PONTIFÍCIA UNIVERSIDADE CATÓLICA
DO RIO DE JANEIRO

Carolina Irurita Ballesteros

Repercussions of Maternal Omega 3 (n-3) LC-PUFA and Mental Health on Early Neuropsychological Development

TESE DE DOUTORADO

Thesis presented to the program de Pós- graduação em Psicologia (Psicologia Clínica) of PUC- Rio in partial fulfillment of the requirements for the degree of Doutor em Psicologia (Psicologia Clínica).

Advisor: Prof. Jesus Landeira-Fernandez

Rio de Janeiro
March 2018

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Bibiliographic data

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Repercussions of maternal omega 3 (n-3) LC-PUFA and mental health on early neuropsychological development / Carolina Irurita Ballesteros ; advisor: J. Landeira-Fernandez. – 2018.

162 f. : il. color. ; 30 cm

Tese (doutorado)–Pontifícia Universidade Católica do Rio de Janeiro, Departamento de Psicologia, 2018.

Inclui bibliografia

1. Psicologia – Teses. 2. Desenvolvimento infantil. 3. Neuropsicologia pediatrica. 4. Neuropsicologia infantil. 5. Nutrição materna. 6. Saúde mental materna. I. Landeira-Fernandez, J. II. Pontifícia Universidade Católica do Rio de Janeiro. Departamento de Psicologia. III. Título.

CDD: 150

I dedicate this doctoral thesis to the two loves of my life: my husband David F. Henao and my daughter Valentina Henao Irurita who several times were left without my company, exercised their patience to wait and they were always proud of me.

I love you with all my heart.

Acknowledgments

To my advisor Prof. Dr. J. Landeira-Fernandez, thank you for trust since the very first time I knocked on your door. You will always be an important reference in my life;

Dr. Luciene Rocinholi, I sincerely appreciate your enormous complicity in my academic career. The result of these work years could not have a better outcome than a true and forever friendship;

To my daughter Valentina, my greatest gift of God. You inspire me to become a better person every single day, just watching you smile makes me realize how beautiful my life is. I love you to the moon and back.

To my beloved husband, there are so many things my heart wants to say to you, all of which can be summed up in just three words – thanks for everything. I love you.

To my parents Kenny Ballesteros and Alvaro Irurita, thank you for always trusting me, for giving me all your love and knowing when to correct me if necessary. You have taught me to value everything and for me, you are the best parents in the world.

Diana and Gerardo, thank you for the unconditional affection;

To my brothers, Alejandra, Nestor, Alvaro E., Maria Fernanda and Jorge Andrés, you will always be in my heart.

Carlitos: Cousins or siblings? Much of both... thanks for your trust and always be by my side. Your speedy recovery is my greatest dream.

To my nephews, Alvaro Fernando and Emilio, you are more precious than gold because you keep your aunt from getting old, love you!

To my abuelita Nelly, I will never forget all the encouragements you've given me as a child in my failures. Thank you for all you have offered to me, Love you forever.

To my mother in law, thank you so much for all the love and support you have given me during this "thesis" time, love you.

Elodie Bertrand, I am very grateful to have such a colleague, and friend during the PhD program. Thank you for this friendship that indisputably crosses the borders.

Prof. Dr Deusivania, thank you for your loving, clever and dedicated presence. I do believe that your unconditionality was a golden key to this work. I feel very happy and lucky to have you in my life.

To my collegues: Vitor Gomes, Silvia Massonetti, Flavia Pereira, Emmy Uhera, Luciana Brooking, Luiz Felipe Tavares, Heloisa Veiga, e Amanda Videira, you are amazing friends and will always be in my heart.

Érica de Lana e Ana Carolina Fioravantti, thanks a lot for encouraging me into the academic life. I still remember our first course as if it were just yesterday.

Manuel Herrera: Thanks for all your support, your friendship has made a big difference in this new life stage.

Prof. Dra. Julianne Borsa, I really wanted to address you in my acknowledgements, your presence in my academic life certainly had a positive purpose in my professional growth. You are a great and wonderful professor!

Prof. Dr. Gilberto Kac, thank for the opportunity to carry out this work.

Verinha e Marcelina, two little angels who always welcomed me with a smile. Thank you.

Dale Zieglar, Thank you for your generous support. I am grateful to have you in my life.

Prof. Dr. Rapport and CLC team, thanks for letting me be a part of your lab.

Abstract

Irurita-ballesteros, C; Landeira-Fernandez, Jesus (Advisor); Rocinholi, Luciene de Fatima (Co-advisor). **Repercussions of Maternal Ômega 3 (n-3) LC-PUFA and Mental Health in the Early Neuropsychological Development** Rio de Janeiro, 2018. 162p. Tese de Doutorado - Departamento de Psicologia, Pontificia Universidade Católica do Rio de Janeiro.

The present doctoral thesis entitled "Repercussions of Omega 3 (n-3) AGPI-CL and Maternal Mental Health on Child Neuropsychological Development" had the general objective to investigate variables inherent to nutrition and maternal mental health related to childhood development. The first section of the thesis was a transversal cohort article that aimed to investigate the influence of maternal intake of EPA and DHA during the first trimester of pregnancy period on child cognitive development during the first two years of life. Pooled results from this study showed that high serum concentrations of DHA and EPA during the first trimester of pregnancy were positively correlated with cognitive development during the second year of life. Length at birth, socioeconomic level and parental education were also predictive variables for cognitive development at 18 and 24 months of age (Article 1). The second article of this thesis explored the effects of LCPUFA on child development through a systematic and meta-analysis review (Article 2). Based on our results, the hypothesis that supplementation with n-3 LCPUFA during pregnancy improves infant neurological development cannot be accepted or rejected based on data reported by randomized control trials included in the present review. The third article was a multiple case study conducted with three dyads (mother-baby) aiming to understand the complexity of the subjects' interrelations in their context in detail. Based on the results of this study, low levels of parental education, precarious socioeconomic conditions and unemployment may trigger maternal mental health, impacting negatively child's motor development and motivation to explore his or her own environment (Article 3). In addition, a single case study was conducted (mother-baby dyad) with the objective to investigate maternal mental health and

social support received during the perinatal period. Repercussions of these variables on child development were addressed. It has been suggested that a child's exposure to maternal mental health problems and fragile social support, accompanied by low socioeconomic status might make them more vulnerable to other factors that might impair socio-emotional and behavioral development (Article 4).

Keywords

Child development; Omega-3-fatty acids; maternal mental health and pediatric neuropsychology

Resumo

Irurita-ballesteros, C; Landeira-Fernandez, Jesus (Orientador); Rocinholi, Luciene de Fatima (Co-orientador). **Repercussões do Ômega 3 (n-3) AGPI-CL e da Saúde Mental Materna no Desenvolvimento Neuropsicológico na Infância**. Rio de Janeiro, 2018. 162p. Tese de Doutorado – Departamento de Psicologia, Pontificia Universidade Católica do Rio de Janeiro

A presente tese intitulada "Repercussões do Ômega 3 (n-3) AGPI-CL e da Saúde Mental Materna no Desenvolvimento Neuropsicológico na Infância", teve por objetivo geral investigar variáveis inerentes à nutrição e à saúde mental materna relacionando-as com o desenvolvimento na primeira infância. A organização deste trabalho deu-se em formato de artigos científicos. A primeira parte da tese foi um artigo de coorte transversal que objetivou investigar a influencia da ingestão materna de EPA e DHA durante o primeiro trimestre da gestação e o desenvolvimento cognitivo das crianças aos 18 e 24 meses de idade. A literatura monstra correlação positiva entre a ingestão destes ácidos graxos durante a gravidez e o desenvolvimento infantil. os dados da presente pesquisa revelaram que altas concentrações de DHA e EPA durante o primeiro trimestre da gravidez estão positivamente correlacionadas com o desenvolvimento cognitivo aos 18 e 24 meses de idade. O comprimento ao nascer, o nível socioeconômico e de educação paterna, também, foram variáveis preditoras para o desenvolvimento cognitivo aos 18 e 24 meses de idade. O segundo artigo desta tese foi dedicado à exploração dos efeitos dos AGPICL no desenvolvimento infantil mediante a realização de uma revisão sistemática e meta-análise. Portanto, a hipótese de que a suplementação com n-3 LCPUFA durante a gravidez melhora o desenvolvimento neurológico infantil não pode ser aceita ou rejeitada com base nos estudos incluídos nesta revisão. O terceiro artigo foi um estudo de casos múltiplos, e consistiu em desenvolver conhecimentos detalhados sobre três díades (mãe-bebê) com o objetivo de investigar a complexidade das inter-relações dos sujeitos em seu contexto. Com base nos resultados deste estudo foi observado como o baixo nível de escolaridade materna

e paterna, as precárias condições socioeconômicas, e o desemprego podem desencadear doenças relacionadas à saúde mental materna, repercutindo negativamente sobre o desenvolvimento motor e a motivação da criança para explorar seu próprio ambiente. Adicionalmente, o quarto artigo versou sobre um estudo de caso (díade mãe-bebê) em que se objetivou investigar indicadores de saúde mental materna e o apoio social recebido durante a gravidez e o período pós-parto, avaliando as influências e repercussões dessas variáveis sobre o desenvolvimento de uma criança. Evidenciou-se que a criança exposta à problemas de saúde mental materna e frágil apoio social, acompanhado de baixo nível socioeconômico está mais vulnerável à fatores que prejudicam o desenvolvimento socioemocional e comportamental, afetando de forma indireta o desenvolvimento cognitivo.

Palavras-chave

Desenvolvimento Infantil; Omega 3, ácidos graxos; saúde mental materna; neuropsicologia pediátrica.

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List of abbreviations

AA: Arachidonic Acid

AGE: Ácido Graxos Essenciais

ALA: Ácido Alfa Linolêico

BSID: Bayley Scales of Infant Development

CMA: Comprehensive Meta-Analysis

CNS: Central Nervous System

DHA: Docosahexaenoic Acid

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders - 4ª edição

DSM-V: Diagnostic and Statistical Manual of Mental Disorders - 5ª edição

EPA: Eicosapentaenoic Acid

EPDS: Edinburgh Postnatal Depression Scale

FA: Fatty Acid

IQ: Intelligence Quotient

LA: Linoleic Acid

LCPUFA: Long Chain Polyunsaturated Fatty Acids

NS: Nervous System

PEDro: Physiotherapy Evidence Database

PND: Post-Natal Depression

PPD: Post-Partum Depression

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis

PUFA: Polyunsaturated Fatty Acids

RCT: Randomized Control Trials

SES: SocioEconomic Status

SFA: Saturated Fatty Acid

SMD: Standardized Mean Difference

STAI: State Trait Anxiety Inventory

1. THESIS PRESENTATION

This thesis entitled “Repercussions of Omega-3 (n-3) LCPUFA and Maternal Mental Health on Neuropsychological Development in Childhood” aimed to investigate the effects of nutrition and maternal mental health on early childhood development. This study was organized in the form of scientific articles, aiming at submission and publication in national and international scientific journals. Four articles are presented, the first is a cross-sectional study that investigated the relationship between maternal mental health, socioeconomic level and maternal education level and maternal serum omega-3 concentrations – LC-PUFA (Long Chain Poly-Unsaturated Fatty Acid) during gestation on cognitive development during the second year of life; the second is a systematic review and meta-analysis on the effects of Omega-3 LC-PUFA supplementation of mothers during gestation and the infant neuropsychological development; the third is a multiple case study analyzing the interdependence of maternal mental health and child development considering the importance of the family and social context, and the last article is a single case study that investigated maternal mental health indicators and the social support received during pregnancy and postpartum, assessing the influences and repercussions of these variables on development during the first two years of the baby’s life.

2. THEORETICAL BACKGROUND

Maternal and child health has been investigated by numerous researchers highlighting the importance of the period between the three months preceding pregnancy and the first two years of life (KINGSTON E TOUGH, 2014; DEVAKUMAR *et al.*, 2016; MAHER *et al.*, 2017; VAIVADA *et al.*, 2017; ADAMS E THOMAS, 2018). In this way, the gestational period should be carefully evaluated, especially due to the occurrence of psychic, metabolic and behavioral changes in the mother (BENAIM *et al.*, 2017; KROB *et al.*, 2017). Unwanted complications during gestation, such as maternal mental health problems and intrauterine malnutrition, can lead to deficits in physical growth and cognitive development in the first 24 months of the child's life (FLORES *et al.*, 2012; BELTRAMI *et al.*, 2013; VIVETTE, 2014; GOULD *et al.*, 2014; MENNITTI *et al.*, 2015; JULVEZ *et al.*, 2016; SUNDELIN-WAHLSTEN *et al.*, 2017). These alterations occur to protect the demands of the pregnant woman, the fetus and the child after birth (Leung *et al.*, 2011; Koutra *et al.*, 2013).

Early life is of relevant importance to humans, since the development of the nervous system begins in embryogenesis and continues during a relatively short period of postnatal life, ending at the end of the early years (CASEY *et al.*, 2000). In this period, the brain is more vulnerable to environmental factors, including nutritional factors, since the processes involved in brain development occur very rapidly (KNICKMEYER *et al.*, 2008). From conception to birth, the child is influenced by innumerable biological and environmental factors, such as socioeconomic elements; health; social support; genetic load; mental health and maternal nutrition (SCHWARTZ *et al.*, 2011; GLOVER, V., 2014; DIMASUAY *et al.*, 2016). The mother's health and nutrition intimately influence the baby's genes while building the foundation of the brain structure, including affecting the cellular migration in the developing brain (GEORGIEFF, 2007).

Basic neural functions such as the processing of sensory information and the perception of corresponding sensations as well as the execution of motor tasks can be affected in varied extensions and in proportion to the intensity and duration of exposure to environmental factors, for instance, nutritional deficiencies

(GRJIBOVSKI *et al.*, 2004). This also occurs in the case of more elaborate functions, such as those involving cognition, consciousness, emotion, learning and memory, processes whose disturbance in childhood can lead to important pathological conditions in adult life that are capable of interfering with the quality of life of the individual and in the society in which it lives (GUERRINI *et al.*, 2007).

Studies carried out by MAKRIDES *et al.* (2010); RAMAKRISHNAN *et al.* (2010); CARDOSO *et al.* (2017) showed that both maternal nutrition and mental health can influence the social and behavioral development of the child in the first years of life. Likewise, VAN GOOR *et al.* (2011); SUDFELD *et al.* (2015) reported that children exposed to intrauterine malnutrition revealed low indices on scales that assessed cognitive development. Thus, adequate nutrition, associated with variables such as genetic load, psychological and socioeconomic environment, exerts a decisive influence on cognitive, psychomotor, behavioral and social development throughout life.

1. Maternal Nutrition

Among the macronutrients that influence the process of brain maturation, lipids appear as determining factors for the development of neural functions (INNIS E FRIESEN, 2008). Lipids form 60% of the mass of brain tissue and, in turn, are made up in a large proportion of fatty acids (FA) (CHEN E BAZAN, 2005). FA are important dietary macronutrients whose ingestion provides the organism with energy and components used for the synthesis of complex lipids. Classified as saturated (SFA), monounsaturated and polyunsaturated (PUFA) fatty acids, according to the presence or absence of double bonds in the carbon chain, almost all lipids can be synthesized by our body from proteins and carbohydrates of the diet, except for linoleic (18: 2 n-6) (LA) and alpha-linolenic (18: 3 n-3) (ALA) acids. For this reason, LA and ALA are called essential fatty acids (EFA), justifying the fact that lipid intake is essential and/or vital for the human species, since these FA come exclusively from the diet (CHEN E BAZAN, 2005; INNIS, 2007). Mammals have the ability to elongate and desaturate the PUFAs and then to convert them into longer chain PUFA (LC-PUFA) only from precursors present in the diet. This is the case of LA, which originates, among others, arachidonic acid (C20: 4,

n-6) (AA). The AA, in turn, is an important precursor of eicosanoids of the paracrine system (prostaglandins, leukotrienes, prostacyclins, thromboxanes and hydroxy acids). The ALA allows the formation of three important LC-PUFAs, eicosapentaenoic acid (C20: 5, n-3) (EPA), docosapentaenoic acid (C22: 5, n-3) (DPA) and docosahexaenoic acid, n-3) (DHA) (SPRECHER *et al.*, 1995). The EPA is also an important precursor of another series of eicosanoids, some with an antagonistic action against those formed from AA.

The LC-PUFA of the *n*-6 family are found in many vegetable oils commonly consumed by the population, such as corn, sunflower and soybean oils (LEMAHIEU *et al.*, 2015). Soybean oil has a suitable balance of FA, rich in EFA, 55% linoleic acid and 7% α-linolenic acid, and with 24% oleic acid (C18: 1 *n*-9) (LEMAHIEU *et al.*, 2015). In turn, the LC-PUFA of the *n*-3 family are in lower percentage in vegetable oils; the source of these fatty acids are the oils extracted from soybean, walnuts and linseed. Linseed oil has a high α-linolenic acid content (C18: 3 *n*-3), contributing with more than 50g of this FA per 100g of total FA (THOMPSON E CUNNANE, 2003). Other representatives of the *n*-3 family, such as eicosapentaenoic acid (EPA, C20: 5 *n*-3) and docosahexaenoic acid (DHA, C22: 6 *n*-3), are essentially found in fish oils and marine animals (GIL E GIL, 2015).

The types of FA in the diet determine the types of FA that are available for the composition of cell membranes (YEHUDA, S. *et al.*, 2005). PUFA-LA and PUFA-ALA are important for the fluidity of the membrane, consequently, facilitate the rearrangement of the membranes; and especially in the nervous system, this factor can promote better cellular communication and guarantee the efficacy of brain functions[12]. The cell membranes present phospholipoproteic composition, and the elements that contain the fatty acids are the phospholipids. If the diet is rich in PUFA, the cell membranes of these individuals will be more fluid, which will facilitate the organization of the other elements, such as proteins, in these membranes (INNIS, 2003). In addition, FA participate in the composition of the myelin layer, thus improving nervous impulse conduction and expression of the NS functions (SALVATI *et al.*, 2000). PUFA have also produced other effects on brain functions, such as: modification of cell membrane enzyme activities, modification of receptor number and affinity, modification of ion channel function, modification

of neurotransmitter production and activity, and change in neuronal growth factor (YEHUDA, S *et al.*, 2005).

Reductions in concentrations of n-3 LC-PUFA are frequently related to some psychiatric disorders, such as depression (SONTROP E CAMPBELL, 2006), schizophrenia (ASSIES *et al.*, 2001), dyslexia, dyspraxia, attention deficit hyperactivity disorder (ADHD) and changes in neurocognitive functioning in women in the gestation period, in which there is a decrease in n-3 LC-PUFA (DE GROOT *et al.*, 2003). Thus, an optimal status of n-3 LC-PUFA seems to be necessary for the infant cognitive functioning.

It has been reported that children of mothers who had high blood levels of DHA had a better development of attention in childhood (COLOMBO *et al.*, 2004) and also that children of mothers who were supplemented with cod liver oil during gestation and lactation presented better mental development at 4 years of age than children whose mothers received corn oil in this period (HELLAND *et al.*, 2003). Essential fatty acids are important for myelin synthesis and if they are not available at this time deficiency in the myelination of the nervous system may occur (AUESTAD, 2000). The effects of nutritional deficiencies on the brain and behavior are more intense if occurring during the period of "rapid brain growth" that coincides with the peak of myelin synthesis, in which there is cellular hypertrophy. This period, in children, begins in gestation and continues until two years of age (REED *et al.*, 2005).

Because n-3 LC-PUFA are important for learning and memory processes and are involved in the myelination of the nervous system (SALVATI *et al.*, 2000; UAUY *et al.*, 2000; YEHUDA, S *et al.*, 2005), and this occurs intensely during the critical period of brain development, many studies investigating omega-3 deficiency recommend n-3 LC-PUFA supplementation during pregnancy and/or lactation (MULDER *et al.*, 2014; MELDRUM *et al.*, 2015; VOLLET *et al.*, 2017). The deficiency of these unsaturated lipids, by delaying the process of myelination, promotes sensory deficits (vision, hearing, taste and smell) (DIJCK-BROUWER *et al.*, 2005), and in the development of neurological reflexes in infants (DIJCK-BROUWER *et al.*, 2005). Other studies have shown that n-3 LC-PUFA deficiency

implies alterations in hippocampal neurons (CALDERON E KIM, 2004), being the adequate functioning of this structure related to learning and memory. Some studies suggested that high concentrations of DHA and EPA during pregnancy are associated with better child cognitive development during the first two years of life ASSISI *et al.*, 2006; HIBBLEN, JOSEPH R. *et al.*, 2007; DUNSTAN *et al.*, 2008; KELLY *et al.*, 2011; VALENT *et al.*, 2013; DE GIUSEPPE *et al.*, 2014)

Some studies have shown that if n-3 LC-PUFA deficiency occurs during the postnatal period, it will also result in damage to the myelination process, which will be accompanied by deficits in learning, motor aspects and visual and auditory abnormalities (BAACK *et al.*, 2016). Similar cognitive and myelination impairments have also been reported in protein malnutrition (ROCINHOLI *et al.*, 2001), protein-calorie malnutrition (ROCINHOLI E LANDEIRA-FERNANDEZ, 2011) and iron deficiency (ROCINHOLI *et al.*, 2008) in children and animals.

n-3 LC-PUFA play a key role in growth and intellectual development during the neonatal and early childhood period (VOLLET *et al.*, 2017). As brain development, especially the pre-frontal cortex responsible for executive functions, continues during late childhood (THATCHER, 1991), it has been suggested that polyunsaturated fatty acids could play an important role in the cognitive functions of children (Sinn e BRYAN, 2007). However, few studies (HELLAND *et al.*, 2008; CAMPOY *et al.*, 2011; MELDRUM *et al.*, 2015) investigated the effects of n-3 LC-PUFA supplementation on the cognition of older children.

2. Maternal Mental Health

Gestation is a moment of transition that generates physical, hormonal, psychic and social insertion changes, which may directly reflect on women mental health, being extremely significant throughout life and requiring numerous adaptations (ANDERSON, 2005; MURGATROYD *et al.*, 2015; HOEKZEMA *et al.*, 2017). In addition to being among the most exposed to the risks of mental disorders, women are more vulnerable to the development of these psychic disorders during pregnancy and the puerperium, since they are more expressive during this period

(CAMACHO *et al.*, 2007; JONES *Et al.*, 2014; KNUESEL *et al.*, 2014). These disorders may cause harm to the health of the pregnant woman, as well as to the fetus, and their intensity will depend on family, marital, social, cultural and personality factors of the pregnant woman (CAMACHO *et al.*, 2007).

Mental disorders can begin with the presentation of negative feelings, which if occur infrequently, can be considered common. However, minor psychiatric morbidity is understood as being very common disorders, difficult to characterize. Most individuals with minor psychiatric morbidities present complaints such as sadness, anxiety, fatigue, decreased concentration, somatic concern, irritability, and insomnia. Minor psychiatric morbidities may also be termed common mental disorders, a comprehensive term that reinforces their frequent occurrence. Depression, anxiety, somatoform disorders and neurasthenia are common mental disorders (CAMACHO *et al.*, 2007).

In addition, some studies have pointed to mental disorders, which are underdiagnosed and without adequate treatment in pregnant women, as a determinant of several maternal and fetal outcomes (JABLENSKY *et al.*, 2005; ROMANO-SILVA, 2009; MALM *et al.*, 2015; GENTILE, 2017). The presence of anxiety can negatively affect gestation because it is considered a mediator of endocrine changes as well as certain risk behaviors, such as smoking, delay and/or inadequate access to prenatal care, inadequate feeding and gestational weight gain (MALM *et al.*, 2015; MEIRELES *et al.*, 2017; YONKERS *et al.*, 2017).

With regard to the mental health of women in the perinatal period, disorders common to the postpartum are added to the common mental disorders. Postpartum depression (PPD) has been considered a major public health problem today due to its high prevalence in the population and its high social costs. Nevertheless, its early identification, as well as other psychiatric disorders, is not part of the routine of health institutions, both public and private. Besides that, there is evidence of the relationship between the occurrence of mental disorders in the prenatal period or in previous moments of life with the occurrence of such disorders in postpartum (ROBERTSON *et al.*, 2004; BOYCE E HICKEY, 2005; Jones *et al.*, 2014; GENTILE, 2017).

If during the prenatal consultations, no psychiatric morbidities are investigated during pregnancy, in the postpartum period this condition does not change. Women only have their first visit with the obstetrician about 6 weeks after childbirth, with the focus on the baby (EARLS *et al.*, 2010). There is no space in this model of care for the identification of psychiatric disorders in the population that is precisely one of the most vulnerable to their occurrence. There is increasing evidence that psychosocial factors can affect health through biological effects and changes in mental health (KLIEMANN *et al.*, 2017).

Several authors associate these psychosocial factors with PPD, such as: belonging to lower social classes; history of psychiatric illness; history of depression and recent treatment for depression; vulnerable personality; occurrence of stressful events during pregnancy and after delivery; complications during pregnancy; dissatisfaction with the partner and problems in the marital relationship; and inadequate social support (BOYCE E HICKEY, 2005; DE SOUZA E BAPTISTA, 2017; KLIEMANN *et al.*, 2017).

Some studies have shown that PPD is associated with cognitive, socioemotional and behavioral adverse effects in children (CID E MATSUKURA, 2010; Mcdonald *et al.*, 2016; CARDOSO *et al.*, 2017). PPD is presenting a higher prevalence in the age group in which women usually become mothers, affecting, therefore, the main responsible for the care of the child. Thus, maternal depression is an important risk factor for child development (BRUM & SCHERMANN, 2006). The duration of PPD is related to a reduction in affectivity and child-directed care, resulting in developmental impairment during the first year of life (NARDI *et al.*, 2015). According to HUDSON *et al.* (2015); NARDI *et al.* (2015); CARDOSO *et al.* (2017), there is an association between PPD and later developmental problems in children, including conduct disorders, language development, physical health impairment, unsafe connections and depressive episodes. Symptoms of depression interfere in all interpersonal relationships, especially in the development of the interaction between the mother and the baby.

3. Child Development: Considerations on the Neuropsychological Perspective

3.1 Brain development and its first implications

The process of human development has a multidimensional character, such as the cognitive, motor, emotional and social dimension, to which all these dimensions communicate in an integrated way (COLE & COLE, 2003). More specifically, the ontogenesis of cognitive functions is strongly influenced by genetic and maturational factors, as well as social interactions, socioeconomic level and cultural values. Although all brains have similar basic structures, size, organization, and functioning vary and change throughout life, depending on the genes, environment, and experience of each individual.

3.2 The importance of the first years of life

Neuroscience has provided evidence that early experiences affect brain development and may have a long-term effect on the child's well-being, whether in relation to physical and mental health, or learning and behavior. For example, according to (SHORE, 2001), the first three years are the fastest growing period of sensitive periods specific to optimal learning in certain areas.

From conception to birth, the child is influenced by several factors. The health and nutrition of the pregnant mother intimately influences the genes while building the foundation of the brain structure, including affecting cell migration in the developing brain. Before the end of the first year of life, brain development lacks the protective barrier of cells that restrict the entry of toxins from the bloodstream into brain cells. Thus, inadequate maternal nutrition and exposure to dangerous pollutants and toxins (such as pesticides, viruses, prescription drugs, and recreational drugs, including nicotine and alcohol) significantly compromise the developing brain, causing brain cells to acquire abnormal properties and make dysfunctional connections with other brain cells (LEVITT, 2003).

The quality of the relationship between parents (and the close family) and children is fundamental for the effective development of brain architecture, its functions and ability (FOGEL *et al.,* 2009). Parental care practices such as reading, complex language use and sensitivity in interactions are associated with improved developmental outcomes (BRADLEY, 2002). Research has shown that babies with a more loving and safe parental relationship have a lower response to stress and are more likely to achieve a higher level of happiness, health, productivity and creativity (RAPOPORT, 2003; AZEVEDO, 2013; LISBOA, 2018). Positive affect can measurably alter developing trajectories, including emotional development and social cognition (GOSWAMI, 2008).

In relation to the development of the central nervous system, it begins soon after conception and develops sequentially, cumulatively and integratedly continuing throughout life. The brain matures from the bottom up. The lower part (the brainstem), which controls the automatic functions, matures first and must be formed at the time of birth for survival. Following the development of the higher parts - such as the midbrain, which mediates sensory and motor integration; the limbic system, where much emotional information is kept; and the prefrontal cortex along with the neocortex that control abstract thinking and memory (PERRY, 2000).

The development of the highest (top) level is based on the development of the lower (bottom) structures. For the higher levels to develop and function fully, it depends on accurate and precise inputs from the lower levels (KNUDSEN, 2004). Higher level adaptation is more difficult if the lower level is compromised, i.e., the good development of basic skills generates more complex skills. For example, in infants, emotional, sensory, and social experiences are essential to optimize the development of lower levels in the brain. Children, however, mature more sophisticatedly from a variety of experiences, which are essential to improve the development of higher levels (NSCDC, 2007).

3.3 Brain development and cognitive functions

The brain is composed of a set of integrated systems, which participate intensely in the performance of cognitive functions (MIRANDA & MUSZKAT, 2004). It is

from the integration of all cognitive functions that human cognition is constituted as a biological phenomenon where being, doing and knowing are indissociably aspects of behavior. Due to the particular abilities of each cognitive function, each of them has a specific ontogenesis with maturation and internalization at different moments (PIRES, 2010).

Sensation and perception are functions that are dependent on the biological system, as well as on the experience and action. That is, at birth, the fundamental sensory elements are already practically developed, but it is through social interaction and adult care that these abilities are stimulated and reinforced. As the capabilities of each sense become more precise, inter-sensory coordination develops, becoming more complex (LICKLITER, 2011). Thus, perception is constituted as an individual construction, which allows to build a vision of reality, where each one can assign a particular meaning to these processes.

Attention is a cognitive function that involves cognitively directing, selecting information, responding to and inhibiting external and internal stimuli (LURIA, 1981) and improves with age, especially those aspects that are related to stability and adaptability, and can be maintained until adolescence. During the first months, attention is elementary and involuntary, and there is no control of it (POSNER, 2014).

From the maturation of certain structures, new skills and behaviors emerge, gradually allowing greater control over the attentional processes. This has a great impact on the individual behavior and is closely associated with the development of executive functions. This process stabilizes at about 5 or 6 years of age, when it is expected that attention will be voluntary; however, the full development of selective and sustained attention, visual processing speed, and inhibitory control will only occur at twelve years of age. This process occurs from the interaction with the adults, that is, with the social interactions that the child establishes, since it is from the adult communication and speech that the attentional process is internalized (LURIA AND YUDOVICH, 1971). Thus, the language of the adult guides the way the stimulus will be oriented. Therefore, language becomes important for proper development of the attentional process. Attention is a complex process that depends

on other cognitive functions and emotional functions as well, involving “inputs” of information and performance of complex behaviors. (NABAS AND XAVIER, 2004)

For clinical purposes, the attentional process is subdivided into four subcategories that are related to the procedures involved during the performance of a task: (1) selective attention; (2) divided attention; (3) sustained attention (vigilance and concentration) and (4) alternated attention (STERNBERG AND BEN-ZEEV, 2001).

In turn, the development of memory is closely associated with the maturation of numerous brain structures, especially the hippocampus region and frontal areas (PRESTON & EICHENBAUM, 2013). Memory is a cognitive function that develops among biological and social aspects, accompanying the various changes that occur in ontogenesis.

Memory as a cognitive function can be presented among different stages and types, each with a specific mode of operation but working together as a whole memory system. The first stage is the codification and learning of new information, the second is the retention and consolidation of information, which includes sensory memory, short- and long-term memory and the third stage is evocation of information (COWAN, 1988; BADDELEY *et al.*, 2001; BADDELEY, 2002).

Human memory can be classified into two types of storage: Short-term memory and Long-Term memory. Short-term memory is an active process of storing and retaining information for a limited period of time. Long-term memory is divided into two systems: explicit (conscious) memory and implicit (non-conscious) memory. Explicit memory is divided into episodic (events and experiences) and semantic (theories and concepts) (SQUIRE, 2009)

According to CARNEIRO (2008), memory undergoes several transformations throughout human development. During the first months of life, there is a rudimentary recognition of memory (BAUER, 2008) and can be assessed through

imitation: (1) immediately, called elicited imitation and (2) after an interval, called differed imitation (MELTZOFF, 1988; BAUER *et al.*, 2002).

During the pre-school age, it is possible to follow the explicit memory through language development (NELSON & FIVUSH, 2004). In other words, language acquisition and development are also important factors for a more flexible and efficient memory (DIAS & LANDEIRA-FERNANDEZ, 2011). During school age, it is suggested that mnemonic processes can be differentiated. According to GRAF (1990), implicit memory becomes functional before explicit memory because it requires translation of instructions, planning to store new information, planning and access to long-term memory.

Emotional processes in young children also have a strong impact on the development of cognitive abilities (BLAIR, 2002), so an event can be remembered when it was unique and full of emotionality, or even when it was very important (FIVUSH & SCHWARZMUELLER, 1998). The diverse modalities of the memory system are presented within different courses of development; however, the improvement of the attentional focus along with the emergence of storage and retrieval strategies definitely helps to improve the mnemonic processes.

The development of language is related to both, the biological maturity aspects of the CNS and to the interactions between the baby and its environment, which plays a relevant role throughout this process of language acquisition and improvement (BARBOSA, 2009).

The language relates the ability to understand and express thoughts, ideas and feelings constructed of words, gestures and visual and auditory stimuli. The linguistic abilities accompany a course of brain myelination and maturation, occurring in a postero-anterior gradient (PUJOL *et al*, 2006). The Broca's area, responsible for the articulation of speech (expressive language) and Wernicke's area, responsible for understanding the language (receptive language), thus, the receptive and semantic functions of language, develop prior to expressive functions and morphosyntactic functions. However, exposure to an environment where language use is present is necessary for this maturation to occur and more complex language abilities to develop (BARBOSA, 2009).

Language is considered to be the first form of socialization of the child and, in the majority of the times, it is explicitly performed by parents through verbal instructions during daily activities, as well as through stories that express cultural values. Socialization through language can also occur implicitly, through participation in verbal interactions.

The process of language acquisition involves the development of four interdependent systems: (1) Phonological, related to the perception and production of sounds to form words; (2) Pragmatic, refers to the use of language for communication purposes within a social context; (3) Semantic, attribution of meaning to words; (4) Orthographic, knowledge of rules and norms related to the ability of building sentences. According to STERNBERG & BEN-ZEEV, (2001); BARBOSA (2014) regardless of the language that is acquired, children seem to follow the same pattern of development.

Numerous definitions for the concept of executive functions have emerged, as well as for the possible subcomponents integrating them. (MILLER & COHEN, 2001) consider the construct as an "umbrella" term that encompasses several cognitive processes related to oriented behavior. Executive abilities present an important adaptive value for the individual, allowing a rapid and flexible change of behavior in response to new environmental requirements (ZELAZO *et al.*, 2003). These functions enable us to interact with the world in the most diverse situations that we encounter in our daily lives, through which it is possible to organize the thoughts, taking into account the experiences and knowledge stored in the memory, as well as the expectations regarding the future (LEFÈVRE, 2004)

Recently, MÜLLER *et al.* (2005) proposed a dichotomous classification of executive functions by dividing into "hot", related to affective and emotional aspects and "cold "executive processes, related to cognitive aspects. Therefore, executive functions encompass a highly complex set of interrelated skills such as selective attention, vigilance, impulse control and self-regulation, working memory, mental flexibility, organization and planning, problem solving, verbal

fluency, and creativity. In addition, they allow the norms within a society to be respected in a behavioral pattern considered appropriate for a given context.

The multidimensional nature of executive skills and the interdependence of related neural circuits have an impact on the development of other related skills. Prolonged maturation of the frontal lobes makes executive functions take longer to develop fully. For a long time, it was believed that the cerebral location of the executive functions was exclusive to the prefrontal lobe; currently, through neuroimaging techniques, it is known that this construct is associated with regions of the frontal lobes (STUSS & ALEXANDER, 2000) as well as distributed in a wide brain network, which includes subcortical structures and thalamus pathways. Over the years, executive circuits have become more refined and better connected.
Consequently, they have a more efficient character in the organization and monitoring of human behavior. Thus, this cognitive function becomes the last to have its development completed in the process of human cognitive development (PIRES, 2010). Executive functions seem to improve sequentially over the years due to maturation of the frontal lobes between birth and two years of age, from seven to nine, and a final leap in adolescence, between sixteen and nineteen years of age (ANDERSON *et al.*, 2001).

3.4 Neuropsychological assessment in childhood

Developmental neuropsychology is a branch of the neuropsychology that studies, on the one hand, the interaction between the social background of the child and the development of its mental functions and personality and, on the other hand, the ontogenetic development of the brain under normal and pathological conditions.

Child neuropsychology along with developmental neuropsychology has emerged in innumerable ways. Among the main objectives of the child neuropsychological assessment, stand out the prevention and early identification of cognitive and behavioral changes, qualitative and quantitative mapping of brain areas and their correlates, differential diagnosis, treatment of developmental disorders, therapeutic intervention programs and study of the learning development process (ELLISON & SEMRUD-CLIKEMAN, 2007). In this way, the neuropsychological assessment is an excellent tool for the clinical practice, especially in the pediatric age group,

since prognostic changes could act as a protective factor, preventing secondary cognitive and behavioral dysfunctions arising from family, occupational and educational constraints.

Child neuropsychological assessments requires specific instruments that seek to understand the cognitive (praxis, attention, language, memory, perception, and executive functioning), emotional (self-regulation and social development) and behavioral functioning of the child within a specific age range through standardized tests and instruments. The interpretation of results requires knowledge of cognitive, affective aspects, as well as factors that can be inferred in a task. Knowledge related to the normal and pathological development of the central nervous system as well as the critical periods of development. In this way, the generated report can act on the possible changes (recommendations and accommodations) resulting from a brain injury or impairment or anticipate atypical development through cognitive stimulation and compensate observed deficits.

Another specificity of the child neuropsychology is the importance of guidance to parents and/or teachers. The orientation is fundamental for the acceptance of the difficulties that the child presents and the viability of favorable situations to optimize child development.

