IDEAPUZZLE
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Linking obesity-induced inflammation and metabolic disease: from adolescence to adulthood

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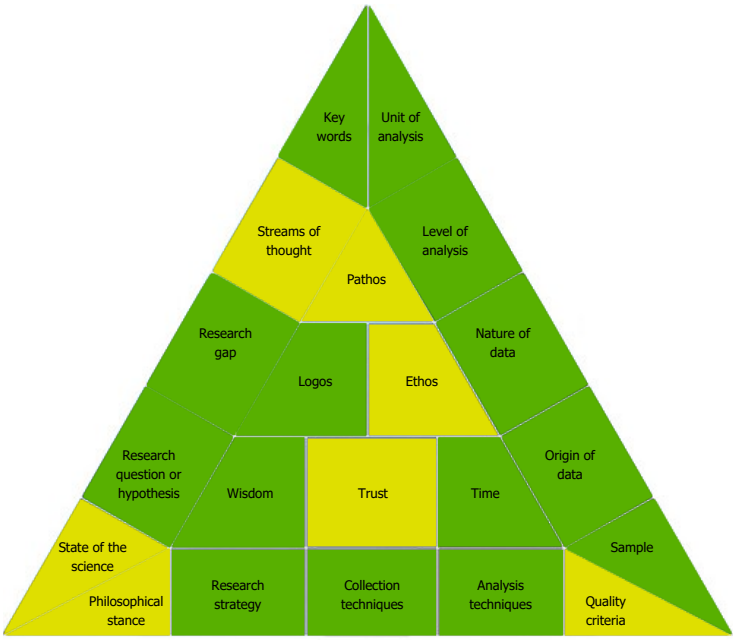
Date: 2016-05-30 - 14:54:13 (GMT)
Self-evaluation: 83%



Key words

1/21. Theoretical question: which are the two main keywords of your research?

The focus of my research is the relationship between obesity-induced inflammation and metabolic disease, with a special interest on understanding whether diet as the potential to modulate this relationship.
Obesity-induced inflammation, also known as metaflammation, is a proposed concept to describe the chronic low-grade inflammatory response to obesity (Hotamisligil, 2006;Lumeng & Saltiel, 2011).
Metabolic disease is a metabolic dysfunction associated to excess adipose tissue that may partly result from an imbalance in the expression of pro- and anti-inflammatory cytokines thereby contributing to the development of obesity-related disorders such as cardiovascular diseases (Ouchi et al, 2011).

References:
Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006;444(7121):860-7.
Lumeng CN, Saltiel AR. Inflammatory links between obesity and metabolic disease. J Clin Invest. 2011;121(6):2111-7.
Ouchi N, Parker JL, Lugus JJ, Walsh K. Adipokines in inflammation and metabolic disease. Nat Rev Immunol. 2011;11(2):85-97.

Self-evaluation: 100%

Streams of thought

2/21. Theoretical question: which are the two main streams of thought of your literature review?

Two streams of thought about my research project are the role of inflammation in the occurrence of disease, particularly cardiovascular disease; and the pro and anti-inflammatory potential of food as a possible moderator of the relationship between metaflammation and metabolic disease.
Metabolic diseases have been linked to inflammatory processes. A growing body of evidence demonstrates that increased adipose tissue mass contributes directly towards an increase in systemic inflammation. It is suggested that the initial signal of this type of inflammation is an excessive food intake, with the signaling pathway starting in the metabolic cells with a resulting increase in cytokine production, recruitment of immune cells inducing a pro-inflammatory state (Hotamisligil, 2006; Ruiz-Nunez et al, 2013).
On the other hand, diet comprises components with both pro and anti-inflammatory potential, which can turn into an instrument that may modify the relationship between obesity induced inflammation and metabolic disease (Ruiz-Nunez et al, 2013; Gonzalez-Gil et al, 2015). The lower consumption of saturated fatty acids and industrially produced trans fatty acids (Mozaffarian, 2006), a higher intake of long-chain polyunsaturated fatty acids (LCP) of the n-3 series (LCPn-3) (He et al, 2009), the consumption of carbohydrates with a low glycemic index (Liu et al, 2002) are amongst the anti-inflammatory dietary components that may play a crucial role in modulating inflammation.
Geoffrey Rose proposed that early approaches to prevention by screening to identify individuals at risk of disease require understanding of how risk factors are distributed in the population and how they relate to the disease. This leads to the major insight that the total burden of disease in a community depend on the numbers of people exposed to a particular risk factor, i.e. the population distribution of a risk factor. A large number of people in the center of the distribution, exposed to small elevations in risk, contribute more cases to a population than a small number of people at the extreme of the distribution exposed to a very high risk. Thus, prevention of cardiovascular disease needs to consider not just screening at treatment in those at very high risk at the extremes of the distribution, but reduction of risk factors in the large number of those in the middle of the distribution with moderately elevated risk. Hence, prevention strategies, to be effective, need not only to focus on the high-risk individuals at one extreme of the distribution, but need also to address the population distribution (Rose, 1992). Therefore, population-based interventions add great value to public health.

