day symposium on "The impact of diet and weight on mental health and psychological wellbeing" was organized in London.

The **iCASE** consortium generated several positions including 2 master students, 2 PhD students, 2 Postdocs and a half position for a medical technical assistant as well as several student research assistants, one bachelor student and one intern.

14 master students, 4 PhD students, 3 Postdocs and 1 research assistant were hired during the runtime of the **D-CogPlast** consortium. The consortium organized the course "DIET & HEALTH: Mediterranean and Nordic diet. Different dietary patterns in the promotion of healthy living habits" in Barcelona and "Innovating the Joy of Eating for Healthy Aging (INJOY). Furthermore, two workshops were arranged

about “Nutrition for the ageing brain” in Barcelona and in Copenhagen as well as one workshop about “Neural stem cells theory and practice” in London.

Two bachelor students, 4 master students, 3 Postdocs and 3 research assistants were hired for the **MiTyrAge** consortium.

The **SELENIUS** consortium generated 3 master student positions, 1 PhD and 1 Postdoc position and 2 research assistant positions.

No further training activities were organized either in the **MiTyrAge** or in the **SELENIUS** consortium.

3.3.1.7 Data and Knowledge Sharing

All consortia stated to work according to the FAIR (**F**indable, **A**ccessible, **I**nteroperable and/or **R**eusable) data principle. An overview of the used data sources in the different consortia can be found in table 5.

Table 5: Handling of data source in the NutriCog funded consortia

	AMBROSIAC	iCASE	D-CogPlast	MiTyrAge	SELENIUS
FAIR principles	yes	yes	yes	yes	yes
use of samples from existing cohorts and / or other epidemiological studies	yes	yes	yes	yes	yes
use of existing data or pooled data	yes	yes	yes	no	yes
creation of new or further development existing tools and/or infrastructure	no	yes	yes	yes	no
use of samples from bio-bank or/and other disease register sample collections	no	no	yes	no	no

AMBROSIAC used samples as well as pooled information from the Rhineland study to generate new data and support their findings. Exploitation of data from the project was performed by publications (newsletters, open access journals), presentations (conferences, forums, stakeholder meetings, public engagement events) and reports (commission, policy makers and key stakeholders). The data will be preserved securely beyond the project runtime for additional uses e.g. population health or compilation of statistics. While respecting a study participant’s wishes and autonomy at all times, data will be made available to other researchers where the research is of high societal relevance and impact and the study has been approved by an appropriate research ethics committee. Appropriate technical procedures were established to ensure that unauthorized access, loss or misuse of data does not occur.

The project of the **iCASE** consortium used samples from the Bonn Gene Brain Behavior Project (BGBBP) for their genetic analyses. The genetic data of the participants of BGBBP were correlated with new data collected ("Reading the Mind in the Eyes Test" (RMET) and moral tasks, questionnaires, and information about nutritional habits) in an online experiment performed by **iCASE**. Furthermore, a matlab based analysis pipeline for dietary data was developed which can be used by others in the future. The consortium supports data sharing initiatives and will make their data available after the funding period according to the guidelines for data sharing as developed by the German Psychological Association. *Functional magnetic resonance imaging* (FMRI) and genetic data will not be freely accessible due to data protection but statistical maps can be shared with other scientists upon request.

D-CogPlast consortium uses samples from the 3C-study from Bordeaux and Dijon. Samples from the 3C-Bordeaux cohort were used for the biomarker discovery quantification stage of the project whereas

samples from the 3C-Dijon cohort were used for the validation stage of the project. It is envisaged that the datasets will be available as appropriate 6 months after the end of the project and maintained for a period of at least 10 years. All data will be deposited as appropriate in the JPI HDHL Meta Database.

The **MiTyrAge** consortium used data from the existing SALIA cohort which were part of the analysis in WP1. The consortium developed a new *C. elegans* transgenic strain to investigate the role of mitochondrial stress response and Abl tyr kinase in Alzheimer's disease as well as new human cell lines to investigate the role of transcription factor NRF2 in Alzheimer's disease. In the first step, the consortium planned to make the data fully accessible inside the consortium in order to compare them with the ones obtained by studies performed in the different models. The second step will be accessibility to the scientific community through publication in international peer-reviewed scientific journals, as well as conference presentations and press releases. Access to the data obtained by silencing, genome wide association study (GWAS) and -omics approaches will be provided through a publicly accessible database.

