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Relação Mãe-Bebê: comportamento, cognição e inflamação

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RESUMO

A relação mãe-bebê é um complexa interação entre dois indivíduos que pode trazer consequências no desenvolvimento infantil a longo prazo e aumentar o risco de psicopatologias. Alguns comportamentos maternos parecem ser mais benéficos para o desenvolvimento infantil, como a habilidade materna de perceber e se adequar às demandas de seu bebê, ter afeto positivo em relação a ele e a forma como a mãe o olha, toca e fala com ele. A presente tese buscou analisar fatores que possivelmente influenciam a habilidade materna de se tornar sensível às necessidades de seu bebê, tendo como principais focos o processamento cognitivo e fatores inflamatórios maternos. Oitenta e duas mães foram visitadas em suas casas um mês após o parto a fim de analisarmos o comportamento materno através do manual *Coding Interactive Behavior* (CIB), verificarmos o processamento cognitivo materno através de uma tarefa *go/no-go* com faces de adultos e bebês expressando diferentes emoções como estímulo e realizarmos uma coleta de sangue para análise de interleucinas inflamatórias. Os três artigos produzidos para esta tese reforçam a importância do processamento cognitivo materno na interação mãe-bebê. O primeiro deles é um artigo de revisão sobre viés atencional para faces infantis, sugerindo que este viés atencional é influenciado por diversos fatores, incluindo a parentalidade. O segundo e terceiro artigos foram elaborados utilizando a pesquisa original realizada para a presente tese. No segundo artigo, é demonstrada uma correlação positiva entre maior engajamento do sistema atencional para faces de bebês em sofrimento e a habilidade materna de perceber, interpretar e responder adequadamente aos sinais emitidos pelo bebê. O terceiro artigo integra três diferentes aspectos maternos que parecem se relacionar com a sensibilidade materna: o tempo de reação materna na tarefa de processamento cognitivo, o nível sérico de interleucina 6 (Il-6) e o nível socioeconômico materno. A forma com que a mãe olha, toca, fala com seu bebê e seu afeto durante a interação se correlacionou com o maior engajamento para faces independentemente da emoção expressa. A Il-6 esteve correlacionada negativamente com o comportamento materno sensível e positivamente com o tempo de reação na tarefa de processamento cognitivo. Os níveis periféricos de Il-6 e o comportamento materno diferiram conforme o nível socioeconômico materno, sendo que um nível socioeconômico mais baixo apresentou níveis mais elevados de Il-6 e menos comportamento materno sensível.

Esta tese reforça a ideia de que múltiplos fatores, como o processamento cognitivo, inflamação e nível socioeconômico influenciam a delicada relação mãe-bebê desde o pós-parto, e podem ser marcadores da vulnerabilidade dessa relação, ou de um comportamento materno menos sensível.

Palavras-chave: relação mãe-bebê, sensibilidade materna, processamento cognitivo, interleucina 6, nível socioeconômico

ABSTRACT

The mother-infant relationship is a complex interaction that might have long-term impact on child development and risk for psychopathology. Some maternal behaviors seem to be essential to optimize infant development, such as the maternal ability to perceive and adjust to the demands of the newborn, a positive affect towards the child, and the way she looks, touches, and talks to her infant. The present thesis sought to analyze factors that influence the maternal ability to become sensitive to her child's needs, having as main focuses the maternal cognitive processing and maternal inflammatory factors. Eighty-two mother and infant dyads were visited at home one month after delivery. In this encounter, mother-infant interaction was recorded for posterior analyses using the Coding Interactive Behavior (CIB) manual. Mothers also performed a go/no-go task with adult and infant faces expressing different emotions as stimulus as a measure of cognitive processing, and maternal blood was collected to analyze interleukins. The three articles produced for this thesis reinforce the importance of maternal cognitive processing for mother-infant interaction. The first article is a systematic review on attention bias towards infant faces, suggesting that this behavior is influenced by many factors including the parental status. The second and third articles used data of the original research carried out for the present thesis. In the second article we demonstrate a positive correlation between attentional engagement for infant faces of distress and the maternal ability to perceive, interpret and respond adequately to the signals emitted by the baby. The third article integrates three different aspects related to maternal sensitivity: maternal reaction time in cognitive processing task, serum levels of interleukin 6 (Il-6) and maternal income. The way the mother looks, touches and talks to her child, as well as her affect during the interaction correlates with greater engagement to infant and adults faces, independently of the expressed emotion. Il-6 was negatively correlated with sensitive maternal behavior and positively correlated with the reaction time in the cognitive processing task. Il-6 and maternal behavior differed according to maternal income, with lower income mothers having higher Il-6 levels and decreased scores of maternal behavior. This thesis reinforces the idea that multiple factors, such as cognitive processing, inflammation, and socioeconomic status, influence the delicate mother-infant relationship since the early postpartum period, highlighting markers of vulnerability to altered maternal sensitivity.