4. Child Development: Considerations on the Bioecological Perspective

Child development is a continuous and dynamic process that promotes changes in several areas, namely: cognitive, social, emotional and physical, in a complex interaction between them and the environment in which each stage is constructed from the previous stages (FIGUEIRAS *et al.*, 2005; HALPERN, 2015). Development can be understood from the bioecological model of development, in which it expands from biology and the environment to a broader concept, which encompasses epigenetics and neuroscience (BRONFENBRENNER, 2011; HALPERN, 2015).

Bronfenbrenner developed the theory of human development, published in the late 1970s, presenting to the scientific field important premises for the planning and

development of studies in natural environments. The bioecological model considers that the human being is biopsychologically active in evolution with the people, objects and symbols that are present in its environment. Thus, development consists of a process of reciprocal interaction between the person and its context through time, being a function of the forces that arise from multiple circumstances and the relation between them ((BRONFENBRENNER & MORRIS, 1998), This process occurs throughout the life cycle and the generations (BRONFENBRENNER, 2001), where the family is the main nucleus where the child's first social interactions occur. The learning of concepts, rules and cultural practices that support socialization processes begins in it (BRONFENBRENNER, 2005).

Human development occurs through gradually more complex processes of reciprocal interaction of an active subject and the people, environments, and symbols of its immediate environment. This process of reciprocity is called a proximal process, which, in order to have developmental effects, must occur regularly over an extended period of time (BRONFENBRENNER, 1995). In this context, the concept of development is seen as the result of a joint function between a proximal process, the characteristics of the developing person, the immediate context in which the person lives, and the amount and frequency of time in which the developing person has been exposed to a specific proximal process and the environment.

The PPCT model of development (Process-Person-Context-Time) stresses that for the development of the person to occur, it needs to actively participate in reciprocal interactions of increasing complexity with people with whom it develops attachment and, over time, commit to the well-being and development of others, preferably for life. In this direction, the establishment and maintenance of the interactions between the caregiver and the child depends on the availability and involvement of another adult (third person) who supports and encourages the person who cares for and interacts with the child (BRONFENBRENNER & EVANS, 2000). In this way, the person is a producer and, at the same time, a product of development (BRONFENBRENNER, 1999).

Family has been the main context of child development. However, it is directly and indirectly affected by other sociocultural contexts. BRONFENBRENNER & VASTA (1989) also proposed that the effective functioning of the process of educating children in the family context and in other contexts (e.g. schools, kindergartens) requires mutual trust and the existence of established and continuous patterns of information exchange in the main environments in which children and their families live. In this direction, processes that occur in different contexts are interdependent and affect each other in a reciprocal way.

For an adequate development at this early stage, the child needs a warm, harmonious environment rich in experiences from the prenatal period through the care of the mother and the environment in which it lives. This context should be promoted intensively after birth. The involvement and participation of the family, the social support network and the public policies that organize the services to support the needs of families and children and optimize their development is therefore crucial. According to BRONFENBRENNER (1996), the concept of support network is related to an evolutionary conception of the person in the interacting ecological context, and to the increasing capacity to discover, sustain or modify the properties of the environment.

Based on these considerations, the present thesis sought to include the different dimensions presented by the Bioecological Approach to Human Development: Process, Person, Context and Time.

3. OBJECTIVES

Based on the theoretical revision presented above, the present thesis will be composed of four articles with the following objectives:

- To evaluate the effects of maternal n-3 LCPUFA supplementation on offspring's neurobehavioral development without the potential effects of breastfeeding through a systematic review and meta-analysis.

- To investigate the association between maternal mental health, socioeconomic status and maternal serum concentrations of eicosapentaenoic acid (EPA; omega-3) and docosahexaenoic acid (DHA; omega-3) during early pregnancy and infant cognitive development at 18 and 24 months of age.

- To characterize the impact of maternal mental health conditions on child development from pregnancy to two years of age. This is a multiple case longitudinal study, considering three mother-infant dyads.

- This single case study aimed to investigate indicators of maternal mental health and social support received during the gestational and post-partum period on child development during the first two years of life.

4. ARTICLE SECTION

ARTICLE 1

Irurita-Ballesteros, C., Herrera-Legon, M., DVS, Falcão., Rocinholi, L., Landeira-fernandez, J. Effects of omega-3 LCPUFA supplementation during pregnancy on child neurodevelopmental outcomes: A systematic review and meta-analysis of randomized controlled trials**.** **(**Article submitted)

ABSTRACT

Previous studies have suggested that prenatal n-3 long-chain polyunsaturated fatty acid (LCPUFA) supplementation may have a positive impact on child neurodevelopment later in life. The aim of this review was to evaluate the effects of maternal n-3 LCPUFA supplementation on offspring's neurobehavioral development without the potential effects of breastfeeding. A search of two electronic databases was conducted to identify randomized controlled trials that used maternal n-3 LCPUFA supplementation and assessed offspring's neurodevelopmental outcomes. After meeting the inclusion criteria, the trials were evaluated using the Physiotherapy Evidence Database scale. Standardized mean differences (SMDs), 95% confidence intervals, and heterogeneity were calculated using Comprehensive Meta-Analysis software.

Out of the 341 total studies that were identified in the database search, 10 trials met the inclusion criteria. These 10 trials included a total of 4041 participants. No significant difference was found between the n-3 LCPUFA supplementation group and placebo group in cognition, receptive or expressive language, fine and gross motor skills, and socio-emotional outcomes. A small effect size was found for the behavioral outcome (SMD = 0.140 [0.039,0.242], $p = 0.007$), but these results had significant heterogeneity. The pooled results for anthropometric measures were significant, in which birth weight (SMD = 0.104 [0.043,0.164], $p = 0.001$) and birth length (SMD = 0.111 [0.011,0.212], $p = 0.030$) significantly increased in the supplementation group. The results from the present meta-analysis do not support the hypothesis that maternal supplementation with n-3 LCPUFAs improves childhood neurodevelopment. Further studies are needed to consolidate and extend the hypothesis.

Key words: omega-3 - fatty acids; maternal nutrition. child neuropsychological development; cognitive assessment.

RESUMO

Alguns estudos têm sugerido que a suplementação de ácidos graxos polinsaturados de cadeia longa n-3 (AGPICL) no período pré-natal pode ter um impacto positivo no desenvolvimento neurológico infantil. O objetivo desta revisão, foi avaliar os efeitos da suplementação materna de AGPICL n-3 sobre o desenvolvimento neuropsicologico das crianças sem considerar os efeitos potenciais da amamentação. Foi conduzida uma busca bibliográfica em duas bases de dados eletrônicas com o objetivo de identificar ensaios controlados randomizados (ECR) que utilizaram a suplementação materna de AGPICL n-3 e posteriormente, avaliaram o desenvolvimento neuropsicologico das crianças. Depois de atender aos critérios de inclusão, os ECR foram avaliados utilizando a escala da base de dados de Physiotherapy Evidence Database Scale (PEDro). As diferenças entre médias (SMDs), os intervalos de confiança de 95% e a heterogeneidade foram calculados usando o software Comprehensive Meta-Analysis (CMA). Dos 341 estudos extraídos na busca bibliográfica, 10 estudos atenderam aos critérios de inclusão. Os resultados não encontraram diferença significativa nos domínios da cognição, linguagem receptiva e expressiva, motor fino e grosso e socioemocional para os grupos de suplementação de AGPICL n-3 e os grupos placebo. A analise apontou um tamanho de efeito pequeno para o domínio comportamental (SMD = 0.140 [0.039.0.242], p = 0.007), porem, os dados apresentaram uma heterogeneidade significativa. Houve diferenças significativas entre os grupos controle e suplementação no peso corporal (SMD = 0,104 [0,043,0,164], p = 0,001) e comprimento ao nascer (SMD = 0,1111 [0,011,0212], p = 0,030). Os resultados da presente meta-análise apontam para a necessidade de mais estudos que elucidem a hipótese de que a suplementação materna com n-3 AGPICL melhore o desenvolvimento neuropsicologico infantil.

Palavras chave: ácidos graxos – ômega 3; nutrição materna; desenvolvimento neuropsicologico infantil; avaliação cognitiva.

1. Introduction

The ability of supplementation with long-chain polyunsaturated fatty acids (LCPUFAs) during gestation to improve the healthy development of the fetus has being debated for years. LCPUFAs, such as eicosapentaenoic acid (EPA; C20:5ω-3), docosahexaenoic acid (DHA; C22:6ω-3), and arachidonic acid (AA; C20:4ω-6), are structural and functional components of cell membranes and involved in numerous neuronal processes, ranging from effects on membrane fluidity to the the regulation of gene expression (SCHUCHARDT *et al.*, 2010). Deficiencies and imbalances in these nutrients not only during the developmental phase but also throughout life have significant effects on brain function (BARKER e CLARK, 1997; UAUY *et al.*, 2000).

PUFAs of the ω-3 and ω-6 families are essential nutrients that cannot be synthesized by the human body; therefore, they must be obtained exclusively from a nutritional diet (MENNITTI *et al.*, 2015). The maternal diet during pregnancy is a major factor that influences fetal development and metabolism. LCPUFAs affect several aspects of fetal programming (MATHIAS *et al.*, 2014). A study of individuals who were exposed *in utero* to the Dutch famine of the winter of 1944-1945 showed that inadequate nutrition during pregnancy, particularly after mid-pregnancy, diminished fetal growth and glucose tolerance in adults at ≥ 50 years of age. These results suggest that malnutrition during gestation can negatively affect fetal metabolic control systems (RAVELLI *et al.*, 1998).

Numerous studies have shown that LCPUFAs may positively influence both maternal health during pregnancy and fetal and child health (INNIS, 2007; CETIN e KOLETZKO, 2008; SCHUCHARDT *et al.*, 2010). LCPUFAs are important and beneficial for the physiological development of offspring who receive n-3 fatty acids via the placenta during critical periods of development. Therefore, it has been proposed that additional maternal supplementation with LCPUFAs during pregnancy may improve offspring's early cognitive and visual development (INNIS, 2007; EMMETT *et al.*, 2015).

The present systematic review and meta-analysis of randomized controlled trials (RCTs) investigated the potential effects of interventional LCPUFA supplementation during the gestational period on offspring's neurobehavioral development, without the potential effects of breastfeeding. The primary outcome of this review was developmental scores in the following domains: cognition, language, motor skills, socio-emotional behavior, and adaptive behavior, based on standardized psychometric scales in which the mean is 100 and the SD is 15. The secondary outcomes were birth weight and birth length.

2. Methods

This review and meta-analysis adhered to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (MOHER *et al.*, 2009).

2.1. Search strategy

An electronic database search was conducted using PubMed and PsycINFO. We searched for articles that were published from 2006 to the end of April 2016. The PubMed search terms were the following: "pregnant women" OR "pregnan* AND fatty acids-omega 3" OR LCPUFA AND child development. The official subject terms that were selected for the PubMed database were based on MeSH terms. The PsycINFO search terms were the following: pregnan* AND "fatty acids" OR "LCPUFA" AND childhood development. The reference lists of all of the articles that were selected for this study were also checked for the possible inclusion of additional studies. The search results were reviewed based on the titles and abstracts, followed by retrieval of the full-text of the article for evaluation by two authors (CIB and MHL). Studies were selected according to eligibility criteria. Searches of references published papers were also conducted.

2.1.1. Criteria for inclusion of studies

The studies that were included in this systematic review and meta-analysis had to be RCTs that compared the effects of oral LCPUFA supplementation and placebo or no supplementation during pregnancy on the neurobehavioral development of

offspring. Studies that assessed neurobehavioral development outcomes (cognition, language, motor skills, socio-emotional behavior, and adaptive behavior) or IQ were included in this review.

2.1.2. Criteria for exclusion of studies

Review papers, uncontrolled trials, dissertations, studies that included premature infants or children with disabilities or developmental delays, studies that did not adjust for the potential effects of breastfeeding, and animal studies were excluded.

2.2. Quality assessment

A quality assessment of the included studies was performed using the modified Physiotherapy Evidence Database (PEDro) scale (MAHER *et al.*, 2003). The PEDro scale contemplates two aspects of trial quality: the internal validity of the trial and whether the trial contains adequate statistical information to make it interpretable (MAHER *et al.*, 2003). The majority of the items on this scale are based on the well-validated Delphi list (VERHAGEN *et al.*, 1998), except for two items (items 8 and 10). Points were granted if the criteria according to the PEDro guidelines were met. Higher points indicate higher quality of the trial (DE MORTON, 2009). This scale was not used as exclusion criteria. Its purpose was to measure the quality of the RCTs. The PEDro scale was completed by the first two authors of the present study (CIB and MHL).

2.3. Outcome measures

The first two authors of this study (CIB and MH) independently performed data extraction. A semi-structured form was used to extract the following specific information: characteristics of the participants and methodological information of each trial, including sample size, type of supplementation, and neurodevelopmental instruments that were used to assess the primary outcomes. The quality of the assessment instruments was also established as part of the data extraction. The primary outcomes for the present study were the offspring's scores on five neurodevelopmental domains that were measured using global well-standardized instruments (cognition, language, motor skills, social-emotional behavior, and adaptive behavior), including subcategories for language (expressive and receptive language) and motor skills (fine and gross motor skills). Intelligence Quotient (IQ)

scores were considered as a cognitive measure. Therefore, IQ values were also included as primary outcomes. Anthropometric measurements were considered second outcomes.

2.3.1. Primary outcomes

Federal, state, and professional standards for early childhood assessment require that cognition, language, motor skills, social-emotional, and behavioral domains are evaluated (WEISS *et al.*, 2010). Therefore, these domains are emphasized in the Individuals with Disabilities Educational Improvement Act of 2004 (YELL *et al.*, 2006) as critical to the comprehensive assessment of young children because they are key for documenting delays and are pertinent to inform response-to-intervention efforts. In this analysis, IQ was included as part of the cognitive domain.

2.3.2. Secondary outcomes

As part of early physical development, birth weight and birth length were used as secondary outcomes.

2.4. Data extraction and synthesis

After data from the studies were extracted and reviewed by both authors (CIB and MH), further clarification of trial details and unpublished outcome data were requested by e-mail from the studies' authors. Only one of the studies that were included in the qualitative analysis was not included in the quantitative analysis because unpublished outcome data could not be obtained from its authors (VOLLET *et al.*, 2017).

2.5. Statistical analysis

The main objective of this study was to investigate whether there are associations between n-3 LCPUFA supplementation during pregnancy and (*i*) the five developmental domains (cognition, language, motor skills, social-emotional behavior, and adaptive behavior) and/or IQ scores and (*ii*) anthropometric measures (birth weight and birth length). The analyses of the primary and secondary outcomes were performed independently according to each domain. Age ranges were not separated.

Comprehensive Meta-Analysis (CMA) 3.0 software was used to analyze the data. Heterogeneity was quantified using the I^2 statistic. With the absence of substantial heterogeneity, the results were pooled using a fixed-effects model. The level of significance was set at $p < 0.05$, and 95% confidence intervals were determined. The figures were produced using CMA 3.0 software.

2.5.1. Computation of effect sizes

Effect sizes for each study, represented by Cohen's *d*, were calculated using means, standard deviations (SDs), and samples sizes for the studies that reported these statistics. Effect sizes for the other studies were calculated using odd ratios or median and interquartile ranges when means and SDs were irrelevant or not provided. Cohen's *d* effect sizes are in SD units, such that an effect size of 1.0 indicates that two groups differ by 1 SD. An effect size of 0.2 is interpreted as small (detectable only through statistics). An effect size of 0.5 is interpreted as medium (detectable to a cautious observer). An effect size of ≥ 0.8 is interpreted as large (clear to any observer) (COHEN, 1988). Using a random-effects model, in which each study is weighted by its inverse variance weight (1/SE2), effect sizes were computed as recommended previously (SCHMIDT e LE, 2004). Separate effect sizes were calculated for each outcome.

3. Results

3.1. Search results

The initial PsycINFO and PubMed database searches yielded 341 studies. An additional 23 studies were identified through other sources, for a total of 364 studies. Of these 364 studies, 72 duplicate studies were removed. Of the remaining 292 studies, 207 were excluded after the titles and abstracts were reviewed because they did not meet the inclusion criteria. Additionally, the full text of four studies could not be obtained. The full text of the remaining 81 studies was then assessed for eligibility. Of these 81 studies, 70 were excluded for the following reasons: not RCTs (*n* = 35), LCPUFA supplementation after the gestational period (*n* = 6), no data adjustment for breastfeeding (*n* = 6), the absence of neurodevelopmental outcomes (*n* = 19), the lack of a standardized scale for the assessment of neurodevelopmental outcomes (*n* = 2), subjects who did not meet the age criteria (*n*

= 1), and animal study (*n* = 1). A total of *n* = 11 articles were included in the qualitative synthesis, and 10 studies were included in the quantitative synthesis meta-analysis (*n* = 10). The reasons for the exclusion of studies after full-text analysis are outlined in Fig. 1 (TOFAIL *et al.*, 2006; DUNSTAN *et al.*, 2008; HELLAND *et al.*, 2008; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; CAMPOY *et al.*, 2011; ESCOLANO-MARGARIT *et al.*, 2011; VAN Goor *et al.*, 2011; MULDER *et al.*, 2014; MELDRUM *et al.*, 2015; VOLLET *et al.*, 2017).

3.2. Quality assessment

For each study that was included in the meta-analysis, the PEDro quality assessment was completed by the two main authors of this study. The average PEDro score was 7.7 ± 1.5 for the RCTs (*n* = 11). Only three studies (TOFAIL *et al.*, 2006; MELDRUM *et al.*, 2015; VOLLET *et al.*, 2017) obtained a moderate score of 6. For the other RCTs (DUNSTAN *et al.*, 2008; HELLAND *et al.*, 2008; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; CAMPOY *et al.*, 2011; ESCOLANO-MARGARIT *et al.*, 2011; VAN GOOR *et al.*, 2011; MULDER *et al.*, 2014), the scores ranged from 7 to 11, indicating moderate to high quality. The average PEDro scores are outlined in Supplementary Table S1.

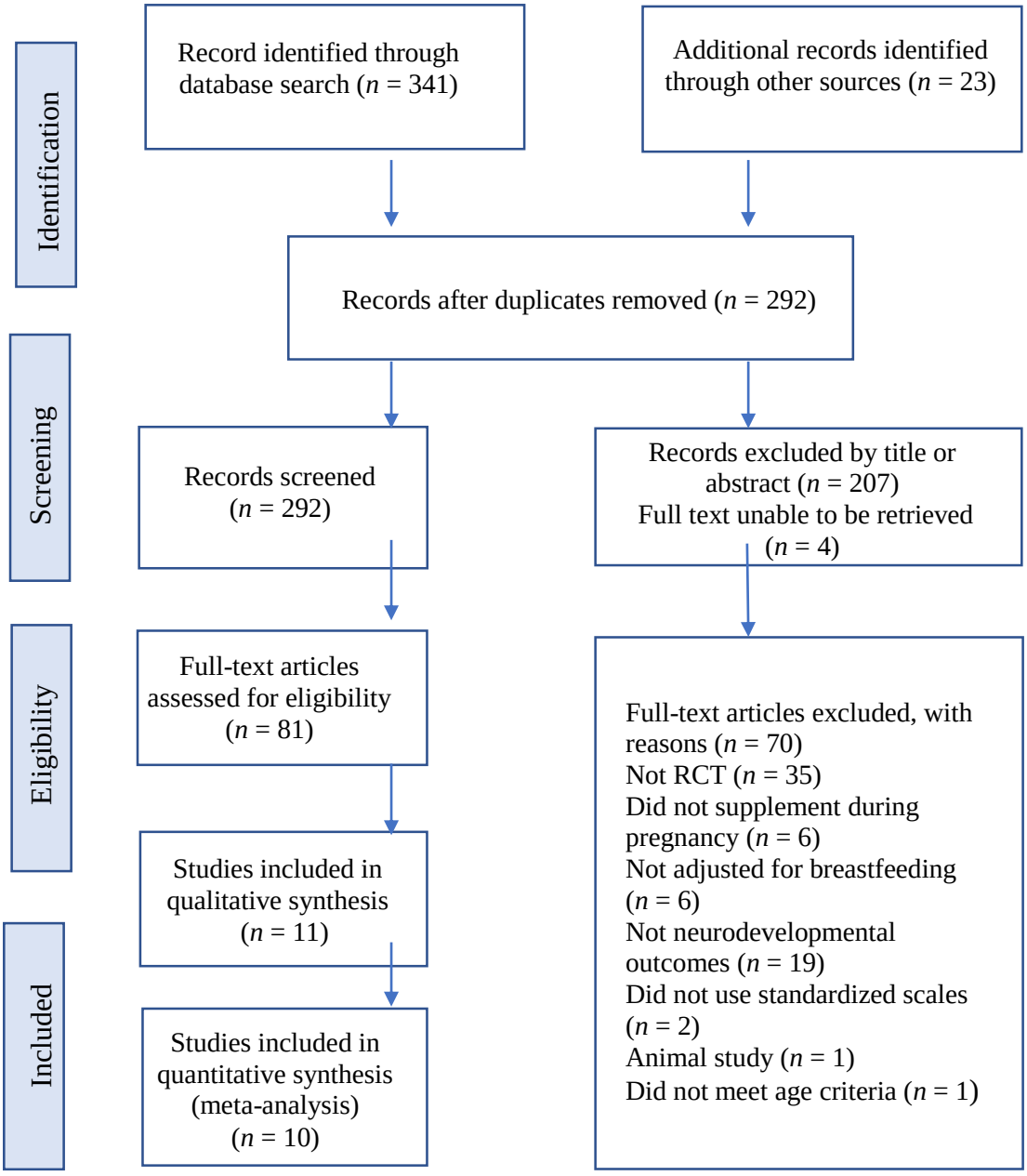

Fig 1. Consort flow chart of search results and papers identified for inclusion

3.3. Participants

The studies that were included in the analysis had a total of 4041 participants (Table 1). The age of the participants was 10 months to 12 years. With the exception of two studies (TOFAIL *et al.*, 2006; VOLLET *et al.*, 2017), RCTs were conducted in more economically developed countries. All but three studies reported the birth length (n = 6) (TOFAIL *et al.*, 2006; DUNSTAN *et al.*, 2008; HELLAND *et al.*, 2008; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; CAMPOY *et al.*,

2011). The mean birth length was 50.4 ± 1.1 cm (range = 47.6-51.4 cm). All of the studies reported the birth weight (*n* = 9) (TOFAIL *et al.*, 2006; DUNSTAN *et al.*, 2008; HELLAND *et al.*, 2008; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; CAMPOY *et al.*, 2011; VAN GOOR *et al.*, 2011; MULDER *et al.*, 2014). The mean birth weight was 3376 ± 242.6 g (range = 2700-3652 g). Singleton pregnancy was used as an inclusion criterion.

3.4. Intervention

All of the RCTs that were included in the present analysis used oral omega-3 LCPUFA supplementation. Oral capsule supplementation was used for the majority of the studies (TOFAIL *et al.*, 2006; DUNSTAN *et al.*, 2008; HELLAND *et al.*, 2008; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; VAN GOOR *et al.*, 2011; MULDER *et al.*, 2014; MELDRUM *et al.*, 2015), with the exception of two studies that used 1 sachet per day with 15 g of a milk-based supplement that contained modified fish oil (CAMPOY *et al.*, 2011; ESCOLANO-MARGARIT *et al.*, 2011) (Table 1). The supplementation period ranged between the 16th and 26th gestational weeks. Eight trials performed supplementation until delivery (TOFAIL *et al.*, 2006; DUNSTAN *et al.*, 2008; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; CAMPOY *et al.*, 2011; ESCOLANO-MARGARIT *et al.*, 2011; MULDER *et al.*, 2014; MELDRUM *et al.*, 2015), with the exception of two trials (HELLAND *et al.*, 2008; VAN GOOR *et al.*, 2011) that continued supplementation for 3 months after delivery. All of the trials included a control group. Of the 10 RCTs, three involved more than two intervention groups (CAMPOY *et al.*, 2011; Escolano-MARGARIT *et al.*, 2011; VAN GOOR *et al.*, 2011), but only the groups that were supplemented with LCPUFAs were included in the present analysis.

Table 1. Summary of randomized controlled trials included.

Study	Country	Intervention	Dose	Follow-Up	Instruments	Outcome										
						Cognition/IQ	Language	Receptive language	Expressive language	Motor skills	Fine Motor skills	Gross motor skills	Socio-emotional behavior	Adaptive Behavior	Birth length	Birth weight
Dunstan et al., 2008	Perth, Australia	Oral capsules from 20th week of gestation	4 capsules/day 3.300 mg LCPUFA	Children's age: 2.5 years	GMDS, PPVT, and CBCL	*n* = 72	*n* = 72				*n* = 72	*n* = 72	*n* = 72		*n* = 72	*n* = 72
Helland et al., 2008	Oslo, Norway	Cod liver oil from 18th week of gestation	Liquid oil 1183 mg DHA 2494 mg LC-PUFA (total)	Children's age: 7 years	K-ABC	*n* = 143									*n* = 143	*n* = 143
Makrides et al., 2010	Australia	Oral capsules from <18-21 weeks of gestation	Twice daily 800 mg DHA	Children's age: 18 months	BSID III	*n* = 726	*n* = 726			*n* = 726			*n* = 726	*n* = 726	*n* = 2399	*n* = 2399
Meldrum et al., 2015	Australia	Oral capsules from 20th week of gestation	Once daily 2200 mg DHA 1100 mg EPA	Children's age: 12 years	WISC-IV, CBCL, TVMI, and CCC-2	*n* = 50	*n* = 47			*n* = 47				*n* = 48		
Mulder et al., 2014	Vancouver, Canada	Oral capsules from 16th week of gestation	Once daily 400 mg DHA	Children's age: 18 months	BSID III	*n* = 200		*n* = 200	*n* = 200		*n* = 200	*n* = 200				*n* = 215
Ramakrishnan et al., 2015	Cuernavaca, Mexico	Oral capsules from 18th-22th week of gestation	Twice daily 400 mg DHA	Children's age: 18 months	BSID II	*n* = 730				*n* = 730				*n* = 730	*n* = 730	*n* = 730
Campoy et al., 2011	Germany, Hungary, and Spain	Sachet supplement from 20th week of gestation	Once daily 500 mg DHA 150 mg EPA	Children's age: 6.5 years	BSID II	*n* = 119									*n* = 119	*n* = 119
Escolano-Margarit et al., 2011	Germany, Hungary, and Spain	Sachet supplement from 20th week of gestation	Once daily 500 mg DHA 150 mg EPA	Children's age: 4 and 5.5 years	Hempel and Touwen					*n* = 127						
van Goor et al., 2011	Groningen, Netherlands	Oral capsules from 16th week of gestation	Once daily 500 mg DHA	Children's age: 18 months	BSID II	*n* = 114				*n* = 114						*n* = 114
Tofail et al., 2006	Dhaka, Bangladesh	Oral capsules from 26th week of gestation	4 capsules/day 1200 mg DHA 1800 mg EPA	Children's age: 10 months	BSIDII and HOME	*n* = 249				*n* = 249					*n* = 249	*n* = 249

DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; GMDS, Griffiths Mental Development Scale; PPVT, Peabody Picture Vocabulary Test; CBCL, Children Behavior Checklist; K-ABC, Kauffman Assessment Battery for Children; BSID III, Bayley Scales of Infant Development, 3rd edition; BSID II, Bayley Scales of Infant Development, 2nd Edition; WISC-IV, Wechsler Intelligence Scale for Children, 4th edition; TVMI, Test of Visual Motor Skills; CCC-2, Children's Communication Checklist, 2nd Edition.

3.5. Neurodevelopmental outcomes

3.5.1. Cognition and IQ

All of the RCTs intended to measure cognitive development. In the present analysis, however, only studies that used standardized scales were included (TOFAIL *et al.*, 2006; DUNSTAN *et al.*, 2008; HELLAND *et al.*, 2008; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; CAMPOY *et al.*, 2011; VAN GOOR *et al.*, 2011; MULDER *et al.*, 2014; MELDRUM *et al.*, 2015). Nine studies reported outcomes within the cognitive domain. The pooled results of the RCTs showed no differences between the intervention and control groups (standardized mean difference [SMD] = 0.06 [-0.003,0.157], $p = 0.06$). The analysis indicated minimal heterogeneity ($I^2 = 0\%$, χ^2 $p = 0.98$; Supplementary Fig. S1).

3.5.2. Language

Some of the RCTs that assessed the language domain reported results in terms of either expressive (MULDER *et al.*, 2014) or receptive (MULDER *et al.*, 2014) language. However, three studies ($n = 3$) measured both as a measure of total language ability (DUNSTAN *et al.*, 2008; MAKRIDES *et al.*, 2010; MELDRUM *et al.*, 2015). In total ($n = 4$), studies assessed for language in any form. Results for total language did not show a significant difference between groups (SMD = 0.105 [-0.030,0.240], $p = 0.13$). The analysis indicated minimal heterogeneity ($I^2 = 0\%$, χ^2 $p = 0.97$; Supplementary Fig. S2). Receptive and expressive language were not included in the meta-analysis because only one study reported these subdomains (MULDER *et al.*, 2014).

3.5.3. Motor skills

Six RCTs (TOFAIL *et al.*, 2006; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; ESCOLANO-MARGARIT *et al.*, 2011; VAN GOOR *et al.*, 2011; MELDRUM *et al.*, 2015) assessed the total motor domain. The results for this specific domain did not show a significant difference between groups (SMD = 0.044 [-0.039,0.127], $p = 0.30$). The analysis indicated minimal heterogeneity ($I^2 = 0\%$, χ^2 $p = 0.85$; Supplementary Fig. S3).

The results for the two RCTs that evaluated the fine motor domain (DUNSTAN *et al.*, 2008; MULDER *et al.*, 2014) did not indicate significant differences between groups (SMD = 0.301 [-

0.001,0.604], p = 0.051). The analysis indicatd moderate heterogeneity (I^2 = 47.76%, χ^2 p = 0.17; Supplementary Fig. S4). The present results may be attributable to the small number of studies that were included in the analysis, and the results should be interpreted with caution.

Two studies (DUNSTAN *et al.*, 2008; MULDER *et al.*, 2014) evaluated the gross motor domain, with no significant difference between groups (SMD = 0.203 [-0.096,0.501], p = 0.184). The analysis indicated moderate heterogeneity (I^2 = 0%, χ^2 p = 0.36; Supplementary Fig. S5).

3.5.4. Socio-emotional behavior

Two RCTs evaluated the socio-emotional domain (DUNSTAN *et al.*, 2008; MAKRIDES *et al.*, 2010), with no significant difference between groups (SMD = 0.072 [-0.067,0.211], p = 0.31). The analysis indicated minimal heterogeneity (I^2 = 0%, p = 0.42; Supplementary Fig. S6).

3.5.5. Adaptive behavior

Of the 10 studies, three evaluated adaptive behavior (MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; MELDRUM *et al.*, 2015) as one domain of child development. The pooled results indicated a significant difference between groups, favoring supplementation with LCPUFAs (SMD = 0.140 [0.039,0.242], p = 0.007). However, the analysis indicated substantial heterogeneity (I^2 = 74.17%, χ^2 p = 0.02; Supplementary Fig. S8). We were unable to identify a plausible explanation for the higher evidence of heterogeneity, and the results should be interpreted with caution (Fig. 2).

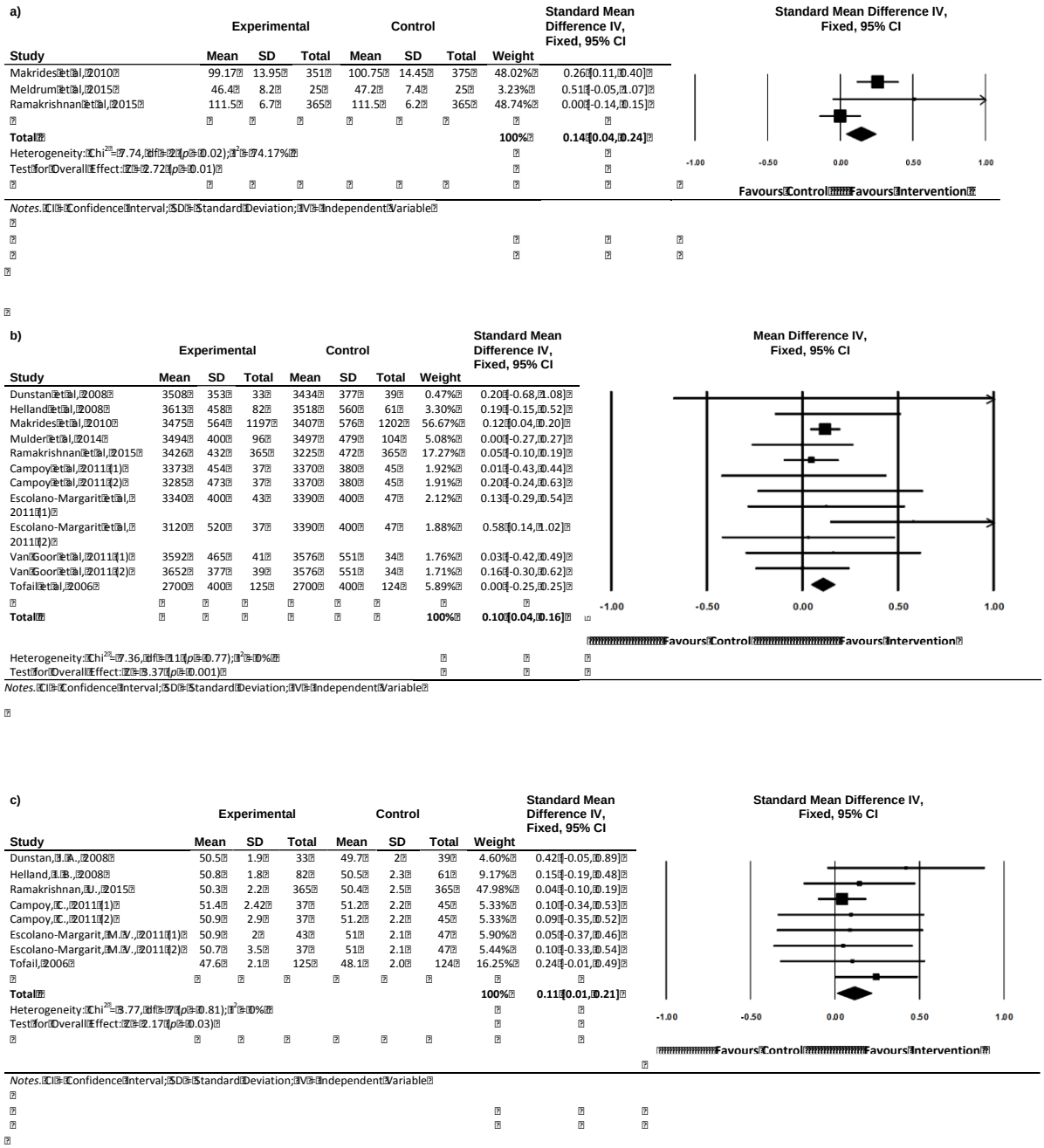

Fig. 2. (a) Forest plot of effect sizes of LC-PUFA supplementation in the behavioral domain. **(b)** Forest plot of effect sizes of LC-PUFA supplementation for birth weight. **(c)** Forest plot of effect sizes of LCPUFA supplementation for birth length.

3.6. Anthropometric measures

3.6.1. Birth weight

Nine RCTs that were included in the present analysis measured birth weight (TOFAIL *et al.*, 2006; DUNSTAN *et al.*, 2008; HELLAND *et al.*, 2008; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; CAMPOY *et al.*, 2011; ESCOLANO-MARGARIT *et al.*, 2011; VAN GOOR *et al.*, 2011; MULDER *et al.*, 2014), with a significant difference between groups (SMD = 0.104 [0.043,0.164], p = 0.001), favoring the intervention group. The analysis indicated minimal heterogeneity (I^2 = 0%, χ^2 p = 0.77; Fig. 2).

3.6.2. Birth length

The pooled results for the six RCTs (TOFAIL *et al.*, 2006; DUNSTAN *et al.*, 2008; HELLAND *et al.*, 2008; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; CAMPOY *et al.*, 2011) that evaluated birth length showed a significant difference between groups (SMD = 0.111 [0.011,0.212], p = 0.030), favoring the supplementation group. The analysis indicated minimal heterogeneity (I^2 = 0%, p = 0.81; Fig. 2).

3.7. Heterogeneity

Cochrane I^2 scores indicated minimal heterogeneity for the majority of the outcomes (birth weight, birth length, cognition, language, receptive language, motor skills, gross motor skills, and socio-emotional behavior). Fine motor skills (47.76%) and the behavioral domain (74.17%) showed moderate and substantial heterogeneity, respectively. Individual results are outlined in each outcome section above.

3.8. Risk of bias

All of the eligible studies were included independently of quality assessment. A funnel plot analysis (Supplementary Fig. S7) and the Duval and Tweedie Trim and Fill procedure (Supplementary Fig. S8) were conducted. The adjusted point estimate of 0.07 suggested a lower risk than the original analysis with the observed studies, in which the point estimate was 0.11, but these are both fairly close to one another, suggesting similar implications with and without missing studies from our meta-analysis. In other words, the risk of bias was minimal in the present study. Additionally, the PEDro scale indicated that only two studies had moderate quality, and nine

studies had high quality. Furthermore, Egger's regression intercept for this meta-analysis was 0.72 (95% confidence interval = 0.37,1.07, $p = 0.001$), indicating a small publication bias.