The **SELENIUS** consortium used samples of the existing cohort REPRO_PL. In the samples collected during pregnancy and in cord blood the micronutrients (Se, Zn, Cu) were already assessed (in previous projects) or have been assessed within SELENIUS (heavy metals Hg and Pb) to achieve a sample size sufficient for further analysis. Additional analysis (inflammatory and oxidative markers) were performed on the stored samples from the REPRO_PL cohort. Furthermore, the data bases PHIME and REPRO_PL were compared including birth cohorts from three EU countries (Croatia, Slovenia and Poland). The coordinator's institution ISS is strongly committed to promoting open science and open data strategies and is a member and coordinator of an inter-institutional working group established within the Italian Ministry of Health Biomedical Research Library Network ("Bibliosan for Open Science"). The consortium exploited the cohort data made available through other collaborative networks like HDHL-INTIMIC Knowledge Platform on Food, Diet, Intestinal Microbiomics and Human Health, ALPHABET project (Early life programming of childhood health: a nutritional and epigenetic investigation of adiposity and bone, cardiometabolic, neurodevelopmental and respiratory health) under the ERA-Net on Biomarkers for Nutrition and Health or SEAFOODTOMORROW (H2020 project).

3.3.1.8 Impact

3.3.1.8.1 Contribution of the project to the coordination/harmonization of research activities

The **AMBROSIAC** consortium investigated the influence of nutrition on stress-induced cognitive deficits in memory and executive functioning from adulthood to old age; and the impact of a nutritional intervention on cognitive ability, stress vulnerability and stress perception. It further studied the molecular mechanisms by which targeted nutritional interventions can improve stress-induced vulnerabilities in cognition in preclinical models. The consortium combined findings from in vitro, preclinical and human intervention studies to investigate the impact of dietary intervention on cognition and stress and where they intersect. They further interrogated the role of the microbiome in their findings as well as changes in inflammatory, endocrine outputs and changes in gene expression. The researchers identified a role for histamine, cortisol, polyphenols and the microbiome in cognitive performance in healthy ageing. Due to their research topic the consortium did not contribute to standardisation of methods, but shared their obtained knowledge and data from the Rhineland study within this JPI project to allow progressive development of therapeutic options for healthy ageing.

The **iCASE** consortium investigated the influence of serotonin levels on cognitive aging processes, in particular with social and affective cognition. Using a multidisciplinary (psychology, genetics, neuroscience, nutrition) and translational approach, they mainly investigated whether tryptophan

supplementation positively influences moral judgements, the mentalization of social signals and how the mechanism of social behaviour is modulated by nutrition. Amongst others they could show that the essential amino acid tryptophan compensated for age-related social cognitive problems with recognizing positive emotions and that a tryptophan-rich diet protected against depression and increased social cognition. For harmonization of methods and data sharing the consortium created a matlab based analyses pipeline for dietary data which can also be used by others in the future.

The **D-CogPlast** consortium hypothesized that a combination of dietary bioactives could be capable of modulating cognition and brain plasticity, dietary modulation of brain plasticity and cognition starts in early life and occurs throughout life and exposure to stress/genetic predisposition are vulnerability factors to consider. The consortium identified several dietary bioactives that influence cognitive ageing in later life and specifically found a protective role of coffee, cocoa, fish and red wine. On the other hand, they found that caffeine could accelerate cognitive ageing. One potential way to trigger this outcome is through reducing proliferation of hippocampal neural progenitor cells. Additionally, they found that hippocampal neurogenesis was associated with future cognitive decline and dementia and that diet and physical exercise can modulate these neurogenic outcomes. A 16-lipid blood signature of accelerated cognitive decline was identified, that is mainly composed of phospholipids, including phospatidilycholines and phosphatidyletalomines. Due to the research topic of the consortium no standardisation of methods could be achieved. However, the consortium developed an analytic databank which was used for data harmonisation and could be also an interesting tool for sharing data and knowledge.