Key words: mother-infant relationship, maternal sensitivity, cognitive processing, interleukin 6, income

LISTA DE ABREVIATURAS E SIGLAS

ABIPEME: Critério Brasil de Classificação Econômica da Associação Brasileira dos Institutos de Pesquisa de Mercado
CIB: *Coding Interactive Behavior*
CPC-HCPA: Centro de Pesquisa Clínica do Hospital de Clínicas de Porto Alegre
CRP: proteína C reativa
EPDS: Escala de Depressão Pós-natal de Edimburgo
GHC: Grupo Hospitalar Conceição – Hospital Nossa Senhora da Conceição
GR: glicocorticoide
HAM-A: escala de Hamilton para ansiedade
HCPA: Hospital de Clínicas de Porto Alegre
HPA: hipotálamo-hipófise-adrenal
Il-10: interleucina 10
Il-1Ra: antagonista do receptor da interleucina 1
Il-1β: interleucina 1 beta
Il-6: interleucina 6
LPNeC: Laboratório de Psicologia Experimental, Neurociência e Comportamento da Universidade Federal do Rio Grande do Sul
MAB: *maternal affiliative behavior*
mRNA: acido ribonucleico mensageiro
ms: milissegundos
PBI: *parental bonding instrument*
SCID: Entrevista Clínica Estruturada para o Manual de Diagnóstico e Estatística das Perturbações Mentais IV – Versão Clínica
SPSS: *Statistical Package for the Social Sciences*
SUS: Sistema Único de Saúde
TCLE: termo de consentimento livre e esclarecido
TLR4: *toll-like receptor 4*
TNFα: fator de necrose tumoral alfa
TR adulto: tempo de reação materno nos blocos de faces de adultos
TR bebê: tempo de reação materno nos blocos de faces de bebês
UAMP: Unidade de Análises Moleculares e de Proteínas
UBS: Unidade Básica de Saúde
UFRGS: Universidade Federal do Rio Grande do Sul

SUMÁRIO

1. INTRODUÇÃO

A relação da mãe com o bebê na espécie humana e em outros mamíferos tem sido extensivamente estudada sob vários enfoques. Os estudos seminais de Ainsworth (1969), Bowlby (1979) e Winnicott (1975) lançam bases fundamentais na elaboração conceitual da relação mãe-bebê (1-3). No campo dos estudos observacional e experimental de várias outras espécies animais, Tinbergen e Lorenz (1961) desenvolvem conceitos básicos da relação parental e suas repercussões no desenvolvimento dos indivíduos da geração que se forma (4, 5). Os conhecimentos dos vários aspectos envolvidos na relação mãe-bebê, tais como psicológicos, cognitivos, além do desenvolvimento neural e fisiológicos, são essenciais. Podemos ressaltar três aspectos que tornam esses conhecimentos fundamentais: o recém-nascido não sobrevive sem o cuidado materno ou de um cuidador; seu desenvolvimento é influenciado pela interação mãe-filho; e a interação mãe-filho pode ter impacto transgeracional.

1.1. Comportamento Materno

A interação mãe-bebê é uma relação complexa e delicada, a qual servirá de padrão de relações interpessoais e de reações perante diversas situações ao longo da vida (2, 3, 6). O cuidado materno inicia-se ainda na gestação (com a adequada alimentação, abstinência de substâncias que possam ser teratogênicas, mudanças de hábitos e surgimento do vínculo) e prolonga-se ao longo da vida da prole, adaptando-se às diferentes fases. O repertório comportamental de cuidados maternos é vasto, englobando o suporte físico e emocional de sua prole. A mãe (ou cuidador) é responsável pela alimentação, higiene, afeto, acolhimento e entendimento das necessidades do bebê.