4. Discussion

The purpose of the present systematic review and meta-analysis was to investigate the effect of omega-3 LCPUFA supplementation during pregnancy on offspring's neurodevelopmental outcomes and anthropometric measures. The cognitive scores (TOFAIL *et al.*, 2006; DUNSTAN *et al.*, 2008; HELLAND *et al.*, 2008; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; CAMPOY *et al.*, 2011; VAN GOOR *et al.*, 2011; MULDER *et al.*, 2014; MELDRUM *et al.*, 2015) of children whose mothers received n-3 LCPUFA supplementation did not significantly differ from the mean scores of children in the control group, with no differences in receptive language (MULDER *et al.*, 2014), expressive language (MULDER *et al.*, 2014), general language (DUNSTAN *et al.*, 2008; MAKRIDES *et al.*, 2010; MELDRUM *et al.*, 2015), fine motor skills (DUNSTAN *et al.*, 2008; MULDER *et al.*, 2014), gross motor skills (DUNSTAN *et al.*, 2008; MULDER *et al.*, 2014), total motor skills (TOFAIL *et al.*, 2006; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; ESCOLANO-MARGARIT *et al.*, 2011; VAN GOOR *et al.*, 2011; MELDRUM *et al.*, 2015), or socio-emotional behavior (DUNSTAN *et al.*, 2008; MAKRIDES *et al.*, 2010).

We detected small effect sizes for the supplementation group in the behavioral domain (MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; MELDRUM *et al.*, 2015) and anthropometric measures (birth weight (TOFAIL *et al.*, 2006; DUNSTAN *et al.*, 2008; HELLAND *et al.*, 2008; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; CAMPOY *et al.*, 2011; VAN GOOR *et al.*, 2011; MULDER *et al.*, 2014)] and birth length (TOFAIL *et al.*, 2006; DUNSTAN *et al.*, 2008; HELLAND *et al.*, 2008; MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; CAMPOY *et al.*, 2011). A significant difference was found between the n-3 LCPUFA supplementation and placebo groups in the behavioral domain. For the RCTs that were included in the present review, behavior was measured based on data that were collected from caregivers' reports (e.g., Home Observation for Measurement (HOME), Child Behavior Checklist (CBCL), and Adaptive Behavior Assessment System (ABAS II) questionnaires) at 18 months and 12 years of age. Some studies suggested that low maternal fish intake may be associated with poor prosocial

behavior and a greater tendency to express hyperactivity in childhood (HIBBELN *et al.*, 2007; GALE *et al.*, 2008). A previous study (STEENWEG-DE GRAAFF *et al.*, 2015) reported associations between maternal n-3 LCPUFA intake and behavioral problems in offspring. Although our analysis detected a small effect size, the results should be considered with caution because of substantial heterogeneity (I^2 = 74.71%). This result may be attributable to the low number of trials that had different sample sizes and measured this outcome. Moreover, global measures of neurodevelopment have the benefit of standardized administration and scoring, but they might be unable to detect specific effects of n-3 LCPUFA supplementation during pregnancy on the behavioral domain. Questionnaires or scales that are used to assess the behavioral domain in children usually evaluate caregivers' perceptions of children's behavior. However, these instruments do not target specific brain functions that are associated with the behavioral domain.

The analysis of secondary outcomes detected greater effect sizes for birth weight and birth length in the n-3 LCPUFA supplementation group. The secondary outcomes also had more participant data to run the analyses compared with the primary outcome data from RCTs. An epidemiological study (OLSEN *et al.*, 1986) reported that omega-3 fatty acid supplementation may result in a greater birth weight by prolonging gestation and affecting the metabolism of endogenous prostaglandins. Furthermore, a meta-analysis indicated that n-3 LCPUFA supplementation was associated with a significantly longer gestational age at delivery (CHEN *et al.*, 2016), which might account for the birth length outcome. Therefore, n-3 LCPUFA supplementation increases gestation length, thus increasing birth weight and birth length.

According to the results of the present meta-analysis, the effect of n-3 LCPUFA supplementation on childhood development is uncertain because of methodological weaknesses. Therefore, the hypothesis that supplementation with n-3 LCPUFAs during pregnancy improves child neurodevelopment cannot be either accepted or rejected based solely on the studies that were included in the present analysis. Small sample sizes were one of the greatest methodological flaws that were detected. PEDro scores indicated that all of the studies except for three (MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010; VAN GOOR *et al.*, 2011) were able to use 85% of their initial sample size, and all but one study failed to report baseline similarities (MAKRIDES *et al.*, 2010) to allow assessments of risk of bias.

Future research is needed to evaluate periods of fetal brain development that may be sensitive to n-3 LCPUFAs by including multiple assessments of prenatal LCPUFA status.

4.1. Strengths of this review

The present systematic review and meta-analysis were conducted in accordance with PRISMA guidelines (MOHER *et al.*, 2009). Thus, our review provides a comprehensive view of the literature to date regarding the impact of n-3 LCPUFA supplementation during the perinatal period on subsequent childhood development without the potential effects of breastfeeding or dietary supplementation.

4.2. Limitations of studies and future research

Several limitations should be considered when interpreting these findings. With regard to sample sizes, most of the RCTs that were included in this review had small sample sizes, except for two studies (MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010) that had $n < 300$ per group. The small sample sizes may have resulted in the loss of statistical power. Furthermore, half of the studies did not report random group allocation, which might have affected the initial randomization. Another limitation is that the RCTs that were included in this review used different doses of LCPUFA supplementation during the gestational period, although the dose of n-3 LCPUFAs was sufficiently high to meet the recommendations for DHA intake during pregnancy (> 200 mg/day) (KOLETZKO *et al.*, 2007). Supplementation did not begin during the same gestational period for all subjects, and this discrepancy between different periods of supplementation might be a confounding variable.

REFERENCES

BARKER, D. J.; CLARK, P. M. Fetal undernutrition and disease in later life. **Reviews of Reproduction,** v. 2, n. 2, p. 105-12, May 1997. ISSN1359-6004 (Print) 1359-6004(Linking).Disponível em:<https://www.ncbi.nlm.nih.gov/pubmed/9414472.

CAMPOY, C. et al. Effects of prenatal fish-oil and 5-methyltetrahydrofolate supplementation on cognitive development of children at 6.5 y of age. **The American journal of clinical nutrition,** v. 94, n. 6 Suppl, p. 1880S-1888S, 2011. ISSN 0002-9165.

CETIN, I.; KOLETZKO, B. Long-chain omega-3 fatty acid supply in pregnancy and lactation. **Curr Opin Clin Nutr Metab Care,** v. 11, n. 3, p. 297-302, May 2008. ISSN 1363-1950 (Print) 1363-1950.

CHEN, B. et al. Fish oil supplementation improves pregnancy outcomes and size of the newborn: a meta-analysis of 21 randomized controlled trials. **The Journal of Maternal-Fetal & Neonatal Medicine,** v. 29, n. 12, p. 2017-2027, 2016. ISSN 1476-7058.

COHEN, J. Statistical power analysis for the behavioral sciences . Hilsdale. **NJ: Lawrence Earlbaum Associates,** v. 2, 1988.

DE MORTON, N. A. The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. **Australian Journal of Physiotherapy,** v. 55, n. 2, p. 129-133, 2009/01/01/ 2009. ISSN 0004-9514. Disponível em: < http://www.sciencedirect.com/science/article/pii/S0004951409700431

DUNSTAN, J. et al. Cognitive assessment of children at age 2½ years after maternal fish oil supplementation in pregnancy: a randomised controlled trial. **Archives of Disease in Childhood-Fetal and Neonatal Edition,** v. 93, n. 1, p. F45-F50, 2008. ISSN 1359-2998.

EMMETT, P. M.; JONES, L. R.; GOLDING, J. Pregnancy diet and associated outcomes in the Avon Longitudinal Study of Parents and Children. **Nutr Rev,** v. 73 Suppl 3, p. 154-74, Oct 2015. ISSN 0029-6643.

ESCOLANO-MARGARIT, M. V. et al. Prenatal DHA status and neurological outcome in children at age 5.5 years are positively associated. **The Journal of nutrition,** v. 141, n. 6, p. 1216-1223, 2011. ISSN 0022-3166.

GALE, C. R. et al. Oily fish intake during pregnancy–association with lower hyperactivity but not with higher full-scale IQ in offspring. **Journal of Child Psychology and Psychiatry,** v. 49, n. 10, p. 1061-1068, 2008. ISSN 1469-7610.

HELLAND, I. B. et al. Effect of supplementing pregnant and lactating mothers with n-3 very-long-chain fatty acids on children's IQ and body mass index at 7 years of age. **Pediatrics,** v. 122, n. 2, p. e472-e479, 2008. ISSN 0031-4005.

HIBBELN, J. R. et al. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study. **The Lancet,** v. 369, n. 9561, p. 578-585, 2007. ISSN 0140-6736.

INNIS, S. M. Fatty acids and early human development. **Early human development,** v. 83, n. 12, p. 761-766, 2007. ISSN 0378-3782.

KOLETZKO, B.; CETIN, I.; BRENNA, J. Child Health Foundation; Diabetic Pregnancy Study Group; European Association of Perinatal Medicine; European Association of Perinatal Medicine; European Society for Clinical Nutrition and Metabolism; European Society for Paediatric Gastroenterology, Hepatology and Nutrition, Committee on Nutrition; International Federation of Placenta Associations; International Society for the Study of Fatty Acids and Lipids. Dietary fat intakes for pregnant and lactating women. **British Journal of Nutrition,** v. 98, n. 5, p. 873-877, 2007.

MAHER, C. G. et al. Reliability of the PEDro scale for rating quality of randomized controlled trials. **Physical therapy,** v. 83, n. 8, p. 713-721, 2003. ISSN 0031-9023.

MAKRIDES, M. et al. Effect of DHA supplementation during pregnancy on maternal depression and neurodevelopment of young children: a randomized controlled trial. **Jama,** v. 304, n. 15, p. 1675-1683, 2010. ISSN 0098-7484.

MATHIAS, P. C. et al. Maternal diet, bioactive molecules, and exercising as reprogramming tools of metabolic programming. **European journal of nutrition,** v. 53, n. 3, p. 711-722, 2014. ISSN 1436-6207.

MELDRUM, S. et al. Maternal fish oil supplementation in pregnancy: a 12 year follow-up of a randomised controlled trial. **Nutrients,** v. 7, n. 3, p. 2061-2067, 2015.

MENNITTI, L. V. et al. Type of fatty acids in maternal diets during pregnancy and/or lactation and metabolic consequences of the offspring. **Journal of Nutritional Biochemistry,** v. 26, n. 2, p. 99-111, Feb 2015. ISSN 0955-2863.

MOHER, D. et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. **PLOS Medicine,** v. 6, n. 7, p. e1000097, 2009. Disponível em: < https://doi.org/10.1371/journal.pmed.1000097 >.

MULDER, K. A.; KING, D. J.; INNIS, S. M. Omega-3 fatty acid deficiency in infants before birth identified using a randomized trial of maternal DHA supplementation in pregnancy. **PLoS One,** v. 9, n. 1, p. e83764, 2014. ISSN 1932-6203.

OLSEN, S. et al. Intake of marine fat, rich in (n-3)-polyunsaturated fatty acids, may increase birthweight by prolonging gestation. **The Lancet,** v. 328, n. 8503, p. 367-369, 1986. ISSN 0140-6736.

RAMAKRISHNAN, U. et al. Effects of docosahexaenoic acid supplementation during pregnancy on gestational age and size at birth: randomized, double-blind, placebo-controlled trial in Mexico. **Food and nutrition bulletin,** v. 31, n. 2_suppl2, p. S108-S116, 2010. ISSN 0379-5721.

RAVELLI, A. C. et al. Glucose tolerance in adults after prenatal exposure to famine. **The Lancet,** v. 351, n. 9097, p. 173-177, 1998. ISSN 0140-6736.

SCHMIDT, F. L.; LE, H. Software for the Hunter-Schmidt meta-analysis methods. **University of Iowa, Department of Management & Organization, Iowa City, IA,** v. 42242, 2004.

SCHUCHARDT, J. P. et al. Significance of long-chain polyunsaturated fatty acids (PUFAs) for the development and behaviour of children. **European journal of pediatrics,** v. 169, n. 2, p. 149-164, 2010. ISSN 0340-6199.

STEENWEG-DE GRAAFF, J. C. et al. Maternal LC-PUFA status during pregnancy and child problem behavior: the Generation R Study. **Pediatric research,** v. 77, n. 3, p. 489, 2015. ISSN 1530-0447.

TOFAIL, F. et al. Supplementation of fish-oil and soy-oil during pregnancy and psychomotor development of infants. **Journal of Health, Population and Nutrition**, p. 48-56, 2006. ISSN 1606-0997.

UAUY, R.; MENA, P.; ROJAS, C. Essential fatty acids in early life: structural and functional role. **Proc Nutr Soc,** v. 59, n. 1, p. 3-15, Feb 2000. ISSN 0029-6651 (Print) 0029-6651 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/10828169 >.

VAN GOOR, S. A. et al. The influence of supplemental docosahexaenoic and arachidonic acids during pregnancy and lactation on neurodevelopment at eighteen months. **Prostaglandins, Leukotrienes and Essential Fatty Acids (PLEFA),** v. 84, n. 5, p. 139-146, 2011. ISSN 0952-3278.

VERHAGEN, A. P. et al. The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. **Journal of clinical epidemiology,** v. 51, n. 12, p. 1235-1241, 1998. ISSN 0895-4356.

VOLLET, K. et al. Prenatal fish oil supplementation and early childhood development in the Upstate KIDS Study. **Journal of Developmental Origins of Health and Disease**, p. 1-9, 2017. ISSN 2040-1744.

WEISS, L. G.; OAKLAND, T.; AYLWARD, G. P. **Bayley-III clinical use and interpretation**. Academic Press, 2010. ISBN 0080921078.

YELL, M. L.; SHRINER, J. G.; KATSIYANNIS, A. Individuals with disabilities education improvement act of 2004 and IDEA regulations of 2006: Implications for educators, administrators, and teacher trainers. **Focus on exceptional children,** v. 39, n. 1, p. 1, 2006. ISSN 0015-511X.

Artigo 2

Irurita - Ballesteros, C., Landeira - Fernandez, J., Kac, G., Rocinholi, L. Association between Maternal n-3 Polyunsaturated Fatty Acid Concentrations during Early Pregnancy and Cognitive Development during offspring's Second Year of Life: A Prospective Cohort Study in Brazil

Abstract

This study investigated the association between maternal mental health, socioeconomic stautus (SES) and maternal serum concentrations of eicosapentaenoic acid (EPA; omega-3) and docosahexaenoic acid (DHA; omega-3) during early pregnancy and infant cognitive development at 18 and 24 months of age. Maternal long-chain polyunsaturated fatty acid concentrations were determined in serum samples between 5 and 13 weeks of gestation. Infant cognitive development was assessed using the Bayley Scales of Infant and Toddler Development (BSID-III) at 18 and 24 months of age. Data from 33 mother-infant pairs were included in the analysis. The regression analysis included sociodemographic data, maternal mental health status, and concentrations of DHA and EPA during early pregnancy, which were associated with higher BSID-III scores during the second year of life ($F_{5,26} = 5.091$, $p < 0.002$, $R^2 = 0.5$, and $F_{3,29} = 7.427$, $p < 0.001$, $R^2 = 0.434$, respectively).

These results suggest that the following predictive factors were associated with better cognitive development at 18 and 24 months of age: socioeconomic status, parental education, and maternal serum concentrations of *n*-3 long-chain polyunsaturated fatty acids (EPA and DHA) during the first trimester of pregnancy.

Key words: infant development; cognitive development; early pregnancy, omega-3 fatty acids, prenatal; Bayley Scales

RESUMO

O objetivo do presente estudo foi investigar a associação entre o nível socioeconômico, a saúde mental e as concentrações séricas maternas do ácido eicosapentaenoico (EPA; omega-3) e ácido docosaexaenoico (DHA; omega-3) durante o inicio da gestação e o desenvolvimento cognitivo durante o segundo ano de vida. As concentrações maternas de ácidos graxos poli-instaurados foram determinadas através das amostras de sangue coletadas na 5ª e 13ª semana do período gestacional. O desenvolvimento cognitivo das crianças foi avaliado utilizando as Escalas Bayley do Desenvolvimento Infantil (BSID III) aos 18 e 24 meses de idade. Dados sobre (n=33) díades mãe-bebê foram incluídos nas analises.

Os dados foram analisados através de uma analise de regressão, incluindo o nível sócio econômico, *status* da saúde mental materna, e concentrações de DHA e EPA no inicio da gestação, as quais foram associadas a maiores scores na BSDI-III durante o segundo ano de vida ($F_{5,26} = 5.091$, $p < 0.002$, $R^2 = 0.5$, e $F_{3,29} = 7.427$, $p < 0.001$, $R^2 = 0.434$, respectivamente). Estes resultados indicam que os seguintes preditores foram associados com um melhor desempenho na escala cognitiva aos 18 e 24 meses de vida: nível socioeconômico, educação parental, e concentrações maternas séricas de EPA e DHA durante o primeiro trimestre da gestação.

Palavras chave: desenvolvimento infantil; desenvolvimento cognitivo; Omega 3-acidos graxos; prenatal; gestacão; escalas Bayley

1. Introduction

The intrauterine environment and maternal nutrition have a substantial influence on fetal development, affecting the health and well-being of individuals throughout life (BARLER E CLARK, 1997; BERTI *et al.*, 2017). Several studies have reported that optimum fetal neurodevelopment depends on specific nutrients that are solely derived from dietary sources, including omega-3 (n-3) long-chain polyunsaturated fatty acids (LCPUFAs), such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) (SALEM *et al.*, 2001; SALEM E EGGERSDORFER, 2015).

DHA and EPA are the two most biologically active n-3 PUFAs (COLETTA *et al.*, 2010). These fatty acids are found in large amounts in the lipid membrane of gray matter in the cerebral cortex and retina (MARTINEZ E MOUGAN, 1998; UAUY *et al.*, 2000; MARTINEZ, 2001; GERMAN, 2011). During pregnancy, significant amounts are transferred to the fetus via the placenta and after birth through breastfeeding (INNIS E FRIESEN, 2008). The maternal intake of sufficient amounts of n-3 PUFAs has been shown to be important both before conception and during pregnancy (HADDERS-ALGRA, 2005). These essential lipids are involved in many neurological functions, including the maintenance of membrane fluidity (LAURITZEN *et al.*, 2001), gene expression, signal transduction, neural growth (COLETTA *et al.*, 2010), and myelination (YEHUDA *et al.*, 2005). PUFAs in the diet during pregnancy are important for fetal development and metabolism (MENNITTI *et al.*, 2015). High concentrations of EPA and DHA in blood samples in pregnant women were associated with improvements in vocabulary comprehension, verbal intelligence, motor and cognitive development, and visual skills in offspring (GOULD *et al.*, 2013; WEISER *et al.*, 2016).

Perinatal maturation reaches a peak rate of growth during the third trimester of pregnancy when the accumulation of LCPUFAs in neural tissue occurs most rapidly (GOULD *et al.*, 2014; GOULD *et al.*, 2016). During this phase, the hippocampus and frontal lobes, which are involved in higher cognitive function, undergo an intense period of growth (DOBBING, 1973). In severe cases of DHA deprivation, such as Zellweger disease and paroxysmal disorders, mental retardation is common, and the restoration of DHA intake in the diet improves clinical outcomes and neuronal

myelination (MARTINEZ E MOUGAN, 1998; BRYANTON *et al.*, 2014). After birth, in addition to consuming an adequate diet, newborns depend on environmental stimuli that are fundamentally mediated by parents and caregivers. Mothers are the main caregivers and educators at home, and parental levels of education are a strong predictor of child development (CHEVALIER, 2012). Low socioeconomic status (SES), low parental education, and the fragility of family ties have been reported to be environmental risk factors that can adversely affect child development (BRADLEY E CORWYN, 2002).

Several studies have reported that children's scholastic achievement and performance on tests of cognitive ability are associated with SES. Children from advantaged homes and neighborhoods present higher scholastic achievement than children from disadvantaged homes and neighborhoods (KLEBANOV *et al.*, 1998; BRADLEY E CORWYN, 2002; POWER *et al.*, 2006; KIERNAN E HUERTA, 2008; SANTOS *et al.*, 2008); in the latter case, an early assessment of the developmental functioning using instruments such as the Bayley Scales of Infant and Toddler Development, 3rd edition (BSID-III) may identify suspected developmental delays (BAYLEY, 2006). It is now stablished that the quality of early mother-child relationship does have an influence on later child and cognitive and language development (MCELWAIN *et al.*, 2003; CUEVAS *et al.*, 2014). Maternal mental health, including anxiety in the pre- and postnatal phases, can have adverse effects on the well-being of the mother and impair fetal development, including emotional, cognitive, and behavioral development throughout all stages of life (FLORES *et al.*, 2012; BELTRAMI *et al.*, 2013).

As well as mother-child, the importance of father-child relationships has become increasingly evident, especially the role of paternal sensitivity on cognitive and language outcomes in early childhood (PANCSOFAR *et al.*, 2010; MALMBERG *et al.*, 2016). The present study investigated the effects of maternal serum concentrations of LCPUFAs (DHA and EPA) during pregnancy, maternal anxiety, SES, and parental levels of education on children's cognitive development at 18 and 24 months of age.

2. Materials and Methods

2.1 Study design and eligibility criteria

The present study was conducted in two phases. Phase 1 was a prospective cohort study of pregnant women who received prenatal care at a public health center in the city of Rio de Janeiro, Brazil, from November 2009 to October 2011. The eligibility criteria for the first phase were the following: (a) between gestational weeks 5 and 13 at the time of recruitment, (b) between 20 and 40 years of age, (c) no known chronic diseases (except obesity), (d) singleton pregnancy, (e) residence near the study catchment area, and (f) receiving prenatal care where the study was performed. The women were followed across four time points: weeks 5-13 of pregnancy (first trimester), weeks 20-26 of pregnancy (second trimester), weeks 30-36 of pregnancy (third trimester), and 30-45 days postpartum. A total of 322 women were invited to participate, and 299 were enrolled in the study. After baseline clinical evaluation, 70 women were excluded for the following reasons: missing information regarding fatty acid (FA) data or dietary intake (n = 3), miscarriage (n = 25), chronic arterial hypertension (n = 2), twin pregnancy (n = 4), advance pregnancy (n = 15), confirmed pre-pregnancy diagnosis of chronic non-communicable diseases (n = 11), and did not attend the baseline interview (n = 10). Additionally, 41 women who were initially enrolled in the study were excluded from the analyses because they were encouraged to participate in a nested randomized control trial on the effects of n-3 PUFAs on postpartum depression that was associated with this cohort of subjects. Therefore, the baseline sample comprised 188 pregnant women, 155 women participated from the baseline to the second trimester, and the third trimester was comprised for 154 women. Extensive information about the cohort and procedures for data collection is provided elsewhere (BENAIM *et al.*, 2017). Briefly, all of the women completed a questionnaire that covered sociodemographic information, obstetric information, lifestyle, psychosocial conditions, and mental health status during pregnancy. The women also had complete data on maternal FA status based on blood samples that were collected during prenatal screening. The socioeconomic data were obtained through a standardized questionnaire from the Brazilian Association of Research Companies (ABEP) that evaluates the amount of goods purchased and level of education of heads of households. Scores ranged from 0 to 46. The respondents were then distributed into eight economic classes: A1, A2, B1, B2, C1, C2, D, and E.

Phase 2 of the present study was a transverse cross-sectional study in which the offspring from the mothers from phase 1 underwent a neuropsychological evaluation from June 2012 to December

2014. All of the women whom participated in phase 1 and whose gestational age was greater than 36 weeks were invited to participate in phase 2. However, only fifty pairs mother-child (n = 50) agreed to register into phase 2. For the assessment, the BSID-III was used at 6 months of age (n = 10), 12 months of age (n = 11), 18 months of age (n = 15), and 24 months of age (n = 14). The instrument was administered by three graduate students from the Department of Psychology, Pontifical Catholic University.

2.2 Serum fatty acid composition

During phase 1, maternal blood samples were collected in Vacutainer tubes during three different clinical visits (first, second, and third gestational trimesters). Blood collection was performed by a trained professional after the women underwent 12 h of fasting. The samples were immediately centrifuged at 5000 rotations per minute and stored at -80°C until analysis. We used serum samples to determine the blood FA composition. The serum samples were shipped on dry ice to the Section of Nutritional Neuroscience, Laboratory of Membrane Biochemistry and Biophysics, National Institutes of Health (Bethesda, MD, USA). Fatty acids were identified using high-throughput robotic direct methylation coupled with fast gas-liquid chromatography, which was developed and validated by the National Institutes of Health to enable large-scale analysis (LIN *et al.*, 2012). The analyses were performed using a HP 6890 Plus gas LAN chromatograph equipped with three flame ionization detectors (Agilent Technologies, Santa Clara, CA, USA) coupled to a fused silica capillary column (Agilent 127-32 H2, 15 m × 0.1 mm). Fatty acid concentrations are expressed as absolute values (μg/ml).

We evaluated the serum concentrations of EPA+DPA, total n-3 PUFAs (18:3 n-3 + 20:5 n:3 + 22.5 n-3 + 22:6 n-3), and total n-6 PUFAs (18:3 n-6 + 20:2 n:6 + 20:3 n-6 + 20:4 n-6 + 22:4 n-6 + 22:5 n-6). All FA concentrations are expressed as relative values (% of total FAs) because the metabolism of the various unsaturated FAs depends on the balanced amount of each FA precursor and/or product (ARTERBURN *et al.*, 2006). EPA and DHA were analyzed together because both are products of α-linilenic acid (ALA) conversion and are related to a lower risk of undesirable maternal/fetal outcomes (BENAIM *et al.*, 2017).

2.3 Assessment of maternal anxiety during pregnancy

During phase 1, pregnant women who were eligible for participation (*n* = 154) were interviewed to collect sociodemographic data, and the State Trait Anxiety Inventory (STAI) was applied on the same day. This questionnaire was completed between 5 and 13 weeks of gestation (1st trimester), between 20 and 26 weeks of gestation (2nd trimester), and between 30 and 36 weeks of gestation (3rd trimester). The STAI is one of the most used self-report measures of anxiety in research and clinical settings across different cultures (LONNER E IBRAHIM, 1989). This self-report questionnaire is divided into two scales with the aim of measuring two different components of anxiety: state and trait. State anxiety (STAI-S) measures the transitory emotional state, characterized by subjective feelings or tension that may vary in intensity over time. Trait anxiety (STAI-T) measures the relatively stable disposition to respond to stress with anxiety and a tendency to perceive a wider range of situations as threatening (CATTELL E SCHEIER, 1961). Each of these scales consists of 20 statements. A score of 1 to 4 is assigned to each item on both scales, with a total score that ranges from 20 (minimum) to 80 (maximum). When answering this questionnaire, the subject should consider that "state" means "as the subject feels at that particular moment," and "trait" mean "as the subject generally feels herself." The scores indicate a low degree of anxiety (0-30), medium degree of anxiety (31-49), and high degree of anxiety (> 50) (SPIELBERGER, 2010).

2.4 Assessment of infant neurodevelopmental outcome

The neuropsychological assessment of infants occurred at 6 months (*n* = 10), 12 months (*n* = 11), 18 months (*n* = 15), and 24 months (*n* = 14) using the BSID-III (BAYLEY, 2006). The translated, adapted, and validated version of this instrument for Brazilian Portuguese was used (MADASCHI, 2012), (MADASCHI *et al.*, 2016). Well-trained students from the Department of Psychology, Pontifical Catholic University, performed all of the neuropsychological assessments. The BSID-III is composed of five scales: cognitive, language, motor, socio-emotional, and adaptive. However, only the cognitive, language, and motor scales were included in the present study. The cognitive scale evaluates such abilities as sensorimotor development, exploration, manipulation, object relatedness, concept formation, memory, and simple problem solving. The language scale is a composite of receptive communication (verbal comprehension, vocabulary) and expressive communication (babbling, gesturing, and utterances). The motor scale evaluates both gross and fine motor functioning. The raw scores for each of the scales are standardized to a mean of 100

with an SD of 15 (range, 50-150). The standardized scores were also classified into categories of accelerated performance (115), within normal limits (85-115), and delayed performance (85). The last BSID-III assessment of the present study was completed on December 16, 2014.

2.5 Statistical analysis

We conducted a regression analysis with backward methodology using cognitive development as the dependent variable. The statistical analysis included children of ages 18 and 24 months; since these were the groups with higher participants (6 months, n = 15; 12 months, n = 18; 18 months, n = 25; 24 months, n = 27). Thus, according to this criterion, children who were evaluated at 18 and 24 months (n = 33) were selected for inclusion in this analysis. Additionally, correlations were determined among z-scores of cognitive development and sociodemographic data (Table 1; maternal and paternal level of education, socioeconomic status, gender, and age-anthropometric measures and mental health variables (maternal STAI-T scores during each pregnancy trimester). All predictors were initially included in the first model and gradually removed until the most parsimonious one was reached.

The data analysis was performed using SPSS 20.0 software. Descriptive statistics were used to illustrate the sample characteristics. Stepwise regression models were calculated separately for maternal serum n-3 (EPA and DHA) concentrations during each pregnancy trimester to explore relationships between predictors. EPA and DHA concentrations were highly correlated (r_{33} = 0.49, $p < 0.001$). Regression models were performed independently to avoid an increase in collinearity. The models were chosen based on R^2 and Adjusted R^2. To check the assumption of multicollinearity (collinearity diagnostics), we used variance inflation factor (VIF) and Durbin Watson to test the assumption of independent errors (FIELD, 2009).

Table 1. Maternal and infant characteristics.

	Mean	Std. Deviation	N
Cognitive Developmental Z-Scores	0.3031	0.91774	33
Mother's age (in years)	27.53	6.175	33
Mother educational level (in years)	8.31	3.021	33
Socioeconomic Status (ABEP)	18.16	4.371	33
Father educational level (in years)	7.97	4.052	33
Birth Length (in cm)	49.53	2.700	33
Mother's anxiety (IDATE-T) scores during 1st trimester	41.53	7.964	33
Mother's DHA serum concentrations during 1st trimester (g/day)	0.03656	0.036774	33
Mother's EPA serum concentrations during 1st trimester (g/day)	0.02697	0.024301	33

3. Results

3.1 Regression model with predictors for cognitive development (DHA)

The first regression model included the following independent variables: socioeconomic status, mother's age, years of education (father), years of education (mother), birth length, mother's anxiety during the 1st trimester, and serum concentrations of DHA during the 1st trimester of pregnancy. The second model (Table 2) showed the highest explained variance (R^2) and cross validity (adjusted R^2; $F_{5,26} = 5.091$, $p < 0.002$, $R^2 = 0.5$). This model included socioeconomic status, years of education (father), concentration of DHA during the 1st trimester, birth length, anxiety during the first trimester, mother's age, and years of education (mother). The latter two variables were excluded in the second model, which led to better cross validity, but the nonsignificant variables in each model were retained because of a suppression effect. We found no evidence of collinearity in the analysis, based on VIF (FIELD, 2009).

Table 2. Regression model with predictors for cognitive development (DHA).

Variable	Model 1		Model 2		Model 3	
	β	p-value	β	p-value	β	p-value
Mother's age in years	0.1	0.572				
Years of education (mother)	0.19	0.3				
Socio economic status	0.5	**0.012**	0.48	**0.007**	0.49	**0.007**
Years of education (father)	-0.44	**0.021**	-0.38	**0.028**	-0.44	**0.014**
Birth Length	0.23	0.129	0.24	0.101		
Anxiety during the 1st trimester	0.15	0.316	0.14	0.35		
DHA during the 1st trimester	0.42	**0.008**	0.42	**0.008**	0.44	**0.006**
Model p-value		**0.008**		0.363		0.118
R2	0.52		0.5		0.43	
Adjusted R2	0.38		0.4		0.37	

3.2 Regression model with predictors for cognitive development (EPA)

Table 3 shows the regression model (model 3), which presented the best trade-off between explained variance (R^2) and cross validity (adjusted R^2; $F_{3,29} = 7.427$, $p < 0.001$, $R^2 = 0.434$). Further inspection of the predictive factors revealed that socioeconomic status, birth length, and serum concentrations of EPA during the 1st trimester significantly contributed to the model. The nonsignificant variables in this model (e.g., socioeconomic status) were retained because of a suppression effect (FIELD, 2009). This analysis did not indicate collinearity according to VIF (FIELD, 2009).

Table 3. Regression model with predictors for cognitive development (EPA).

Variable	Model 1		Model 2		Model 3	
	β	p-value	β	p-value	β	p-value
Mother's s age in years	0.09	0.581				
Years of education (mother)	0.14	0.466	0.11	0.507		
Socio economic status	0.26	0.154	0.25	0.142	0.22	0.132
Years of education (father)	-0.15	0.45	-0.15	0.413		
Birth Length	0.27	0.11	0.31	**0.044**	0.3	**0.046**
Anxiety during the 1st trimester	-0.08	0.627				
EPA during the 1st trimester	0.61	**0.001**	0.59	**0.001**	0.62	**0.001**
Model p-value		**0.018**		0.61		0.51
R2	0.47		0.45		0.43	
Adjusted R2	0.31		0.35		0.38	

4. Discussion

Numerus studies have reported a positive correlation between the intake of LCPUFAs during pregnancy and infant outcomes (HIBBELN *et al.*, 2007; LEMAITRE *et al.*, 2011; OKEN *et al.*, 2016). The two most biologically active n-3 PUFAs are DHA and EPA (COLETTA *et al.*, 2010). Substantial evidence indicates that these fatty acids are essential for optimal brain function later in life (MENDEZ *et al.*, 2009). Additionally, research suggests that DHA and EPA supplementation during pregnancy improves child cognitive and visual development (ASSISI *et al.*, 2006; HIBBELN *et al.*, 2007; DUNSTAN *et al.*, 2008; KELLY *et al.*, 2011; VALENT *et al.*, 2013).

Most studies have suggested that the placental transfer of LCPUFAs occurs predominantly during the last trimester of pregnancy when brain growth is most rapid (STRAIN *et al.*, 2015). According to previous studies (SMUTS *et al.*, 2003; RAMAKRISHNAN *et al.*, 2010), the intake of LCPUFAs during the third trimester of the gestational period may also prolong pregnancy to full term, without detrimental effects on the growth of the fetus or the course of labor. In contrast, our data indicate that high concentrations of LCPUFAs only during the first trimester of pregnancy are positively correlated with cognitive development at 18 and 24 months of age. By the end of the 3rd week of pregnancy, the neural folds begin moving together and fuse, forming the neural tube, and

such fusion progresses both cranially and caudally in a zipperlike manner ((RICE E BARONE, 2000)52-54). DHA and EPA facilitate this fusion and contribute to proper development of the neural tube, thus contributing to the overall development of structures of the nervous system (UAUY *et al.*, 1996; KIDD, 2007; GUESNET E ALESSANDRI, 2011).

The present study examined the beneficial effects of high serum concentrations of DHA and EPA during the first trimester of pregnancy in women in Brazil. Our first regression model (Table 2) indicated that high serum concentrations of DHA during the first trimester of pregnancy, paternal level of education, and family SES were predictors of cognitive development at 18 and 24 months of age. The second regression model (Table 3) indicated that high serum concentrations of EPA during the first trimester of gestation, SES, and birth length were predictors of cognitive development in infants at the same ages.

Consistent with a recent systematic review (LINSELL *et al.*, 2015) that evaluated prognostic factors for the underdevelopment of cognition, the present results indicated that the mother's mental health (although not statistically significant), SES, birth length, and parental education were factors that are involved in early childhood development. We found that children with a longer length at birth and parents with a higher SES presented better cognitive performance, which supports data in the literature. Children with good neonatal health status, longer birth length, and heavier birth weight enroll at school with greater cognitive development advantages in general and remain stable during the elementary and middle school years (FIGLIO *et al.*, 2016), (KRISHNA *et al.*, 2017). Moreover, children of mothers and fathers with a higher SES (PAXSON E SCHADY, 2007) and higher levels of education (HOWARD *et al.*, 2011; ADAMS-CHAPMAN *et al.*, 2013) presented better performance, reflected by higher cognitive test scores.

In the present study, the level of parental education was negatively correlated with cognitive development scores. Fathers who had a low level of education had children who had higher scores on the BSID-III. Although the mothers' level of education had no effect on their children's cognitive development, our data corroborate studies that also separated parental education into maternal and paternal, suggesting that the father's level of education produced less of an effect on the child's cognitive development compared with the mother's level of education (HOLMLUND

et al., 2006; HOWARD *et al.*, 2011).

In this study, father's low level of education did not impair and even improved the children's cognitive development, even though, this finding was somewhat unexpected, as previous studies have found fathers' and mothers' sensitivity to have similar effects on child cognitive outcome (RYAN *et al.*, 2006; MARTIN *et al.*, 2007). The higher scores on the cognitive assessments in these children may have occurred because most of these fathers spent more time with their children and thus interacted with them more.

The sensitive fathering may be particularly important in families where the father takes on the role of the primary care-giver (PCG), a decision influenced by a series of economic, attitudinal and cultural variables found that PCG fathers have lower occupational status and provide a lower proportion of family income than non-PCG fathers (LEWIS *et al.*, 2009; WEST *et al.*, 2009). Maternal anxiety was a nonsignificant predictive factor in the regression models. This result in consistent with a previous study (KEIM *et al.*, 2011) but contrasts with other studies (GLOVER, 1999; TEIXEIRA *et al.*, 1999; BERGMAN *et al.*, 2010; DUNKEL SCHETTER e TANNER, 2012) that found that anxiety is detrimental to the child's cognitive development, which was caused by higher cortisol levels *in utero*.

5. Conclusions

In conclusion, our data suggest that high serum concentrations of n-3 LCPUFAs (EPA and DHA) during the first trimester of pregnancy are necessary for enhancing child development at 18 and 24 months of age in healthy children who were born at term. We also found that the level of paternal education, birth length, and SES were predictors of cognitive development. Further studies with larger sample sizes and supplementation that begins at the first trimester of pregnancy are required to corroborate these results.

REFERENCES

ADAMS-CHAPMAN, I. et al. Association between feeding difficulties and language delay in preterm infants using Bayley Scales of Infant Development-Third Edition. **Journal of Pediatrics,** v. 163, n. 3, p. 680-5 e1-3, Sep 2013. ISSN 1097-6833 (Electronic) 0022-3476 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/23582139 >.