The **MiTyrAge** consortium specifically addressed whether selected nutrients, mainly polyphenols found in fruits and vegetables, regulate a mitochondria-tyr kinase crosstalk and can delay and/ or prevent the neuronal and cognitive decline observed during physiological and accelerated aging. Different model systems and approaches (like in-vitro mechanistic studies on mammalian cells, in vivo lifespan and neuronal behavioral assays in C. elegans and mice) were combined with epidemiological research to obtain new results on neuronal aging. By this, the consortium found a positive impact of dietary compounds associated with a Mediterranean diet on signs and symptoms of age-associated neuronal decline. So far, the consortium did not aim for harmonization of data, but the data will be shared through a publicly accessible database.

SELENIUS evaluated the specific role of selenium in relation to other nutrients and trace elements in favouring brain and behavioural plasticity by investigating the role of oxidative stress and inflammation as key processes. A multidisciplinary approach was adopted including ex vivo and in vitro models and transcriptomic, proteomic and metabolomic/lipidomic technology, measurement of oxidative stress and inflammatory pathways in different target organs and the experimental approach was combined with human cohort studies. Results from experimental studies and human cohort observations indicate a detrimental effect of suboptimal selenium intake on behavioural development and the adverse influence of early exposure to Pb in the absence of optimal selenium intake.

3.3.1.8.2 Contribution to Public Health

The results of all consortia are relevant for a wide range of different target groups. An overview about the specific target groups of each consortium is depicted in table 6.

Table 6: Target groups of the NutriCog funded consortia

Target groups	AMBROSIAC	iCASE	D-CogPlast	MiTyrAge	SELENIUS
Patients	**x**	**x**	**x**	**/**	**/**
Scientists (researchers, clinicians)	**x**	**x**	**x**	**x**	**x**
Consumers	**x**	**x**	**x**	**/**	**x**
Policy makers	**x**	**/**	**x**	**/**	**x**
Biomedical and food industry	**/**	**/**	**x**	**/**	**/**
Special aged groups	**adults, 60+ age**	**adults, 60+ age**	**60+ age**	**60+ age**	**children (up to 5 years), adults**

The **AMBROSIAC** consortium monitored both sexes in the epidemiological and human intervention studies and studied aspects of sex differences across the interventions performed by the consortia partners. The **iCASE** consortium used gender as a covariate but did no specific analysis on gender effects. **D-CogPlast** constructed a case-control study nested within the 3C-Bordeaux cohort including the matching of participants by age, gender, and education. Moreover, the impact of gender and APOEe4 genetics status on cognitive decline and fatty acid metabolism was explored in the study. **SELENIUS** considered the two sexes at different ages separately, either in experimental studies or cohort studies. The results of the **SELENIUS** consortium were intensively disseminated and it is expected that they may have an impact for the scientific community and more generally for the amelioration of health in the population

3.3.1.8.3 Activities towards innovation

Due to the preclinical setting of all consortia no new products or patents were developed. The obtained results are more important for the development and improvement of dietary guidelines and the application in future interventions.

The **AMBROSIAC** consortium collaborated with the industrial partner Nutricia Danone. Furthermore, the investigated levels of cortisol could be used in the future as biomarker to identify individuals that may be more susceptible to dietary interventions for the improvement of cognitive performance.

The **iCASE** consortium created a matlab based analyses pipeline for dietary data which can also be used by others in the future.

The **D-CogPlast** consortium has developed an analytical databank for chemicals and their metabolites representative of the food metabolome and/or associated with Mediterranean diet and for endogenous compounds that were recognized to be associated with cognitive decline. A further databank including biomarkers for intake of specific foods and scripts to automatically search matches with ions of metabolomics datasets was developed.

The **MiTyrAge** consortium developed a behavioral assay (for mice) to monitor neuronal alterations which can be used for neurotoxicology studies. Furthermore, the use of organotypic slice cultures to evaluate chronic effects of nutraceuticals on neuronal viability and neuronal resilience against toxic insults may represent an interesting research tool for the scientific community.

An animal model (rat) was developed by the **SELENIUS** consortium allowing to study the effect of selenium intake levels challenging the brain development and cognitive function without dramatically affecting reproduction and other vital functions.