References:
Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006;444(7121):860-7.
Ruiz-Nunez B, Pruimboom L, Dijck-Brouwer DA, Muskiet FA. Lifestyle and nutritional imbalances associated with Western diseases: causes and consequences of chronic systemic low-grade inflammation in an evolutionary context. J Nutr Biochem. 2013;24(7):1183-201.
Gonzalez-Gil EM, Santabarbara J, Russo P, Ahrens W, Claessens M, Lissner L, et al. Food intake and inflammation in European children: the IDEFICS study. Eur J Nutr. 2015.
Mozaffarian D, Katan MB, Ascherio A, Stampfer MJ, Willett WC. Trans fatty acids and cardiovascular disease. The New England journal of medicine. 2006;354(15):1601-13.
He K, Liu K, Daviglus ML, Jenny NS, Mayer-Davis E, Jiang R, et al. Associations of dietary long-chain n-3 polyunsaturated fatty acids and fish with biomarkers of inflammation and endothelial activation (from the Multi-Ethnic Study of Atherosclerosis [MESA]). The American journal of cardiology. 2009;103(9):1238-43.
Liu S, Manson JE, Buring JE, Stampfer MJ, Willett WC, Ridker PM. Relation between a diet with a high glycemic load and plasma concentrations of high-sensitivity C-reactive protein in middle-aged women. The American journal of clinical nutrition. 2002;75 (3):492-8.
Rose G. The strategy of preventive medicine. The strategy of preventive medicine. 1992.

Self-evaluation: 50%

Research gap

3/21. Theoretical question: which is the main gap that your research addresses?

Longitudinal studies have shown that adiposity from early life tracks into and predicts the occurrence of cardiovascular disease in adulthood, even if they are not obese adults, placing individuals at risk for lifelong metainflammation (Skinner et al, 2010). Most studies have focused on the role of changes throughout childhood. However, though adolescence is the second period with the fastest changes in the biological, psychological and social characteristics (Loomba-Albrecht & Styne, 2009), it has not been extensively studied as in early life and adulthood when disease is already established. As verified by our research group, adiposity varies during adolescence with impact on cardiovascular risk factors (Araujo et al, 2014; Araujo et al, 2015). However, it is still necessary to understand the impact that such changes have on inflammatory markers and its metabolic consequences.
Additionally, diet presents components with both pro and anti-inflammatory potential, which can turn into an instrument that may modify the relationship between obesity induced inflammation and metabolic disease (Lopes et al, 2007;Holt et al, 2009). Despite the potential of these components, many clinical trials with supplements are inconclusive (Tavani et al, 1999), which makes it essential to better understand the effect of nutrients and dietary patterns in a real context. In the present context, where obesity prevalence is increasing, it becomes essential to better understand the real role of diet in order to define efficient measures to prevent an early onset of the low-grade inflammation, for which my population-based approach is a valuable asset.

References:
Skinner AC, Steiner MJ, Henderson FW, Perrin EM. Multiple markers of inflammation and weight status: cross-sectional analyses throughout childhood. Pediatrics. 2010;125(4):e801-9.
Loomba-Albrecht LA, Styne DM. Effect of puberty on body composition. Curr Opin Endocrinol Diabetes Obes. 2009;16(1):10-5.
Araujo J, Barros H, Severo M, Lopes C, Ramos E. Longitudinal changes in adiposity during adolescence: a population-based cohort. BMJ Open. 2014;4(6):e004380.