A relação que a mãe desenvolve com seu bebê nos primeiros anos de vida influencia o seu desenvolvimento neurobiológico, fisiológico e emocional (7-12). Estudos observacionais demonstram a associação positiva entre a responsividade materna a emoções de seu bebê com a formação de um apego seguro na relação mãe-bebê e também com o desenvolvimento cognitivo e emocional a longo prazo (11, 13-15). Na mesma linha, estudos descrevem a associação entre distúrbios na interação mãe-bebê e sintomas de sofrimento psíquico e psicopatologias ao longo da vida (16, 17).

Há indicativos de que os primeiros meses após o parto são um período sensível no neurodesenvolvimento humano (18). Raby *et al.,* 2015 utilizam dados de um estudo prospectivo longitudinal que acompanhou indivíduos do nascimento até os 32 anos de vida para propor que a sensibilidade materna nos primeiros três anos prediz a capacidade de estabelecer relações positivas com os pares na infância e adolescência, de estabelecer relações amorosas e um bom cuidado parental na sua vida adulta. Para Raby *et al*., 2015, esta é uma sequência que se alimenta progressivamente: quanto mais sensível o cuidado recebido, melhor será a relação com os pares; isso influenciará a capacidade de estabelecer vínculos amorosos estáveis, o que por sua vez afeta a qualidade do cuidado proporcionado à prole (7).Relações disfuncionais e transtornos psiquiátricos maternos durante a gestação e nos primeiros anos de vida da criança impactam negativamente o desenvolvimento infantil (16, 19-22). A revista *Lancet* em novembro de 2014 publicou três revisões a respeito da saúde mental materna no período perinatal (16, 23, 24). No artigo *Effects of perinatal mental disorders on the fetus and child* são abordadas as consequências de transtornos psiquiátricos maternos durante a gestação e no puerpério para o feto e o bebê (16). Neste interessante artigo, Stein *et al.,* 2014 apontam para a relação dos transtornos mentais maternos, sendo depressão puerperal o mais estudado, com alterações no desenvolvimento da prole: dificuldades de sociabilização ao longo da infância, pior desenvolvimento cognitivo, mais sintomas e episódios depressivos na infância e adolescência. De grande importância, os autores ressaltam que o cuidado parental atua como mediador da relação entre transtornos psiquiátricos e o desenvolvimento infantil. E de especial interesse para o Brasil está o dado de que o baixo nível socioeconômico possa ser um agravante dessa relação entre os transtornos mentais maternos e o desenvolvimento da prole(16).

Transtornos psiquiátricos maternos podem ser relacionados a alterações dramáticas na interação entre mães e filhos, porém mesmo modificações mais sutis do comportamento materno parecem estar associadas a alterações persistentes no desenvolvimento das crianças. Com o avanço das pesquisas sobre relação mãe-bebê, a análise dessa interação pode ser refinada. Além de se pesquisar casos extremos, como comparar mães deprimidas a mães não deprimidas, passou-se a avaliar também variações comportamentais maternas sutis que poderiam ser benéficas para a prole (18).

Estudos relacionam a influência de determinados fatores ambientais do início da vida com alterações no desenvolvimento e na expressão da carga genética do indivíduo, determinando um padrão de saúde-doença peculiar. Agravos ambientais ocorridos na vida fetal ou nas fases iniciais da vida extrauterina relacionam-se com o surgimento de doenças crônicas ao longo da vida (25). Vários estudos em roedores demonstram que o cuidado materno e o ambiente neonatal influenciam o desenvolvimento do filhote a longo prazo e a próxima geração através de alterações epigenéticas (18, 26-29). Déficits na qualidade do cuidado materno ofertado no início da vida estão associados à redução na expressão de receptores glicocorticoides no hipocampo, afetando a retroalimentação negativa do eixo hipotálamo-hipófise-adrenal, e, portanto, modificando a resposta dos indivíduos a estímulos estressores na vida adulta (29).

Além disso, cada vez mais fica evidenciado que a qualidade dos cuidados oferecidos para a prole no início da vida se associa ao nível de cuidados que ela será capaz de promover para a sua própria prole (30). Existem evidências de transmissão transgeracional de traços afetivos, estilo parental e aspectos maternais como apego e vínculo (31, 32). Nesse sentido, os benefícios de programas de intervenção precoce podem ser ainda maiores do que os geralmente relatados, tendo em vista a transgeracionalidade do estilo parental e a possível transmissão do efeito da intervenção entre gerações (7, 10, 17). Ou seja, promovendo a saúde mental de uma díade possivelmente abre-se o caminho para proporcionar uma relação mais sensível e adaptada nas gerações futuras.