3.3.1.8.4 New strategies/applications to reduce incidence of diet related chronic diseases

The **AMBROSIAC** consortium identified that short-chain fatty acids, Ω-3 fatty acid-rich and docosahexanoic acid (DHA) rich supplementation have anti-inflammatory properties reversing stress-induced deficits in behaviour and cognitive performance. The beneficial effect on cognitive behaviour, stress and weight reduction was furthermore associated with changes in specific gut bacteria composition. Identified individuals susceptible to cognitive decline or stress (e.g. those with higher cortisol levels) could be prophylactically treated with a diet positively modulating the microbiome resulting in reduced inflammatory markers, decreased cognitive impairments and thereby in healthier aging. Therefore, the results can contribute in the future to the research field in the development of dietary interventions that improve health outputs.

The results of **iCASE** demonstrate that regarding social cognition especially individuals with reduced tryptophan availability, genetic or other risk factors related to diminished serotonin availability in the brain, and elderly people can profit from tryptophan supplementation. This can be used in individualized diet or supplementation recommendations and might therefore augment and ameliorate existing interventions making an important step towards developing diets that are tailored to individual needs and help to promote well-being and healthy aging.

The **D-CogPlast** consortium showed that diet plays an important role in the trajectory of cognitive decline and dementia. A protective role of coffee, cocoa, fish, and red wine was found against accelerated cognitive decline in later life in an older population of males and females living in Bordeaux. Moreover, it was shown that diet and exercise can modulate neurogenesis outcomes long before the onset of cognitive decline and dementia and that altered hippocampal neurogenesis could signify the start of the pathological process, potentially representing a biomarker for cognitive decline and dementia. By this, the consortium has provided the scientific foundations for evidence-based recommendations for optimal nutrition/new nutritional targets that incorporate long-term health outcomes, focusing on cognitive ageing. It is expected that the bioactives identified and validated will lead to dietary interventions and recommendations for cognitive decline prevention and have societal impact across all ages.

The result of the **MiTyrAge** consortium indicate that flavonoids (like quercentin, abundant in the Mediterranean diet) mainly found in fruits and vegetables can help to delay age-associated neuronal decline and associated neuronal pathologies like Alzheimer's disease. In the long term, preventive strategies could be developed that may contribute to ameliorating the diet and lifestyle in order to prevent oxidative stress associated with aging and neurological decline in several pathologies. A further possibility would be new treatment options referring to senolytic treatment (quercentin in combination with dasatinib) of neurodegenerative disorders like Alzheimer's disease. However, validation in mammalian models and translational approaches have to be carried out before providing guidelines for clinicians for preventive/therapeutic opportunities with these nutraceuticals (mainly polyphenols).

The **SELENIUS** consortium provided evidence for a detrimental effect of suboptimal selenium intake on behavioural development and the adverse influence of early exposure to Pb in the absence of optimal selenium intake. The results also underlined the effects of dietary selenium on neuroinflammation and neuroplasticity. Therefore, these results could have an impact on the consumption habits, to ameliorate health of populations suffering from partial selenium deficiency and exposed to chemical stressors, in particular during pregnancy and in childhood. New nutritional recommendation could be developed for pregnancy to promote brain and behaviour development of the offspring.

3.3.1.9 Experts' assessment on general aspects and the specific aims of NutriCog

For the external evaluation of **AMBROSIAC, iCASE, D-CogPlast, MiTyrAge** and **SELENIUS** one expert from the Stakeholder Advisory Board (SHAB) and one expert from the Scientific Advisory Board (SAB) of JPI HDHL have answered general questions regarding the projects.

1. *Contribution of the JFA to fill relevant research gaps in the field*

Both experts agreed that the JFA contributed to fill some relevant research gaps in this area. All projects contributed significantly and relevantly to the knowledge of how and to what extent diet influences brain functions. However, both think that many significant gaps still remain.

2. *Contribution of the JFA to better coordination and collaboration*

From the experts view the JFA contributed to new collaborations and networks, with experts in neurology and brain getting engaged more with experts in nutrition and related fields resulting in enhanced progress and quality in this research field.

3. *(Future) Impact of JFA results for changes/improvement in the food and/or public health sector*

One expert stated, that at least some of the projects were too complex to be completed in the time scheduled and there seems to be much work left over. Nevertheless, both experts stated that the projects were likely to expand the knowledge of certain aspects of brain physiology and biochemistry, i.e. in basic science. It is not quite clear whether, when completed, the projects will contribute to development of new approaches of prevention and / or treatment, leading to genuine health gain. But the results and further research will help shape dietary recommendations further down the line, and induce changes in the public sector (prevention of cognitive decline through healthy lifestyle) in the near future.