Araujo J, Severo M, Barros H, Mishra GD, Guimaraes JT, Ramos E. Developmental trajectories of adiposity from birth until early adulthood and association with cardiometabolic risk factors. Int J Obes (Lond). 2015;39(10):1443-9.
Lopes C, Aro A, Azevedo A, Ramos E, Barros H. Intake and adipose tissue composition of fatty acids and risk of myocardial infarction in a male Portuguese community sample. Journal of the American Dietetic Association. 2007;107(2):276-86.
Holt EM, Steffen LM, Moran A, Basu S, Steinberger J, Ross JA, et al. Fruit and vegetable consumption and its relation to markers of inflammation and oxidative stress in adolescents. Journal of the American Dietetic Association. 2009;109(3):414-21.
Tavani A, La Vecchia C. Beta-carotene and risk of coronary heart disease. A review of observational and intervention studies. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie. 1999;53(9):409-16.

Self-evaluation: 100%

Research question or hypothesis

4/21. Theoretical question: which is the main question or hypothesis of your research?

My research question is whether and how the relationship between inflammatory markers and metabolic disease is influenced by adiposity trajectory and pattern of distribution, and whether diet can be used as an instrument to modify this relationship.

Self-evaluation: 100%

State of the science

5/21. Theoretical question: which is the current answer to your research question or hypothesis?

There is not yet a consensual answer to this question.
Current knowledge shows that obesity causes metaflammation and that this type of inflammation is one of the pathways that explains obesity consequences (DeBoer, 2013). On the other hand, current evidence supports the theoretical potential of diet to induce or reduce inflammation, however its effect at a population level is not yet clear (Gonzalez-Gil et al, 2015).

References:
Gonzalez-Gil EM, Santabarbara J, Russo P, Ahrens W, Claessens M, Lissner L, et al. Food intake and inflammation in European children: the IDEFICS study. Eur J Nutr. 2015.
DeBoer MD. Obesity, systemic inflammation, and increased risk for cardiovascular disease and diabetes among adolescents: a need for screening tools to target interventions. Nutrition (Burbank, Los Angeles County, Calif). 2013;29(2):379-86.

Self-evaluation: 50%

Philosophical stance

6/21. Methodological question: which is the philosophical stance of your research?

The specific term for the philosophical stance of my research is quantitative objectivism.

Self-evaluation: 50%

Research strategy

7/21. Methodological question: which is the qualitative, quantitative or mixed method of your research?

My research strategy is a quantitative and longitudinal research study (Rothman et al, 2008).

References:
Rothman KJ, Greenland S, Lash TL. Modern epidemiology: Lippincott Williams & Wilkins; 2008.

Self-evaluation: 100%

Collection techniques

8/21. Methodological question: which are the data collection techniques of your research?

Data is collected through the use of standardized procedures that included questionnaires and physical examinations. All evaluations are performed by a team of experienced health professionals, which include food intake questionnaires, anthropometric assessment, blood pressure measurement and fasting blood sample collection.

Self-evaluation: 100%

Analysis techniques

9/21. Methodological question: which are the data analysis techniques of your research?

The data analysis techniques adopted in my research are longitudinal data analysis to evaluate adiposity trajectories, food intake and cardiometabolic markers. We will use structural equation models (e.g. path analysis or causal models with latent variables) in order to quantify the associations and to understand the exposures%u2019 effect throughout the study period.
The software adopted in my research to conduct all statistical analysis are SPSS version 20.0 (IBM® SPSS® Statistics), R software, version 3.0.1 (R Foundation for Statistical Computing, Austria, 2013) and MPlus, version 5.2.

Self-evaluation: 100%

Quality criteria

10/21. Methodological question: which are the tactics of your research to ensure scientific quality criteria?