ARTERBURN, L. M.; HALL, E. B.; OKEN, H. Distribution, interconversion, and dose response of n-3 fatty acids in humans. **American Journal of Clinical Nutrition,** v. 83, n. 6 Suppl, p. 1467S-1476S, Jun 2006. ISSN 0002-9165 (Print) 0002-9165 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/16841856 >.

ASSISI, A. et al. Fish oil and mental health: The role of n-3 long-chain polyunsaturated fatty acids in cognitive development and neurological disorders. **International Clinical of Psychopharmacology**, US**,** v. 21, n. 6, p. 319-336, 2006. ISSN 1473-5857(Electronic);0268-1315(Print).

BARKER, D. J.; CLARK, P. M. Fetal undernutrition and disease in later life. **Review of Reproduction ,** v. 2, n. 2, p. 105-12, May 1997. ISSN 1359-6004 (Print) 1359-6004 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/9414472 >.

BAYLEY, N. **Bayley scales of infant and toddler development: Bayley-III**. Harcourt Assessment, Psych. Corporation San Antonio, Tex, USA, 2006.

BELTRAMI, L.; DE MORAES, A. B.; DE SOUZA, A. P. R. Ansiedade materna puerperal e risco para o desenvolvimento infantil. **Distúrbios da Comunicação. ISSN 2176-2724,** v. 25, n. 2, 2013. ISSN 2176-2724.

BENAIM, C. et al. Early pregnancy body mass index modifies the association of pre-pregnancy dietary patterns with serum polyunsaturated fatty acid concentrations throughout pregnancy in Brazilian women. **Maternal & Child Nutrition**, Jun 21 2017. ISSN 1740-8709 (Electronic)
1740-8695 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/28635163 >.

BERGMAN, K. et al. Maternal prenatal cortisol and infant cognitive development: moderation by infant-mother attachment. **Biological Psychiatry,** v. 67, n. 11, p. 1026-32, Jun 01 2010. ISSN 1873-2402 (Electronic) 0006-3223 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/20188350 >.

BERTI, C. et al. Early-life nutritional exposures and lifelong health: immediate and long-lasting impacts of probiotics, vitamin D, and breastfeeding. **Nutrition Reviews,** v. 75, n. 2, p. 83-97, Feb 01 2017. ISSN 1753-4887 (Electronic) 0029-6643 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/28130504 >.

BRADLEY, R. H.; CORWYN, R. F. Socioeconomic status and child development. **Annual Review of Psychology,** v. 53, p. 371-99, 2002. ISSN 0066-4308 (Print) 0066-4308 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/11752490 >.

BRYANTON, J. et al. Incidence of prenatal alcohol exposure in Prince Edward Island: a population-based descriptive study. **CMAJ open,** v. 2, n. 2, p. E121, 2014.

CATTELL, R. B.; SCHEIER, I. H. The meaning and measurement of neuroticism and anxiety. 1961.

CHEVALIER, S. Active trilingualism in early childhood: The motivating role of caregivers in interaction. **International Journal of Multilingualism,** v. 9, n. 4, p. 437-454, 2012. ISSN 1479-0718.

COLETTA, J. M.; BELL, S. J.; ROMAN, A. S. Omega-3 Fatty acids and pregnancy. **Reviews in Obstetrics and Gynecology,** v. 3, n. 4, p. 163-71, Fall 2010. ISSN 2153-8166 (Electronic) 1941-2797 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/21364848 >.

CUEVAS, K. et al. What's mom got to do with it? Contributions of maternal executive function and caregiving to the development of executive function across early childhood. **Developmental Science,** v. 17, n. 2, p. 224-238, 2014. ISSN 1467-7687.

DOBBING, J. Proceedings: Growth retardation and the human fetal brain. **Archives of Disease in Childhood,** v. 48, n. 10, p. 828, Oct 1973. ISSN 1468-2044 (Electronic) 0003-9888 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/4796012 >.

DUNKEL SCHETTER, C.; TANNER, L. Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice. **Current Opinion in Psychiatry,** v. 25, n. 2, p. 141-8, Mar 2012. ISSN 1473-6578 (Electronic) 0951-7367 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/22262028 >.

DUNSTAN, J. A. et al. Cognitive assessment of children at age 2(1/2) years after maternal fish oil supplementation in pregnancy: a randomised controlled trial. **Archives of Disease in Child Fetal Neonatal Ed,** v. 93, n. 1, p. F45-50, Jan 2008. ISSN 1359-2998.

FIELD, A. **Discovering statistics using SPSS**. Sage publications, 2009. ISBN 1847879071.

FIGLIO, D. N. et al. Long-term Cognitive and Health Outcomes of School-Aged Children Who Were Born Late-Term vs Full-Term. **JAMA Pediatrics,** v. 170, n. 8, p. 758-64, Aug 01 2016. ISSN 2168-6211 (Electronic) 2168-6203 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/27271240 >.

FLORES, M. R. et al. Associação entre indicadores de risco ao desenvolvimento infantil e estado emocional materno. **Revista CEFAC,** v. 15, n. 2, p. 348-360, 2012.

GERMAN, J. B. Dietary lipids from an evolutionary perspective: sources, structures and functions. **Matern Child Nutrition,** v. 7 Suppl 2, p. 2-16, Apr 2011. ISSN 1740-8709 (Electronic) 1740-8695 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/21366863 >.

GLOVER, V. Maternal stress or anxiety during pregnancy and the development of the baby. **The Practising Midwife,** v. 2, n. 5, p. 20-2, May 1999. ISSN 1461-3123 (Print)1461-3123 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/12024606 >.

GOULD, J. F. et al. Randomized controlled trial of maternal omega-3 long-chain PUFA supplementation during pregnancy and early childhood development of attention, working memory, and inhibitory control. **American Journal of Clinical Nutrition,** v. 99, n. 4, p. 851-9, Apr 2014. ISSN 0002-9165.

GOULD, J. F.; SMITHERS, L. G.; MAKRIDES, M. The effect of maternal omega-3 (n-3) LCPUFA supplementation during pregnancy on early childhood cognitive and visual development: a systematic review and meta-analysis of randomized controlled trials. **American Journal of Clinical Nutritional ,** v. 97, n. 3, p. 531-44, Mar 2013. ISSN 1938-3207 (Electronic) 0002-9165 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/23364006 >.

GOULD, J. F. et al. Does n-3 LCPUFA supplementation during pregnancy increase the IQ of children at school age? Follow-up of a randomised controlled trial. **BMJ Open,** v. 6, n. 5, p. e011465, May 17 2016. ISSN 2044-6055 (Electronic) 2044-6055 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/27188814 >.

GUESNET, P.; ALESSANDRI, J. M. Docosahexaenoic acid (DHA) and the developing central nervous system (CNS) - Implications for dietary recommendations. **Biochimie,** v. 93, n. 1, p. 7-12, Jan 2011. ISSN 1638-6183 (Electronic) 0300-9084 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/20478353 >.

HADDERS-ALGRA, M. The neuromotor examination of the preschool child and its prognostic significance. **Mental Retardation and Developmental Disabilities Research Reviews,** v. 11, n. 3, p. 180-8, 2005. ISSN 1080-4013 (Print) 1080-4013 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/16161096 >.

HIBBELN, J. R. et al. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): An observational cohort study. **The Lancet**, United Kingdom**,** v. 369, n. 9561, p. 578-585, 2007. ISSN 1474-547X(Electronic);0140-6736(Print). HOLMLUND, H.; LINDAHL, M.; PLUG, E. Estimating intergenerational schooling effects: a comparison of methods. 2006.

HOWARD, K. et al. Biological and environmental factors as predictors of language skills in very preterm children at 5 years of age. **Journal of Developmental & Behavioral Pediatrics,** v. 32, n. 3, p. 239-249, 2011. ISSN 0196-206X.

INNIS, S. M.; FRIESEN, R. W. Essential n-3 fatty acids in pregnant women and early visual acuity maturation in term infants. **American Journal of Clinical Nutrition,** v. 87, n. 3, p. 548-57, Mar 2008. ISSN 1938-3207 (Electronic) 0002-9165 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/18326591 >.

KEIM, S. A. et al. A prospective study of maternal anxiety, perceived stress, and depressive symptoms in relation to infant cognitive development. **Early Human Development,** v. 87, n. 5, p. 373-80, May 2011. ISSN 1872-6232 (Electronic) 0378-3782 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/21420261 >.

KELLY, L. et al. The polyunsaturated fatty acids, EPA and DPA exert a protective effect in the hippocampus of the aged rat. **Neurobiology of Aging,** v. 32, n. 12, p. 2318 e1-15, Dec 2011. ISSN 1558-1497 (Electronic)
0197-4580 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/20570403 >.

KIDD, P. M. Omega-3 DHA and EPA for cognition, behavior, and mood: clinical findings and structural-functional synergies with cell membrane phospholipids. **Alternative medicine review,** v. 12, n. 3, p. 207, 2007. ISSN 1089-5159.

KIERNAN, K. E.; HUERTA, M. C. Economic deprivation, maternal depression, parenting and children's cognitive and emotional development in early childhood. **Br J Sociol,** v. 59, n. 4, p. 783-806, Dec 2008. ISSN 1468-4446 (Electronic) 0007-1315 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/19035922 >.

KLEBANOV, P. K. et al. The contribution of neighborhood and family income to developmental test scores over the first three years of life. **Child Development,** v. 69, n. 5, p. 1420-36, Oct 1998. ISSN 0009-3920 (Print)
0009-3920 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/9839425 >.

KRISHNA, M. et al. Birth size, risk factors across life and cognition in late life: protocol of prospective longitudinal follow-up of the MYNAH (MYsore studies of Natal effects on Ageing and Health) cohort. **BMJ Open,** v. 7, n. 2, p. e012552, Feb 16 2017. ISSN 2044-6055 (Electronic) 2044-6055 (Linking). Disponível em: <https://www.ncbi.nlm.nih.gov/pubmed/28209604 >.

LAURITZEN, L. et al. The essentiality of long chain n-3 fatty acids in relation to development and function of the brain and retina. **Prog Lipid Res,** v. 40, n. 1-2, p. 1-94, Jan-Mar 2001. ISSN 0163-7827 (Print)0163-7827 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/11137568 >.

LEMAITRE, R. N. et al. Genetic loci associated with plasma phospholipid n-3 fatty acids: a meta-analysis of genome-wide association studies from the CHARGE Consortium. **PLoS Genet,** v. 7, n. 7, p. e1002193, Jul 2011. ISSN 1553-7404 (Electronic) 1553-7390 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/21829377 >.

LEWIS, S. et al. A comparison of father–infant interaction between primary and non-primary care giving fathers. **Child: care, health and development,** v. 35, n. 2, p. 199-207, 2009. ISSN 1365-2214.

LIN, Y. H. et al. Automated high-throughput fatty acid analysis of umbilical cord serum and application to an epidemiological study. **Lipids,** v. 47, n. 5, p. 527-539, 2012. ISSN 0024-4201.

LINSELL, L. et al. Prognostic Factors for Poor Cognitive Development in Children Born Very Preterm or With Very Low Birth Weight: A Systematic Review. **JAMA Pediatr,** v. 169, n. 12, p. 1162-72, Dec 2015. ISSN 2168-6211 (Electronic) 2168-6203 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/26457641 >.

LONNER, W. J.; IBRAHIM, F. A. Assessment in cross-cultural counseling. 1989. ISSN 082481231X.

MADASCHI, V. Tradução, adaptação transcultural e evidências de validade das Escalas Bayley III de Desenvolvimento Infantil em uma população do Município de Barueri, São Paulo. 2012.

MADASCHI, V. et al. Bayley-III Scales of Infant and Toddler Development: Transcultural Adaptation and Psychometric Properties. **Paidéia (Ribeirão Preto),** v. 26, p. 189-197, 2016. ISSN 0103-863X. Disponível em: < http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0103-863X2016000200189&nrm=iso >.

MALMBERG, L. E. et al. The influence of mothers' and fathers' sensitivity in the first year of life on children's cognitive outcomes at 18 and 36 months. **Child Care Health Development,** v. 42, n. 1, p. 1-7, Jan 2016. ISSN 1365-2214 (Electronic) 0305-1862 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/26538379 >.

MARTIN, A.; RYAN, R. M.; BROOKS-GUNN, J. The joint influence of mother and father parenting on child cognitive outcomes at age 5. **Early Childhood Research Quarterly,** v. 22, n. 4, p. 423-439, 2007. ISSN 0885-2006.

MARTINEZ, M. Restoring the DHA levels in the brains of Zellweger patients. **J Mol Neurosci,** v. 16, n. 2-3, p. 309-16; discussion 317-21, Apr-Jun 2001. ISSN 0895-8696 (Print) 0895-8696 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/11478386 >.

MARTINEZ, M.; MOUGAN, I. Fatty acid composition of human brain phospholipids during normal development. **Journal of Neurochemistry,** v. 71, n. 6, p. 2528-33, Dec 1998. ISSN 0022-3042 (Print)0022-3042 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/9832152 >.

MCELWAIN, N. L. et al. Differentiating among insecure mother-infant attachment classifications: a focus on child-friend interaction and exploration during solitary play at 36 months. **Attachment & Human Development,** v. 5, n. 2, p. 136-64, Jun 2003. ISSN 1461-6734 (Print)1461-6734 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/12791564 >.

MENDEZ, M. A. et al. Maternal fish and other seafood intakes during pregnancy and child neurodevelopment at age 4 years. **Public Health Nutrition,** v. 12, n. 10, p. 1702-10, Oct 2009. ISSN 1475-2727 (Electronic)
1368-9800 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/19026093 >.

MENNITTI, L. V. et al. Type of fatty acids in maternal diets during pregnancy and/or lactation and metabolic consequences of the offspring. **J Nutrition Biochemistry,** v. 26, n. 2, p. 99-111, Feb 2015. ISSN 0955-2863.

OKEN, E. et al. Maternal prenatal fish consumption and cognition in mid childhood: Mercury, fatty acids, and selenium. **Neurotoxicology and Teratology,** v. 57, p. 71-78, Sep - Oct 2016. ISSN 1872-9738 (Electronic)
0892-0362 (Linking). Disponível em: <https://www.ncbi.nlm.nih.gov/pubmed/27381635 >.

PANCSOFAR, N.; VERNON-FEAGANS, L.; INVESTIGATORS, F. L. P. Fathers' early contributions to children's language development in families from low-income rural communities. **Early childhood research quarterly,** v. 25, n. 4, p. 450-463, 2010. ISSN 0885-2006.

PAXSON, C.; SCHADY, N. Cognitive development among young children in Ecuador the roles of wealth, health, and parenting. **Journal of Human resources,** v. 42, n. 1, p. 49-84, 2007. ISSN 0022-166X.

POWER, C. et al. The influence of birth weight and socioeconomic position on cognitive development: Does the early home and learning environment modify their effects? **Journal of Pediatrics,** v. 148, n. 1, p. 54-61, Jan 2006. ISSN 0022-3476 (Print) 0022-3476 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/16423598 >.

RAMAKRISHNAN, U. et al. Effects of docosahexaenoic acid supplementation during pregnancy on gestational age and size at birth: randomized, double-blind, placebo-controlled trial in Mexico. **Food and Nutrition Bulletin,** v. 31, n. 2 Suppl, p. S108-16, Jun 2010. ISSN 0379-5721 (Print) 0379-5721 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/20715595 >.

RICE, D.; BARONE, S., Jr. Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. **Environment Health Perspectives,** v. 108 Suppl 3, p. 511-33, Jun 2000. ISSN 0091-6765 (Print) 0091-6765 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/10852851 >.

RYAN, R. M.; MARTIN, A.; BROOKS-GUNN, J. Is one good parent good enough? Patterns of mother and father parenting and child cognitive outcomes at 24 and 36 months. **Parenting,** v. 6, n. 2-3, p. 211-228, 2006. ISSN 1529-5192.

SALEM, N., Jr.; EGGERSDORFER, M. Is the world supply of omega-3 fatty acids adequate for optimal human nutrition? **Current Opinion in Clinical Nutrition & Metabolic Care,** v. 18, n. 2, p. 147-54, Mar 2015. ISSN 1473-6519 (Electronic) 1363-1950 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/25635599 >.

SALEM, N., Jr. et al. Mechanisms of action of docosahexaenoic acid in the nervous system. **Lipids,** v. 36, n. 9, p. 945-59, Sep 2001. ISSN 0024-4201 (Print) 0024-4201 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/11724467 >.

SANTOS, D. N. et al. Determinants of cognitive function in childhood: a cohort study in a middle income context. **BMC Public Health,** v. 8, p. 202, Jun 06 2008. ISSN 1471-2458 (Electronic) 1471-2458 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/18534035 >.

SMUTS, C. M. et al. A randomized trial of docosahexaenoic acid supplementation during the third trimester of pregnancy. **Obstetrics Gynecologist,** v. 101, n. 3, p. 469-79, Mar 2003. ISSN 0029-7844 (Print) 0029-7844 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/12636950 >.

SPIELBERGER, C. D. **State-Trait anxiety inventory**. Wiley Online Library, 2010. ISBN 0470479213.

STRAIN, J. J. et al. Prenatal exposure to methyl mercury from fish consumption and polyunsaturated fatty acids: associations with child development at 20 mo of age in an observational study in the Republic of
Seychelles. **American Journal of Clinical Nutrition,** v. 101, n. 3, p. 530-7, Mar 2015. ISSN 0002-9165.

TEIXEIRA, J. M.; FISK, N. M.; GLOVER, V. Association between maternal anxiety in pregnancy and increased uterine artery resistance index: cohort based study. **BMJ,** v. 318, n. 7177, p. 153-7, Jan 16 1999. ISSN 0959-8138 (Print) 0959-535X (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/9888905 >.

UAUY, R.; MENA, P.; ROJAS, C. Essential fatty acids in early life: structural and functional role. **Proc Nutr Soc,** v. 59, n. 1, p. 3-15, Feb 2000. ISSN 0029-6651 (Print)

0029-6651 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/10828169 >.

UAUY, R. et al. Role of essential fatty acids in the function of the developing nervous system. **Lipids,** v. 31 Suppl, p. S167-76, Mar 1996. ISSN 0024-4201 (Print) 0024-4201 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/8729114 >.

VALENT, F. et al. Associations of prenatal mercury exposure from maternal fish consumption and polyunsaturated fatty acids with child neurodevelopment: a prospective cohort study in Italy. **Journal of Epidemiology,** v. 23, n. 5, p. 360-70, Sep 05 2013. ISSN 1349-9092 (Electronic) 0917-5040 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/23933621 >.

WEISER, M. J.; BUTT, C. M.; MOHAJERI, M. H. Docosahexaenoic Acid and Cognition throughout the Lifespan. **Nutrients,** v. 8, n. 2, p. 99, Feb 17 2016. ISSN 2072-6643 (Electronic) 2072-6643 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/26901223 >.

WEST, A. F. et al. Why do some fathers become primary caregivers for their infants? A qualitative study. **Child: care, health and development,** v. 35, n. 2, p. 208-216, 2009. ISSN 1365-2214.

YEHUDA, S.; RABINOVITZ, S.; MOSTOFSKY, D. I. Essential fatty acids and the brain: from infancy to aging. **Neurobiology of Aging,** v. 26 Suppl 1, p. 98-102, Dec 2005. ISSN 0197-4580 (Print) 0197-4580 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/16226347 >.

Article 3

Irurita-Ballesteros, C., DVS, Falcão., Rocinholi, L., Landeira-fernandez, J. Depression, Anxiety and Social Support for the Mother: Repercussions on Infant Development. (Article Submitted)

RESUMO

O desenvolvimento humano consiste em um processo de interação entre a pessoa e seu contexto. O papel da mãe é fundamental no desenvolvimento da criança e parece amenizar o impacto de condições ambientais desfavoráveis. Prejuízos na saúde mental materna na gestação e pós-parto podem reduzir as interações mãe-criança. O objetivo deste estudo foi caracterizar o impacto das condições de saúde mental materna no desenvolvimento das crianças da gestação aos dois anos de idade. Trata-se de um estudo longitudinal de delineamento de casos múltiplos, considerando três díades mãe-bebê. Na primeira fase avaliou-se: aspectos sociodemográficos, ansiedade, saúde mental (gestação) e depressão materna (gestação e pós-parto). Na segunda fase, as crianças foram avaliadas através das escalas Bayley do Desenvolvimento Infantil III (BSID III), aos 6, 12, 18 e 24 meses de idade. Na díade 1, foram identificadas dificuldades de linguagem na primeira avaliação, que foram melhoradas com a facilitação social no ambiente de creche. Nas díades 2 e 3, foram identificadas dificuldades motoras nas crianças associadas à presença de ansiedade e depressão maternas. Os três casos podem auxiliar na compreensão da interdependência da saúde mental materna e o desenvolvimento do bebê, considerando a importância do contexto social e familiar.

Palavras chave: Ansiedade materna; Desenvolvimento inicial; Psicologia pediátrica; Desenvolvimento cognitivo; Desenvolvimento psicomotor

ABSTRACT

Human development consists of a process of interaction between the person and its context. The role of the mother is fundamental in child development and appears to mitigate the impact of unfavorable environmental conditions. Maternal mental health impairment during perinatal and postnatal period may reduce mother-child interaction. The objective of this study was to characterize the impact of maternal mental health conditions on the child development from pregnancy to two years of age. This is a multiple case longitudinal study, considering three mother-infant dyads. In the first phase, we evaluated sociodemographic aspects, anxiety, mental health (pregnancy) and maternal depression (pregnancy and postpartum). In the second phase, infants were evaluated through the Bayley Scales of Infant Development III (BSID III) at 6, 12, 18 and 24 months of age. In the first dyad, we identified infant language difficulties during the first evaluation; which were overcome by socialization in the day care environment. In the second and third dyads, we identified infant motor difficulties associated with the presence of maternal anxiety and depression. These three case studies can help in understanding the interdependence of maternal mental health and the development of the baby, considering the importance of the social and family context.

Key words: maternal anxiety, early childhood development; pediatric psychology; cognitive development, psychomotor development.

1. Introduction

Human development has been explained by systemic theoretical models based on the interaction effects of the person in different contexts (LERNER, 2006). The bioecological model considers that the human being is biopsychologically active in evolution with the people, objects and symbols that are present in its environment. Development consists of a process of reciprocal interaction between the person and its context through time, being a function of the forces that arise from multiple circumstances and the relation between them (BRONFENBRENNER AND MORRIS, 1998). Therefore, it is a process that occurs throughout the life cycle and the generations (BRONFENBRENNER, 2001), where the family is the main nucleus where the first social interactions of the child occur. It is in it that the learning of concepts, rules and cultural practices that underlie the processes of socialization of individuals begins (BRONFENBRENNER, 2005).

Within the family, the role of the mother is highlighted in the literature as of fundamental importance in the development of the child. Her ability to take care of children properly and to improve the available resources seems to mitigate the impact of an unfavorable condition, especially during the first thousand days, from conception to the end of the second year of life, a sensitive or critical period of development (BEEBE *et al.*, 2016; BERG, 2016).

In another perspective, the Attachment Theory emphasized the importance of the child growing up in a relationship of attachment with the mother so that a good affective, social and cognitive development occurs. In this way, maternal care is closely linked to attachment behavior, since the act of caring for the baby causes the mother to be constantly close, almost always within reach of its eyes or ears, so that she remains attentive to child's needs and can supply them when needed (BOWLBY, 2002).

In this sense, adequate maternal performance may decrease the effects of stress variables on the internal and external environment of the baby, favoring the child's development (DE OLIVEIRA *et al.*, 2017). However, when the mother cannot provide adequate protection and stimulation, the chances of damage in this area increase significantly, with repercussions in the medium and long term (BRETHERTON, 1992; PEREIRA *et al.*, 2014; BERNIER *et al.*, 2016).

Maternal mental health impairments may reduce mother-child interactions (FLYKT *et al.*, 2010) and are among the most common morbidities in pregnancy and postpartum, with about 25% of women experiencing stress, depression or anxiety in this period (KINGSTON *et al.*, 2012). Although attention has been directed more often to postpartum, the prevalence of prepartum depression ranges from 7 to 15% in high-income countries and 19 to 25% in low- and middle-income countries (RAHMAN *et al.*, 2003). Depression negatively affects the formation of the mother-baby bond. Studies have indicated that 50-70% of women with anxiety and depression in the gestational period developed chronic symptoms that were perpetuated during child rearing in their early years (HORWITZ *et al.*, 2009; WOOLHOUSE *et al.*, 2015; GOODMAN AND GARBER, 2017), increasing the risk of the child having adverse outcomes, such as emotional difficulties, symptoms of attention deficit hyperactivity disorder, or impairment of cognitive, neurological, linguistic and socioemotional development in the long-term (GLOVER, 2014; PEREIRA PRETTO CARLESSO *et al.*, 2014). Some risk factors for maternal depression are related to the higher number of children; low schooling; low socioeconomic status; women with a history of physical, psychological and sexual abuse in childhood; history of mental illness in the family; hormonal imbalances; single marital status; instability in the affective relationship; history of previous abortion; unwanted and unplanned pregnancy; father's negative reaction to pregnancy; low perception of social support (SILVA, 2012; LUCCI E OTTA, 2013).

While all of these factors increase the risk of depression in women during the pregnancy and postpartum periods, increased social support plays a buffering role against depression (HUNG, 2004). Thus, identification of the desire to become pregnant in women and the type of social support they receive during prenatal care visits are necessary to provide adequate guidelines that favor their mental health during the gestational period (DIBABA *et al.*, 2013).

There is a lack of literature on longitudinal studies on the role of maternal mental health in the pre- and postpartum periods as well as on parental practices and care. A systematic review of the literature has indicated that most research in this area comes from developed countries and has historically focused on the adverse effects of postpartum depression (KINGSTON *et al.*, 2015). However, the epidemiological evidence of prenatal anxiety and depression rates, similar or superior to the postnatal rates, favored the interest of investigations on the influence of: maternal mental health throughout the perinatal period; the postnatal environment to alleviate the risk

occurred during prenatal period; and the long-term impact on child development (VAN DEN BERGH *et al.*, 2005; KINGSTON *et al.*, 2015).

In this context, it is necessary to diagnose delays in child development, as early as possible, in order to detect risk and protection factors, both biological and environmental, in order to intervene and improve the prognosis and quality of life of children, their caregivers and relatives. Based on this information, this study aimed at identifying and characterizing in three mother-infant dyads the impact of the maternal mental health conditions in the three trimesters of gestation and forty-five days after delivery on the development of children in the first two years of life. Specifically, we sought to assess the indicators of depression and anxiety that may interfere with the mother-baby bond during the pre- and postpartum period, and also evaluate the role of the social support network for dyad well-being and for the child development.

2. Method

2.1 Design

This is a longitudinal multiple case research (YIN, 1994), which consists of developing a detailed knowledge about a small number of related cases and proposes to investigate the complexity of the subjects' interrelationships in their context, contributing to a better understanding of the investigated phenomenon.

2.2 Study site

Phase 1 of the research was developed at the Heitor Beltrão Municipal Health Center (CMS), located in the Tijuca neighborhood of the city of Rio de Janeiro, State of Rio de Janeiro. Phase 2 was conducted in a room of the Pontifical Catholic University of Rio de Janeiro (PUC-Rio), prepared appropriately for the accomplishment of the neuropsychological evaluations of the babies.

2.3 Participants

Three mother-baby dyads participated in the study, presented with the fictitious names of Maria and Lucas (dyad 1); Diana and Alice (dyad 2) and; Beatriz and Felipe (dyad 3). All had low

socioeconomic status and lived in the city of Rio de Janeiro. The eligibility criteria for mothers were: a) gynecological and obstetric follow-up at the study site; b) be between 20 and 40 years of age; c) do not present chronic non-communicable disease (except obesity); d) participated in the first phase of the research. For the children the inclusion criteria were: a) term birth; b) the mother's participation in the first phase of the research; c) carry out pediatric follow-up and vaccination control at the study site.

2.4 Instruments

2.4.1 Sociodemographic questionnaire:

Composed of closed questions and elaborated from the literature review. The following variables were evaluated: parents' age, marital status, schooling, socioeconomic classification, subjective perception of the pregnant woman regarding social support (companion, family, friends and neighbors). Socioeconomic status was measured through the Brazilian Association of Research Companies (ABEP) instrument. This classification maps individuals based on certain "comfort indexes", such as television, refrigerator, radio, automobile and domestic servant, in addition to the schooling of the head of the family.

2.4.2 The State Trait anxiety inventory (STAI)

This instrument translated, adapted and validated in Brazil (Biaggio and Natalício, 1979) was used to evaluate anxiety during pregnancy. It is based on the dualistic conception that distinguishes anxiety in two states: Trait-Anxiety (trait-a) and State-Anxiety (state-a) (CATTELL & SCHEIER, 1961). STAI-E was applied in each trimester of gestation, by trained interviewers, totaling three evaluations in this period.

2.4.3. Mini International Neuropsychiatric Interview (MINI)

The Mini International Neuropsychiatric Interview (MINI) is a standardized instrument, divided into modules by diagnostic categories and with brief application, around 15 minutes (DE AZEVEDO MARQUES AND ZUARDI, 2008). This study investigated the presence of mental disorders classified in DSM IV (ASSOCIATION, 2000) through the (MINI) version 5.0.0. The

instrument was applied during gestation by a mental health professional with previous training and knowledge of psychopathology.

2.4.4. Edinburgh Postnatal Depression Scale (EPDS)

The Edinburgh Postnatal Depression Scale (EPDS) was used to evaluate the pregnant and postpartum women in phase 1 of the present study. The validated EPDS in Brazil (SANTOS *et al.*, 1999) is a self-applied, quick and simple scale composed of 10 items designed to identify depression during pregnancy and postpartum. Its score is made of options from 0 to 3 points according to the presence and intensity of the depressive symptom, each item is summed to obtain the general score, and the total of 12 points or more indicates the probability of the occurrence of depression, but does not indicate its severity (MURRAY AND COX, 1990).

2.4.5. Bayley Scales of Infant Development (BSID III)

In 1953, the first version of the Bayley Scales of Infant Development was published by its main author, Nancy Bayley, PhD. In 1977, it was revised, then creating the second version and finally in 2006, the third and current version of the Bayley (BSID III) was published (Bayley, 2006). BSID III is composed of the following scales: a) Cognitive Scale, which aims to evaluate sensorimotor development, exploration and manipulation, concept formation, memory and other aspects of cognitive processing; b) Language Scale, composed of receptive and expressive communication items, forming two distinct subtests; c) Motor Scale, which aims to evaluate motor skills in general (large muscles) and fine motor skills; d) Social-emotional Scale, aims to identify the main milestones of social and emotional development at certain ages; e) Adaptive Behavior Scale, which accesses functional abilities of the child's daily life. Both the social-emotional scale and the behavioral scale are filled by the primary caregiver. According to the study (SWEENEY AND SWANSON, 2004), the Bayley scales present high sensitivity and specificity as well as adeuqate predictive values. BSID III is considered one of the best instruments in the area of for the evaluation of child development, being considered as "gold standard" by several authors, especially since it includes an extremely complete and detailed evaluation of neuropsychomotor development (MADASCHI AND PAULA, 2011). For this study, a validation and cross-cultural adaptation for Brazil was used ((MADASCHI, 2012).

2.5 Ethical Aspects

The study was submitted to the National Commission for Research Ethics CONEP (registration 16647) through the Institute of Psychiatry of the Federal University of Rio de Janeiro and was approved on 01/03/2012 by means of opinion 099/2012. The research is in accordance with the ethical principles contained in Resolution 196/96 of the National Health Council and was conditioned upon the signing of a free and informed consent term.

2.6 Procedures for data collection and analysis

The study had two phases: a) during the first phase (2009-2011), pregnant women were evaluated at three follow-up points during pregnancy and forty-five days postpartum; b) in the second phase (2012-2014), the children were evaluated at 6, 12, 18 and 24 months of age.During the three trimesters of gestation, we sought information on sociodemographic aspects and desire to become pregnant, as well as applied anxiety (IDATE-E), mental health (M.I.N.I) and depression (Edinburgh) scales. In the postpartum period, the Edinburgh postnatal depression scale was applied. After birth, children were analyzed for anthropometric measures and child development assessments were performed through BSDI III. During the collection, a database with 52 mother-baby dyads was composed; however, only three children completed the Bayley scales evaluations for the 4 established points, and they were selected for this study.

3. Results and Discussion

The results of the assessments of all children in the first two years of life, in which the cognitive, language and motor scales of BSID III were applied, can be found in Table 1.

3.1 Case 1 - Dyad Maria (mother) - Lucas (child)

Maria declared that she had a stable marital status. At the beginning of the study, she was 37 years old, 12 years older than her spouse. Both worked outside the home (she as domestic worker and he in general services); he had complete higher education and she, incomplete elementary school. The monthly family income was 1,072 reais. Maria had three children from the first marriage and noted that she had no desire to get pregnant again because she did not want to raise more children, since the oldest was 18 years old and the youngest was 8 years old. However, her husband had no children and had a great desire to be a father; he longed to have a child with Maria and always

asked her to fulfill that desire. Lucas's pregnancy was not planned, but it was accepted and well received by both.

3.1.1 Experiences from pregnancy to birth

During the gestational period, the mother showed happiness with the arrival of the baby. She had maternity leave from the 35th week of gestation, after feeling that she had difficulty developing her activities outside the home. Lucas was born at the 38th week of natural delivery, with a weight of 3.660 kg and 49 cm in length. During pregnancy, Maria verbalized that she was satisfied with the social support offered by her husband, her older children and her mother.

It was verified that she did not present symptoms of anxiety, depression or the presence of other mental disorders after analyzing the data obtained with the application of the scales, and that corroborated her reports about being calm and satisfied with the arrival of the child but concerned about the financial situation of the family.

3.1.2 Postpartum experiences

After delivery, Maria reported that she had a good recovery. Neither she nor the child suffered nor suffered any danger. The social support received was favorable, showing satisfaction with the support of the medical doctors and all hospital staff, as well as with the employers, who agreed to maternity leave. In addition, the baby's maternal grandmother went to live with the family after the child was born, providing the support they needed. It should be emphasized that no symptoms related to postpartum depression were detected.

3.1.3 Child development:

3.1.3.1 History of development

Lucas was a child in normal development. Since he was a baby he has shown to be affectionate, explorer and with an easy temper. It was found that he did not have problems sleeping or eating, being breastfed up to 15 months. At birth, he was under the care of her mother, father and maternal grandmother, and her grandmother was the main caretaker until the age of 14 months. After this period, he began attending the public day care center in the neighborhood where they lived.

3.1.3.2 Behavioral observations

Lucas always attended the neuropsychological assessments dressed properly and in good conditions of personal hygiene. During the evaluation periods, he revealed cooperativeness and motivation to what was requested. As for the relationship with the mother, he always showed affection and responsiveness.

3.1.3.3 Results

The first assessment of Lucas was performed at 6 months and 28 days of age and revealed within-average scores for the cognition and motor development scales. However, the child presented borderline performance on the language scale, and did not score in the first three items of the age group corresponding to his age (G range: 6 months and 16 days - 8 months and 30 days). Therefore, it was necessary to go back to the items of the scale that corresponded to the age group prior to the child's age (D range: 5 months and 16 days - 6 months and 15 days), as established in the protocol for application of the BSID III scales, to give continuity to the process. However, Lucas still had difficulty responding to the subtests of the language scale (receptive and expressive). On the second (12 months and 28 days) and third (18 months and 6 days) evaluations, the scores related to the language presented improvements, and Lucas reached values within the average and the superiority, respectively.

Based on the evaluator's observation and experience, Lucas had a significant advance in social skills that helped him improve his language, and all his scores; at 18 months, scores were higher than the average for his age range. His last evaluation was performed at 25 months and 2 days of age. In this evaluation, he continued to present scores in the upper average scores for cognitive evaluation, average scores for language and upper scores for the motor scale.

3.1.3.4 Diagnosis/ clinical impressions

In general, Lucas' neurodevelopmental skills were in the middle range on all BSID III scales used. During the visits, it was observed that the child always showed improvement in the performance of items that showed higher cortical processes involved in associative and integrative neural circuits, such as concept formation, planning and memory, among others (WEISS *et al.*, 2010;

PELA, 2016). In the initial evaluation, he was a little indifferent to the toys and did not try to interact with the evaluator, revealing difficulties in responding to items related to the identification of certain objects and requests for social routines, such as clapping, bye-bye or send a kiss. After analyzing the child performance in this first evaluation, the examiner identified discrepancies between the subtests of the language scale (expressive and receptive), however, it was considered early to point out to the caregivers any difficulty related to the communication. At about 12 months (second evaluation), it was observed that Lucas learned to use gestures to communicate, responded only to his name and followed the commands given by the evaluator or his mother, when necessary, showing difficulties in communicating. Thus, in the first and second evaluations, certain aspects of communication were identified that became worrisome when associated with the reduction of the language scale score. Therefore, it was considered important to perform a meeting to discuss the neuropsychological report with the primary caregiver in order to present recommendations to benefit child development.

Although he was very affectionate with his mother during the first sessions, he did not show high social skills; on the contrary, his interactive skills in social routines presented low scores on the language scale. Interventions that focus on the development of interactive skills positively affect more pronounced pre-linguistic abilities such as gestures, vocalization and eye contact, and later use of words and word combinations (CALANDRELLA AND WILCOX, 2000).

Based on the child responsiveness to his mother, it was suggested to increase his social interaction with other children, in order to facilitate the acquisition of language. In the last evaluation performed, at 25 months and 2 days, the child scored on average or above average for all scales, showing the occurrence of rapid changes due to the maturity that acquired along the development associated with the environmental factors that he may have been exposed (DICKINSON AND MCCABE, 1991). As highlighted by his mother, after Lucas entered the day care center, he became more interested in the environment and social interactions with the family, which certainly favored the development of language.

3.2 Case 2 - Dyad Diana (mother) - Alice (child)

Diana had a stable marital status since the beginning of the research. This was her second pregnancy, as the couple had a six-year-old son. The age difference between Alice's parents was 17 years old, the father was 45 years old and the mother was 28 at the beginning of gestation. As for schooling, neither had completed elementary school. According to Diana, her husband was the family head, worked as a porter, and the couple's monthly income was 850 reais, however, he preferred that she stay at home taking care of the home. Both were surprised and worried about the news of the pregnancy because they were clear that they did not want more children, having taken precautions to avoid it. When they found out that they were pregnant with a girl, Diana reported that the world turned "pink" and soon became enthusiastic about the arrival of the child, naming it immediately Alice.