Table 7: Impact of funded projects

Results of JFA have or will generate	End of the project	In the coming years
New suitable strategies	**expert 1**: Not at this stage. **expert 2**: /	**expert 1**: In some cases, possibly. **expert 2**: yes
Recommendations	**expert 1**: There may be recommendations at the end of some projects. **expert 2**: /	**expert 1**: There will almost certainly be recommendations flowing from some of these projects in subsequent years. **expert 2**: yes
Applications	**expert 1**: / **expert 2**: /	**expert 1**: / **expert 2**: yes
Products to reduce the incidence of chronic diseases	**expert 1**: Not at this stage. **expert 2**: /	**expert 1**: Some of these projects may lead to the production of products that might have places in the prevention and treatment of non-communicable disease. **expert 2**: yes
Induce changes/improvements in the food and drink sector	**expert 1**: Not immediately. **expert 2**: /	**expert 1**: Some guidance may emerge which could be of use and applicable within this sector. **expert 2**: /
Induce changes/improvements in the public sector	**expert 1**: No, certainly not immediately. **expert 2**: /	**expert 1**: Some of these projects may lead to the generation of new hypotheses, and further useful research may follow on from them. **expert 2**: /

4. *Any other comment on this funding measure:*

One expert stated that most of the projects appear likely to provide useful results in the research area, and to that limited extent the research outcomes appear to justify the expenditure on them. One expert was quite impressed by the high standards of the demonstrated work including the formulation of hypotheses, study design, the used methods and the way of carrying these out. It was also mentioned that one project was rather weaker in comparison to the other projects.

5. *Did the project generate a substantial progress to unravel the links between dietary factors and cognitive function?*
6. *Any other comments on the projects*

One expert mentioned that these projects did achieve small steps in this direction, and they appear likely to be able to make some useful justifiable statements to clarify some links between dietary factors and cognitive function. However, these will be only the first steps on a long road of further research work to come in this area.

Table 8: Experts' comments on funded projects

Name of consortium	Comment
AMBROSIAC	The study concerned stress, its effects on cognitive functioning and whether these can be influenced through nutritional counselling, dietary change or dietary supplementation. The study included both human populations and rat studies. Both experts mentioned that there are interesting initial findings which have been already published like results about fecal transplantation in mice. More research is still in progress like gut-brain axis, compounds omega-3 fatty acids and vitamin A and resveratrol. One expert sees that the studies on interaction between dietary factors and stress are an asset and highlighted the good output of publications and the new developed network. The other expert however mentioned that the results will unlikely lead to practical recommendations either for health service practice or for food production. Nevertheless, the project may lead to new hypothesis resulting in further research.
iCASE	The project studied levels of 5-hydroxy-tryptamine (serotonin) on social cognition having the hypothesis that poor social cognition is associated with low levels of serotonin in the brain. The study investigated whether foods rich in tryptophan and certain probiotics might improve social cognition. The partners investigated whether appropriate food supplements improve social functioning in a human sample, as compared to that in another group taking placebo. Both experts mentioned, that so far, no real results on diet-cognition relationship were presented and therefore it is unclear whether useful results will emerge from this project. On expert also mentioned that even the extension of the project might not be enough to finish the work.
D-CogPlast	The project investigated brain plasticity and the effects of dietary factors on this. The dietary records of a French population which had suffered cognitive decline were compared with those of a similar population which had not suffered such decline. The project proceeded to measure modulation of neurogenesis and microglial function by taking physiological samples from human subjects and testing foods hypothesized to protect young developing brains from stress. Both experts agreed that practical and useful recommendations may emerge from the results of the study. The metabolomic data point about coffee and red wine and the results may also underpin potential beneficial effects of Mediterranean diet studied in