Several criteria will be used to guarantee the quality of my research. These comprise external validity, internal validity, construct validity, convergent validity and reliability (McDowell, 2006).
First, the research will be performed using a large population-based sample for inferential statistical generalization. Second, the inductive reasoning for theory development, and peer debriefing will be used to assure internal validity. Third, the use of standardized questionnaires validated for the Portuguese population, the participants' explanation about the study, the research assistants available to assist participants whenever necessary with consistent evaluation throughout the data collection process, and the open and close-ended participants' response to the questionnaire items will assure construct validity. Fourth, convergent validity will be assured by the triangulation of streams of thought, collection techniques, and data origin. Finally, the informed consent form given to adolescents and their legal guardians, and the standardized techniques for the data collection will assure reliability.

References:
McDowell I. Measuring health: a guide to rating scales and questionnaires: Oxford University Press; 2006.

Self-evaluation: 50%

Unit of analysis

11/21. Empirical question: which is the unit of analysis of your research?

The unit of analysis that I compare in reality to operationalize the relationship between obesity-induced inflammation and metabolic disease are adolescents from a population-based cohort (EPITeen).
Each individual was measured several times over 12 years of follow-up. Therefore, we have not only the individual at each moment, but also its trajectory as a unit of analysis.

Self-evaluation: 100%

Level of analysis

12/21. Empirical question: which is the level of analysis of your research?

The level of analysis of the unit of analysis of my research is individual.

Self-evaluation: 100%

Nature of data

13/21. Empirical question: which is the nature of the data of your research?

The quantitative data collected in my research are numbers corresponding to close-ended questions, to the questionnaires coding, to inflammation markers, to CVD risk factors and to anthropometric measurements.

Self-evaluation: 100%

Origin of data

14/21. Empirical question: which is the origin of the data of your research?

My research includes only primary data, resulting from answers to close-ended questions, anthropometric measurement and fasting blood sample measurement, evaluated at least 4 times over the 12 years of follow-up.

Self-evaluation: 100%

Sample

15/21. Empirical question: which is the sample of your research?

The sample are participants of the Epidemiological Health Investigation of Teenagers in Porto (EPITeen), a cohort that includes detailed dietary information as well as information on biomarkers of cardio-metabolic disease risk (anthropometrics, blood pressure, fasting glucose, insulin, triglycerides, and cholesterol).

The EPITeen is a cohort of 2942 adolescents born in 1990 and recruited at Porto private and public schools. The cohort comprises, so far, three assessments. At baseline, in 2003/2004, 2159 adolescents were evaluated (77.5% of participation). In 2007/2008, 1716 (79.4%) adolescents were reevaluated and 783 additional adolescents, also born in 1990, were recruited for the first time. In 2011/2013, 1764 were reevaluated (60.0%).
During 2016 we will re-evaluate the participants with valid data on anthropometrics in three previous evaluations, in order to take advantage of a longitudinal approach. An increase on refusals at this age might be expected, however, since we are restricting to those more regular participants (having at least three evaluations), we expect to re-evaluate in this wave approximately 1200 of the 2942 participants.

Self-evaluation: 100%

Pathos

16/21. Rhetorical question: which are the positive and negative emotions of your research?

The longitudinal perspective of this research will contribute to study adolescence as a possible sensitive period, aiming to identify the extent to which changes in adiposity during adolescence influence the future risk of cardiovascular disease. Also, it will broaden the knowledge about the role of diet on the inflammatory chain and in the incidence of cardiovascular disease. This calls for more research on dietary intake that could be translated to important and practical public health messages. We believe that it is important to identify whether there are key dietary components that can modify the obesity inflammatory potential. Furthermore, we believe that understanding how adolescence conditions the trajectories of adiposity can help emphasizing the importance of this period in the development of strategies to reduce the impact of obesity.
Besides the contribution to the understanding of disease mechanisms, this population-based project will be central to design appropriate health promotion strategies for the Portuguese population.
My research is not associated with negative emotions in terms of ethics and conflicts of interest. The EPITeen cohort received ethical approval by the Ethical Committee of São João Hospital/ University of Porto Medical School and complies with the Helsinki Declaration and the current national legislation. Participants were informed about the study aim and data confidentiality, as well as benefits and potential discomfort. They provided written informed consent for participation at baseline and re-evaluations.

Self-evaluation: 50%

Logos

17/21. Rhetorical question: which is the scientific logic of your research?

