

SHORT TERM SCIENTIFIC MISSION (STSM) SCIENTIFIC REPORT

This report is submitted for approval by the STSM applicant to the STSM coordinator

Action number: **CA18211**

STSM title: **Stress, nutritional behaviour and epigenetics in mothers living in Nord Europe**

STSM start and end date: **13/08/2021 to 21/08/2021**

Grantee name: **Rosita Gabbianelli**

PURPOSE OF THE STSM:

Early life stress has been associated with changes which influence brain development and metabolic responses later in life [1,2]. Furthermore, stress can vary nutritional behaviour changing the quantity and quality of food intake [2]; fats and carbohydrates may be differently consumed, and their quality if not well controlled could promote negative health effects on the mother and the fetus/infant [3]. In particular, stress and food behaviour can modulate the epigenome of the fetus/infant leading to long term effects at adulthood [4]. In addition, maternal stress can also vary the immunological and metabolic responses of the mother, and with breastfeeding the infant can receive pro-inflammatory cytokines as well as food metabolites from fats and carbohydrates according to maternal food intake, that can impact his/her epigenome [5].

The aim of this STSM is to explore the main aspects associated with maternal stress and the consequence on her nutritional behaviour. In collaboration with Prof. Sigfríður Inga Karlsdóttir the goal of this STSM was to explore how stress can impact maternal nutritional behaviour (i.e. the quality and the quantity of food intake, the kind of food), and if stress can modify macronutrient intake (i.e. proteins, lipids, carbohydrates and micronutrients) in the mothers leaving in Nord Europe.

To reach this goal a questionnaire is a useful tool to collect these data from mother, and to inform her on the key role of maternal nutrition in the modulation of offspring's epigenome. Furthermore, to inform the mother, a simple and exhaustive short white paper to help her how manage the stress events during pregnancy, the impact of the quality and the quantity of food intake on fetus/offspring during neonatal life (the first 1000 days of life), needs to be prepared and given to the mothers. The knowledge of the key role of maternal nutrition in the programming of child health and the knowledge of what can happen during pregnancy/childbirth could support the mother to manage/prevent a traumatic stress and finally it can support the mother during her pregnancy and birthchild.

This pilot study with the questionnaire and the white paper for mother leaving in the Nord of Europe (Island), could be adapted and translate in other languages within the CA18211 and used by the other members of CA18211 to collect data and transfer useful suggestions to the mothers.

References

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- 2.Bordoni L, Petracci I, Calleja-Agius J, Lalor JG, Gabbianelli R. NURR1 Alterations in Perinatal Stress: A First Step towards Late-Onset Diseases? A Narrative Review. *Biomedicines.* 2020;8(12):584. Published 2020 Dec 8. doi:10.3390/biomedicines8120584

3. Gabbianelli R, Bordoni L, Morano S, Calleja-Agius J, Lalor JG. *Nutri-Epigenetics and Gut Microbiota: How Birth Care, Bonding and Breastfeeding Can Influence and Be Influenced?*. *Int J Mol Sci.* 2020;21(14):5032. Published 2020 Jul 16. doi:10.3390/ijms21145032
4. Gabbianelli R, Damiani E. *Epigenetics and neurodegeneration: role of early-life nutrition.* *J Nutr Biochem.* 2018 Jul;57:1-13. doi: 10.1016/j.jnutbio.2018.01.014. Epub 2018 Feb 9. PMID: 29529489.
5. Cook N, Ayers S, Horsch A. *Maternal posttraumatic stress disorder during the perinatal period and child outcomes: A systematic review.* *J Affect Disord.* 2018 Jan 1;225:18-31. doi: 10.1016/j.jad.2017.07.045. Epub 2017 Jul 27. PMID: 28777972.

DESCRIPTION OF WORK CARRIED OUT DURING THE STSMS

During the STSM I met with Prof Sigfríður Inga Karlsdóttir to discuss and to understand about maternal stress occurrence and which kinds of stress the mothers can live during pregnancy and childbirth. At the time of STSM I had prepared a proof of the questionnaire containing general questions and only data about nutrition.