Dentro do espectro de cuidados maternais, alguns elementos da relação mãe-bebê parecem ser decisivos para o desenvolvimento do bebê (18). O termo “sensibilidade materna” aparece na literatura como sendo um comportamento materno positivo, relacionado à formação de vínculos seguros entre a mãe e o bebê e ao desenvolvimento infantil favorável como um todo. A sensibilidade materna é caracterizada pela habilidade da mãe de entrar em contato com o filho através da comunicação verbal e não verbal, de perceber, interpretar e responder de forma adequada aos sinais de seu bebê (33). Nos primeiros meses de vida, o afeto positivo, o olhar para a face do bebê, o toque afetuoso (como, por exemplo, abraçar, beijar, fazer carinho) e o “mamanhês” (fala em tom mais agudo de uso frequente quando se conversa com bebês) são comportamentos associados a uma melhor qualidade de cuidado materno. Esses comportamentos devem estar coordenados com sinais emitidos pelo bebê para o estabelecimento de uma maternagem sensível (18, 34-36).

O grupo da Professora Dra. Ruth Feldman (Bar-Ilan University, Israel) desenvolve trabalhos de pesquisa na área da relação mãe-bebê que contribuem de maneira expressiva para o conhecimento desta complexa relação, integrando medidas comportamentais, de neuroimagem e hormonais. Em 1998, Feldman estabelece um manual de codificação de interações pais/ filhos, o *Coding Interactive Behavior* (CIB). Este se baseia na pesquisa da autora e em outras fontes importantes como Bowlby, Stern, Winnicott, Mahler, entre outros. Esse manual é composto por 43 itens, sendo 22 referentes ao comportamento de adultos, 16 infantis e cinco itens referentes à dupla. Cada item é pontuado entre um e cinco conforme a frequência e a intensidade do comportamento avaliado. O manual inicialmente foi criado para ser utilizado na codificação da relação mãe/pai-bebê de dois a 36 meses e foi ampliado para versões de codificação da relação com recém-nascidos, adolescentes e codificação de interação familiar não diádica.

Através do uso do manual, criaram-se seis constructos de caráter interativo para o primeiro ano de vida (que focam na interação e momentos de sincronia da díade): sensibilidade parental (*parental sensitivity*), “invasão” parental (*parental intrusiveness*), envolvimento social da criança (*child social involvement*), estado emocional negativo da criança (*child negative emotionality*), reciprocidade diádica (*dyadic reciprocity*) e estados diádicos negativos (*dyadic negative states*). Através desse manual, o grupo da autora ampliou o conhecimento da relação mãe-bebê de forma consistente e significativa. Diversos estudos foram realizados e publicados utilizando o CIB, incluindo coortes que acompanham as famílias desde o nascimento do bebê. Esses estudos apontam a relação entre características do comportamento materno avaliado pelo CIB e o desenvolvimento infantil (18).

1.2 Processamento Cognitivo

Diversos autores já revisaram e enfatizaram a importância do processamento cognitivo para o desenvolvimento da sensibilidade materna (17, 37, 38). Em destaque está a capacidade materna de perceber diferentes sinais, por muitas vezes sutis, emitidos pelo bebê e de priorizar estímulos e demandas do bebê em ambientes complexos com diferentes níveis de estimulação (17).

Sander *et al.,* 2003 propõem que a saliência de um estímulo não depende apenas de suas características de medo e ameaça. Eles sugerem que a amígdala tem um papel de detector de relevância do estímulo para priorizar seu processamento, a fim de desencadear o comportamento adequado para cada situação. O processamento cognitivo, principalmente a atenção, é modulado pela relevância biológica do estímulo para sobrevivência, pelo aprendizado prévio em relação ao estímulo e por sua capacidade de estimular o sistema de recompensa (39, 40). Nesse contexto, faces humanas parecem ser estímulos salientes a serem priorizados pelo sistema de atenção. Bindemann *et al.,* 2005 demonstraram a preferência do sistema de atenção de adultos por faces de outros adultos, conhecidos e desconhecidos, em relação a objetos e a grafia de nomes de pessoas conhecidas (41).