	other projects. One expert furthermore highlighted the high-quality work and the good output.
MiTyrAge	This project concerned the functioning of mitochondria, and in particular the mitochondria-tyr kinase axis, with a focus to determining strategies to prevent neuronal decline. Both human and mice studies were conducted. The partners investigated whether certain polyphenols found in particular vegetables might contribute to such prevention. One expert mentioned that the epidemiological study showed some interesting results on the potential of Mediterranean diet for reducing cognitive impairment in elderly women. The interaction with apoE4, a risk factor for Alzheimer's disease was demonstrated as well as a potential mechanism of quercentin. A lot of work was done, but for one expert it was not possible to tell whether or not the findings will result in practical applications. The other expert highlighted the good work but was a bit concerned about the validity of the genetic analysis because of the low number of GWAS.
SELENIUS	This project was designed to study the effects of selenium levels in the body on the developing brain. A substantial part of the study related to a cohort of mothers and their young children in Poland. The project aimed to identify the effects of different diets on behavioral development, cognitive functions, hippocampal synaptic plasticity and peripheral and central inflammation, etc. Both experts agreed that the project was delayed by the involved rat studies. One expert thought that scientific progress has not only been made for selenium but also on potential harmful effects of lead exposure in early life and highlighted the interesting results and the good consortium.

3.3.2 Conclusions

The aim of the NutriCog call was to promote research activities that address the interrelation of diet and cognitive function used as basis for dietary preventive strategies and recommendations to guide individuals and populations towards health promoting dietary habits.

During the runtime of the consortia regular meetings (physical or online) were arranged with the partners. Although, the number of meetings varied between the consortia, the number of meetings does not correlate with the success of the consortium. It seems more important for the success of the consortium that the work in the single work packages was well distributed amongst the partners. **AMBROSIAC**, **D-CogPlast** and **SELENIUS** divided the work of one work package between up to 4 partners, resulting in a high number of publications per consortium and demonstrating the close transnational and transdisciplinary collaboration. The partners of **iCASE** and **MiTyrAge** mostly took on one work package alone, which might be because of only 3 partner per consortium resulting in a slightly reduced publication rate. Nevertheless, all consortia published their results (58 published papers) or are still finishing last experiments (2 papers in preparation and 3 under review). Furthermore, the consortia established a lot of collaborations with other JPI HDHL funded projects like DEDIPAC, ENPADASI, FoodBall, MaPLE or DiGuMet which will support the dissemination of results in these new developed networks also in the future.

Due to the basic research orientated approach of all consortia, they focused on dissemination of results and data sharing within the scientific community reflected by the high numbers of presentation, data sharing plans and the development of a matlab based analyses pipeline for dietary data (**iCASE**) or analytical databanks (**D-CogPlast**).

A lot of interesting findings regarding nutrition and cognitive function were obtained by the consortia pointing to an important role of Ω-3 fatty acids, tryptophan, flavonoids and selenium intake in reducing cognitive decline or neurodegenerative diseases. The data of the consortia are the basis for further research which could result in improved dietary guidelines for pregnant women and elderly but also into therapeutic treatment or prevention strategies for neurodegenerative disorders in the long run.

3.4 Annexes

3.4.1 Annex 1: List of NutriCog partners

Due to data protection regulations the list of NutriCog partners was removed.

3.4.2 Annex 2: Used data sources

Call Text "Joint Action: Nutrition and Cognitive Function (NutriCog)" published via https://www.healthydietforhealthylife.eu/images/documents/Call_Text_NutriCog.pdf

NutriCog full proposals submitted by 8th of June 2015.

NutriCog final report from AMBROSIAC, iCASE, D-CogPlast, MiTyrAge and SELENIUS were submitted on 28.05.2020, 30.07.2021, 31.07.2020, 15.04.2020 and 30.06.2020, respectively.

Written feedback to NutriCog final symposia from Stakeholder Advisory Board (SHAB) and Scientific Advisory Board (SAB) members.