3.2.1 Experiences from pregnancy to birth

Early in her pregnancy, Diana stated that she had been very anxious and concerned about the situation. However, she was very hopeful about the idea of being the mother of a girl. During the gestational period, Diana did not do any kind of work outside the home, wanting to be quiet at home. The scales applied during the three trimesters of gestation and postpartum revealed that Diana exhibited symptoms of high levels of anxiety only during the first trimester of gestation. In the other trimesters, the scales did not indicate symptoms of anxiety, although she rated herself as a very anxious person. No depressive symptoms or the presence of other psychiatric disorders were detected.

Alice was born at 40 weeks, in a natural and uncomplicated delivery, presenting a weight of 3,095 kg and 53 cm in length.

3.2.2 Postpartum experiences

Diana showed calmness after the baby's birth, feeling well treated by the hospital staff. As for the perception of social support, she pointed out that her husband and some family members helped her a lot in the first month after Alice's arrival. However, she said that she tried to spend most of her time with the oldest son because he was "jealous". The assessments indicated that no data were found related to postpartum depression.

3.2.3 Child development

3.2.3.1 History of development

Alice had typical developmental patterns. Since she was a baby she was very attached to her mother and just calmed down on her lap. Diana stated that she had difficulty sleeping and only slept if she remained suckling the breast. After 11 months of age, Alice got to sleep all night, becoming a little more independent.

3.2.3.2 Behavioral observations

Alice always attended neuropsychological evaluations with her mother and maternal grandmother, using large colored hair ribbons made by her grandmother. She was a collaborative, cooperative, and motivated child. She showed affection with her mother and often interrupted the session to be breastfed.

3.2.3.3 Results

The initial evaluation of Alice occurred at 6 months and 17 days of age, with within-average scores detected for the three scales. The second evaluation was performed at 13 months and 1 day of age and, although it was within the average for the cognitive and language scales, she achieved a lower mean performance on the motor scale, specifically, on the fine motor development scale. It was observed a difficulty in the performance of the items that involved the movement of forceps. At 17 months and 25 days, the third evaluation was performed, in which Alice showed an improvement in her fine motor development. The last developmental evaluation was performed at 24 months and 6 days of age. The child continued to score on average for the language scale and within the upper average for the cognitive scale. She showed a great evolution in the motor scale, obtaining higher scores for both sub scales.

3.2.3.4 Diagnosis clinical/ impressions

Alice's developmental skills, as measured by BSID III, were within the average scores for the three scales applied and compared to children of the same age. She developed rhythmic and consistent development during her first 24 months of life. The fact that she obtained scores within

the lower average for the fine motor scale in the second evaluation alerted the team involved about the more delicate movements and subsequent consequences that involve this domain. Although the results were not seen as quantitative discrepancies, the observation of these data helped the motor evaluation in a qualitative way.

Scholars of child development have shown that while most babies follow a sequence of milestones related to typical development, the way in which they develop their abilities often varies and differs among infants, such as early reach patterns (THELEN *et al.*, 1993) and crawling forms (ADOLPH *et al.*, 1993). These researches have shown that babies organize motor actions around functional goals; that is, the development of motor skills is influenced by what the physical environment provides for the child, including the objects that are available to the child.

Babies adjust their locomotion patterns when they detect different possibilities of action. Learning new patterns of movement and motor skills is a complex interaction of multiple factors. As the baby develops strength and balance, its ability to develop possibilities for motor actions is improved. They often learn by attempting to perform various movements through the consequences of their actions (ADOLPH *et al.*, 1993; LOCKMAN, 2000; BERGER AND ADOLPH, 2007).

3.3. Case 3 - Dyad Beatriz (mother) - Felipe (child)

Felipe's parents had a stable marital status from the beginning of his pregnancy. She became pregnant at the age of 21 and he was 32 years old. Both had a complete elementary school, but they always found it difficult to get a job in the city of Rio de Janeiro. The couple's family income was around 600 reais per month. He did not have a permanent job and she worked outside the home (in the same neighborhood where she lived) as a nanny.

3.3.1 Experiences from pregnancy to birth

Felipe's parents expressed a strong desire to get pregnant, since he was the first child. Beatriz mentioned that in the beginning of her pregnancy she suffered a lot of nausea, feeling very worried about having a baby at home. Because of this condition, she left her job. After this decision, the family began to live financially through occasional and short-term services performed by the

father. By the end of the first trimester, the mother got better, but she began to argue a lot with her husband, as he attended many parties, drinking and spending most of his time alone and away from home. She said she regretted getting pregnant, cried almost every day of the second and third trimester of pregnancy.

The baby arrived at 39 weeks of gestation, of natural childbirth, with 3,395 kg and 50 cm in length. The mother reported having felt a lot of sadness and abandonment during pregnancy. In the IDATE-E applications, high anxiety scores were detected in the second and third gestational trimesters. Beatriz also had high scores of depression during pregnancy and postpartum in the Edinburgh scale. She pointed out that she had no interest in having more children, was not happy to have been pregnant, felt ugly, lonely and very unprotected by her husband. It was difficult for her to have to change the pace of life and not accompany him at parties and nightlife.

3.3.2 Postpartum experiences

After delivery by natural means, Beatriz recovered quickly, having no help from third parties with the baby during this period. As for the perception of social support, it was found that she felt sad, lonely, abandoned and forgotten by family and friends. In this context, symptoms related to postpartum depression were detected.

3.3.3 Child development:

3.3.3.1 History of development

Felipe presented typical development. Beatriz mentioned that, since newborn, he has always been "very quiet" and she has managed to breastfeed him until about 6 months of age. At 18 months, Felipe went to public day care in the neighborhood where they lived.

3.3.3.2 Behavioral observations

The boy always attended the neuropsychological assessments dressed properly and in company of his mother; they were never seen in the company of his father. He was quiet, unresponsive to his mother, but cooperative in his tasks. The fact that he was a little apathetic and indifferent to the toys was remarkable. For several times, the evaluator had to insist to keep him focused on the

evaluation. However, his performance improved and with the passage of time he showed greater interaction with the evaluator.

3.3.3.3 Results

The first evaluation was performed at 6 months and 17 days, in which, Felipe obtained higher scores, in the upper average and on the average for the cognition, language and motor scales, respectively. On the second (13 months and 08 days) and third (17 months and 16 days) evaluations, Felipe was more interested in interacting with the toys and with the evaluator, presenting upper average scores and average scores in both evaluations, both for the cognitive scale and for the language scale. However, when assessed with the motor scale, discrepancies between fine and gross motor scale values were detected.

During the second evaluation, the team noticed a great difficulty in Felipe's strength and balance, when responding to the items of the gross motor scale, because he could not perform movements, such as standing and standing alone or sitting with control. In the third evaluation, he showed no impulse to start walking alone, nor to move from sitting to standing without support. The fourth and final evaluation was performed at 23 months and 3 days of age, in which the child scored within the average for the cognitive and language scales and lower average scores for the motor scale. His difficulty in responding to the items that compose the gross motor scale remained remarkable, however, compared with his performance in the previous evaluations, he presented better motor development scores in this last evaluation.

3.3.3.4 Diagnosis/ clinical impressions

During the assessments, low scores on motor scale items were detected, especially for those related to gross motor development, compared to children of his age. The scores obtained by Felipe on the motor subscales showed a discrepancy between them, revealing higher scores for the fine motor than for the gross motor. Although he had lower scores than expected in the two subscales, he presented greater difficulty in the items that evaluated balance, muscle tone and strength. In the initial evaluation, it was verified that Felipe did not like to be in the prone position and demonstrated irritation. Around the first year, he was very afraid of trying to stand or even squat without support. Learning to walk also seemed to be something that did not interest him and

showed a lot of insecurity in his movements. Considering these aspects, a qualitative evaluation of the responses to the motor scale items that were most related to the cognitive development of the child was carried out, in order to understand if the motor difficulty of Felipe could be neurological or have origin from another nature.

In the assessment of fine motor development, the child showed difficulties in the patterns of grabbing (pencil and glass). However, in the items correlated with cognition such as motor planning and motor and visual coordination, the child showed a good performance. Therefore, it was associated the difficulty with the lack of security and motivation to execute movements unheard of for him, disregarding neurological causes at that moment of development.

Functional tasks begin their organization by the action of the child (GIBSON, 1988; HUMPHREY, 2009) and these actions are guided by their objectives and goals (THELEN *et al.*, 2001); that is, the child organizes its movements when it is interested in making them to play (functional purposes). Thus, the movements are organized after the period of exploration of available objects in the environment in which they are (perceptual learning) and can be related to both social aspects (mother's smile) and physical aspects (toy noise). Some studies have shown the influence of the physical and social context on the child development (GIBSON, 1988; LOCKMAN, 2000; HUMPHREY, 2009) and indicated that the parents' presence would aim to encourage and promote feelings of safety and comfort for the infant during its motor development, since its performance depends on the context in which it develops.

Overall, throughout developmental evaluations, it was identified that on the one hand Felipe showed insecurity in relation to his mother, and on the other, the mother showed rejection and negligence in relation to him. Another aspect identified was the importance of daycare in Felipe's motor development, who after admission to the institution showed an improvement in motor development, although he did not reach the expected average for children of his age. At the last meeting, he appeared less insecure in his movements and more sociable with the evaluation team.

Table 1. Interpretation of the scores obtained through BSID III

			Cognition	Language	Motor
Lucas	1st Semester	Z-score	0	-1.4	-0.4
		Percentile	50	8	34
		Classification	M	L	M
	2nd Semester	Z-score	1.4	-0.4	0.8
		Percentile	92	34	79
		Classification	S	M	MS
	3rd Semester	Z-score	1.6	1.4	1.4
		Percentile	95	92	92
		Classification	S	S	S
	4th Semester	Z-score	1	0	1.4
		Percentile	84	50	92
		Classification	MS	M	S
Alice	1st Semester	Z-score	1	-0.2	-0.2
		Percentile	84	42	42
		Classification	MS	M	M
	2nd Semester	Z-score	0	0.2	-0.8
		Percentile	50	58	21
		Classification	M	M	MI
	3rd Semester	Z-score	0.7	0	1
		Percentile	76	50	84
		Classification	MS	M	MS
	4th Semester	Z-score	0	0.4	1.7
		Percentile	50	66	96
		Classification	MS	M	S
Felipe	1st Semester	Z-score	1.6	0.8	-0.4
		Percentile	95	79	34
		Classification	S	MS	M
	2nd Semester	Z-score	1.4	-0.2	-1.4
		Percentile	92	42	8
		Classification	S	MS	L
	3rd Semester	Z-score	3	0	-1.2
		Percentile	12	50	12
		Classification	M	M	MI
	4th Semester	Z-score	0	-0.5	-0.8
		Percentile	50	31	21
		Classification	M	M	MI

4. Final Considerations

The present study highlighted the importance of expanding the focus of health care with special attention to maternal mental health, in order to protect the child in development. The three cases presented may contribute to understand the interdependence in the mother-baby relationship,

taking into account the importance of the social support received by the mother and the socio-familial, educational, cultural and economic context experienced by both (SILVA, 2012; LUCCI AND OTTA, 2013).

As highlighted on the third dyad, the mother reported that she did not receive support from her husband, who did not understand the needs of her pregnant state or the social environment in which they lived. On the contrary, she reported feeling excluded, since the habits of entertainment, previously shared in her environment, were no longer considered adequate by her, in the care of her health or that of her baby during pregnancy. In addition, she emphasized that the husband did not offer minimum conditions of economic security for her and for the child.

In Bronfenbrenner's perspective (BRONFENBRENNER, 2005; 2011), the variables related to the person must include individual characteristics that can be related to the diversities in the socio-cultural systems, the contemporary differences in the access to the resources, and also the prevalent modes of family interaction. In this sense, the interaction between the variables of the person and the context is neither linear nor additive, but rather synergistic. Thus, the ecological model adopts a point of view where the qualitative differences in the individual development result from the variations in the attributes of the social partners and the patterns of social exchange.

In this study, it was verified that the family arrangements and the differentiated modes of care with the children indicated that the baby occupies a prominent place in the family promoting reorganization of the relations between the members (AMORIM *et al.*, 2012). As shown on the first dyad, the mother's need to work outside the home made the maternal grandmother move to the family home and then become the baby's primary caregiver. This new family arrangement seems to have been positive for the child who during the evaluations was affectionate and sociable.

The transformations occurring in society and in family structures have pointed out that the child can have an adult as a reference and not just the mother, as was shown in some of the dyads of this work. The reference adults of a child are those who live with them most of the day and establish the closest affective bonds during childhood. It is expected that biological parents will be responsible for facilitating the development of their children. However, the tendency of today's families to be more and more symmetrical in the distribution of roles and obligations, lead to greater involvement of parents, grandparents and educators in the daycare while mothers work

outside the home. With the increase in the demand for daycare centers to assist in the care of children, the professionals of these institutions become, increasingly, important figures of secondary attachment to the children, after their parents or their main caregivers (ALLEN, 2014).

The literature has pointed out that daycare centers can become a possible intervention route for the interaction of babies and depressed mothers due to a compensatory effect of care for the baby and the opportunity of early identification of maternal mental health needs (PAPERO, 2005). In dyad 3, we identified the presence of depressive characteristics in the mother and difficulties in the motor development of the child, who, after joining the daycare center, showed improvement in this aspect of development. We consider that the provision of care for the child, through the daycare center, was an intervention measure of high potentiality, as a protective factor for the development of the child, whose mother presents depressive characteristics in the perinatal period. In addition, we emphasize that the father's negative reaction and affective instability throughout the pregnancy period may have contributed to maternal depression and consequent presentation of Felipe's motor difficulties (SILVA, 2012; LUCCI AND OTTA, 2013).

In addition, the daycare center seems to be an important device to leverage the development of children, even if their mothers do not present characteristics of perinatal depression, evidenced by the improvement in language development after Lucas (dyad 1) entered the day care center at 14 months of age.

It is important to emphasize that the couples in the present study presented low level of education, except for one of the parents, who although had a higher education level, had a low income. During the interviews, the mothers pointed to the great financial difficulties caused by their husbands' job shortages. Low levels of schooling, precarious economic conditions, unemployment or underemployment are risk factors described in the literature that may affect the cognitive development of the child (POWER et al., 2006; KIERNAN AND HUERTA, 2008).

These variables may become precursors of diseases related to maternal mental health, causing negative effects on children development (DUNKEL SCHETTER AND TANNER, 2012; BRAITHWAITE *et al.*, 2017). As it was identified in the third dyad, maternal depression had a negative influence on the child's motor development, limiting the motivation to explore his own environment and, at the same time, creating insecurity patterns in relation to himself.

Future studies on the subject require an expanded sample and the insertion of varied methods to understand and identify the influence of predictors of child development during pregnancy.

REFERENCES

ADOLPH, K. E.; EPPLER, M. A.; GIBSON, E. J. Crawling versus walking infants' perception of affordances for locomotion over sloping surfaces. **Child Dev,** v. 64, n. 4, p. 1158-74, Aug 1993. (Print) 0009-3920 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/8404262 >.

ALLEN, E. **The Influence of an Attachment Theory-based Professional Development on the Day-to-day Interactions Between Early Childhood Professionals and Infants in Childcare Facilities**. 2014. Saint Joseph's University

AMORIM, K. d. S. et al. O bebê e a construção de significações, em relações afetivas e contextos culturais diversos. **Temas em Psicologia,** v. 20, n. 2, p. 309-326, 2012. ISSN 1413-389X.

ASSOCIATION, A. P. Diagnostic and statistical manual, 4th edn, Text Revision (DSM-IV-TR). **American Psychiatric Association, Washington**, 2000.

BAYLEY, N. **Bayley scales of infant and toddler development: Bayley-III**. Harcourt Assessment, Psych. Corporation San Antonio, Tex, USA, 2006.

BEEBE, B. et al. A systems view of mother–infant face-to-face communication. **Developmental psychology,** v. 52, n. 4, p. 556, 2016.

BERG, A. **The importance of the first 1 000 days of life**: Taylor & Francis 2016.

BERGER, S. E.; ADOLPH, K. E. Learning and development in infant locomotion. **Prog Brain Res,** v. 164, p. 237-55, 2007. ISSN 0079-6123 (Print)0079-6123 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/17920435 >.

BERNIER, A.; CALKINS, S. D.; BELL, M. A. Longitudinal associations between the quality of mother–infant interactions and brain development across infancy. **Child development,** v. 87, n. 4, p. 1159-1174, 2016. ISSN 1467-8624.

BIAGGIO, A.; NATALÍCIO, L. Manual para o inventário de ansiedade Traço-Estado (IDATE). **Rio de Janeiro: CEPA,** v. 15, 1979.

BOWLBY, J. Apego e perda: apego. **Apego e perda: apego,** v. 1, 2002.

BRAITHWAITE, E. C. et al. Modifiable predictors of depression following childhood maltreatment: a systematic review and meta-analysis. **Translational psychiatry,** v. 7, n. 7, p. e1162, 2017.

BRETHERTON, I. The origins of attachment theory: John Bowlby and Mary Ainsworth. **Developmental psychology,** v. 28, n. 5, p. 759, 1992. ISSN 1939-0599.

BRONFENBRENNER, U. Human development, bioecological theory of. 2001.

BRONFENBRENNER, U. **Making human beings human: Bioecological perspectives on human development**. Sage, 2005. ISBN 0761927123.

BRONFENBRENNER, U. **Bioecologia do desenvolvimento humano: tornando os seres humanos mais humanos**. Artmed Editora, 2011. ISBN 853632645X.

BRONFENBRENNER, U.; MORRIS, P. A. The ecology of developmental processes. 1998. ISSN 0471055271.

CALANDRELLA, A. M.; WILCOX, M. J. Predicting language outcomes for young prelinguistic children with developmental delay. **J Speech Lang Hear Res,** v. 43, n. 5, p. 1061-71, Oct 2000. ISSN 1092-4388 (Print)
1092-4388 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/11063230 >.

DE AZEVEDO MARQUES, J. M.; ZUARDI, A. W. Validity and applicability of the Mini International Neuropsychiatric Interview administered by family medicine residents in primary health care in Brazil. **General hospital psychiatry,** v. 30, n. 4, p. 303-310, 2008. ISSN 0163-8343.

DE OLIVEIRA, M. E.; SIQUEIRA, A. C.; ZANDONADI, A. C. A importância do afeto materno através do toque para o desenvolvimento saudável da criança. **Revista FAROL,** v. 3, n. 3, p. 97-110, 2017. ISSN 2525-5908.

DIBABA, Y.; FANTAHUN, M.; HINDIN, M. J. The association of unwanted pregnancy and social support with depressive symptoms in pregnancy: evidence from rural Southwestern Ethiopia. **BMC pregnancy and childbirth,** v. 13, n. 1, p. 135, 2013. ISSN 1471-2393.

DICKINSON, D.; MCCABE, A. The acquisition and development of language: A social interactionist account of language and literacy development. 1991. ISSN 0912752297.

DUNKEL SCHETTER, C.; TANNER, L. Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice. **Current Opinion in Psychiatry,** v. 25, n. 2, p. 141-8, Mar 2012. ISSN 1473-6578 (Electronic)0951-7367 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/22262028 >.

FLYKT, M. et al. Maternal depression and dyadic interaction: the role of maternal attachment style. **Infant and Child Development,** v. 19, n. 5, p. 530-550, 2010. ISSN 1522-7219.

GIBSON, E. J. Exploratory behavior in the development of perceiving, acting, and the acquiring of knowledge. **Annual review of psychology,** v. 39, n. 1, p. 1-42, 1988. ISSN 0066-4308.

GLOVER, V. Maternal depression, anxiety and stress during pregnancy and child outcome; what needs to be done. **Best practice & research Clinical obstetrics & gynaecology,** v. 28, n. 1, p. 25-35, 2014. ISSN 1521-6934.

GOODMAN, S. H.; GARBER, J. Evidence-Based Interventions for Depressed Mothers and Their Young Children. **Child Development,** v. 88, n. 2, p. 368-377, 2017. ISSN 1467-8624.

HORWITZ, S. M. et al. Persistence of maternal depressive symptoms throughout the early years of childhood. **Journal of Women's Health,** v. 18, n. 5, p. 637-645, 2009. ISSN 1540-9996.

HUMPHREY, J. H. Child undernutrition, tropical enteropathy, toilets, and handwashing. **The Lancet,** v. 374, n. 9694, p. 1032-1035, 2009. ISSN 0140-6736.

HUNG, C. H. Predictors of postpartum women's health status. **Journal of Nursing Scholarship,** v. 36, n. 4, p. 345-351, 2004. ISSN 1547-5069.

KIERNAN, K. E.; HUERTA, M. C. Economic deprivation, maternal depression, parenting and children's cognitive and emotional development in early childhood. **Br J Sociol,** v. 59, n. 4, p. 783-806, Dec 2008. ISSN 1468-4446 (Electronic)0007-1315 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/19035922 >.

KINGSTON, D. et al. Factors associated with perceived stress and stressful life events in pregnant women: findings from the Canadian Maternity Experiences Survey. **Maternal and child health journal,** v. 16, n. 1, p. 158-168, 2012. ISSN 1092-7875.

K
INGSTON, D. et al. Association between prenatal and postnatal psychological distress and toddler cognitive development: a systematic review. **PloS one,** v. 10, n. 5, p. e0126929, 2015. ISSN 1932-6203.

LERNER, R. M. Developmental science, developmental systems, and contemporary theories of human development. **Handbook of child psychology**, 2006. ISSN 0470147652.

LOCKMAN, J. J. A perception--action perspective on tool use development. **Child Dev,** v. 71, n. 1, p. 137-44, Jan-Feb 2000. ISSN 0009-3920 (Print)

0009-3920 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/10836567 >.

LUCCI, T. K.; OTTA, E. Postpartum depression and child development in first year of life. **Estudos de Psicologia (Campinas),** v. 30, n. 1, p. 7-17, 2013. ISSN 0103-166X.

MADASCHI, V. Tradução, adaptação transcultural e evidências de validade das Escalas Bayley III de Desenvolvimento Infantil em uma população do Município de Barueri, São Paulo. 2012.

MADASCHI, V.; PAULA, C. S. Medidas de avaliação do desenvolvimento infantil: uma revisão da literatura nos últimos cinco anos. **Cadernos de Pós-Graduação em Distúrbios do Desenvolvimento, São Paulo,** v. 11, n. 1, p. 52-56, 2011.

MURRAY, D.; COX, J. L. Screening for depression during pregnancy with the Edinburgh Depression Scale (EDDS). **Journal of reproductive and infant psychology,** v. 8, n. 2, p. 99-107, 1990. ISSN 0264-6838.

PAPERO, A. L. Is early, high-quality daycare an asset for the children of low-income, depressed mothers? **Developmental Review,** v. 25, n. 2, p. 181-211, 2005. ISSN 0273-2297.

PELA, C. C. d. N. C. Funções Executivas e Desenvolvimento na primeira Infância: habilidades necessárias para a autonomia. Estudo III. 2016.

PEREIRA PRETTO CARLESSO, J.; RAMOS DE SOUZA, A. P.; BRAGANÇA DE MORAES, A. Análise da relação entre depressão materna e indicadores clínicos de risco para o desenvolvimento infantil. **Revista CEFAC,** v. 16, n. 2, 2014. ISSN 1516-1846.

PEREIRA, V. A. et al. Desenvolvimento do bebê nos dois primeiros meses de vida: variáveis maternas e sociodemográficas. **Pensando familias,** v. 18, n. 1, p. 64-77, 2014. ISSN 1679-494X.

POWER, C. et al. The influence of birth weight and socioeconomic position on cognitive development: Does the early home and learning environment modify their effects? **J Pediatr,** v. 148, n. 1, p. 54-61, Jan 2006. ISSN 0022-3476 (Print)0022-3476 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/16423598 >.

RAHMAN, A.; IQBAL, Z.; HARRINGTON, R. Life events, social support and depression in childbirth: perspectives from a rural community in the developing world. **Psychological medicine,** v. 33, n. 7, p. 1161-1167, 2003. ISSN 1469-8978.

SANTOS, M. F. d.; MARTINS, F. C.; PASQUAL, L. Escala de auto-avaliaçäo de depressäo pós-parto: estudo no Brasil. **Arch. clin. psychiatry (São Paulo, Impr.),** v. 26, n. 2, p. 90-5, 1999. ISSN 0101-6083.

SILVA, S. **Vinculação materna durante e após a gravidez: ansiedade, depressão, Stress e suporte social**. 2012. Tese de mestrado não publicada, Universidade Fernando Pessoa, Faculdade de Ciências Humanas e Sociais, Portugal

SWEENEY, J.; SWANSON, M. Crianças de baixo peso ao nascer: cuidados neonatais e acompanhamento. **Umphred DA. Reabilitação neurológica. 4ª ed. São Paulo: Manole**, p. 213-71, 2004.

THELEN, E. et al. The transition to reaching: mapping intention and intrinsic dynamics. **Child Dev,** v. 64, n. 4, p. 1058-98, Aug 1993. ISSN 0009-3920 (Print)0009-3920 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/8404257 >.

THELEN, E. et al. The dynamics of embodiment: a field theory of infant perseverative reaching. **Behavioral Brain Science,** v. 24, n. 1, p. 1-34; discussion 34-86, Feb 2001. ISSN 0140-525X (Print)0140-525X (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/11515285 >.

VAN DEN BERGH, B. R. et al. Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: links and possible mechanisms. A review. **Neuroscience & Biobehavioral Reviews,** v. 29, n. 2, p. 237-258, 2005. ISSN 0149-7634.

WEISS, L. G.; OAKLAND, T.; AYLWARD, G. P. **Bayley-III clinical use and interpretation**. Academic Press, 2010. ISBN 0080921078.

WOOLHOUSE, H. et al. Maternal depression from early pregnancy to 4 years postpartum in a prospective pregnancy cohort study: implications for primary health care. **BJOG: An International Journal of Obstetrics & Gynaecology,** v. 122, n. 3, p. 312-321, 2015. ISSN 1471-0528.

YIN, R. **Case study research: Design and methods . Beverly Hills**: CA: Sage publishing 1994.

ARTICLE 4

Irurita-Ballesteros, C., DVS, Falcão., Rocinholi, L., Landeira-fernandez, J. Mental Health and Maternal Social Support: Influence on Infant Development in the First Two Years (Article accepted for publication).

Resumo

Este estudo de caso (díade mãe-bebê) baseado no modelo bioecologico de Bronfenbrenner objetivou investigar indicadores de saúde mental materna e o apoio social recebido durante a gravidez e o pós-parto, avaliando as influências e repercussões dessas variáveis sobre o desenvolvimento durante os dois primeiros anos de vida do bebê. A mãe foi submetida a entrevistas clínicas e as avaliações da saúde mental utilizando o Medical Outcomes Study (MOS), o Inventário de Ansiedade Traço-Estado (IDATE), a Escala de depressão pós-natal de Edinburgh (EPDS) e o Mini International Neuropsychiatry Interview (M.I.N.I) durante quatro pontos de seguimento: três na gestação e um no pós-parto. O bebê completou três avaliações com as escalas Bayley do Desenvovlvimento Infantil (BSID III) realizadas durante o primeiro e o segundo ano de vida. Verificou-se que a mãe apresentou sintomas depressivos durante o primeiro trimestre gestacional e quarenta e cinco dias após o parto. Traços de ansiedade na mãe e frágil apoio social foram encontrados durante todos os trimestres da gestação e no puerpério. Este estudo evidenciou que a criança exposta à depressão materna e a uma rede de apoio social frágil desde o início da vida, está mais vulnerável a fatores de risco que prejudicam o desenvolvimento.

Palavras-chave: relacionamento mãe-bebê; saúde mental materna; desenvolvimento infantil

Abstract

This case study (mother-child dyad) based on the bioecological model of Bronfenbrenner aimed to investigate indicators of maternal mental health and social support received during the gestational and post-partum period on child development during the first two years of life. Clinical interviews and mental health assessments were performed in the mother using the Medical Outcomes Study (MOS), State-Trait Anxiety Inventory (STAI), Edinburgh Post-natal Depression Scale (EPDS) and the Mini International Neuropsychiatry Interview (M.I.N.I) at one point of each gestational trimester and fourty five days after delivery; in addition, the child completed three neurodevelopmental assessment with the Bayley Scales of Infant Development III (BSID III) throughout the first and second year of life. It was verified that mother exhibited depressive symptoms during the first trimester of pregnancy and in the postpartum period. Traits of anxiety and fragile social support were detected during all gestational trimesters and post-partum as well. Results showed that the earlier a child is exposed to maternal depression and poor social support, the higher the vulnerability to risk factors that might affect development.

Keywords: mother-child relationship; maternal mental health; infant development

1. Introduction

Maternal mental health has been an important topic discussed in recent years, due to the high prevalence of depression, anxiety and other disorders in women of childbearing age, and the harmful consequences in the mother-child relationship (BENER, GERBER, & SHEIKH, 2012; KLIEMANN, BÖING, & CREPALDI, 2017; LI, LIU, & ODOULI, 2008; STEIN et al., 2010). Depression is the most prevalent mental disorder during pregnancy and the puerperal period (COATES, SCHAEFER, & ALEXANDER, 2004). In this context, the prevalence of depression seems to vary according to the degree of development of the country (LIMA, TSUNECHIRO, BONADIO, & MURATA, 2017). In developed countries, such as the United States, England, Canada and Sweden, prevalence rates are lower, around 10% and 15%, while in developing countries, such as Brazil, Bangladesh and South Africa, the average is around 25% (FISHER et al., 2012). RUSCHI et al. (2007) found a prevalence of maternal depression of 39.4% for the Brazilian population, corroborating the results of other national studies (DA SILVA CRUZ, SIMÕES, & FAISAL-CURY, 2005; SKAZUFKA, 2000).

The main risk factors for the onset of perinatal depression are the following: mental health history; socioeconomic factors; educational level; absence or fragile social support network; cognitive problems; violence; family structure; stressful events during pregnancy; maternal age; pregnancy planning; problematic marital relationship and the use of psychoactive substances (KLIEMANN et al., 2017; MARTINI et al., 2015; SILVERMAN et al., 2017). Some studies have shown a higher incidence of prenatal depression compared to postnatal depression, in addition to consider it the main risk factor for the occurrence of postnatal depression, as it is often a continuation of depression initiated during pregnancy (ANDERSSON, SUNDSTRÖM-POROMAA, WULFF, ÅSTRÖM, & BIXO, 2006; LOVISI, LOPEZ, COUTINHO, & PATEL, 2005; MCHICHI ALAMI, KADRI, & BERRADA, 2006).

The impact of maternal depression on the interactions with the baby during the first year of life may constitute a greater risk of developing emotional, behavioral, affective, cognitive and social disorders in the long term (GLOVER, 2014). The negative repercussions of maternal depression

on baby health make this a fundamental issue in the development of public health policies for mothers and children (DE CASTRO ALMEIDA & DA ROCHA ARRAIS, 2016).

Women commonly experience ambivalent feelings about the experience of motherhood, since if on the one hand, they feel very happy and ecstatic with the arrival of their babies, on the other they present feelings of anxiety (RAPOPORT & PICCININI, 2011), another mental disorder with great incidence during pregnancy and the postpartum period (KLIEMANN et al., 2017). Anxiety is very frequent during the pregnancy-puerperal cycle; it is estimated that 20% of the women present symptoms of this disease during pregnancy (ARAÚJO, PEREIRA & KAC, 2007). DONELLI, CHEMELLHO, AND LEVANDOWSKI (2017) found that anxiety in the context of motherhood is a multifactorial phenomenon, related to different variables (e.g., sociodemographic, psychosocial) that can trigger an anxious state in the mother, anxiety of those who already have it as a personality trait. Research (KLIEMANN et al., 2017; PEREIRA & LOVISI, 2008) indicated that the presence of persistent states of anxiety along with depression during pregnancy is associated with obstetric outcomes such as preterm delivery, low birth weight and harmful effects on child development, which may adversely affect cognitive and motor development, regulation of attention, temperament, and emotional regulation in the child's early years (SCHETTER & TANNER, 2012).

Maternal consumption of alcohol in large doses can also result in irreversible damage to the fetus, such as physical, mental, behavioral (SUNDELIN-WAHLSTEN, HALLBERG, & HELANDER, 2017; WARE et al., 2012), psychosocial (LYNCH, KABLE, & COLES, 2015), learning (BERTRAND, FLOYD, & WEBER, 2005) alterations, and in more severe cases, fetal alcohol syndrome (DOYLE & MATTSON, 2015). However, it is not well established in the literature whether maternal alcohol consumption during pregnancy at low to moderate levels has marked effects on the development of the child. Studies have suggested that, in a small amount, alcohol does not appear to cause harm (COOPER, PETHERICK, & WRIGHT, 2013; PATRA et al., 2011), while others emphasized that it could lead to negative consequences even if consumption occurred in low doses (ANDERSEN, ANDERSEN, OLSEN, GRØNBÆK, & STRANDBERG-LARSEN, 2012; FLAK et al., 2014; NYKJAER et al., 2014).

Besides that, studies have reported that it is still unknown whether there are behavioral differences

among children due to exposure to alcohol in low to moderate amounts in the fetal period (SUNDELIN-WAHLSTEN et al., 2017). In addition to the risk factors for children of mothers with mental disorders, we can observe the protection factors, which can be understood as personal or social resources that soften or inhibit the impact of risk and may favor human development. In this sense, social support has been the target of several studies evaluating the importance of this variable in the gestational period (MANENTE & RODRIGUES, 2016; MARANHÃO, GOMES, & DA SILVA, 2014). Social support is a dynamic and complex process that concerns the support usually provided by the family or friends, favoring the feeling of care, support, understanding and assistance (SCHWARTZ, VIEIRA, & GEIB, 2011). In this scenario, the family is understood as the primary network of social interaction and provider of support indispensable to the maintenance of the physical and psychological integrity of the individual (DE SOUZA & BAPTISTA, 2017). It is in it that an individual establishes the first bonds of a group coexistence, being a mediator of the relation of the individual with the world, providing affective and material support (RODRIGUEZ CEBERIO & WATZLAWICK, 2006). The support given to women by relatives, friends and neighbors during the pregnancy-puerperal process is of paramount importance and can be considered a decisive protective factor in maternal mental health and adherence to breastfeeding (PRATES, SCHMALFUSS, & LIPINSKI, 2015).

From a systemic perspective, it is observed that the mother-baby interaction and its repercussions throughout the development of the child must be understood through biopsychosocial, historical, economic, cultural, familiar, situational factors, besides the personal characteristics of the parents and the children. The theoretical-methodological model of BRONFENBRENNER (2005) encompasses these dimensions since it involves four interdependent nuclei in the understanding of the phenomena: the Person, the Process, the Context and Time. The Person nucleus represents the human being or the developing family group through its biopsychosocial characteristics and their interactions. The Process nucleus relates to how the subject or family means their experiences and interprets the environment throughout life. The Context nucleus is seen as the ecological environment in which individuals develop throughout their histories, and such interposed contexts are called the microsystem, mesosystem, exosystem, and macrosystem. The Time nucleus is linked to the cultural influences and heritages of families, denoting the historical roots of society, ethnic backgrounds and the valorization or not of a certain ritualistic or cultural practice. This nucleus

also organizes chronologically the routines and the events, allowing to know the previous history and the expectations of the future (BRONFENBRENNER, 1996).

Considering this information, the present study was developed with the goal of investigating maternal mental health indicators and the social support received during pregnancy and postpartum, evaluating the influence and repercussion of these variables on infant development during the first two years of life.

2. Method

2.1. Contextualization

This study derives from a partnership between two universities in the city of Rio de Janeiro, Brazil, and is part of a larger research whose objective was to investigate the effect of changes in maternal mental health on inflammatory markers and hormones during pregnancy on the birth weight, physical growth, body composition and neuropsychological development in the first two years of life. The research was approved by FAPERJ 19/2011 – "Pensa Rio" Program (FAPERJ E-26/110681/2012).

2.2. Design

This is a case study. According to Goode and Hatt (1952), the case study is a means of organizing the data, preserving the unitary character of the studied object. In this context, it considers the unit as a whole, including its development (person, family, set of relations or processes, etc).

2.3. Participants

A mother-baby dyad was selected to participate in the study, whose inclusion criterion was: a) to be part of the major research mentioned above; b) the mother was evaluated at four follow-ups during pregnancy and postpartum; c) the baby has completed three developmental assessments performed during the first and second year of life.

2.4. Instruments

A. A socioeconomic interview script: used to investigate the following characteristics: the age of the pregnant woman; schooling; profession; marital status; housing arrangement;

monthly income; number of children; body weight before, during and after gestation; lifestyle and consumption of psychoactive substances.

B. M.I.N.I. (Mini International Neuropsychiatry Interview, version 5.0, DSM-IV): this is a rapid diagnostic interview (approximately 15 minutes) that explores the main psychiatric disorders of Axis I of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) (American Psychiatric Association, 1994). This instrument is divided by independent diagnostic modules and each contains a series of questions regarding the following psychiatric disorders: phobias; major depressive episodes; generalized anxiety disorder; manic and hypomanic episodes; obsessive and compulsive disorder; panic disorder; dysthymic disorder; post-traumatic stress disorder, alcohol/drug abuse/dependence, and bulimia nervosa (HERGUETA, BAKER, & DUNBAR, 1998).

C. The State-Trait Anxiety Inventory (STAI): The STAI was translated, adapted and validated in Brazil by BIAGGIO AND NATALÍCIO (1979) and is based on the dualistic conception proposed by CATTELL AND SCHEIER (1961), which distinguishes anxiety in two concepts: Trait- Anxiety(trait-a) and State-Anxiety (state-a) is used to evaluate maternal anxiety by trained interviewers and standardized techniques.