Tendo em vista a importância do sistema de atenção no comportamento materno, o primeiro artigo elaborado para esta tese visa analisar se faces de bebês podem ser consideradas um estímulo saliente o suficiente para serem priorizadas pelo sistema atencional de adultos (homens e mulheres) em relação a outros estímulos. O artigo de revisão sistemática "*Attentional Bias Toward Infant Faces – Review of the Adaptive and Clinical Relevance*", publicado na revista *International Journal of Psychophysiology* (página 31), reúne um conjunto de dados evidenciando que faces de bebês são um estímulo saliente para adultos, sendo que a intensidade da saliência é influenciada pela parentalidade e sexo do participante. Faces de crianças capturam mais a atenção de mulheres do que de homens e mais de mães e pais do que de pessoas sem filhos (42).

Em mulheres que são mães, a maior saliência de faces de bebês provavelmente tem relação com a importância que o cuidado materno desempenha na sobrevivência da espécie humana. A maior atenção para sinais infantis pode ter sido uma adaptação evolutiva, já que nos primeiros meses após o nascimento a comunicação do bebê é predominantemente não verbal (43). A visualização de faces humanas ativa regiões do sistema nervoso central relacionadas à atenção (região parietal, sulco intraparietal, pre-cúneo e córtex cingulado anterior), ao processamento de emoções (córtex orbitofrontal, córtices cingulado anterior e medial, ínsula) e de prazer (por exemplo: núcleo accumbens e amígdala), à empatia (córtex cingulado anterior) e ao comportamento motor (por exemplo: giro frontal superior), sendo que estímulos envolvendo faces de crianças geram ativação de maior intensidade nessas regiões do que estímulos com faces de adultos (37, 44, 45). Desta forma, possivelmente o processamento cognitivo de faces infantis desencadeia o comportamento da mãe.

De fato, estudos de neuroimagem demonstram que mães com diferentes características de comportamento materno apresentam variações na ativação cerebral quando expostas a imagens e sons de crianças (46-49). Mães com comportamento mais sensível em relação ao bebê apresentam ativação mais sincrônica da rede da amígdala medial (a rede da amígdala medial é descrita pelos autores como conexão entre núcleo accumbens, amígdala medial, hipotálamo rostral, córtex pré-frontal ventromedial, córtex cingulado anterior subgenual e córtex cingulado posterior) do que mães menos sensíveis (50). Os mesmos autores em estudo anterior já haviam demonstrado que mães que apresentavam maior sensibilidade materna, avaliada por suas habilidades em perceber sinais emitidos pelo bebê e reagir de forma adequada a eles, apresentam diferenças no padrão de ativação neuronal quando comparadas a mães com comportamento invasivo. O comportamento materno invasivo neste estudo foi caracterizado por momentos em que a mãe interrompe, redireciona a atenção ou estimula de forma inapropriada o bebê sem respeitar os sinais emitidos por ele. Enquanto a sensibilidade é caracterizada por uma interação orientada pelos sinais do bebê , no comportamento invasivo o desejo da mãe direciona a interação mesmo que se oponha aos sinais emitidos pelo bebê. Um exemplo de comportamento invasivo é estimular fisicamente ou com aumento da intensidade da voz um bebê que está bocejando, emitindo sinais de que está com sono. Ao serem expostas a vídeos de seus filhos, mães com maior sensibilidade apresentam maior ativação do núcleo accumbens esquerdo e menor da amígdala direita do que mães invasivas (47). As mães com maior sensibilidade apresentam um padrão organizado e previsível de ativação dessa circuitaria límbica durante a visualização do comportamento maternal com seu próprio filho; já as mães com comportamento invasivo apresentam um padrão não organizado de funcionamento desta mesma região (47). Ambos estudos reforçam a importância do sistema de recompensa e empatia para a sensibilidade materna, em especial a importância da organização da ativação dessas regiões para o comportamento materno.

Estudos que não utilizam neuroimagem também evidenciam a associação entre diferenças no processamento de estímulos com alterações do comportamento materno (51-54). A Dra. Rebecca Pearson (Bristol University) desenvolveu uma tarefa de processamento cognitivo do tipo *go/no-go* utilizando faces de bebês e adultos expressando emoções (52). A tarefa é composta por seis blocos (três representando faces infantis e três representando adultos), sendo que cada bloco possui faces expressando uma emoção diferente (alegre/neutro/sofrimento nos bebês, alegre/neutro/com medo nos adultos). A tarefa tem por objetivo avaliar o engajamento do sistema atencional por cada estímulo através do tempo de reação para cada bloco. Em uma sequência de artigos, Pearson demonstra que gestantes ao longo da gravidez apresentam viés atencional para faces de bebês em sofrimento. A autora argumenta que a maior saliência do sofrimento infantil para o sistema atencional materno pode ser adaptativo devido à importância de a mãe perceber o sofrimento do bebê de forma prioritária, tendo em vista que esse pode significar um maior risco para a integridade física ou emocional do bebê (51, 52, 55, 56).