The scientific logic adopted in my research is hypothetic-deductive, based on a longitudinal approach in order to trace back the impact that obesity-induced inflammation and its determinants have on metabolic disease from adolescence into adulthood.

Self-evaluation: 100%

Ethos

18/21. Rhetorical question: which are the limitations of your research?

The main theoretical limitation of my research is the absence of other streams of thought specifically about obesity-induced inflammation and metabolic disease.
The main methodological limitation of my research are the losses to follow up and the restraints inherent to data collection regarding food intake.
The main empirical limitation of my research are the economic constraints that limit the choice of the inflammatory markers to assess, and the absence of data regarding genetic information.

Self-evaluation: 50%

Wisdom

19/21. Authorial question: which is your education and experience related with your research?

My background combines public health and nutritional sciences, which are crucial to the successful development of this research project.
I have a bachelor degree in Nutritional Sciences obtained from the Faculty of Food and Nutrition Sciences of the University of Porto, a masters degree in Public Health from the University of Porto Medical School, with the thesis entitled "Vitamin D and metabolic syndrome among Portuguese adolescents: the EPITeen project". Now, I am a PhD candidate of a doctoral programme in Global Public Health based on the wide ranging teaching and research experience of four Portuguese Schools: the Institute of Public Health of the University of Porto, the Institute of Hygiene and Tropical Medicine, the Nova Medical School and the National School of Public Health.
The theoretical training distributed by the different schools, allowed me to contact with different views of Epidemiology and Public Health, as well as to acquire knowledge in diverse areas, since each school has a different approach to Public Health, allowing me to explore the different working methodologies.
Since obesity is a multifactorial disease, a transdisciplinary approach is key for its understanding, as well as for the design of public health interventions.

My previous experience as a research fellow allowed me to enhance my research skills in public health, developing my understanding of police and practice and giving me the tools to make original contributions to knowledge development.
My experience in a hospital setting, in the nutrition department of the University Hospital of Coimbra, and in a foreign research centre, in the Nutritional Epidemiology department of the Faculty of the Federal University of Rio de Janeiro, provided me with a broad perspective of nutrition and public health.
Additionally, prior to the PhD I have worked as a research fellow in the Angola Health Research Centre, a partnership between the Gulbenkian Foundation and the Angolan Government.
Finally, I have worked as a research fellow in the Institute of Public Health of the University of Porto together with the Department of Clinical Epidemiology, Predictive Medicine and Public Health of the University of Porto Medical School, in which I had the opportunity to work in several stages of research, from fieldwork to data analysis, namely in the EPITeen cohort, in which I will base my investigation.

Self-evaluation: 100%

Trust

20/21. Authorial question: who are the partners of your research?

Our Research Unit has Epidemiology and Public Health as main scientific domains, with large experience in cohort studies' methodology, having already developed previous work on the project's topic, which will contribute to the feasibility of the thesis project. I belong to the Nutrition and Obesity Epidemiology research group, which has numerous publications in the highest impact factor journals in the field.
Additionally, my supervisor is a Nutritionist and Assistant Professor of Epidemiology in the Porto Medical School, with large research experience, particularly in nutritional epidemiology, with a special interest in obesity and its link to cardiovascular diseases.
Moreover, the existing connection with various research groups of the São João Hospital Centre, enables the deepening of the clinical relevance of the research, namely with the department of Biochemistry and with the central pathology laboratory of the University Hospital of São João, whose director is involved the project planning and conduction.
Furthermore, the research group has also developed work with external collaborations, which might allow me to do an internship abroad, providing me with a different perspective and an added value to the methodological strategies that I will implement in the conduction of the thesis.

Self-evaluation: 50%

Time

21/21. Authorial question: which is your availability of time and resources for your research?

I have a doctoral grant from the Foundation for the Science and Technology to develop my research during the four years in an exclusive basis. Therefore, I have full-time availability to conduct my research project (PD/BD/105824/2014).
Additionally, this thesis project will be part of an already financed FCT project (PTDC/DTP-EPI/6506/2014), in which I am a team member. The project provides funding for the field work implementation, however, it does not allow me to deepen my training. Therefore, this grant will be essential to facilitate the conditions for course attendance, for training improvement and to contact with other researchers.

Self-evaluation: 100%