3.4.3 Annex 3: Overview on general indicators

4.1.1 Alignment of national funding					
- Number of countries/partners participating in the call	10 JPI HDHL partner countries and 12 funding organisations				
- total committed budget	9.2 Mio €				
4.1.2 Involvement of national scientific communities					
- Number of submitted pre/full-proposals per country/funding organisation	39 full proposals (35 eligible proposals)				
- Number of accepted proposals per country/ funding organization	15 consortia recommended for funding 5 consortia funded				
- Committed budget per country	9.2 Mio € in total				
- Budget requested /allocated per country	34.9 Mio € requested / 4.9 Mio € allocated in total				
- % of the total budget spent	53.6 % (4.9 Mio € spent in total)				
-Committed budget per consortium	**AMBROSIAC:** 1.9 Mio €	**iCASE:** 1.0 Mio €	**D-CogPlast:** 1.0 Mio €	**MiTyrAge:** 0.8 Mio €	**SELENIUS:** 1.0 Mio €
- Number and type (Research/SME/Large industry) of organisations/teams in the funded consortia	**AMBROSIAC:** 6 partners (all from research institutes and academia)	**iCASE:** 4 partners (all from research institutes and academia)	**D-CogPlast:** 6 partners (all from research institutes and academia)	**MiTyrAge:** 4 partners (all from research institutes and academia)	**SELENIUS:** 6 partners (all from research institutes and academia)
- Gender of Coordinators and PI's	60% female and 40% male coordinators; 69% female and 41% male PI's				
4.1.3 Success of implementing collaboration					
- Interdisciplinary collaboration					
Number of disciplines per consortium	**AMBROSIAC:** 10	**iCASE:** 4	**D-CogPlast:** 7	**MiTyrAge:** 9	**SELENIUS:** 5
list of disciplines	**AMBROSIAC:** animal	**iCASE:** genetics,	**D-CogPlast:** nutrition,	**MiTyrAge:** cell biology,	**SELENIUS:** biochemistry,

	science, biochemistry, food metabolomics, food science, microbiology, microbiomics, molecular biology, neurosciences, nutriceutics, nutrition	neurosciences, nutrition, psychology	cognition, ageing, brain plasticity, metabolomics, lipidomics, *in vitro* parabiosis	neuroscience, physiology, biogerontology, geriatrics, molecular and cellular neurology, neuropathology, nutrition	cell biology, molecular biology, neurosciences, nutrition
- Success of transnational collaboration					
Number of new collaborations with academia	**AMBROSIAC:** 5	**iCASE:** /	**D-CogPlast:** 1	**MiTyrAge:** /	**SELENIUS:** /
Number of collaborations with other JPI funded projects	**AMBROSIAC:** DEDIPAC, ENPADASI, HEALTHMARK	**iCASE:** /	**D-CogPlast:** FoodBall, MaPLE DiGuMet	**MiTyrAge:** /	**SELENIUS:** HDHL-INTIMIC Knowledge Platform on Food, Diet, Intestinal Microbiomics and Human Health
- Number of project coordinators/partner per country	**AMBROSIAC:** see Figure 3	**iCASE:** see Figure 4	**D-CogPlast:** see Figure 5	**MiTyrAge:** see Figure 6	**SELENIUS:** see Figure 7
- Intensity of Collaboration					
Number of Meetings	**AMBROSIAC:** 2 physical meetings	**iCASE:** 4 physical meetings, 10 online meetings, regular telephone meetings	**D-CogPlast:** 4 physical meetings, 20 online meetings	**MiTyrAge:** regular telephone meetings	**SELENIUS:** 3 physical meetings, 5 online meetings
Number of mobility/lab visits within a consortium	**AMBROSIAC:** 3 lab exchanges	**iCASE:** 3 lab exchanges	**D-CogPlast:** 4 lab exchange	**MiTyrAge:** /	**SELENIUS:** 1 lab exchange
4.1.4 Success of scientific collaboration					
- Number of new publications related to the project	**AMBROSIAC:** 18	**iCASE:** 3 + 2 in preparation	**D-CogPlast:** 25 + 3 under review	**MiTyrAge:** 6	**SELENIUS:** 6
- Number of presentations related to the project	**AMBROSIAC:** 53 oral and 25 poster presentations	**iCASE:** 3 oral and 4 poster presentations	**D-CogPlast:** 23 oral and 15 poster presentations	**MiTyrAge: 4** oral and 2 poster presentationsn	**SELENIUS:** 10 oral and 17 poster presentations
- New funding obtained	**AMBROSIAC:** 1	**iCASE:** no	**D-CogPlast:** 3	**MiTyrAge:** 1	**SELENIUS:** no
4.1.5 Involvement in other JPI HDHL activities	**AMBROSIAC:** 3	**iCASE:** 3	**D-CogPlast:** 3	**MiTyrAge:** 2	**SELENIUS:** 4