D. The Edinburgh Postnatal Depression Scale (EPDS): The EPDS scale, used to evaluate maternal depression, was developed by Cox, Holden, and Sagovsky (1987) and consists of a self-assessment instrument composed of 10 statements, with options scored from 0 to 3 according to the presence and intensity of the depressive symptom. Several studies have cited and used the EPDS because it is a questionnaire that is easily applied and understood by woman, besides being very efficient in the identification of postpartum depression (BOYCE & HICKEY, 2005; DA SILVA CRUZ ET AL., 2005; KNIGHT, MARTIN, & PATIL, 2016; TENDAIS, COSTA, CONDE, & FIGUEIREDO, 2014). Santos, Martins, and & Pasquali (2000) conducted a study in Brazil with the objective of validating the said scale for Portuguese. It was found that the instrument had reasonable internal consistency, with a Chronbach alpha coefficient of 0.80 for suspected postpartum depression (PPD). In the present study, the 11/12 score is defined as the cutoff point. For suspected depression

during pregnancy, Su et al. (2007), suggested that cutoff points should vary for each gestational trimester. In the sample in which this group validated EPDS for use in pregnant women, a good positive prediction of depression was found when the cutoff points used were 13/14 for the second trimester and 12/13 for the third trimester. In this case study, the scale was applied in all follow-ups meetings in order to follow the pattern of occurrence of depression in different gestational and puerperium trimesters.

E. Medical Outcomes Study (MOS) (GRIEP, CHOR, FAERSTEIN, WERNECK, & LOPES, 2005): this instrument proposes to evaluate social support in a practical and brief way with a self-response and multidimensional scale composed of five domains: a) material support consisting of four questions that seek to ascertain the provision of material aid or assistance; b) affective support which evaluates physical demonstrations of affection and love through three questions; c) social interaction that seeks to measure the existence of other people with whom they can do interesting and fun things through four questions; d) informational support, consisting of guidance and feedback that help to find a solution to a problem through four questions and; e) emotional support, measured through four questions that evaluate the expression of positive affection, empathic understanding and encouragement of the expression of feelings (RIBEIRO, 2009).

F. Bayley Scales of Infant Development (BSID III) (BAYLEY, 2006): BSID is an instrument developed in the United States, currently in its third edition and aims to evaluate the development of children between 16 days and 42 months of age. BSID consists of 5 scales: a) Cognitive Scale, which aims to evaluate sensorimotor development, exploration and manipulation, concept formation, memory and other aspects of cognitive processing; b) Language Scale, composed of receptive and expressive communication items, forming two different sub-tests; c) Motor Scale, which aims to evaluate motor skills in general (large muscles) and fine motor skills; d) Socioemotional Scale, aims to identify the main milestones of social and emotional development at certain ages. It also examines the development of emotional skills, self-control and interest in the world, communication needs, interest in others and in establishing relationships, use of emotions in relationships, among others; e) Adaptive Behavior Scale, which accesses functional abilities of the

child's daily routine, which must be filled by the examiner. It considers communication, participation in the community (interest in activities outside the home), life at home, health and safety, leisure, self-care, among others. For this study, validation and cross-cultural adaptation were used for the Brazilian population ((MADASCHI, MECCA, MACEDO, & PAULA, 2016).

2.5 Procedures

This study had two phases, Phase 1 (2009-2011) consisting of the gestational period and 45 days after delivery; Phase 2 being the analysis of children's development. The pregnant woman's entry into the cohort was voluntary, lasted 24 months and was closed in October 2011. In Phase 1, the mother was followed during pregnancy once a quarter and the meetings between the 8th and the 13rd week, on the 24th week and in the 36th week. Also, it was evaluated once between 30 and 45 days postpartum. In these follow-ups, Celina (fictitious name) was evaluated through the aforementioned instruments. The child was integrated in the second phase of the project, where it participated in development evaluations in three different points, at 12, 18 and 24 months of age. After the mother completed all assessments during Phase 1, she was invited to participate in Phase 2 of the study in which the baby (Laura, fictitious name) was evaluated with BSID III (BAYLEY, 2006).

The two phases of this research project were approved by the National Committee for Ethics in Research-CONEP (registration 16647) through the Institute of Psychiatry of the Federal University of Rio de Janeiro (UFRJ) and was approved by means of opinion 099/2012. The research is in accordance with the ethical principles contained in Resolution 196/96 of the National Health Council and was conditioned upon the signing of a free and informed consent term. The testing procedure was performed in an appropriate environment at the department of Applied Psychology of the Pontifical Catholic University of Rio de Janeiro (PUC-RJ) by masters and doctoral students previously trained for this type of evaluation. The comfort and safety of the child were highly respected in all stages of the process.

3. Results

The presentation of the results is divided in two parts, the first is a brief history about the gestational period of the evaluated mother and the second refers to the results of the evaluation of the development of the child.

3.1 Mother's gestational period

Celina, 24, lived alone, was the single mother of a 3-year-old daughter and reported receiving the news of her second pregnancy with much sadness and frustration. She attended school for 8 years, having incomplete high school; worked as a cook receiving a monthly salary of R$ 630.00. She began the pregnancy with 48.5 kilograms, ending with 54 kilos. In addition, she did not use any type of medicine, besides the recommended vitamin supplements.

As for mental health, she mentioned that in the family there was no history of depression or suicide, but she declared herself to be a person of 'bad luck' and that 'nothing was right' in her life. Through M.I.N.I., it was found that Celina recognized herself as being a sad, unhappy, tired, depressed woman with little energy, lack of interest and pleasure in life, indicating a history of depression and current dysthymic disorder. In the Edinburgh postnatal depression scale, the respondent scored within the average for all gestational trimesters, except for the first trimester in which a score of> 11 was detected. This period was related to the report that she experienced much sadness and frustration when she came across the news of her gestation.

In addition, she presented moderate anxiety state through the IDATE-E scale with scores ranging from 33 to 35 during the four evaluations. However, the scores obtained on the IDATE-T scale were high during all trimesters of gestation and the puerperium, suggesting exaggerated reactions to situations perceived as aversive or threatening. She further reported that she had consumed alcohol (beer and vodka) throughout her pregnancy three times a week, which she referred to as 'just drinking a little to get out of the rut'.

As for the social support network, Celina did not maintain contact with the relatives of origin and did not have friends to talk about anything. In the application of the MOS scale, she presented a total score of 281.7, obtained through the sum of all the dimensions (material, affective support, social, informational and emotional interaction) of the instrument, showing below-expected scores. General information about these findings is presented in Table 1.

Table 1. Data on maternal mental health and alcohol consumption

	Aspect Investigated	Instrument	Score	Results
First trimester	Gestational depression	EPDS	12	Above the average
	Anxiety	STAI-S	35	Below the average
	Anxiety	STAI -T	55	Above the average
	History of depression	MINI	Cat 3	Current dysthimic disorder
	Consumption of alcohol	Beer and Vodka	Affirmative	Three times a week
Second trimester	Gestational depression	EPDS	9	Above the average
	Anxiety	STAI-S	35	Below the average
	Anxiety	STAI -T	55	Above the average
	History of depression	MINI	Cat 3	Current dysthimic disorder
	Consumption of alcohol	Beer and Vodka	Affirmative	Three times a week
Third trimester	Gestational depression	EPDS	10	Above the average
	Anxiety	STAI-S	32	Below the average
	Anxiety	STAI -T	55	Above the average
	History of depression	MINI	Cat 3	Current dysthimic disorder
	Consumption of alcohol	Beer and Vodka	Affirmative	Three times a week
Postpartum	Gestational depression	EPDS	12	Above the average
	Anxiety	STAI-S	33	Below the average
	Anxiety	STAI -T	55	Above the average
	History of depression	MINI	Cat 3	Current dysthimic disorder
	Consumption of alcohol	Beer and Vodka	Affirmative	Three times a week

3.2 Evaluation of child development

Laura was born naturally after 40 weeks of gestation, weighing 2,795 kg and 47 cm in length. The mother reported that from birth she was always very ‘crying’, did not like to sleep and seemed to constantly fight with sleep. At 5 months of age, she began attending the neighbor’s house that worked as a kindergarten in the neighborhood where she lived. She was breastfed until 8 months, however, she received food supplements from the fourth month of life. During developmental assessments, the child was always dressed appropriately, and, in all encounters, she was observed that she had difficulty staying separated from the mother. However, the mother allowed her to stay in the arms of any of the evaluators even though she was crying because she said that she could not bear her weight and felt very tired.

Developmental assessments were carried out following the BSID III protocol. Although the baby was invited for the first evaluation at 6 months of age, she attended only at 12 months and 27 days.

In the first evaluation, the child scored between the upper and lower average for all scales. During the second assessment, at 18 months and 29 days of age, she scored on average for cognition, language and motor scale; lower average for behavior scale and; deficit score for the socioemotional scale. The third and final evaluation was performed when Laura was 23 months and 15 days old, in which the child scored differently on four of the five scales. In the motor scale, a superior score was detected, demonstrating high locomotion abilities; in language, presented scores on the average and; lower average for the cognitive and behavioral scale. However, the socioemotional scale remained the lowest scoring scale, revealing a threshold score. More detailed information on these results is listed in Table 2.

Table 2. Scores obtained through the Bayley Scales of Infant Development.

	I		II		III	
	Z-score	**Percentil**	**Z-score**	**Percentil**	**Z-score**	**Percentil**
Cognition	0.7	75	-0.3	37	-0.9	18
Language	0.2	58	-0.2	42	0.4	66
Motor	1	84	0.6	75	1.7	96
Social-Emotional	-0.8	21	-2.1	2	-1.5	7
Adaptative Behavor	-0.9	19	-0.9	18	-0.7	23

I= First Assessment, II= Second Assessment, III= Third assessment.

4. Discussion

The exercise of motherhood involves different moments and experiences of women, such as cultural patterns, social support, history and relationship with parental models and access to information on child development. Many authors have pointed out that maternal mental health directly influences the child development (BOLSONI-SILVA, LOUREIRO, & MARTURANO, 2016; GOODMAN et al., 2011; NARDI, RODRIGUES, MELCHIORI, SALGADO, & TAVANO, 2015), and perinatal depression may impair the mother-baby relationship, affecting neurological, linguistic, cognitive, behavioral and socioemotional development (CARLESSO, SOUZA, & MORAES, 2014). In the present study, it was verified that the mother presented

depressive symptoms during the first trimester of pregnancy and in the postpartum period. Also, moderate anxiety was detected during assessments and high anxiety traits during all trimesters of gestation and the puerperium, suggesting exaggerated reactions to situations perceived as aversive or threatening.

Some research has found that stress in parental role performance in women with a history of mental health impairment before the gestational period is related to a higher vulnerability to the onset of depression during the gestational and puerperal period (SEIMYR, WELLES-NYSTRÖM, & NISSEN, 2013). Sociodemographic and mental health data from the present study showed that this mother coexisted with risk factors such as low income, low level of education, consumption of additive substances (e.g. alcohol), stigma associated with being a single mother, lack of marital, family and social support. These results corroborate data from the literature, in which most of the characteristics of this mother are shown as risk indicators for perinatal mental health, suggesting that these factors may have contributed to the onset of Celina's depressive symptoms, leading to dysthymic state during pregnancy and the postpartum period. Moreover, the depressive symptoms may have influenced her to present difficulties to create a positive affective bond with the daughter, being less sensitive to the signs of her. During the interviews, she reported that she sometimes expressed disagreement and negative attitudes, showing little availability, sad, irritable, anxious and with difficulties in disciplinary practices. In addition, she reported having a negative evaluation of the child and the exercise of motherhood.

The presence of a negative maternal affective bond can compromise the child's functioning, triggering even more aggression. The child who commonly acts with anger, provokes anger, receives anger and becomes angry, developing as a sad child. In this way, disturbances in early interactions, especially caused by depressive symptoms of the mother, may contribute to the appearance of emotional and behavioral problems in the child (ALVARENGA & PALMA, 2013). The impact of maternal depressive behavior and the conditions of disadvantaged or risky environments may trigger a possible development of psychopathologies in the child (CARDOSO, SIQUARA, & DE FREITAS, 2017).

Studies have shown that a significant history of maternal depression in early pregnancy carries a cumulative effect on the presence of behavioral problems in children (BAGNER, PETTIT, LEWINSOHN, & SEELEY, 2010). Children exposed to maternal depression early in life are more vulnerable to the development of psychopathologies than children who were not exposed or exposed later in life (CARDOSO et al., 2017). Some studies explain this result suggesting that the sooner the child's exposure to maternal depression occurs, the less years of healthy development he or she has experienced, that is, it will have grown with the negative effects of poor mother-child interaction, low emotional regulation. On the other hand, the later this occurs, the less dependent on their mothers the children will be, due to increased contact with other attachment figures such as teachers, colleagues and friends, as well as the cognitive maturation that allows older children to understand depressive symptoms of their mothers and develop coping strategies (BAGNER et al., 2010; GOODMAN et al., 2011).

CARDOSO et al. (2017) found that maternal depression influences the presence or absence of behavioral problems in children, represented both by higher levels of internalization (thinking problems) and externalization (breaking rules), both of which affect affection levels and socialization of the child. In the present study, it was found that Laura obtained low scores for the domains related to socialization and behavior. Researchers (CID & MATSUKURA, 2010) attempted to explain the association between maternal depression and deficits in the domains named above, suggesting that maternal mental disorder may affect the parental style adopted by some mothers in dealing with their children in different everyday situations, and in turn, the adopted parental style can significantly influence the development of the child.

The microsystems in which Celina participated were mainly the house, the daycare of the neighbor, the work and the public hospital. According to BRONFENBRENNER (1996), the microsystems act in an interrelated way and are the environments in which the developing person participates, allowing the experience of roles, interpersonal relations and patterns of activities. As a support network, these systems act as potential transformers. In this context, the lack of contact with family members and friends, as well as the absence of a stable marital status and a paternal figure were factors that influenced the mother-baby interaction and the behavioral and socioemotional development of LAURA. According to ANDRADE et al. (2005), home stimulation is reduced for

children whose primary caregiver has no stable partner or does not have stable conjugal relationship. The positive presence of the partner may be favorable to the quality of stimulation available in the family environment and may also positively influence maternal function.

According to BRONFENBRENNER and MORRIS (1998), the person's characteristics are not static and can be modified, even if subjected to adverse conditions. In this sense, they are seen both as producers and as products of development, since they are one of the elements that influence the form, power, content and direction of the proximal processes and, at the same time, are the result of the joint interaction of these elements - process, person, context and time (BRONFENBRENNER, 1999). The ability to influence the proximal processes is linked to three groups of personal characteristics, such as demands, dispositions and resources. Several researches have pointed to maternal schooling as a protection factor for the exercise of motherhood and the healthy development of the child (MCDONALD, KEHLER, BAYRAMPOUR, FRASER-LEE, & TOUGH, 2016; MEINCK, CLUVER, BOYES, & MHLONGO, 2015; WALKER et al., 2011).

The more years of mother's education, the greater the language mastery and, probably, the greater the mother-child interaction (HUDSON, LEVICKIS, DOWN, NICHOLLS, & WAKE, 2015). High schooling may be associated with job satisfaction, increasing social ties, positively affecting self-esteem and the motivation to generate rich and positive experiences for the child, allowing access to toys and other elements related to child development (HUDSON et al., 2015; SOUZA, 2006). As observed in the results of the present study, low maternal schooling negatively affected the quality of Laura's development, both in cognitive, social and behavioral terms.

Although the analyzed child had presented adequate developmental patterns revealed in the BSID III cognitive growth score curve, there was a decline in cognitive scores obtained during cognitive assessments. Percentage scores were used to compare Laura with children of her age in the different age groups evaluated and pointed out that she found it difficult to calm herself outside her mother's arms, presenting tantrums and indifference to the evaluators. Concerning the interaction with the instrument, the child showed interest in interacting with some toys, however, she did not show any attention to the imaginative games when requested (e.g. put the doll to sleep, give or make some food to the doll). In the third and final evaluation, Laura seemed irritated, less

interested in interaction with evaluators and toys, and ignored commands given by her mother or other evaluators. Although she demonstrated to understand and communicate as a child of her age, as observed during the evaluation of the language scale, scores related to her social-emotional and behavioral development revealed results below expectations.

Sensory scores on the socioemotional scale indicated a development within the average scores, but she showed a great deal of insecurity in engaging in relationships and even using gestures to interact with others. Laura was unable to solve a problem without using crying and/or screaming, and most of the time she presented herself as an apathetic and aggressive child with her mother, with the evaluators, and sometimes with some objects in the room. These results corroborate the findings of other studies highlighting that the children of depressed mothers are described as opponents, more aggressive, and more prone to the development of antisocial behavior and problems of emotional regulation (KIM-COHEN, MOFFITT, TAYLOR, PAWLBY, & CASPI, 2005; MENDES, LOUREIRO, & CRIPPA, 2008; TRONICK & RECK, 2009).

In the bioecological model, proximal processes can produce two types of effects: 1) competence, which refers to the acquisition and development of skills, knowledge, and ability to conduct its own behavior through evolutionary situations and domains, either individually or through a combination between them and; 2) dysfunction, which refers to the recurrent manifestation of difficulties in maintaining control and integration of behavior through situations and different domains of development (BRONFENBRENNER & MORRIS, 1998) as observed in Laura. The present study corroborates that the negative impact is greater in unfavorable or disorganized environments, because in these environments the manifestations of dysfunction are more frequent and more severe (BRONFENBRENNER, 1999).

5. Final Considerations

Our findings corroborate the literature hypothesis regarding the negative impact of the mental disorders of the pregnant woman on the maternal-fetal relationship. It has been seen that perinatal depression, together with other factors, such as low schooling, fragile social support, low socioeconomic status and alcohol use during pregnancy, are risk factors that may contribute negatively to the mother-baby bond and consequently to the infant development. It is important to

carry out empirical studies and interventions that promote maternal and child health, favoring the understanding of psychosocial variables that influence development processes. Researchers (BYATT et al., 2012) found that, in general, professionals have limited resources, are not prepared to solve these challenges and do not have the necessary skills to deal with these issues, reducing confidence and motivation to deal with this reality.

It is necessary to encourage the improvement of prevention programs aimed at women mental health to be developed before, during and after pregnancy, especially for those with a fragile social support network. Equally important is the accomplishment of programs for evaluating child development; care for the health of children and their development must be an indispensable and urgent task. Much effort has been made for the implementation of rehabilitation programs, but few for prevention programs. The first four years of the child are recognized as critical for establishing a sound foundation for healthy development (GRANTHAM-MCGREGOR et al., 2007). In this sense, the early detection of risk factors that may lead to delays in the development of children's neuropsychological factors contributes to the prevention of both cognitive and emotional deficiencies. Finally, it is suggested to carry out new studies, preferably with a larger sample size, in order to understand more deeply the relations between the factors studied.

Acknowledgements

The authors are grateful to Professor Gilberto Kac (UFRJ) for allowing collaboration of convergent interests between UFRJ, UFRRJ and PUC-Rio.

REFERENCES

ALVARENGA, P., & PALMA, E. M. S. Indicadores de depressão materna e a interação mãe-criança aos 18 meses de vida. **Psicologia***, 44*(3), 402-410, 2013.

ANDERSEN, A.-M. N., ANDERSEN, P. K., OLSEN, J., GRØNBÆK, M., & STRANDBERG-LARSEN, K.. Moderate alcohol intake during pregnancy and risk of fetal death. **International journal of epidemiology***, 41*(2), 405-413, 2012.

ANDERSSON, L., SUNDSTRÖM-POROMAA, I., WULFF, M., ÅSTRÖM, M., & BIXO, M. Depression and anxiety during pregnancy and six months postpartum: A follow-up study. **Acta obstetricia et gynecologica Scandinavica***, 85*(8), 937-944, 2006

ANDRADE, S. A., SANTOS, D. N., BASTOS, A. C., PEDROMÔNICO, M. R. M., ALMEIDA-FILHO, N. D., & BARRETO, M. L. Ambiente familiar e desenvolvimento cognitivo infantil: uma abordagem epidemiológica. **Revista de saúde Pública,** *39*(4), 606-611, 2005.

ASSOCIATION, A. P. Diagnostic and statistical manual, 4th edn, Text Revision (DSM-IV-TR). **American Psychiatric Association, Washington**, 2000.

BAGNER, D. M., PETTIT, J. W., LEWINSOHN, P. M., & SEELEY, J. R. Effect of maternal depression on child behavior: a sensitive period? **Journal of the American Academy of Child & Adolescent Psychiatry,** *49*(7), 699-707, 2010.

BAYLEY, N. *Bayley scales of infant and toddler development: Bayley-III* (Vol. 7): **Harcourt Assessment,** Psych. Corporation San Antonio, Tex, USA, 2006.

BEEBE, B. et al. A systems view of mother–infant face-to-face communication. **Developmental psychology,** v. 52, n. 4, p. 556, 2016.

BERGER, S. E.; ADOLPH, K. E. Learning and development in infant locomotion. **Prog Brain Res,** v. 164, p. 237-55, 2007. ISSN 0079-6123 (Print)0079-6123 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/17920435 >.

BENER, A., Gerber, L. M., & Sheikh, J. Prevalence of psychiatric disorders and associated risk factors in women during their postpartum period: a major public health problem and global comparison. **International journal of women's health***, 4*, 191, 2012.

BERTRAND, J., FLOYD, L., & WEBER, M. Fetal Alcohol Syndrome Prevention Team, Division of Birth Defects and Developmental Disabilities, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC). Guidelines for identifying and referring persons with fetal alcohol syndrome. **MMWR Recommendations and Reports***, 54*, 1-14, 2005.

BIAGGIO, A., & NATALÍCIO, L. Manual para o inventário de ansiedade Traço-Estado (IDATE). *Rio de Janeiro:* **CEPA***, 15*, 1979.

BOLSONI-SILVA, A. T., LOUREIRO, S. R., & MARTURANO, E. M. Comportamentos internalizantes: associações com habilidades sociais, práticas educativas, recursos do ambiente familiar e depressão materna. **Psico***, 47*(2), 111-120, 2016.

BOYCE, P., & HICKEY, A. Psychosocial risk factors to major depression after childbirth. **Social psychiatry and psychiatric epidemiology***, 40*(8), 605-612, 2005.
BRONFENBRENNER, U. *A ecologia do desenvolvimento humano*: Porto Alegre: Artes Médicas,1996.

BOWLBY, J. Apego e perda: apego. **Apego e perda: apego,** v. 1, 2002.

BRAITHWAITE, E. C. et al. Modifiable predictors of depression following childhood maltreatment: a systematic review and meta-analysis. **Translational psychiatry,** v. 7, n. 7, p. e1162, 2017.

BRETHERTON, I. The origins of attachment theory: John Bowlby and Mary Ainsworth. **Developmental psychology,** v. 28, n. 5, p. 759, 1992. ISSN 1939-0599.

BRONFENBRENNER, U. Environments in developmental perspective: Theoretical and operational models, 1999.

BRONFENBRENNER, U. *Making human beings human: Bioecological perspectives on human development*: **Sage**. 2005.

BRONFENBRENNER, U., & MORRIS, P. A. The ecology of developmental processes. 1998.

CALANDRELLA, A. M.; WILCOX, M. J. Predicting language outcomes for young prelinguistic children with developmental delay. **J Speech Lang Hear Res,** v. 43, n. 5, p. 1061-71, Oct 2000. ISSN 1092-4388 (Print)
1092-4388 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/11063230 >.

CARDOSO, T. D. S. G., SIQUARA, G. M., & DE FREITAS, P. M. Relações entre depressão materna e problemas de comportamento em crianças. **Psicologia Argumento***, 32*(79), 2017.

CARLESSO, J. P. P., SOUZA, A. P. R. D., & MORAES, A. B. D. Maternal depression and clinical risk indicators in child development. **Revista CEFAC***, 16*(2), 500-510, 2014.

CATTELL, R. B., & SCHEIER, I. H. The meaning and measurement of neuroticism and anxiety, 1961.

CID, M. F. B., & MATSUKURA, T. S. Mães com transtorno mental e seus filhos: risco e desenvolvimento. **Mundo saúde***, 34*(1), 73-81, 2010.

COATES, A. O., SCHAEFER, C. A., & ALEXANDER, J. L. Detection of postpartum depression and anxiety in a large health plan. **The Journal of Behavioral Health Services and Research***, 31*(2), 117-133, 2004.

COOPER, D. L., PETHERICK, E. S., & WRIGHT, J. The association between binge drinking and birth outcomes: results from the Born in Bradford cohort study. **The Journal of Epidemiology Community Health,** *67*(10), 821-828. 2013.

COX, J. L., HOLDEN, J. M., & SAGOVSKY, R.. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. **The British journal of psychiatry***, 150*(6), 782-786, 1987

DA SILVA CRUZ, E. B., SIMÕES, G. L., & FAISAL-CURY, A. . Rastreamento da depressão pós-parto em mulheres atendidas pelo Programa de Saúde da Família. **Revista Brasileira de Ginecologia e Obstetria***, 27*(4), 181-188, 2005.

DE AZEVEDO MARQUES, J. M.; ZUARDI, A. W. Validity and applicability of the Mini International Neuropsychiatric Interview administered by family medicine residents in primary health care in Brazil. **General hospital psychiatry,** v. 30, n. 4, p. 303-310, 2008. ISSN 0163-8343.

DE CASTRO ALMEIDA, N. M., & DA ROCHA ARRAIS, A. (. O Pré-Natal Psicológico como Programa de Prevenção à Depressão Pós-Parto. **Psicologia Ciência e Profissão,** *36*(4) 2016.

DE OLIVEIRA, M. E.; SIQUEIRA, A. C.; ZANDONADI, A. C. A importância do afeto materno através do toque para o desenvolvimento saudável da criança. **Revista FAROL,** v. 3, n. 3, p. 97-110, 2017. ISSN 2525-5908.

DE SOUZA, M. S., & BAPTISTA, M. N. Associações entre suporte familiar e saúde mental. **Revista Psicologia Argumento***, 26*(54), 207-215, 2017.

DIBABA, Y.; FANTAHUN, M.; HINDIN, M. J. The association of unwanted pregnancy and social support with depressive symptoms in pregnancy: evidence from rural Southwestern Ethiopia. **BMC pregnancy and childbirth,** v. 13, n. 1, p. 135, 2013. ISSN 1471-2393.

DICKINSON, D.; MCCABE, A. The acquisition and development of language: A social interactionist account of language and literacy development. 1991. ISSN 0912752297.

DONELLI, T. M. S., CHEMELLHO, M. R., & LEVANDOWSKI, D. C. Ansiedade materna e maternidade: Revisão crítica da literatura. **Interação em Psicologia,** *21*(1), 2017

DOYLE, L. R., & MATTSON, S. N.. Neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE): review of evidence and guidelines for assessment. **Current developmental disorders report***s, 2*(3), 175-186, 2015

DUNKEL SCHETTER, C.; TANNER, L. Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice. **Current Opinion in**

Psychiatry, v. 25, n. 2, p. 141-8, Mar 2012. ISSN 1473-6578 (Electronic)0951-7367 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/22262028 >.

FLAK, A. L., SU, S., BERTRAND, J., DENNY, C. H., KESMODEL, U. S., & COGSWELL, M. E. The association of mild, moderate, and binge prenatal alcohol exposure and child neuropsychological outcomes: a meta-analysis. **Alcoholism: Clinical and Experimental Research***, 38*(1), 214-226, 2014.

FISHER, J., MELLO, M. C. D., PATEL, V., RAHMAN, A., TRAN, T., HOLTON, S., & HOLMES, W. Prevalence and determinants of common perinatal mental disorders in women in low-and lower-middle-income countries: a systematic review. **Bulletin of the World Health Organization***, 90*(2), 139-149. 2012.

GLOVER, V. Maternal depression, anxiety and stress during pregnancy and child outcome; what needs to be done. **Best practice & research Clinical obstetrics & gynaecology***, 28*(1), 25-35, 2014.

GOODE, W., & HATT, P. The case study. **Methods of Social Research***, New York: McGraw-Hill*, 330-340. 1952.

GOODMAN, S. H., ROUSE, M. H., CONNELL, A. M., BROTH, M. R., HALL, C. M., & HEYWARD, D. Maternal depression and child psychopathology: a meta-analytic review. **Clinical child and family psychology review***, 14*(1), 1-27. 2011.

GRANTHAM-MCGREGOR, S., CHEUNG, Y. B., CUETO, S., GLEWWE, P., RICHTER, L., STRUPP, B., & GROUP, I. C. D. S.. Developmental potential in the first 5 years for children in developing countries. **The Lancet***, 369*(9555), 60-70. 2007.

GRIEP, R. H., CHOR, D., FAERSTEIN, E., WERNECK, G. L., & LOPES, C. S. Validade de constructo de escala de Apoio Social do Medical Outcomes Study adaptada para o português no estudo Pró–Saúde {Construct validity scale of Social Support from the Medical Outcomes Study adapted to Portuguese in Pro study–Health}. **Cadernos de Saúde Pública***, 21*(3), 703-714, 2005.

HERGUETA, T., BAKER, R., & DUNBAR, G. C. The Mini-International Neuropsychiatric Interview (MINI): the development and validation of a structured diagnostic psychiatric interview for DSM-IVand ICD-10. **Journal of Clinical Psychiatry***, 59*(Suppl 20), 2233. 1998

HORWITZ, S. M. et al. Persistence of maternal depressive symptoms throughout the early years of childhood. **Journal of Women's Health,** v. 18, n. 5, p. 637-645, 2009. ISSN 1540-9996.

HUDSON, S., LEVICKIS, P., DOWN, K., NICHOLLS, R., & WAKE, M. Maternal responsiveness predicts child language at ages 3 and 4 in a community-based sample of

slow-to-talk toddlers. **International journal of language & communication disorders**, *50*(1), 136-142, 2015.

HUMPHREY, J. H. Child undernutrition, tropical enteropathy, toilets, and handwashing. **The Lancet,** v. 374, n. 9694, p. 1032-1035, 2009. ISSN 0140-6736.

HUNG, C. H. Predictors of postpartum women's health status. **Journal of Nursing Scholarship,** v. 36, n. 4, p. 345-351, 2004. ISSN 1547-5069.

KIM-COHEN, J., MOFFITT, T. E., TAYLOR, A., PAWLBY, S. J., & CASPI, A. Maternal depression and children's antisocial behavior: nature and nurture effects. **Archives of general psychiatry**, *62*(2), 173-181, 2005.

KINGSTON, D. et al. Factors associated with perceived stress and stressful life events in pregnant women: findings from the Canadian Maternity Experiences Survey. **Maternal and child health journal,** v. 16, n. 1, p. 158-168, 2012. ISSN 1092-7875.

KINGSTON, D. et al. Association between prenatal and postnatal psychological distress and toddler cognitive development: a systematic review. **PloS one,** v. 10, n. 5, p. e0126929, 2015. ISSN 1932-6203.

KLIEMANN, A., BÖING, E., & CREPALDI, M. A. Fatores de risco para ansiedade e depressão na gestação: Revisão sistemática de artigos empíricos. **Mudanças-Psicologia da Saúde**, *25*(2), 69-76, 2017.

KNIGHT, J., MARTIN, J., & PATIL, A. Principal Component Analysis of EPDS Questions to Identify Trends in Depressive Symptoms Among At-Risk Populations [29K]. **Obstetrics & Gynecology**, *127*, 96S-97S, 2016.

LERNER, R. M. Developmental science, developmental systems, and contemporary theories of human development. **Handbook of child psychology**, 2006. ISSN 0470147652.

LEVITT, P. Structural and functional maturation of the developing brain. **Journal of Pediatrics**, 143 (1), 35–45, 2003.

LI, D., LIU, L., & ODOULI, R. Presence of depressive symptoms during early pregnancy and the risk of preterm delivery: a prospective cohort study. **Human Reproduction**, *24*(1), 146-153, 2008.

LIMA, M. D. O. P., TSUNECHIRO, M. A., BONADIO, I. C., & MURATA, M. Sintomas depressivos na gestação e fatores associados: estudo longitudinal. **Acta Paulista de Enfermagem**, *30*(1), 39-46, 2017.

LOCKMAN, J. J. A perception--action perspective on tool use development. **Child Dev,** v. 71, n. 1, p. 137-44, Jan-Feb 2000. ISSN 0009-3920 (Print)

0009-3920 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/10836567

LOVISI, G. M., LOPEZ, J. R. R., COUTINHO, E. S. F., & PATEL, V. Poverty, violence and depression during pregnancy: a survey of mothers attending a public hospital in Brazil. **Psychological medicine,** *35*(10), 1485-1492, 2005.

LUCCI, T. K.; OTTA, E. Postpartum depression and child development in first year of life. **Estudos de Psicologia (Campinas),** v. 30, n. 1, p. 7-17, 2013. ISSN 0103-166X.

LYNCH, M. E., KABLE, J. A., & COLES, C. D. Prenatal alcohol exposure, adaptive function, and entry into adult roles in a prospective study of young adults. **Neurotoxicology and Teratology,** *51*, 52-60, 2015.

MADASCHI, V., MECCA, T. P., MACEDO, E. C., & PAULA, C. S. Bayley-III Scales of Infant and Toddler Development: Transcultural Adaptation and Psychometric Properties. **Paidéia***, 26*, 189-197.

MADASCHI, V.; PAULA, C. S. Medidas de avaliação do desenvolvimento infantil: uma revisão da literatura nos últimos cinco anos. **Cadernos de Pós-Graduação em Distúrbios do Desenvolvimento, São Paulo,** v. 11, n. 1, p. 52-56, 2011.

MANENTE, M. V., & RODRIGUES, O. M. P. R. (2016). Associação entre Depressão Pós-parto, Apoio Social e Satisfação Conjugal*.,* **Maternidade e Trabalho:** *20*(1), 99-111, 2016

MARANHÃO, T. A., GOMES, K. R. O., & DA SILVA, J. M. N. Fatores que influenciam as relações familiares e sociais de jovens após a gestação Factors affecting young mothers' social and family relations after pregnancy Factores que afectan las relaciones familiares. **Cadernos de Saúde Pública***, 30*(5), 998-1008, 2014.

MARTINI, J., PETZOLDT, J., EINSLE, F., BEESDO-BAUM, K., HÖFLER, M., & WITTCHEN, H.-U. Risk factors and course patterns of anxiety and depressive disorders during pregnancy and after delivery: a prospective-longitudinal study. **Journal of Affective Disorders***, 175*, 385-395, 2015.

MCDONALD, S., KEHLER, H., BAYRAMPOUR, H., FRASER-LEE, N., & TOUGH, S. Risk and protective factors in early child development: Results from the All Our Babies (AOB) pregnancy cohort. **Research in developmental disabilities***, 58*, 20-30, 2016.

MCHICHI ALAMI, K., KADRI, N., & BERRADA, S. Prevalence and psychosocial correlates of depressed mood during pregnancy and after childbirth in a Moroccan sample. **Archives of women's mental health***, 9*(6), 343-346, 2006.

MEINCK, F., CLUVER, L. D., BOYES, M. E., & MHLONGO, E. L. Risk and protective factors for physical and sexual abuse of children and adolescents in Africa: A review and implications for practice. **Trauma, Violence, & Abuse***, 16*(1), 81-107, 2015.

MENDES, A. V., LOUREIRO, S. R., & CRIPPA, J. A. S. Depressão materna e a saúde mental de escolares. **Revista de Psiquiatria Clínica***, 35*(5), 178-186., 2008.

MURRAY, D.; COX, J. L. Screening for depression during pregnancy with the Edinburgh Depression Scale (EDDS). **Journal of reproductive and infant psychology,** v. 8, n. 2, p. 99-107, 1990. ISSN 0264-6838.

NARDI, C. G. D. A., RODRIGUES, O. M. P. R., MELCHIORI, L. E., SALGADO, M. H., & TAVANO, L. D. A. Infants with Pierre Robin Sequence: Maternal mental health and mother-infant interaction. **Estudos de Psicologia***, 32*(1), 129-140, 2015.

NYKJAER, C., ALWAN, N. A., GREENWOOD, D. C., SIMPSON, N. A., HAY, A. W., WHITE, K. L., & CADE, J. E. Maternal alcohol intake prior to and during pregnancy and risk of adverse birth outcomes: evidence from a British cohort. **Journal of Epidemiology Community Health,** jech-2013-202934, 2014.

PAPERO, A. L. Is early, high-quality daycare an asset for the children of low-income, depressed mothers? **Developmental Review,** v. 25, n. 2, p. 181-211, 2005. ISSN 0273-2297.

PATRA, J., BAKKER, R., IRVING, H., JADDOE, V. W., MALINI, S., & REHM, J. Dose–response relationship between alcohol consumption before and during pregnancy and the risks of low birthweight, preterm birth and small for gestational age (SGA)—a systematic review and meta-analyses. *BJOG:* **An International Journal of Obstetrics & Gynaecology,** *118*(12), 1411-1421, 2011.

PELA, C. C. d. N. C. Funções Executivas e Desenvolvimento na primeira Infância: habilidades necessárias para a autonomia. Estudo III. 2016.

PEREIRA, P. K., & LOVISI, G. M. Prevalência da depressão gestacional e fatores associados. **Revista de psiquiatria clínica***, 35*(4), 144-153, 2008

POWER, C. et al. The influence of birth weight and socioeconomic position on cognitive development: Does the early home and learning environment modify their effects? **J Pediatr,** v. 148, n. 1, p. 54-61, Jan 2006. ISSN 0022-3476 (Print)0022-3476 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/16423598 >.

PRATES, L. A., SCHMALFUSS, J. M., & LIPINSKI, J. M.. Rede de apoio social de puérperas na prática da amamentação. **Escola Anna Nery Revista de Enfermagem***, 19*(2), 310-315, 2015.

RIBEIRO, J. L. P. A importância da qualidade de vida para a psicologia da saúde. **Bem estar e qualidade de vida**: contributos da psicologia da saúde, 2009.

RAHMAN, A.; IQBAL, Z.; HARRINGTON, R. Life events, social support and depression in childbirth: perspectives from a rural community in the developing world. **Psychological medicine,** v. 33, n. 7, p. 1161-1167, 2003. ISSN 1469-8978.