No artigo *Depressive symptoms in early pregnancy disrupt attentional processing of infant emotion*, utilizando sua tarefa de processamento cognitivo, Pearson e seus colegas concluíram que gestantes com sintomas depressivos apresentam alteração do processamento cognitivo de faces infantis expressando sofrimento. Diferentemente de mães sem sintomas depressivos, mães com sintomas depressivos não apresentam viés atencional para faces de bebês em sofrimento (52). O viés atencional para faces de bebê em sofrimento foi calculado subtraindo a média do tempo de reação nos blocos com faces de bebês alegres e neutros do tempo médio de reação dos bebês em sofrimento. Seguindo as mesmas participantes ao longo da gestação e puerpério, a equipe de pesquisadores demonstrou que gestantes com maior viés atencional para faces de sofrimento infantil posteriormente descrevem ter melhor vínculo no pós-parto com seu bebê através de um questionário autoaplicável (51). A tarefa *go/no-go* utilizada pela Dra. Pearson nestes estudos parece ser uma interessante medida do processamento cognitivo materno de diferentes emoções infantis. Apesar dos resultados importantes descritos pela Dra. Pearson e seus colegas , não há dados que correlacionem o processamento cognitivo de faces infantis nessa tarefa com medidas comportamentais da relação mãe-bebê para podermos afirmar que o maior engajamento do sistema atencional para faces de sofrimento está efetivamente relacionado à maior sensibilidade materna.

1.3. Interleucinas Maternas

Tanto aspectos ambientais como biológicos são capazes de influenciar o comportamento materno e também suas várias etapas do processamento cognitivo. O papel do sistema imune, em especial das interleucinas, no comportamento humano tem sido alvo de estudos nos últimos anos. O sistema imune interage com o eixo hipotálamo-hipófise-adrenal (HPA) e com os sistemas serotoninérgico e dopaminérgico (57). Alguns estudos sugerem que estas interações sejam o motivo pelo qual a neuroinflamação está relacionada a transtornos psiquiátricos como depressão, transtorno de humor bipolar e esquizofrenia (57, 58).

As interleucinas inflamatórias são capazes de alterar a ativação do sistema de recompensa, o que por sua vez é fundamental para a expressão do comportamento materno e para o processamento de estímulos (50, 59-61). Um estudo que injetou endotoxinas em humanos observou que índices mais altos de Il-6 e fator de necrose tumoral alfa (TNFα) se correlacionam a um aumento na anedonia e a uma menor ativação do estriado ventral durante uma tarefa que estimulava antecipação de recompensa. Esse estudo sugere que o processo inflamatório influencia o sistema de recompensa diminuindo sua ativação (62). Interleucinas inflamatórias, em especial a Il-6, parecem influenciar o processamento cognitivo. Níveis mais altos de Il-6 estão correlacionados a prejuízo cognitivo em pacientes com doenças cardiovasculares, com cirrose, com transtorno de humor e em dependentes químicos (63-66).

O sistema imune é altamente permeável a estímulos ambientais. Por exemplo, baixo nível socioeconômico vem sendo consistentemente associado a maior nível de Il-6 periférico (67-70). Essa interferência inicia na infância, tendo efeito a longo prazo. Indivíduos criados em um ambiente socioeconômico desfavorável durante a infância apresentam níveis mais altos de Il-6 na vida adulta, sendo que o nível socioeconômico nos primeiros dois anos de vida parece ter um impacto ainda maior (67). Essa relação entre Il-6 e nível socioeconômico na infância é influenciada por eventos estressores e suporte social. Enquanto eventos negativos favorecem o aumento do Il-6 (71), o suporte social parece atuar de forma a reduzir a reatividade do Il-6 em situações de estresse em pessoas que cresceram em ambiente de baixa renda (72).

Apesar da importância do assunto, ainda há poucos estudos que integrem os diversos aspectos que podem influenciar a interação mãe-bebê em amostras comunitárias. Uma análise multidimensional relacionando fatores comportamentais, cognitivos, ambientais e biológicos maternos que podem influenciar a relação mãe-bebê é relevante pela complexidade e abrangência do tema. A caracterização de elementos emocionais, cognitivos, fisiológicos e ambientais que influenciam a delicada relação mãe-bebê pode auxiliar na identificação de díades mais vulneráveis e de possíveis pontos de intervenção.