4.1.6 Capacity Building					
- Training activities	**AMBROSIAC:** 1 (one-day symposium)	**iCASE:** /	**D-CogPlast:** 5 (3 workshop, 2 courses)	**MiTyrAge:** /	**SELENIUS:** /
- New jobs/positions generated in the project	**AMBROSIAC:** 19 (1 master student, 4 PhD students, 4 Postdocs, 10 research assistants)	**iCASE:** 8 (2 master students, 2 PhD students, 2 Postdocs, 1 intern, medical and research assistants)	**D-CogPlast:** 22 (14 master students, 4 PhD students, 3 Postdocs, 1 research assistant)	**MiTyrAge:** 10 (4 master students, 3 Postdocs, 3 research assistants)	**SELENIUS:** 7 (3 master students,1 PhD student, 1 Postdocs, 2 research assistants)
- Use of existing tools and/or development of new capacities or resources (e.g. a transnational database, biobanks, animal models, cohorts)	**AMBROSIAC:** /	**iCASE:** matlab based analyses pipeline for dietary data	**D-CogPlast:** analytical databank for chemicals and their metabolites, databank including biomarkers of intake for specific foods	**MiTyrAge:** developed a behavioral assay to monitor neuronal alterations	**SELENIUS:** animal model (rats) allowing to study the effect of selenium intake levels challenging the brain development
4.1.7 Data and Knowledge Sharing					
- Use of existing data: Has existing data been used / pooled for the project?	**AMBROSIAC:** yes	**iCASE:** yes	**D-CogPlast:** yes	**MiTyrAge:** no	**SELENIUS:** yes
- Has the consortium used samples from existing cohorts and / or other epidemiological studies?	**AMBROSIAC:** yes	**iCASE:** yes	**D-CogPlast:** yes	**MiTyrAge:** yes	**SELENIUS:** yes
- To perform the project, have you used samples (omics-based) from bio-bank or/and other disease register sample collections?	**AMBROSIAC:** no	**iCASE:** no	**D-CogPlast:** yes	**MiTyrAge:** no	**SELENIUS:** no
- FAIR-Data principles: Has the data generated in the project made available by following the FAIR principles?	**AMBROSIAC:** yes	**iCASE:** yes	**D-CogPlast:** yes	**MiTyrAge:** yes	**SELENIUS:** yes
4.1.8 Impact					
- Contribution of the project to the coordination/harmonization of research activities (standardisation of methods and protocols, data harmonisation, data and knowledge sharing)	**AMBROSIAC:** no	**iCASE:** matlab based analysis pipeline	**D-CogPlast:** analytic databanks	**MiTyrAge:** no	**SELENIUS:** no
- Activities towards innovation					

New industry collaboration	**AMBROSIAC:** Nutricia Danone	**iCASE:** no	**D-CogPlast:** Lipotype GmbH (Germany)	**MiTyrAge:** no	**SELENIUS:** no
Development of new methods/research tool/products	**AMBROSIAC:** no	**iCASE:** no	**D-CogPlast:** no	**MiTyrAge:** no	**SELENIUS:** no
Patents: number and geographical scope	**AMBROSIAC:** no	**iCASE:** no	**D-CogPlast:** no	**MiTyrAge:** no	**SELENIUS:** no
- Contribution to public health					
Target groups	**AMBROSIAC:** patients, scientists, consumers, policy maker	**iCASE:** patients, scientists, consumers	**D-CogPlast:** patients, scientists, consumers, policy maker, biomedical and food industry	**MiTyrAge:** scientists	**SELENIUS:** scientists, consumers, policy maker
Interaction with End-Users (e.g. consumers, patients in intervention studies)	**AMBROSIAC:** no	**iCASE:** no	**D-CogPlast:** no	**MiTyrAge:** no	**SELENIUS:** no
- New strategies/applications to reduce incidence of diet related chronic diseases)	**AMBROSIAC:** maybe in the future	**iCASE:** maybe in the future	**D-CogPlast:** maybe in the future	**MiTyrAge:** maybe in the future	**SELENIUS:** maybe in the future