RODRIGUEZ CEBERIO, M., & WATZLAWICK, P. **La construcción del universo: conceptos introductorios y reflexiones sobre epistemología**: constructivismo y pensamiento sistémico. Cap. I. Editora Herder, 2006.

RUSCHI, G. E. C., SUN, S. Y., MATTAR, R., CHAMBÔ FILHO, A., ZANDONADE, E., & LIMA, V. J. D. Aspectos epidemiológicos da depressão pós-parto em amostra brasileira. **Revista de Psiquiatria do Rio Grande do Sul**, 2007.

SANTOS, M., MARTINS, F., & & PASQUALI, L. Escala de auto-registro de depressão pós-parto: estudo no Brasil. **Escalas de avaliação clínica em psiquiatria e psicofarmacologia**. *São Paulo: Lemos*, 97-101, 2000.

SCHWARTZ, T., VIEIRA, R., & GEIB, L. T. C. Apoio social a gestantes adolescentes: desvelando percepções. **Ciência & Saúde Coletiva**, *16*(5) 2011.
SHORE, R. *A tale of two hemispheres*: Brain research, policy and politics, in proceedings of Excellence for Children: AECA Biennial Conference, **Australian Early Childhood Association**, Sydney, 2001.

SWEENEY, J.; SWANSON, M. Crianças de baixo peso ao nascer: cuidados neonatais e acompanhamento. **Umphred DA. Reabilitação neurológica. 4ª ed. São Paulo: Manole**, p. 213-71, 2004.

SILVA, S. **Vinculação materna durante e após a gravidez: ansiedade, depressão, Stress e suporte social**. 2012. Tese de mestrado não publicada, Universidade Fernando Pessoa, Faculdade de Ciências Humanas e Sociais, Portugal

SILVERMAN, M. E., REICHENBERG, A., SAVITZ, D. A., CNATTINGIUS, S., LICHTENSTEIN, P., HULTMAN, C. M., SANDIN, S. The risk factors for postpartum depression: A population-based study. **Depression and anxiety**, *34*(2), 178-187, 2017.

SKAZUFKA, E. T. **Prevalência da depressão pós-parto e fatores associados em mães que deram à luz em um hospital universitário do município de São Paulo**. Faculdade de Medicina, Universidade de São Paulo.,2000.

SOUZA, R. A criança na família em transformação: um pouco de reflexão e um convite à investigação. Psic Rev 1997;(5): 33-51. SOUZA, Celina. Políticas Públicas: uma revisão da literatura. In: **Sociologia** (16), 209-244, 2006

SPIELBERGER, C. D. **State-Trait anxiety inventory**: Wiley Online Library, 2010.
STEIN, A., ARTECHE, A., LEHTONEN, A., CRASKE, M., HARVEY, A., COUNSELL, N., & MURRAY, L. Interpretation of infant facial expression in the context of maternal postnatal depression. **Infant Behavior and Development,** *33*(3), 273-278, 2010

SU, K.-P., CHIU, T.-H., HUANG, C.-L., HO, M., LEE, C.-C., WU, P.-L., & CHIU, W.-C. Different cutoff points for different trimesters? The use of Edinburgh Postnatal Depression Scale and Beck Depression Inventory to screen for depression in pregnant Taiwanese women. **General hospital psychiatry***, 29*(5), 436-441, 2007

SUNDELIN-WAHLSTEN, V., HALLBERG, G., & HELANDER, A. Higher alcohol consumption in early pregnancy or low-to-moderate drinking during pregnancy may affect children's behaviour and development at one year and six months. **Acta Paediatrica***, 106*(3), 446-453, 2017.

TENDAIS, I., COSTA, R., CONDE, A., & FIGUEIREDO, B.. Screening for depression and anxiety disorders from pregnancy to postpartum with the EPDS and STAI. **The Spanish journal of psychology***, 17*, 2014.

THELEN, E. et al. The transition to reaching: mapping intention and intrinsic dynamics. **Child Dev,** v. 64, n. 4, p. 1058-98, Aug 1993. ISSN 0009-3920 (Print)0009-3920 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/8404257 >.

THELEN, E. et al. The dynamics of embodiment: a field theory of infant perseverative reaching. **Behavioral Brain Science,** v. 24, n. 1, p. 1-34; discussion 34-86, Feb 2001. ISSN 0140-525X (Print)0140-525X (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/11515285 >.

TRONICK, E., & RECK, C. Infants of depressed mothers. **Harvard review of psychiatry***, 17*(2), 147-156, 2009

WALKER, S. P., WACHS, T. D., GRANTHAM-MCGREGOR, S., BLACK, M. M., NELSON, C. A., HUFFMAN, S. L., LOZOFF, B. Inequality in early childhood: risk and protective factors for early child development. **The Lancet***, 378*(9799), 1325-1338, 2011.

5. GENERAL DISCUSSION

The general objective of this doctoral thesis was to investigate variables inherent to maternal nutrition and mental health, relating them to early childhood development. In this context, we sought to contribute to a better understanding of the repercussions of these aspects on the neuropsychological development of the child.

The first article of this thesis aimed at exploring the effects of LC-PUFA on child development through a systematic review and meta-analysis. A systematic search of randomized controlled trials (RCT) was conducted to analyze the effects of maternal supplementation with omega-3 (n-3) LC-PUFA during pregnancy on infant development. According to the results found in this meta-analysis, the effect of n-3 LC-PUFA supplementation on childhood development is uncertain due to methodological limitations. Small sample sizes represented the major flaw detected in the studies. Scores on the PEDro scales showed that all but three surveys were able to use 85% of the initial sample size. Moreover, all but one did not report baseline similarities, allowing the risk of bias judgment. Further, the studies presented different methods to evaluate the maternal FA, which may have compromised the comparison between the studies. Another factor that limited the comparison between them was the difference in the assessment instruments used to accompany neuropsychological development.

Future research is required to identify the periods of fetal development sensitive to n-3 LC-PUFA, including multiple assessments of the antenatal status of LC-PUFA, since, the occurrences of methodological limitations, several studies have reported that high maternal consumption or maternal supplementation with omega-3 is positively associated with high scores in tests that evaluate language (Daniels *et al.*, 2004; OKEN *et al.*, 2014), cognition (Hibbeln, J. R. *et al.*, 2007; MENDEZ *et al.*, 2009), intelligence (GALE *et al.*, 2008) and behavior (MAKRIDES *et al.*, 2010; RAMAKRISHNAN *et al.*, 2010).

The second study aimed to understand the influence of blood concentrations of DHA and EPA during gestation on the neuropsychological development of children during the first two years of life. Our data revealed that high concentrations of DHA and EPA during the first trimester of

pregnancy are positively correlated with the cognitive development of children at 18 and 24 months of age and corroborate research suggesting that supplementation of DHA and EPA during gestation improves both cognitive and visual development (ASSISI *et al.*, 2006; HIBBLEN, JOSEPH R. *et al.*, 2007; DUNSTAN *et al.*, 2008; KELLY *et al.*, 2011; VALENT *et al.*, 2013; DE GIUSEPPE *et al.*, 2014). These results suggested that both DHA and EPA facilitate the fusion of the neural tube and contribute to its optimal development, favoring the maturation of the structures of the NS in general (Uauy *et al.*, 1996; Kidd, 2007; Guesnet e Alessandri, 2011).

Several researchers have reported a positive correlation between LC-PUFA ingestion during pregnancy and child development (HIBBLEN, JOSEPH R. *et al.*, 2007; Lemaitre *et al.*, 2011; MELDRUM *et al.*, 2015; OKEN *et al.*, 2016; VOLLET *et al.*, 2017), but most studies have indicated placental transference of LC-PUFA predominantly in the last trimester of pregnancy, when brain growth is faster. Although these studies agree that LC-PUFA, used by the pregnant woman, improves infant development, they reported this benefit only during the last trimester of gestation, while our results revealed that the ingestion in the first trimester also appears to be important for cognitive development between 18 and 24 months.

Moreover, length at birth, socioeconomic level and parental education were also predictive variables for cognitive development at 18 and 24 months of age (RYAN *et al.*, 2006; HOWARD *et al.*, 2011; FIGLIO *et al.*, 2016).

The third article was a multiple case study and consisted of developing detailed knowledge about three dyads (mother-baby) in order to investigate the complexity of the subjects' interrelations in their context. Many authors have pointed out that maternal mental health directly influences the presence or absence of socioemotional impairments in the child's life (GODDMAN *et al*., 2011; MENDES, LOUREIRO & CRIPPA, 2008; BRUM & SCHERMAN, 2006). Characteristics of the maternal behavior of women with mental illness increase the risk that children develop behavior problems, cognitive, social difficulties and even mental disorders in the course of their developmental process (MALM et al., 2015; GENTILE, 2017).

Aiming at understanding the interaction and behaviors emitted by the mother-baby dyad in a bioecological perspective, it is crucial to take into account the interdependence between them, the circular causality, the context in which they live, as well as the proximal processes that can produce two types of effects: 1) competence, which refers to the acquisition and development of skills, knowledge, and ability to conduct their own behavior through evolutionary situations and domains, either individually or through a combination of them; 2) dysfunction, which refers to the recurrent manifestation of difficulties in maintaining control and integration of behaviors through situations in different domains of development (BRONFRENBRENNER & MORRIS 1998) as this was observed in the third case.

We verified the importance of maternal mental health, the social support received by the mother and the educational, cultural and economic context experienced by the family to protect the child in development. As in one of the dyads, low levels of schooling, precarious socioeconomic conditions, unemployment or underemployment can trigger diseases related to maternal mental health, negatively affecting motor development and the child's motivation to explore their own environment (POWER *et al.*, 2006; KIERNAN E HUERTA, 2008; BRAITHWAITE *et al.*, 2017). Functional tasks begin their organization by the action of the child (GIBSON, 1988; HUMPHREY, 2009) and these actions are guided by their objectives and goals (THELEN *et al.*, 2001); that is, the child organizes its movements when it is interested in making them to play (functional purposes). The brain is composed of a set of integrated systems, which participate intensely in the performance of cognitive functions (MIRANDA & MUSZKAT, 2004), As per ELLISON AND SEMRUD-CLIKEMAN (2007), an adequate neuropsychological assessment, especially in the pediatric age group, is suggested to be an excellent tool to enhance child development in general since prognostic change at this age acts as a protective factor, preventing secondary neuropsychological dysfunctions arising from the environment or neurological development.

Additionally, the fourth article focused on a case study (mother-baby dyad) in which the objective was to investigate indicators of maternal mental health and the social support received during pregnancy and the postpartum period, evaluating the influences and repercussions of these variables on the development of a child at 12, 18 and 24 months of age. Mother's assessments

results showed depressive symptoms, traces of anxiety, fragile social support and alcohol consumption during pregnancy. It has been shown that the child exposed to maternal mental health problems and fragile social support, accompanied by low socioeconomic status, is more vulnerable to factors that impair social-emotional and behavioral development, indirectly affecting cognitive development (KIM-COHEN *et al.*, 2005; MMENDES *et al.*, 2008; TRONICK E RECK, 2009).

Researchers have shown that a significant history of maternal depression in early pregnancy carries a cumulative effect on the presence of behavioral problems in children (BAGNER, PETTIT, LEWINSOHN, & SEELEY, 2010). This mother's depression may have been one of the factors that negatively impacted the initial interactions with her daughter, favoring risks for the development of behavioral, affective and social disorders, as indicated in other studies (BRUM AND SCHERMANN, 2006; BRENNAN, AND NAJMAN, 2014). CARDOSO *et al*. (2017) identified that maternal depression influences the presence of behavioral problems in children, represented both by higher levels of internalization (thinking problems) and externalization (breaking rules), both of which have repercussions on levels of affection and socialization of the child. It is understood that the social support network helps in times of stress and favors the overcoming of adversities that arise throughout life, being a factor of protection for the exercise of motherhood. Such a support network is part of the community context and, as such, impacts family relationships and the mother-baby dyad. The microsystems in which this mother participated were mainly the house, the nursery of the neighborhood, her job and the public hospital. According to BRONFENBRENNER (1996) the microsystems act in an interrelated way and are the environments in which the developing person participates, allowing the experience of roles, interpersonal relationships and patterns of activities. As a support network, these systems act as potential transformers. In this context, Celina had a weak support network due to the lack of contact with family and friends, the absence of a stable marital status and a paternal figure. These factors may have negatively influenced the mother-baby interaction, as well as Laura's behavioral and social-emotional development. Celina's lack of family support revealed the lack of solidity of the social support network, evidencing an impoverishment in the interaction between microsystems (BRONFENBRENNER, 1996).

Like this, the risk-generating or protective factors linked to the mother-baby dyad were related to the context they were inserted. The way this mother identified and sought the support network depended on the interaction with the context where it resided, forming a cycle of feedback between the dyad and the community, producing risk results.

It is worth mentioning that these studies present some methodological limitations, such as the impossibility of generalizing the results due to the small number of participants, however the case studies demonstrate particular aspects that refer us to conditions that can occur on a large scale if there are ways to establish regular and mass assessments, applied at certain periods of development and in different social conditions.

Nutritional aspects have revealed that the cultural characteristics of the sample composed of women of low socioeconomic status and who commonly consume low dietary sources of LC-PUFA should also be considered. Regarding the meta-analysis, it was seen that the effect of n-3 LC-PUFA supplementation on development in childhood is uncertain due to methodological uncertainties; therefore, the hypothesis that supplementation with n-3 LC-PUFA during pregnancy improves infant neurological development cannot be accepted or rejected based on the included studies.

The contributions presented at the end of this study indicated the need for future research that broadens the knowledge about the variables investigated. Experimental studies and with larger samples may be very useful for understanding the importance of LC-PUFA concentration during the first trimester of gestation and its relation to infant development. Longitudinal studies may help in understanding the relationship between omega-3 and cognitive development. In addition, neuroimaging studies could aid in the understanding of differences in nervous system formation when using omega-3 supplementation during the first trimester of pregnancy.

We emphasize that high concentrations of LC-PUFA (EPA and DHA) during the first trimester of gestation are important to potentiate the cognitive development of infants at 18 and 24 months of age. In the same way, through the case studies, we verified that in addition to nutritional information, psychological monitoring is of paramount importance during the perinatal period,

aiming at improving the quality of mother's life style, and limiting exposure to risk factors, which can lead to mental health impairments. In summary, these results may contribute to the elaboration of public policies aimed to promote maternal and child health and indicating the relevance of neuropsychological assessments during early childhood as a preventive way to improve the prognosis of certain developmental delays.

6. REFERENCES

ACEVEDO-POLAKOVICH, I. D., NIEC, L. N., BARNETT, M. L., & BELL, K. Incorporating natural helpers to address service disparities for young children with conduct problems. **Children and youth services review**, *35*(9), 1463-1467, 2013.

ADAMS-CHAPMAN, I. et al. Association between feeding difficulties and language delay in preterm infants using Bayley Scales of Infant Development-Third Edition. **Journal of Pediatrics,** v. 163, n. 3, p. 680-5 e1-3, Sep 2013. ISSN 1097-6833 (Electronic) 0022-3476 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/23582139 >.

ADAMS, C.; THOMAS, S. P. Alternative prenatal care interventions to alleviate Black–White maternal/infant health disparities. **Sociology Compass,** v. 12, n. 1, 2018.

ADOLPH, K. E.; EPPLER, M. A.; GIBSON, E. J. Crawling versus walking infants' perception of affordances for locomotion over sloping surfaces. **Child Dev,** v. 64, n. 4, p. 1158-74, Aug 1993. (Print) 0009-3920 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/8404262 >.

ALLEN, E. **The Influence of an Attachment Theory-based Professional Development on the Day-to-day Interactions Between Early Childhood Professionals and Infants in Childcare Facilities**. 2014. Saint Joseph's University

ALVARENGA, P., & PALMA, E. M. S. Indicadores de depressão materna e a interação mãe-criança aos 18 meses de vida. **Psicologia***, 44*(3), 402-410, 2013.

AMORIM, K. d. S. et al. O bebê e a construção de significações, em relações afetivas e contextos culturais diversos. **Temas em Psicologia,** v. 20, n. 2, p. 309-326, 2012. ISSN 1413-389X.

ANDERSEN, A.-M. N., ANDERSEN, P. K., OLSEN, J., GRØNBÆK, M., & STRANDBERG-LARSEN, K.. Moderate alcohol intake during pregnancy and risk of fetal death. **International journal of epidemiology***, 41*(2), 405-413, 2012.

ANDERSON, G. D. Pregnancy-induced changes in pharmacokinetics. **Clinical pharmacokinetics,** v. 44, n. 10, p. 989-1008, 2005.

ANDERSON, V. A., ANDERSON, P., NORTHAM, E., JACOBS, R., & CATROPPA, C. Development of executive functions through late childhood and adolescence in an Australian sample. **Developmental neuropsychology**, *20*(1), 385-406, 2001.

ANDRADE, S. A., SANTOS, D. N., BASTOS, A. C., PEDROMÔNICO, M. R. M., ALMEIDA-FILHO, N. D., & BARRETO, M. L. Ambiente familiar e desenvolvimento

cognitivo infantil: uma abordagem epidemiológica. **Revista de saúde Pública,** *39*(4), 606-611, 2005.

ARTERBURN, L. M.; HALL, E. B.; OKEN, H. Distribution, interconversion, and dose response of n-3 fatty acids in humans. **American Journal of Clinical Nutrition,** v. 83, n. 6 Suppl, p. 1467S-1476S, Jun 2006. ISSN 0002-9165 (Print) 0002-9165 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/16841856 >.

ASSIES, J. et al. Significantly reduced docosahexaenoic and docosapentaenoic acid concentrations in erythrocyte membranes from schizophrenic patients compared with a carefully matched control group. **Biological psychiatry,** v. 49, n. 6, p. 510-522, 2001.

ASSISI, A. et al. Fish oil and mental health: The role of n-3 long-chain polyunsaturated fatty acids in cognitive development and neurological disorders. **International Clinical Psychopharmacology**, US**,** v. 21, n. 6, p. 319-336, 2006.

AUESTAD, N. Infant nutrition–brain development–disease in later life. **Developmental neuroscience,** v. 22, n. 5-6, p. 472-473, 2000..

BAACK, M. L. et al. Daily enteral DHA supplementation alleviates deficiency in premature infants. **Lipids,** v. 51, n. 4, p. 423-433, 2016.

BADDELEY, A.; VARGHA-KHADEM, F.; MISHKIN, M. Preserved recognition in a case of developmental amnesia: implications for the acaquisition of semantic memory? **Journal of Cognitive Neuroscience,** v. 13, n. 3, p. 357-369, 2001.

BADDELEY, A. D. Is working memory still working? **European psychologist,** v. 7, n. 2, p. 85, 2002.

BAGNER, D. M., PETTIT, J. W., LEWINSOHN, P. M., & SEELEY, J. R. Effect of maternal depression on child behavior: a sensitive period? **Journal of the American Academy of Child & Adolescent Psychiatry,** *49*(7), 699-707, 2010.

BARBOSA, T., MIRANDA, M. C., SANTOS, R. F., & BUENO, O. F. A. Phonological working memory, phonological awareness and language in literacy difficulties in Brazilian children. **Reading & Writing**, 22, 201-218. 2009

BARKER, D. J.; CLARK, P. M. Fetal undernutrition and disease in later life. **Reviews of Reproduction,** v. 2, n. 2, p. 105-12, May 1997. ISSN1359-6004 (Print) 1359-6004(Linking).Disponível em:<https://www.ncbi.nlm.nih.gov/pubmed/9414472.

BAUER, P. J. The cognitive neuroscience of the development of memory. In: (Ed.). **The development of memory in infancy and childhood**: Psychology Press,. p.127-156. 2008

BAUER, P. J.; WENNER, J. A.; KROUPINA, M. G. Making the past present: Later verbal accessibility of early memories. **Journal of Cognition and Development,** v. 3, n. 1, p. 21-47, 2002.

BAYLEY, N. **Bayley scales of infant and toddler development: Bayley-III**. Harcourt Assessment, Psych. Corporation San Antonio, Tex, USA, 2006.

BELTRAMI, L.; DE MORAES, A. B.; DE SOUZA, A. P. R. Ansiedade materna puerperal e risco para o desenvolvimento infantil. **Distúrbios da Comunicação,** v. 25, n. 2, 2013.

BENAIM, C. et al. Early pregnancy body mass index modifies the association of pre-pregnancy dietary patterns with serum polyunsaturated fatty acid concentrations throughout pregnancy in Brazilian women. **Matern Child Nutr**, 2017. (Electronic)1740-8695 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/28635163 >.

BERGMAN, K. et al. Maternal prenatal cortisol and infant cognitive development: moderation by infant-mother attachment. **Biological Psychiatry,** v. 67, n. 11, p. 1026-32, Jun 01 2010. ISSN 1873-2402 (Electronic) 0006-3223 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/20188350 >.

BERTI, C. et al. Early-life nutritional exposures and lifelong health: immediate and long-lasting impacts of probiotics, vitamin D, and breastfeeding. **Nutrition Reviews,** v. 75, n. 2, p. 83-97, Feb 01 2017. ISSN 1753-4887 (Electronic) 0029-6643 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/28130504 >.

BERTRAND, J., FLOYD, L., & WEBER, M. Fetal Alcohol Syndrome Prevention Team, Division of Birth Defects and Developmental Disabilities, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC). Guidelines for identifying and referring persons with fetal alcohol syndrome. **MMWR Recommendations and Reports***, 54*, 1-14, 2005.

BIAGGIO, A., & NATALÍCIO, L. Manual para o inventário de ansiedade Traço-Estado (IDATE). *Rio de Janeiro:* **CEPA***, 15*, 1979.

BLAIR, C. School readiness: Integrating cognition and emotion in a neurobiological conceptualization of children's functioning at school entry. **American psychologist,** v. 57, n. 2, p. 111, 2002.

BOLSONI-SILVA, A. T., LOUREIRO, S. R., & MARTURANO, E. M. Comportamentos internalizantes: associações com habilidades sociais, práticas educativas, recursos do ambiente familiar e depressão materna. **Psico***, 47*(2), 111-120, 2016.

BOYCE, P.; HICKEY, A. Psychosocial risk factors to major depression after childbirth. **Social psychiatry and psychiatric epidemiology,** v. 40, n. 8, p. 605-612, 2005.

BRADLEY, R. Environment and parenting. Em: Bornstein, M (ed). Handbook of parenting. **Lawrence Erlbaum: Hillsdale**. v. 2, n 281-314, 2002

BRAITHWAITE, E. C. et al. Modifiable predictors of depression following childhood maltreatment: a systematic review and meta-analysis. **Translational psychiatry,** v. 7, n. 7, p. e1162, 2017.

BAGNER, D. M., PETTIT, J. W., LEWINSOHN, P. M., & SEELEY, J. R. Effect of maternal depression on child behavior: a sensitive period?. **Journal of the American Academy of Child & Adolescent Psychiatry**, *49*(7), 699-707, 2010.

BRONFENBRENNER, U. **A ecologia do desenvolvimento humano**. Porto Alegre: Artes Médicas, 1996.

BRONFENBRENNER, U. **Environments in developmental perspective: Theoretical and operational models.** 1999.

BRONFENBRENNER, U. **Human development, bioecological theory of**. In N. J. Smelser & P. B. Baltes. pp. 6963- 6970. Oxford, UK: Elsevier. 2001.

BRONFENBRENNER, U. **Making human beings human: Bioecological perspectives on human development**. Sage, 2005. ISBN 0761927123.

BRONFENBRENNER, U. **Bioecologia do desenvolvimento humano: tornando os seres humanos mais humanos**. Artmed Editora, 2011. ISBN 853632645X.

BRONFENBRENNER, U.; EVANS, G. W. Developmental science in the 21st century: Emerging questions, theoretical models, research designs and empirical findings. **Social development,** v. 9, n. 1, p. 115-125, 2000.

BRONFENBRENNER, U.; MORRIS, P. A. The ecology of developmental processes. 1998. ISSN 0471055271.

BRONFENBRENNER, U.; VASTA, R. Six theories of child development. **VASTA, R.(Ed)**, 1989.

BRUM, E. H. M., & SCHERMAN, L. O impacto da depressão materna nas interações iniciais. PSICO, Porto Alegre, 37(2), 151-158, 2006

BRYANTON, J. et al. Incidence of prenatal alcohol exposure in Prince Edward Island: a population-based descriptive study. **CMAJ open,** v. 2, n. 2, p. E121, 2014.

CALDERON, F.; KIM, H. Y. Docosahexaenoic acid promotes neurite growth in hippocampal neurons. **Journal of neurochemistry,** v. 90, n. 4, p. 979-988, 2004.

CAMACHO, I. et al. Incidencia de patología psiquiátrica menor en los estudiantes de primero a cuarto año de la Escuela de Medicina “José María Vargas”, año 2005. Caracas, Venezuela. **Acta Científica Estudiantil,** v. 5, n. 1, p. 14-32, 2007.

CAMPOY, C. et al. Effects of prenatal fish-oil and 5-methyltetrahydrofolate supplementation on cognitive development of children at 6.5 y of age. **The American journal of clinical nutrition,** v. 94, n. 6 Suppl, p. 1880S-1888S, 2011. ISSN 0002-9165.

CARDOSO, T. d. S. G.; SIQUARA, G. M.; DE FREITAS, P. M. Relações entre depressão materna e problemas de comportamento em crianças. **Psicologia Argumento,** v. 32, n. 79, 2017. ISSN 1980-5942.

CARNEIRO, M. P. Memory development in children: what changes with age? **Psicologia: Reflexão e Crítica,** v. 21, n. 1, p. 51-59, 2008.

CARLESSO, J. P. P., SOUZA, A. P. R. D., & MORAES, A. B. D. Maternal depression and clinical risk indicators in child development. **Revista CEFAC***, 16*(2), 500-510, 2014.
CASEY, B.; GIEDD, J. N.; THOMAS, K. M. Structural and functional brain development and its relation to cognitive development. **Biological psychology,** v. 54, n. 1-3, p. 241-257, 2000.

CATTELL, R. B.; SCHEIER, I. H. The meaning and measurement of neuroticism and anxiety. 1961.

CETIN, I.; KOLETZKO, B. Long-chain omega-3 fatty acid supply in pregnancy and lactation. **Curr Opin Clin Nutr Metab Care,** v. 11, n. 3, p. 297-302, May 2008. ISSN 1363-1950 (Print) 1363-1950.

CHEN, C.; BAZAN, N. G. Lipid signaling: sleep, synaptic plasticity, and neuroprotection. **Prostaglandins & other lipid mediators,** v. 77, n. 1-4, p. 65-76, 2005.

CHEVALIER, S. Active trilingualism in early childhood: The motivating role of caregivers in interaction. **International Journal of Multilingualism,** v. 9, n. 4, p. 437-454, 2012. ISSN 1479-0718.

CID, M. F. B.; MATSUKURA, T. S. Mães com transtorno mental e seus filhos: risco e desenvolvimento. **Mundo saúde (Impr.),** v. 34, n. 1, p. 73-81, 2010.

CLAYTON, E. H. et al. Long chain omega-3 polyunsaturated fatty acids in the treatment of psychiatric illnesses in children and adolescents. **Acta Neuropsychiatrica,** v. 19, n. 2, p. 92-103, 2007.

COATES, A. O., SCHAEFER, C. A., & ALEXANDER, J. L. Detection of postpartum depression and anxiety in a large health plan. **The Journal of Behavioral Health Services and Research***, 31*(2), 117-133, 2004.

COLE, M., & COLE, S. R. **O desenvolvimento da criança e do adolescente** *(4ª edição)*. Porto Alegre: ARTMED, 2003

COLETTA, J. M.; BELL, S. J.; ROMAN, A. S. Omega-3 Fatty acids and pregnancy. **Reviews in Obstetrics and Gynecology,** v. 3, n. 4, p. 163-71, Fall 2010. ISSN 2153-8166 (Electronic) 1941-2797 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/21364848 >.

COLES, C. D., SOWELL, E. R. Executive function predicts adaptive behavior in children with histories of heavy prenatal alcohol exposure and attention-deficit/hyperactivity disorder. **Alcoholism: Clinical and Experimental Research,** *36*(8), 1431-1441, 2012

COLOMBO, J. Maternal DHA and the development of attention in infancy and toddlerhood. **Child development,** v. 75, n. 4, p. 1254-1267, 2004.

COOPER, D. L., PETHERICK, E. S., & WRIGHT, J. The association between binge drinking and birth outcomes: results from the Born in Bradford cohort study. **The Journal of Epidemiology Community Health,** *67*(10), 821-828. 2013.

COWAN, N. Evolving conceptions of memory storage, selective attention, and their mutual constraints within the human information-processing system. **Psychological bulletin,** v. 104, n. 2, p. 163, 1988.

COX, J. L., HOLDEN, J. M., & SAGOVSKY, R.. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. **The British journal of psychiatry***, 150*(6), 782-786, 1987

CUEVAS, K. et al. What's mom got to do with it? Contributions of maternal executive function and caregiving to the development of executive function across early childhood. **Developmental Science,** v. 17, n. 2, p. 224-238, 2014. ISSN 1467-7687.

DANIELS, J. L. et al. Fish intake during pregnancy and early cognitive development of offspring. **Epidemiology,** v. 15, n. 4, p. 394-402, 2004.

DA SILVA CRUZ, E. B., SIMÕES, G. L., & FAISAL-CURY, A. . Rastreamento da depressão pós-parto em mulheres atendidas pelo Programa de Saúde da Família. **Revista Brasileira de Ginecologia e Obstetria***, 27*(4), 181-188, 2005.

DE CASTRO ALMEIDA, N. M., & DA ROCHA ARRAIS, A. (. O Pré-Natal Psicológico como Programa de Prevenção à Depressão Pós-Parto. **Psicologia Ciência e Profissão,** *36*(4) 2016.

DE GIUSEPPE, R.; ROGGI, C.; CENA, H. n-3 LC-PUFA supplementation: effects on infant and maternal outcomes. **European journal of nutrition,** v. 53, n. 5, p. 1147-1154, 2014.

DE GROOT, R. H.; ADAM, J. J.; HORNSTRA, G. Selective attention deficits during human pregnancy. **Neuroscience letters,** v. 340, n. 1, p. 21-24, 2003. ISSN 0304-3940.

DE MORTON, N. A. The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. **Australian Journal of Physiotherapy,** v. 55, n. 2, p. 129-133, 2009/01/01/ 2009. ISSN 0004-9514. Disponível em: < http://www.sciencedirect.com/science/article/pii/S0004951409700431

DE SOUZA, M. S.; BAPTISTA, M. N. Associações entre suporte familiar e saúde mental. **Revista Psicologia Argumento,** v. 26, n. 54, p. 207-215, 2017. ISSN 1980-5942.

DEVAKUMAR, D. et al. Maternal antenatal multiple micronutrient supplementation for long-term health benefits in children: a systematic review and meta-analysis. **BMC medicine,** v. 14, n. 1, p. 90, 2016.

DIJCK-BROUWER, D. J. et al. Lower fetal status of docosahexaenoic acid, arachidonic acid and essential fatty acids is associated with less favorable neonatal neurological condition. **Prostaglandins, leukotrienes and essential fatty acids,** v. 72, n. 1, p. 21-28, 2005.

DIMASUAY, K. G. et al. Placental responses to changes in the maternal environment determine fetal growth. **Frontiers in physiology,** v. 7, p. 12, 2016.

DIAS, L. B. T., & LANDEIRA-FERNANDEZ, J. Neuropsicologia do desenvolvimento da memória: da pré-escola ao período escolar. **Revista Neuropsicologia Latinoamericana**, *3*(1), 19-26, 2011

DOBBING, J. Proceedings: Growth retardation and the human fetal brain. **Archives of Disease in Childhood,** v. 48, n. 10, p. 828, Oct 1973. ISSN 1468-2044 (Electronic) 0003-9888 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/4796012 >.

DONELLI, T. M. S., CHEMELLHO, M. R., & LEVANDOWSKI, D. C. Ansiedade materna e maternidade: Revisão crítica da literatura. **Interação em Psicologia,** *21*(1), 2017

DUNKEL SCHETTER, C.; TANNER, L. Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice. **Current Opinion in Psychiatry,** v. 25, n. 2, p. 141-8, Mar 2012. ISSN 1473-6578 (Electronic) 0951-7367 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/22262028 >.

DUNSTAN, J. A. et al. Cognitive assessment of children at age 2(1/2) years after maternal fish oil supplementation in pregnancy: a randomised controlled trial. **Arch Dis Child Fetal Neonatal Ed,** v. 93, n. 1, p. F45-50, Jan 2008..

EARLS, M. F.; CHILD, C. o. P. A. o.; HEALTH, F. Incorporating recognition and management of perinatal and postpartum depression into pediatric practice. **Pediatrics,** v. 126, n. 5, p. 1032-1039, 2010.

ELLISON, P. A. T.; SEMRUD-CLIKEMAN, M. Neuropsychological Intervention and Treatment Approaches for Childhood and Adolescent Disorders. **Child Neuropsychology: Assessment and Interventions for Neurodevelopmental Disorders**, p. 217-240, 2007.

EMMETT, P. M.; JONES, L. R.; GOLDING, J. Pregnancy diet and associated outcomes in the Avon Longitudinal Study of Parents and Children. **Nutr Rev,** v. 73 Suppl 3, p. 154-74, Oct 2015. ISSN 0029-6643.

ESCOLANO-MARGARIT, M. V. et al. Prenatal DHA status and neurological outcome in children at age 5.5 years are positively associated. **The Journal of nutrition,** v. 141, n. 6, p. 1216-1223, 2011. ISSN 0022-3166.

FIELD, A. **Discovering statistics using SPSS**. Sage publications, 2009. ISBN 1847879071.

FIGLIO, D. N. et al. Long-term Cognitive and Health Outcomes of School-Aged Children Who Were Born Late-Term vs Full-Term. **JAMA Pediatr,** v. 170, n. 8, p. 758-64, Aug 01 2016. ISSN 2168-6211 (Electronic) 2168-6203 (Linking) Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/27271240 >.

FIGUEIRAS, A. C. et al. **Manual para vigilância do desenvolvimento infantil no contexto da AIDPI**: Organização Pan-Americana da Saúde 2005.
FLORES, M. R. et al. Associação entre indicadores de risco ao desenvolvimento infantil e estado emocional materno. **Revista CEFAC,** v. 15, n. 2, p. 348-360, 2012.

FISHER, J., MELLO, M. C. D., PATEL, V., RAHMAN, A., TRAN, T., HOLTON, S., & HOLMES, W. Prevalence and determinants of common perinatal mental disorders in women in low-and lower-middle-income countries: a systematic review. **Bulletin of the World Health Organization***, 90*(2), 139-149. 2012.

FIVUSH, R.; SCHWARZMUELLER, A. Children remember childhood: Implications for childhood amnesia. **Applied Cognitive Psychology: The Official Journal of the Society for Applied Research in Memory and Cognition,** v. 12, n. 5, p. 455-473, 1998. ISSN 0888-4080.

FLAK, A. L., SU, S., BERTRAND, J., DENNY, C. H., KESMODEL, U. S., & COGSWELL, M. E. The association of mild, moderate, and binge prenatal alcohol exposure and child neuropsychological outcomes: a meta-analysis. **Alcoholism: Clinical and Experimental Research***, 38*(1), 214-226, 2014.

FLORES, M. R. et al. Associação entre indicadores de risco ao desenvolvimento infantil e estado emocional materno. **Revista CEFAC,** v. 15, n. 2, p. 348-360, 2012.

FOGEL, A, KING, B, & SHANKER, S. Human Development in the 21st Century, **Cambridge University Press: Cambridge UK**, 2009.

GALE, C. R. et al. Oily fish intake during pregnancy–association with lower hyperactivity but not with higher full-scale IQ in offspring. **Journal of Child Psychology and Psychiatry,** v. 49, n. 10, p. 1061-1068, 2008. ISSN 1469-7610.

GENTILE, S. Untreated depression during pregnancy: Short-and long-term effects in offspring. A systematic review. **Neuroscience,** v. 342, p. 154-166, 2017. ISSN 0306-4522.

GEORGIEFF, M. K. Nutrition and the developing brain: nutrient priorities and measurement–. **The American journal of clinical nutrition,** v. 85, n. 2, p. 614S-620S, 2007. ISSN 0002-9165.

GERMAN, J. B. Dietary lipids from an evolutionary perspective: sources, structures and functions. **Matern Child Nutrition,** v. 7 Suppl 2, p. 2-16, Apr 2011. ISSN 1740-8709 (Electronic) 1740-8695 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/21366863 >.

GIBSON, E. J. Exploratory behavior in the development of perceiving, acting, and the acquiring of knowledge. **Annual review of psychology,** v. 39, n. 1, p. 1-42, 1988. ISSN 0066-4308.

GIL, A.; GIL, F. Fish, a Mediterranean source of n-3 PUFA: benefits do not justify limiting consumption. **British Journal of Nutrition,** v. 113, n. S2, p. S58-S67, 2015. ISSN 0007-1145.

GLOVER, V. Maternal depression, anxiety and stress during pregnancy and child outcome; what needs to be done. **Best Practice Research Clinical Obstetrician Gynaecology,** v. 28, n. 1, p. 25-35, Jan 2014. ISSN 1532-1932 (Electronic) 1521-6934 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/24090740 >.

GOODE, W., & HATT, P. The case study. **Methods of Social Research***, New York: McGraw-Hill*, 330-340. 1952.

GOODMAN, S. H., ROUSE, M. H., CONNELL, A. M., BROTH, M. R., HALL, C. M., & HEYWARD, D. Maternal depression and child psychopathology: a meta-analytic review. **Clinical child and family psychology review***, 14*(1), 1-27. 2011.

GOSWAMI, U. Mental Capital and wellbeing: making the most of ourselves in the 21st century, **Government Office for Science**: UK, 2008 Disponível em:

http://www.foresight.gov.uk/Mental%20Capital/SR-E1_MCW.pdf

GOULD, J. F. Randomized controlled trial of maternal omega-3 long-chain PUFA supplementation during pregnancy and early childhood development of attention, working memory, and inhibitory control. **The American Journal of Clinical Nutrition,** v. 99, n. 4, p. 851-9, Apr 2014. (Electronic)0002-9165 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/24522442 >.