From the first day of meeting with Prof. Sigfríður Inga Karlsdóttir we discussed about how to optimize the questionnaire to improve the gaps and to include the main questions on maternal stress. Prof. Sigfríður Inga Karlsdóttir has explained to me all kinds of risk factors associated to maternal stress. To go deeper on this topic she organized also meetings with her colleagues to speak about the different kinds of stress. We met Sigridur Sia Jonsdottir (member of our Cost action) to discuss about the effect of perinatal distress associated with partner relationship, and Sigridur Halldorsdotti, Hulda Sædis Bryngeirsdottir and Karen Birna Torvaldsdottir to discuss about trauma from violence. We discussed with Finnbogi Ritur Tormodsson on stress, epigenetics and neurodegeneration.

The questionnaire was built and revised day by day; for a statistical evaluation of data only closed questions were added and the main work was to identify all the responses to include them in each question. We decided to accept multiple choice response to give to the mother the opportunity to better describe her experience. We discussed about the identification of all kind of traumatic stress and Prof. Sigfríður Inga Karlsdóttir identified the literature to be used (Simson and Catling from *Women and Birth* 29 (2916) 203-217. *Understanding psychological traumatic birth experiences: A literature review*, and also Elmir et al., 2010 *Journal of advanced nursing* 66(109 2142-2153, *Women's perception and experiences of a traumatic birth: a meta-ethnography*).

We discussed about inclusion and if there were any exclusion criteria.

We discussed which questions should have only one answer and which questions would be open to more than one and for this option we specified "you can mark more than one option".

After the general questions (i.e. age, education, marital status), Prof. Sigfríður Inga Karlsdóttir suggested to add a question to screen the mother experience of stress (i.e. *Have you experience of: miscarriage, stillbirth, have you lost child after birth*). The question on the number of children was added after this question to collect data on changes of nutritional behaviour. To help the mother to recognize stress other questions were added; in particular the questionnaire includes "*Have you experience of traumatic stress during pregnancy?*" and "*Have you experience of traumatic stress during/after childbirth?*" Several options and description were added; we discussed about the concept that sometime mothers do not aware about the kind of stress and a list of them could be useful also to give the opportunity to the mother to recognise it, and to think about stress in order to resolve it asking support.

Questions about nutrition were added considering that the questionnaire has to inform the mother; to this aim the questionnaire was prepared with questions like "*Programming of adult health/disease*" means that we can decide on our health; *Have you heard about this concept before?* and *Do you know that during the first 1000 days of life (9 months of pregnancy + 24 months of postnatal life) adult health can be programmed?* and *What a mother eats can programme adult health; Do you know that high or low protein intake during pregnancy can modulate offspring's epigenome increasing the risk to develop obesity in adult life?* Furthermore, in order to screen if stress has modified the nutritional behaviour questions like *Did you change your food intake after a traumatic stress?* and *Did you increase the intake of these macronutrients after traumatic stress?* and *Did you decrease the intake of these macronutrients after traumatic stress?* were added and answers to these questions were detailed with examples to give the opportunity to the mother to respond correctly.

We discussed about the key role of education of the mother to prevent stress and to support her knowledge on physiological changes in her body and the key role of nutrition for her and child wellness; questions about

Who should inform people about this topic? and What would you like to ask for from health care professionals? were added.

We prepared a letter and a poster to introduce the questionnaire and explain to the mother the aim of this investigation.

We suggested that it would be necessary to do a validation of the questionnaire with a small group of women that come from health care clinic for her children and ask to few colleague within the Cost action to read questionnaire before and give her comments.

We suggested to contact the Iceland ethical committee for the required authorization.

We organized the questionnaire using a web platform (google moduli) to facilitate the final elaboration of data and reduce the consume of paper.

To thank for the cooperation of mothers that will fill the questionnaire we decided to prepare a short white paper on what the mother can do during the first 1000 days of life of her child; the mother will get it when she will submit the filled questionnaire. A short white paper has been prepared.

DESCRIPTION OF THE MAIN RESULTS OBTAINED

The questionnaire was prepared and introduced into google moduli in order to be used on line. In this manner it can be spread to the mother easily. Moreover, the use of the platform will permit a proper evaluation of collected data that will be object of discussion within the CA 18211.