GRAF, P. Life-span changes in implicit and explicit memory. **Bulletin of the Psychonomic Society,** v. 28, n. 4, p. 353-358, 1990.

GRANTHAM-MCGREGOR, S., CHEUNG, Y. B., CUETO, S., GLEWWE, P., RICHTER, L., STRUPP, B., & GROUP, I. C. D. S.. Developmental potential in the first 5 years for children in developing countries. **The Lancet***, 369*(9555), 60-70. 2007.

GRIEP, R. H., CHOR, D., FAERSTEIN, E., WERNECK, G. L., & LOPES, C. S. Validade de constructo de escala de Apoio Social do Medical Outcomes Study adaptada para o português no estudo Pró–Saúde {Construct validity scale of Social Support from the Medical Outcomes Study adapted to Portuguese in Pro study–Health}. **Cadernos de Saúde Pública***, 21*(3), 703-714, 2005.

GRJIBOVSKI, A. et al. Housing conditions, perceived stress, smoking, and alcohol: determinants of fetal growth in Northwest Russia. **Acta Obstetricia et Gynecologica Scandinavica,** v. 83, n. 12, p. 1159-1166, 2004.

GUERRINI, I.; THOMSON, A. D.; GURLING, H. D. The importance of alcohol misuse, malnutrition and genetic susceptibility on brain growth and plasticity. **Neuroscience & Biobehavioral Reviews,** v. 31, n. 2, p. 212-220, 2007.

GUESNET, P.; ALESSANDRI, J. M. Docosahexaenoic acid (DHA) and the developing central nervous system (CNS) - Implications for dietary recommendations. **Biochimie,** v. 93, n. 1, p. 7-12, Jan 2011. ISSN 1638-6183 (Electronic) 0300-9084 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/20478353 >.

HADDERS-ALGRA, M. The neuromotor examination of the preschool child and its prognostic significance. **Mental Retardation and Developmental Disabilities Research Reviews,** v. 11, n. 3, p. 180-8, 2005. ISSN 1080-4013 (Print) 1080-4013 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/16161096 >.

HALPERN, R. **Manual de pediatria do desenvolvimento e comportamento**: São Paulo: Manole 2015.

HELLAND, I. B. et al. Effect of supplementing pregnant and lactating mothers with n-3 very-long-chain fatty acids on children's IQ and body mass index at 7 years of age. **Pediatrics,** v. 122, n. 2, p. e472-e479, 2008.

HELLAND, I. B. et al. Maternal supplementation with very-long-chain n-3 fatty acids during pregnancy and lactation augments children's IQ at 4 years of age. **Pediatrics,** v. 111, n. 1, p. e39-e44, 2003.

HERGUETA, T., BAKER, R., & DUNBAR, G. C. The Mini-International Neuropsychiatric Interview (MINI): the development and validation of a structured diagnostic psychiatric interview for DSM-IVand ICD-10. **Journal of Clinical Psychiatry***, 59*(Suppl 20), 2233. 1998

HIBBELN, J. R. et al. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study. **Lancet,** v. 369, n. 9561, p. 578-85, Feb 17 2007.

HOEKZEMA, E. et al. Pregnancy leads to long-lasting changes in human brain structure. **Nature Neuroscience,** v. 20, n. 2, p. 287, 2017.

HOWARD, K. et al. Biological and environmental factors as predictors of language skills in very preterm children at 5 years of age. **Journal of Developmental & Behavioral Pediatrics,** v. 32, n. 3, p. 239-249, 2011.

HUDSON, S. et al. Maternal responsiveness predicts child language at ages 3 and 4 in a community-based sample of slow-to-talk toddlers. **International journal of language & communication disorders,** v. 50, n. 1, p. 136-142, 2015. .

HUMPHREY, J. H. Child undernutrition, tropical enteropathy, toilets, and handwashing. **The Lancet,** v. 374, n. 9694, p. 1032-1035, 2009. ISSN 0140-6736.

INNIS, S. M. Perinatal biochemistry and physiology of long-chain polyunsaturated fatty acids. **The Journal of pediatrics,** v. 143, n. 4, p. 1-8, 2003.

INNIS, S.M. Fatty acids and early human development. **Early human development,** v. 83, n. 12, p. 761-766, 2007.

INNIS, S. M.; FRIESEN, R. W. Essential n-3 fatty acids in pregnant women and early visual acuity maturation in term infants. **Am J Clin Nutr,** v. 87, n. 3, p. 548-57, Mar 2008. ISSN 1938-3207 (Electronic)0002-9165 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/18326591 >.

JABLENSKY, A. V. et al. Pregnancy, delivery, and neonatal complications in a population cohort of women with schizophrenia and major affective disorders. **American Journal of Psychiatry,** v. 162, n. 1, p. 79-91, 2005.

JONES, I. et al. Bipolar disorder, affective psychosis, and schizophrenia in pregnancy and the post-partum period. **The Lancet,** v. 384, n. 9956, p. 1789-1799, 2014.

JULVEZ, J. et al. Maternal Consumption of Seafood in Pregnancy and Child Neuropsychological Development: A Longitudinal Study Based on a Population With High Consumption Levels. **Am J Epidemiol,** v. 183, n. 3, p. 169-82, Feb 01 2016. (Electronic)0002-9262 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/26740026 >.

KELLY, L. et al. The polyunsaturated fatty acids, EPA and DPA exert a protective effect in the hippocampus of the aged rat. **Neurobiol Aging,** v. 32, n. 12, p. 2318 e1-15, Dec 2011. (Electronic)0197-4580 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/20570403 >.

KIDD, P. M. Omega-3 DHA and EPA for cognition, behavior, and mood: clinical findings and structural-functional synergies with cell membrane phospholipids. **Alternative medicine review,** v. 12, n. 3, p. 207, 2007.

KIERNAN, K. E.; HUERTA, M. C. Economic deprivation, maternal depression, parenting and children's cognitive and emotional development in early childhood. **British Journal of Sociology,** v. 59, n. 4, p. 783-806, Dec 2008. ISSN 1468-4446 (Electronic)0007-1315 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/19035922 >.

KIM-COHEN, J. et al. Maternal depression and children's antisocial behavior: nature and nurture effects. **Archives of general psychiatry,** v. 62, n. 2, p. 173-181, 2005.

KINGSTON, D.; TOUGH, S. Prenatal and postnatal maternal mental health and school-age child development: a systematic review. **Maternal and child health journal,** v. 18, n. 7, p. 1728-1741, 2014.

KLEBANOV, P. K. et al. The contribution of neighborhood and family income to developmental test scores over the first three years of life. **Child Development,** v. 69, n. 5, p. 1420-36, Oct 1998. ISSN 0009-3920 (Print)
0009-3920 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/9839425 >.

KLIEMANN, A.; BÖING, E.; CREPALDI, M. A. Fatores de risco para ansiedade e depressão na gestação: Revisão sistemática de artigos empíricos. **Mudanças-Psicologia da Saúde,** v. 25, n. 2, p. 69-76, 2017.

KNICKMEYER, R. C. et al. A structural MRI study of human brain development from birth to 2 years. **Journal of Neuroscience,** v. 28, n. 47, p. 12176-12182, 2008.

KNIGHT, J., MARTIN, J., & PATIL, A. Principal Component Analysis of EPDS Questions to Identify Trends in Depressive Symptoms Among At-Risk Populations [29K]. **Obstetrics & Gynecology***, 127*, 96S-97S, 2016.

KNUDSEN, E. I. Sensitive periods in the development of the brain and behavior. **Journal of cognitive neuroscience**, *16*(8), 1412-1425, 2004.

KNUESEL, I. et al. Maternal immune activation and abnormal brain development across CNS disorders. **Nature Reviews Neurology,** v. 10, n. 11, p. 643, 2014.

KOLETZKO, B.; CETIN, I.; BRENNA, J. Child Health Foundation; Diabetic Pregnancy Study Group; European Association of Perinatal Medicine; European Association of Perinatal Medicine; European Society for Clinical Nutrition and Metabolism; European Society for Paediatric Gastroenterology, Hepatology and Nutrition, Committee on Nutrition; International Federation of Placenta Associations; International Society for the Study of Fatty Acids and Lipids. Dietary fat intakes for pregnant and lactating women. **British Journal of Nutrition,** v. 98, n. 5, p. 873-877, 2007.

KOUTRA, K. et al. Antenatal and postnatal maternal mental health as determinants of infant neurodevelopment at 18 months of age in a mother–child cohort (Rhea Study) in Crete, Greece. **Social psychiatry and psychiatric epidemiology,** v. 48, n. 8, p. 1335-1345, 2013.

KRISHNA, M. et al. Birth size, risk factors across life and cognition in late life: protocol of prospective longitudinal follow-up of the MYNAH (MYsore studies of Natal effects on Ageing and Health) cohort. **BMJ Open,** v. 7, n. 2, p. e012552, Feb 16 2017. ISSN 2044-6055 (Electronic) 2044-6055 (Linking). Disponível em: <https://www.ncbi.nlm.nih.gov/pubmed/28209604 >.

KROB, A. D. et al. Depressão na gestação e no pós-parto e a responsividade materna nesse contexto. **Revista Psicologia e Saúde,** v. 9, n. 3, p. 3-16, 2017.

LAURITZEN, L. et al. The essentiality of long chain n-3 fatty acids in relation to development and function of the brain and retina. **Prog Lipid Res,** v. 40, n. 1-2, p. 1-94, Jan-Mar 2001. ISSN 0163-7827 (Print)0163-7827 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/11137568 >.

LEACH, L. S. et al. Online Recruitment: Feasibility, Cost, and Representativeness in a Study of Postpartum Women. **Journal of medical Internet research,** v. 19, n. 3, 2017.

LEFÈVRE, B. Avaliação neuropsicológica infantil. **Neuropsicologia hoje**, p. 249-263, 2004.

LEMAHIEU, C. et al. Impact of different omega-3 polyunsaturated fatty acid (n-3 PUFA) sources (flaxseed, Isochrysis galbana, fish oil and DHA Gold) on n-3 LC-PUFA enrichment (efficiency) in the egg yolk. **Journal of Functional Foods,** v. 19, p. 821-827, 2015.

LEMAITRE, R. N. et al. Genetic loci associated with plasma phospholipid n-3 fatty acids: a meta-analysis of genome-wide association studies from the CHARGE Consortium.

PLoS Genet, v. 7, n. 7, p. e1002193, Jul 2011. ISSN 1553-7404 (Electronic)1553-7390 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/21829377 >.

LEUNG, B. M.; WIENS, K. P.; KAPLAN, B. J. Does prenatal micronutrient supplementation improve children's mental development? A systematic review. **BMC pregnancy and childbirth,** v. 11, n. 1, p. 12, 2011.

LEVITT, P. Structural and functional maturation of the developing brain. **Journal of Pediatrics**, 143 (1), 35–45, 2003.

LEWIS, S. et al. A comparison of father–infant interaction between primary and non-primary care giving fathers. **Child: care, health and development,** v. 35, n. 2, p. 199-207, 2009. ISSN 1365-2214.

LI, D., LIU, L., & ODOULI, R. Presence of depressive symptoms during early pregnancy and the risk of preterm delivery: a prospective cohort study. **Human Reproduction***, 24*(1), 146-153, 2008.

LICKLITER, R. The integrated development of sensory organization. **Clinics in perinatology,** *38*(4), 591-603, 2011.

LIMA, M. D. O. P., TSUNECHIRO, M. A., BONADIO, I. C., & MURATA, M. Sintomas depressivos na gestação e fatores associados: estudo longitudinal. **Acta Paulista de Enfermagem***, 30*(1), 39-46, 2017.

LIN, Y. H. et al. Automated high-throughput fatty acid analysis of umbilical cord serum and application to an epidemiological study. **Lipids,** v. 47, n. 5, p. 527-539, 2012. ISSN 0024-4201.

LINSELL, L. et al. Prognostic Factors for Poor Cognitive Development in Children Born Very Preterm or With Very Low Birth Weight: A Systematic Review. **JAMA Pediatr,** v. 169, n. 12, p. 1162-72, Dec 2015. ISSN 2168-6211 (Electronic) 2168-6203 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/26457641 >.

LISBOA, N. D. **Estresse, habilidades sociais e percepção de suporte social e familiar em adolescentes**. Dissertação de mestrado- psicologia do Desenvolvimento e Aprendizagem, Universidade Estadual Paulista, São Paulo. 2018

LONNER, W. J.; IBRAHIM, F. A. Assessment in cross-cultural counseling. 1989. ISSN 082481231X.

LOVISI, G. M., LOPEZ, J. R. R., COUTINHO, E. S. F., & PATEL, V. Poverty, violence and depression during pregnancy: a survey of mothers attending a public hospital in Brazil. **Psychological medicine,** *35*(10), 1485-1492, 2005.

LURIA, A. R., & YUDOVICH, F. I. Speech and the Development of Mental Processes in the Child. 1971

LURIA, A. R. Fundamentos da Neuropsicologia. São Paulo*:* EDUSP, 223-44, 1981

LYNCH, M. E., KABLE, J. A., & COLES, C. D. Prenatal alcohol exposure, adaptive function, and entry into adult roles in a prospective study of young adults. **Neurotoxicology and Teratology,** *51*, 52-60, 2015.

MANENTE, M. V., & RODRIGUES, O. M. P. R. (2016). Associação entre Depressão Pós-parto, Apoio Social e Satisfação Conjugal*.,* **Maternidade e Trabalho:** *20*(1), 99-111, 2016

MADASCHI, V. Tradução, adaptação transcultural e evidências de validade das Escalas Bayley III de Desenvolvimento Infantil em uma população do Município de Barueri, São Paulo. 2012.

MADASCHI, V. et al. Bayley-III Scales of Infant and Toddler Development: Transcultural Adaptation and Psychometric Properties. **Paidéia (Ribeirão Preto),** v. 26, p. 189-197, 2016. ISSN 0103-863X. Disponível em: < http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0103-863X2016000200189&nrm=iso >.

MAHER, J. P. et al. Associations Between Maternal Mental Health and Well-being and Physical Activity and Sedentary Behavior in Children. **Journal of Developmental & Behavioral Pediatrics,** v. 38, n. 6, p. 385-394, 2017.

MAKRIDES, M. et al. Effect of DHA supplementation during pregnancy on maternal depression and neurodevelopment of young children: a randomized controlled trial. **Jama,** v. 304, n. 15, p. 1675-1683, 2010.

MALM, H. et al. Pregnancy complications following prenatal exposure to SSRIs or maternal psychiatric disorders: results from population-based national register data. **American Journal of Psychiatry,** v. 172, n. 12, p. 1224-1232, 2015.

MALMBERG, L. E. et al. The influence of mothers' and fathers' sensitivity in the first year of life on children's cognitive outcomes at 18 and 36 months. **Child Care Health Development,** v. 42, n. 1, p. 1-7, Jan 2016. ISSN 1365-2214 (Electronic) 0305-1862 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/26538379 >.

MARANHÃO, T. A., GOMES, K. R. O., & DA SILVA, J. M. N. Fatores que influenciam as relações familiares e sociais de jovens após a gestação Factors affecting young mothers' social and family relations after pregnancy Factores que afectan las relaciones familiares. **Cadernos de Saúde Pública***, 30*(5), 998-1008, 2014.

MARTIN, A.; RYAN, R. M.; BROOKS-GUNN, J. The joint influence of mother and father parenting on child cognitive outcomes at age 5. **Early Childhood Research Quarterly,** v. 22, n. 4, p. 423-439, 2007. ISSN 0885-2006.

MARTINEZ, M. Restoring the DHA levels in the brains of Zellweger patients. **J Mol Neurosci,** v. 16, n. 2-3, p. 309-16; discussion 317-21, Apr-Jun 2001. ISSN 0895-8696 (Print) 0895-8696 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/11478386 >.

MARTINEZ, M.; MOUGAN, I. Fatty acid composition of human brain phospholipids during normal development. **Journal of Neurochemistry,** v. 71, n. 6, p. 2528-33, Dec 1998. ISSN 0022-3042 (Print)0022-3042 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/9832152 >.

MATHIAS, P. C. et al. Maternal diet, bioactive molecules, and exercising as reprogramming tools of metabolic programming. **European journal of nutrition,** v. 53, n. 3, p. 711-722, 2014. ISSN 1436-6207.

MCDONALD, S. et al. Risk and protective factors in early child development: Results from the All Our Babies (AOB) pregnancy cohort. **Research in developmental disabilities,** v. 58, p. 20-30, 2016.

MEINCK, F., CLUVER, L. D., BOYES, M. E., & MHLONGO, E. L. Risk and protective factors for physical and sexual abuse of children and adolescents in Africa: A review and implications for practice. **Trauma, Violence, & Abuse***, 16*(1), 81-107, 2015.

MEIRELES, J. F. F. et al. Body image, eating attitudes, depressive symptoms, self-esteem and anxiety in pregnant women of Juiz de Fora, Minas Gerais, Brazil. **Ciência & Saúde Coletiva,** v. 22, n. 2, p. 437-445, 2017.

MELDRUM, S. et al. Maternal fish oil supplementation in pregnancy: a 12 year follow-up of a randomised controlled trial. **Nutrients,** v. 7, n. 3, p. 2061-2067, 2015.

MENDES, A. V., LOUREIRO, S. R., & CRIPPA, J. A. S. Depressão materna e a saúde mental de escolares. **Revista de Psiquiatria Clínica***, 35*(5), 178-186., 2008.

MENDEZ, M. A. et al. Maternal fish and other seafood intakes during pregnancy and child neurodevelopment at age 4 years. **Public health nutrition,** v. 12, n. 10, p. 1702-1710, 2009.

MENNITTI, L. V. et al. Type of fatty acids in maternal diets during pregnancy and/or lactation and metabolic consequences of the offspring. **The Journal of Nutritional Biochemestry,** v. 26, n. 2, p. 99-111, Feb 2015. (Electronic)0955-2863 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/25459884 >.

MILLER, E. K.; COHEN, J. D. An integrative theory of prefrontal cortex function. **Annual review of neuroscience,** v. 24, n. 1, p. 167-202, 2001.

Miranda, M.C. & Muszkat, M. (2004). *Neuropsicologia do Desenvolvimento.* In: Andrade, V.M., Santos, F.H. dos & Bueno, O.F.A. Neuropsicologia Hoje. São Paulo: Artes Médicas.

MOHER, D. et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. **PLOS Medicine,** v. 6, n. 7, p. e1000097, 2009. Disponível em: < https://doi.org/10.1371/journal.pmed.1000097 >.

MULDER, K. A.; KING, D. J.; INNIS, S. M. Omega-3 fatty acid deficiency in infants before birth identified using a randomized trial of maternal DHA supplementation in pregnancy. **PLoS One,** v. 9, n. 1, p. e83764, 2014. ISSN 1932-6203.

MÜLLER, U.; ZELAZO, P. D.; IMRISEK, S. 2005. Executive function and children's understanding of false belief: How specific is the relation? **Cognitive Development,** v. 20, n. 2, p. 173-189, ISSN 0885-2014.

MURGATROYD, C. A. et al. Early life social stress induced changes in depression and anxiety associated neural pathways which are correlated with impaired maternal care. **Neuropeptides,** v. 52, p. 103-111, 2015. ISSN 0143-4179.

NABAS, T.; XAVIER, G. Neurobiologia da atenção visual. **Neuropsicologia Hoje. São Paulo: Artes Médicas**, p. 101-124, 2004.

NARDI, C. G. d. A. Infants with Pierre Robin Sequence: Maternal mental health and mother-infant interaction. **Estudos de Psicologia (Campinas),** v. 32, n. 1, p. 129-140, 2015. ISSN 0103-166X.

NATIONAL SCIENTIFIC COUNCIL ON THE DEVELOPING CHILD (NSCDC). The Timing and Quality of Early Experiences Combine to Shape Brain Architecture: Working Paper No. 5, 2007. Disponível em: < https://developingchild.harvard.edu/science/national-scientific-council-on-the-developing-child/>.

NELSON, K.; FIVUSH, R. The emergence of autobiographical memory: a social cultural developmental theory. **Psychological review,** v. 111, n. 2, p. 486, 2004. ISSN 1939-1471.

OKEN, E. et al. Assessment of dietary fish consumption in pregnancy: comparing one-, four- and thirty-six-item questionnaires. **Public Health Nutrition,** v. 17, n. 9, p. 1949-59,

NYKJAER, C., ALWAN, N. A., GREENWOOD, D. C., SIMPSON, N. A., HAY, A. W., WHITE, K. L., & CADE, J. E. Maternal alcohol intake prior to and during pregnancy and risk of adverse birth outcomes: evidence from a British cohort. **Journal of Epidemiology Community Health,** jech-2013-202934, 2014.

OKEN, E. et al. Maternal prenatal fish consumption and cognition in mid childhood: Mercury, fatty acids, and selenium. **Neurotoxicology Teratology,** v. 57, p. 71-78, Sep - Oct 2016.

OLSEN, S. et al. Intake of marine fat, rich in (n-3)-polyunsaturated fatty acids, may increase birthweight by prolonging gestation. **The Lancet,** v. 328, n. 8503, p. 367-369, 1986. ISSN 0140-6736.

PANCSOFAR, N.; VERNON-FEAGANS, L.; INVESTIGATORS, F. L. P. Fathers' early contributions to children's language development in families from low-income rural communities. **Early childhood research quarterly,** v. 25, n. 4, p. 450-463, 2010. ISSN 0885-2006.

PATRA, J., BAKKER, R., IRVING, H., JADDOE, V. W., MALINI, S., & REHM, J. Dose–response relationship between alcohol consumption before and during pregnancy and the risks of low birthweight, preterm birth and small for gestational age (SGA)—a systematic review and meta-analyses. *BJOG:* **An International Journal of Obstetrics & Gynaecology,** *118*(12), 1411-1421, 2011.

PAXSON, C.; SCHADY, N. Cognitive development among young children in Ecuador the roles of wealth, health, and parenting. **Journal of Human resources,** v. 42, n. 1, p. 49-84, 2007. ISSN 0022-166X.

PEREIRA, P. K., & LOVISI, G. M. Prevalência da depressão gestacional e fatores associados. **Revista de psiquiatria clínica***, 35*(4), 144-153, 2008

PERRY, R. J., WATSON, P., & HODGES, J. R. The nature and staging of attention dysfunction in early (minimal and mild) Alzheimer's disease: relationship to episodic and semantic memory impairment. *Neuropsychologia*, *38*(3), 252-271, 2000.

PIRES, E. U. Ontogênese das funções cognitivas: uma abordagem neuropsicológica. Dissertação (Mestrado em Psicologia) – Pontifícia Universidade Católica do Rio de Janeiro, Rio de Janeiro. 2010

POSNER, M. I., ROTHBART, M. K., SHEESE, B. E., & VOELKER, P. (2014). Developing attention: behavioral and brain mechanisms. Advances in Neuroscience, 2014.

POWER, C. et al. The influence of birth weight and socioeconomic position on cognitive development: Does the early home and learning environment modify their effects? **Journal of Pediatrics,** v. 148, n. 1, p. 54-61, Jan 2006. ISSN 0022-3476 (Print)0022-3476 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/16423598 >.

PRATES, L. A., SCHMALFUSS, J. M., & LIPINSKI, J. M.. Rede de apoio social de puérperas na prática da amamentação. **Escola Anna Nery Revista de Enfermagem***, 19*(2), 310-315, 2015

PRESTON, A. R., & EICHENBAUM, H. Interplay of hippocampus and prefrontal cortex in memory. **Current Biology,** *23*(17), R764-R773, 2013

PUJOL, J., SORIANO-MAS, C., ORTIZ, H., SEBASTIAN-GALLES, N., LOSILLA, J. M., & DEUS, J. Myelination of language-related areas in the developing brain. **Neurology,** *66*(3), 339-343, 2006

RAMAKRISHNAN, U. et al. Effects of docosahexaenoic acid supplementation during pregnancy on gestational age and size at birth: randomized, double-blind, placebo-controlled trial in Mexico. **Food and nutrition bulletin,** v. 31, n. 2_suppl2, p. S108-S116, 2010. ISSN 0379-5721.

RAPOPORT, A. Da gestação ao primeiro ano de vida do bebê: Apoio social e ingresso na creche. 2003.

REED, U.; NITRINI, R.; BACHESCHI, L. O desenvolvimento normal do sistema nervoso central. **A neurologia que todo médico deve saber. 2ª ed. São Paulo: Atheneu**, p. 395-9, 2005.

RIBEIRO, J. L. P. A importância da qualidade de vida para a psicologia da saúde. **Bem estar e qualidade de vida**: contributos da psicologia da saúde, 2009.

RICE, D.; BARONE, S., Jr. Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. **Environment Health Perspectives,** v. 108 Suppl 3, p. 511-33, Jun 2000. ISSN 0091-6765 (Print) 0091-6765 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/10852851 >.

ROBERTSON, E. Antenatal risk factors for postpartum depression: a synthesis of recent literature. **General hospital psychiatry,** v. 26, n. 4, p. 289-295, 2004.

ROCINHOLI, L.; DE OLIVEIRA, L.; COLAFEMINA, J. Malnutrition and environmental stimulation in rats: Interpeak intervals of the brainstem auditory evoked potentials. **Nutritional Neuroscience,** v. 4, n. 3, p. 189-198, 2001.

ROCINHOLI, L. d. F.; LACHAT, J.-J.; DUTRA DE OLIVEIRA, J. E. Auditory evoked potential in handled and non-handled iron-deficient rats. **Psychology & Neuroscience,** v. 1, n. 2, p. 129, 2008.

ROCINHOLI, L. F.; LANDEIRA-FERNANDEZ, J. Anxiety-like behavior in weanling and young adult male and female malnourished rats. **Physiology & behavior,** v. 102, n. 1, p. 13-16, 2011.

RODRIGUEZ CEBERIO, M., & WATZLAWICK, P. **La construcción del universo: conceptos introductorios y reflexiones sobre epistemología**: constructivismo y pensamiento sistémico. Cap. I. Editora Herder, 2006.

ROMANO-SILVA, M. A. Edinburgh Postnatal Depression Scale for screening in the public health system. **Revista da Saúde Pública,** v. 43, n. Supl 1, 2009.

RUSCHI, G. E. C., SUN, S. Y., MATTAR, R., CHAMBÔ FILHO, A., ZANDONADE, E., & LIMA, V. J. D. Aspectos epidemiológicos da depressão pós-parto em amostra brasileira. **Revista de Psiquiatria do Rio Grande do Sul**, 2007.

RYAN, R. M.; MARTIN, A.; BROOKS-GUNN, J. Is one good parent good enough? Patterns of mother and father parenting and child cognitive outcomes at 24 and 36 months. **Parenting,** v. 6, n. 2-3, p. 211-228, 2006.

SALEM, N., Jr.; EGGERSDORFER, M. Is the world supply of omega-3 fatty acids adequate for optimal human nutrition? **Current Opinion in Clinical Nutrition & Metabolic Care,** v. 18, n. 2, p. 147-54, Mar 2015. ISSN 1473-6519 (Electronic) 1363-1950 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/25635599 >.

SALEM, N., Jr. et al. Mechanisms of action of docosahexaenoic acid in the nervous system. **Lipids,** v. 36, n. 9, p. 945-59, Sep 2001. ISSN 0024-4201 (Print) 0024-4201 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/11724467 >.

SANTOS, D. N. et al. Determinants of cognitive function in childhood: a cohort study in a middle income context. **BMC Public Health,** v. 8, p. 202, Jun 06 2008. ISSN 1471-2458 (Electronic) 1471-2458 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/18534035 >.

SALVATI, S. et al. Diet, lipids and brain development. **Developmental neuroscience,** v. 22, n. 5-6, p. 481-487, 2000.

SCHMIDT, F. L.; LE, H. Software for the Hunter-Schmidt meta-analysis methods. **University of Iowa, Department of Management & Organization, Iowa City, IA,** v. 42242, 2004.

SCHWARTZ, T.; VIEIRA, R.; GEIB, L. T. C. Apoio social a gestantes adolescentes: desvelando percepções. **Ciência & Saúde Coletiva,** v. 16, n. 5, 2011.

SCHUCHARDT, J. P. et al. Significance of long-chain polyunsaturated fatty acids (PUFAs) for the development and behaviour of children. **European journal of pediatrics,** v. 169, n. 2, p. 149-164, 2010. ISSN 0340-6199.

SILVERMAN, M. E., REICHENBERG, A., SAVITZ, D. A., CNATTINGIUS, S., LICHTENSTEIN, P., HULTMAN, C. M., SANDIN, S. The risk factors for postpartum depression: A population-based study. **Depression and anxiety***, 34*(2), 178-187, 2017

SKAZUFKA, E. T. **Prevalência da depressão pós-parto e fatores associados em mães que deram à luz em um hospital universitário do município de São Paulo***.* Faculdade de Medicina, Universidade de São Paulo.,2000.

STEENWEG-DE GRAAFF, J. C. et al. Maternal LC-PUFA status during pregnancy and child problem behavior: the Generation R Study. **Pediatric research,** v. 77, n. 3, p. 489, 2015. ISSN 1530-0447.

SINN, N.; BRYAN, J. Effect of supplementation with polyunsaturated fatty acids and micronutrients on ADHD-related problems with attention and behaviour. Journal of Developmental and Behavioral Pediatrics, 2007,

SMUTS, C. M. et al. A randomized trial of docosahexaenoic acid supplementation during the third trimester of pregnancy. **Obstetrics Gynecologist,** v. 101, n. 3, p. 469-79, Mar 2003. ISSN 0029-7844 (Print) 0029-7844 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/12636950 >.

SONTROP, J.; CAMPBELL, M. K. ω-3 polyunsaturated fatty acids and depression: a review of the evidence and a methodological critique. **Preventive medicine,** v. 42, n. 1, p. 4-13, 2006.

SOUZA, R. A criança na família em transformação: um pouco de reflexão e um convite à investigação. Psic Rev 1997;(5): 33-51. SOUZA, Celina. Políticas Públicas: uma revisão da literatura. In: **Sociologia** (16), 209-244, 2006

SPIELBERGER, C. D. **State-Trait anxiety inventory**: Wiley Online Library, 2010.
STEIN, A., ARTECHE, A., LEHTONEN, A., CRASKE, M., HARVEY, A., COUNSELL, N., & MURRAY, L. Interpretation of infant facial expression in the context of maternal postnatal depression. **Infant Behavior and Development,** *33*(3), 273-278, 201

SPRECHER, H. et al. Reevaluation of the pathways for the biosynthesis of polyunsaturated fatty acids. **Journal of Lipid Research,** v. 36, n. 12, p. 2471-2477, 1995.

SQUIRE, L. R. Memory and brain systems: 1969–2009. **Journal of Neuroscience,** v. 29, n. 41, p. 12711-12716, 2009.

STERNBERG, R. J.; BEN-ZEEV, T. **Complex cognition: The psychology of human thought**. Oxford University Press, 2001.

STRAIN, J. J. et al. Prenatal exposure to methyl mercury from fish consumption and polyunsaturated fatty acids: associations with child development at 20 mo of age in an observational study in the Republic of
Seychelles. **American Journal of Clinical Nutrition,** v. 101, n. 3, p. 530-7, Mar 2015. ISSN 0002-9165.

STUSS, D. T.; ALEXANDER, M. P. Executive functions and the frontal lobes: a conceptual view. **Psychological research,** v. 63, n. 3-4, p. 289-298, 2000.

SUDFELD, C. R. et al. Malnutrition and Its Determinants Are Associated with Suboptimal Cognitive, Communication, and Motor Development in Tanzanian Children–3. **The Journal of nutrition,** v. 145, n. 12, p. 2705-2714, 2015.

SU, K.-P., CHIU, T.-H., HUANG, C.-L., HO, M., LEE, C.-C., WU, P.-L., & CHIU, W.-C. Different cutoff points for different trimesters? The use of Edinburgh Postnatal Depression Scale and Beck Depression Inventory to screen for depression in pregnant Taiwanese women. **General hospital psychiatry***, 29*(5), 436-441, 2007

SUNDELIN-WAHLSTEN, V.; HALLBERG, G.; HELANDER, A. Higher alcohol consumption in early pregnancy or low-to-moderate drinking during pregnancy may affect children's behaviour and development at one year and six months. **Acta Paediatrica,** v. 106, n. 3, p. 446-453, 2017.

TEIXEIRA, J. M.; FISK, N. M.; GLOVER, V. Association between maternal anxiety in pregnancy and increased uterine artery resistance index: cohort based study. **BMJ,** v. 318, n. 7177, p. 153-7, Jan 16 1999. ISSN 0959-8138 (Print) 0959-535X (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/9888905 >.

TENDAIS, I., COSTA, R., CONDE, A., & FIGUEIREDO, B.. Screening for depression and anxiety disorders from pregnancy to postpartum with the EPDS and STAI. **The Spanish journal of psychology***, 17*, 2014.

THATCHER, R. W. Maturation of the human frontal lobes: Physiological evidence for staging. **Developmental Neuropsychology,** v. 7, n. 3, p. 397-419, 1991.

THELEN, E. et al. The dynamics of embodiment: a field theory of infant perseverative reaching. **Behavioral Brain Science,** v. 24, n. 1, p. 1-34; discussion 34-86, Feb 2001. ISSN 0140-525X (Print)0140-525X (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/11515285 >.

THOMPSON, L. U.; CUNNANE, S. C. **Flaxseed in human nutrition**. AOCS Press, 2003.

TRONICK, E., & RECK, C. Infants of depressed mothers. **Harvard review of psychiatry***, 17*(2), 147-156, 2009

UAUY, R.; MENA, P.; ROJAS, C. Essential fatty acids in early life: structural and functional role. **Procedings of the Nutrition Society,** v. 59, n. 1, p. 3-15, Feb 2000. ISSN 0029-6651 (Print) 0029-6651 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/10828169 >.

UAUY, R. et al. Role of essential fatty acids in the function of the developing nervous system. **Lipids,** v. 31 Suppl, p. S167-76, Mar 1996. ISSN 0024-4201 (Print) 0024-4201 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/8729114 >.

VAIVADA, T. et al. Evidence-based interventions for improvement of maternal and child nutrition in low-income settings: what's new? **Current Opinion in Clinical Nutrition & Metabolic Care,** v. 20, n. 3, p. 204-210, 2017. ISSN 1363-1950.

VALENT, F. et al. Associations of prenatal mercury exposure from maternal fish consumption and polyunsaturated fatty acids with child neurodevelopment: a prospective cohort study in Italy. **Journal of Epidemiology,** v. 23, n. 5, p. 360-70, Sep 05 2013. ISSN 1349-9092 (Electronic)0917-5040 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/23933621 >.

VAN DEN BERGH, B. R. et al. Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: links and possible mechanisms. A review. **Neuroscience & Biobehavioral Reviews,** v. 29, n. 2, p. 237-258, 2005. ISSN 0149-7634.

VAN GOOR, S. A. et al. The influence of supplemental docosahexaenoic and arachidonic acids during pregnancy and lactation on neurodevelopment at eighteen months. **Prostaglandins, Leukotrienes and Essential Fatty Acids (PLEFA),** v. 84, n. 5, p. 139-146, 2011. ISSN 0952-3278.

VERHAGEN, A. P. et al. The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. **Journal of clinical epidemiology,** v. 51, n. 12, p. 1235-1241, 1998. ISSN 0895-4356.

VOLLET, K. et al. Prenatal fish oil supplementation and early childhood development in the Upstate KIDS Study. **Journal of Developmental Origins of Health and Disease**, p. 1-9, 2017. ISSN 2040-1744.

WALKER, S. P., WACHS, T. D., GRANTHAM-MCGREGOR, S., BLACK, M. M., NELSON, C. A., HUFFMAN, S. L., LOZOFF, B. Inequality in early childhood: risk and protective factors for early child development. **The Lancet***, 378*(9799), 1325-1338, 2011.

WEISER, M. J.; BUTT, C. M.; MOHAJERI, M. H. Docosahexaenoic Acid and Cognition throughout the Lifespan. **Nutrients,** v. 8, n. 2, p. 99, Feb 17 2016. ISSN 2072-6643 (Electronic) 2072-6643 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/26901223 >.

WEISS, L. G.; OAKLAND, T.; AYLWARD, G. P. **Bayley-III clinical use and interpretation**. Academic Press, 2010. ISBN 0080921078.

WEISS, L. G.; OAKLAND, T.; AYLWARD, G. P. **Bayley-III clinical use and interpretation**. Academic Press, 2010. ISBN 0080921078.

WOOLHOUSE, H. et al. Maternal depression from early pregnancy to 4 years postpartum in a prospective pregnancy cohort study: implications for primary health care. **BJOG: An International Journal of Obstetrics & Gynaecology,** v. 122, n. 3, p. 312-321, 2015. ISSN 1471-0528.

YEHUDA, S.; RABINOVITZ, S.; MOSTOFSKY, D. Essential fatty acids and the brain: from infancy to aging. **Neurobiology of aging,** v. 26, n. 1, p. 98-102, 2005. ISSN 0197-4580.

YEHUDA, S.; RABINOVITZ, S.; MOSTOFSKY, D. I. Essential fatty acids and the brain: from infancy to aging. **Neurobiology of Aging,** v. 26 Suppl 1, p. 98-102, Dec 2005. ISSN 0197-4580 (Print) 0197-4580 (Linking). Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/16226347 >.

YELL, M. L.; SHRINER, J. G.; KATSIYANNIS, A. Individuals with disabilities education improvement act of 2004 and IDEA regulations of 2006: Implications for educators, administrators, and teacher trainers. **Focus on exceptional children,** v. 39, n. 1, p. 1, 2006. ISSN 0015-511X.

YIN, R. **Case study research: Design and methods . Beverly Hills**: CA: Sage publishing 1994.

YONKERS, K. A. et al. Association of Panic Disorder, Generalized Anxiety Disorder, and Benzodiazepine Treatment During Pregnancy With Risk of Adverse Birth Outcomes. **JAMA psychiatry,** v. 74, n. 11, p. 1145-1152, 2017.

ZELAZO, P. D. et al. The development of executive function in early childhood. **Monographs of the society for research in child development**, p. i-151, 2003.