The questionnaire is available at this web site: https://docs.google.com/forms/d/e/1FAIpQLSd3-TFNJzv7KDnraRmAy1Ew5G_C8c42dClfTX_eUXh1Joeg6g/viewform?vc=0&c=0&w=1&flr=0

We have created a QR code to link to the questionnaire.



Besides, a poster was prepared; it will be put in the waiting room where the mothers go for the child's control at 5-9 weeks old. The poster will be useful to inform the mother and invite her to fill the questionnaire.

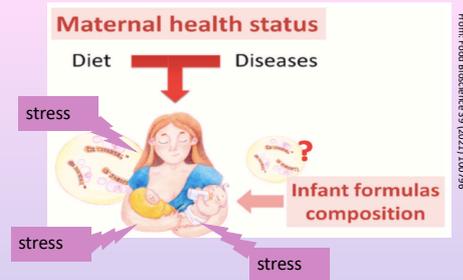
Maternal stress and epigenetics: how maternal nutrition can change and impacts on offsprings' health (CA18211)

Dear Mother,

Nutrition is one of the main factors that can modulate our wellness across our life. What we eat during early life and childhood impacts significantly our health, as well as what the mother eats during pregnancy and lactation. Furthermore, early life stress has been associated with changes which influence brain development and metabolic responses later in life. Additionally, stress can vary nutritional behaviour changing the quantity and quality of food intake; fats (i.e. oils, butter) proteins (i.e. meat, fish, cheese, eggs), simple carbohydrates (i.e. cake, biscuits) and complex carbohydrates (i.e. white/brow pasta, white/brow rice, noodles, white/brow bread) may be differently consumed.

The quality of food if not well controlled could contribute to negative health effects on the mother and the child. Furthermore, stress and food behaviour can modulate the epigenome of the child leading to long term effects at adulthood. In addition, maternal stress can also vary the physiological responses of the mother (i.e. immunological and metabolic responses), and with breastfeeding the infant can receive positive and negative stimuli according to maternal life style. What occurs during pregnancy and neonatal life (9 months of pregnancy plus 24 months of postnatal life) can modulate the offspring epigenome which guides the differentiation of organs (i.e. liver, brain, pancreas etc.,) in child programming his/her adult health.

Please if you are ready to participate use this code:



This study is dedicated to you that have experience pregnancy/childbirth. The inclusion criteria is: To be a mother with a child/children and to have 5-9 weeks old child.

We want to stress that the questionnaire is anonymous and that your name or identity will not be part of the findings and you are free to participate or not, skip answers if you wish. It will take you 5 to 10 minutes to respond to the questionnaire. Your time spent to do the questionnaire will be useful to update knowledge on this topic to help to improve care for the quality of life for children and parents.

To thank you for your kind cooperation when you will have submitted the questionnaire you will get response with information about your child nutritional need during early life to encourage you during this important time of your life.

With kind wishes,

Prof Rosita Gabbianelli, Full professor of Biochemistry, School of Pharmacy, Unit of Molecular Biology and Nutrigenomics, University of Camerino, Italy and Prof Sigríður Inga Karlsdóttir, Full Professor of Midwifery, School of Health Science, University of Akureyri, Iceland.

A letter to inform the mothers has been prepared; it contains the information reported in the poster, an image and the QR code. The letter will be put in the waiting room where the mothers go for the child's control at 5-9 weeks old. The poster will be useful to inform the mother and invite her to fill the questionnaire.

FUTURE COLLABORATIONS (if applicable)

The questionnaire will be translated in icelandic language and used in Iceland after ethical permission and the validation; data will be elaborated (statistical analysis) and share within the CA18211. The questionnaire will be translated in Italian and in cooperation with clinicians and members of the CA18211 used to collect further data useful to write a paper.

Other members of the CA 18211 could be involved to translate the questionnaire in their languages and it will be used to collect data in other counties. All results could be object of a common publication within the CA18211.

A short white paper will be translated in other languages and will be get to mothers involved in other countries within the CA18211.

The validation of the questionnaire will be done with some young mothers in Island and within selected members of CA18211.

If this pilot study it will be useful to inform the mother on the the impact of environmental stimuli on her and child health. Other white papers can be prepared and collected in a book for the mothers.

This report was approved by the host, Prof Sigríður Inga Karlsdóttir on 30th of August 2021.