2. OBJETIVOS

O objetivo do presente estudo foi analisar de forma integrada diferentes aspectos maternais que possam influenciar a relação mãe-bebê em amostra comunitária no primeiro mês após o parto. O trabalho desenvolveu-se através dos seguintes objetivos específicos:

- Revisar a literatura existente sobre viés atencional para faces infantis. Este objetivo resultou no artigo de revisão sistemática "*Attentional Bias Toward Infant Faces – Review Of The Adaptive And Clinical Relevance*", publicado na revista *International Journal of Psychophysiology* em abril de 2017, aqui apresentado no item 6.1, página 31.
- Analisar a correlação entre sensibilidade materna e processamento cognitivo de faces de bebês e adultos expressando diferentes emoções em uma tarefa go/ no-go. Os resultados deste objetivo estão expressos no artigo "*Correlation between Automatic Attention Engagement to Infant Faces and Behavioral Components of Maternal Sensitivity*", página 40, submetido à publicação na revista *Child Development*
- Avaliar a correlação de marcadores de neuroinflamação (interleucina 10 (Il-10), interleucina 1 beta (Il-1β), interleucina 6 (Il-6) e fator de necrose tumoral alfa (TNFα) e processamento cognitivo. Os resultados deste objetivo estão expressos no artigo "*Cognitive Processing, Inflammation, Environment and Maternal Behavior in Early Postpartum*"**,** página 50, submetido à publicação na revista *Biological Psychiatry* e página 78 item 6.4 dos resultados.
- Analisar a correlação entre marcadores de neuroinflamação e comportamento materno. Os resultados deste objetivo também estão expressos no artigo **"***Cognitive Processing, Inflammation, Environment and Maternal Behavior in Early Postpartum***",** página 50 submetido à publicação na revista *Biological Psychiatry.*

3. MATERIAIS E MÉTODOS

3.1. Universo e Amostragem

As participantes deste projeto são provenientes de dois serviços públicos de atendimento à saúde da cidade de Porto Alegre: usuárias do Sistema Único de Saúde (SUS) que frequentavam a Unidade Básica de Saúde Santa Cecília (UBS Santa Cecília) para o seu pré-natal ou que realizaram o parto no Hospital Nossa Senhora da Conceição (GHC) e que preenchiam os critérios de inclusão/exclusão para participar do projeto.

A UBS Santa Cecília fica localizada no bairro Santa Cecília, na região central de Porto Alegre. É vinculada ao Hospital de Clínicas de Porto Alegre (HCPA), à Universidade Federal do Rio Grande do Sul (UFRGS) e à Secretaria Municipal de Saúde. A UBS Santa Cecília é composta por quatro equipes de Saúde da Família. Seu atendimento abrange uma população estimada de 35 mil pessoas (73). Devido a sua localização geográfica, a população atendida apresenta nível socioeconômico heterogêneo, com famílias de classe média, baixa e alguns bolsões de extrema vulnerabilidade social.

O Hospital Nossa Senhora da Conceição é um hospital do SUS com nível de atendimento terciário localizado no bairro Cristo Redentor em Porto Alegre. Atende pacientes de diferentes regiões do Rio Grande do Sul, principalmente da capital. Sua maternidade está entre as maiores do estado, realizando mais de 4 mil partos ao ano.

Critérios de Inclusão

- idade igual ou superior a 18 anos;
- gestante ou puérpera no primeiro mês após o parto de nativivo;
- bebê hígido com nascimento a termo (igual ou superior a 37 semanas gestacionais) que tenha tido alta hospitalar com a mãe após o nascimento;
- morar em Porto Alegre.

Critérios de Exclusão

- gemelaridade;
- malformações congênitas fetais, síndromes congênitas no recém-nascido;

- alterações auditivas, visuais e doenças crônicas no recém-nascido;
- mães com dependência química a substâncias ilícitas;
- ter tido cinco ou mais gestações.

3.2. Logística

O projeto tinha como objetivo realizar três encontros com as participantes: o primeiro para convite, apresentação e aceite do Termo de Consentimento Livre e Esclarecido (TCLE) e coleta de dados sociodemográficos; o segundo e terceiro a serem realizados no domicílio das participantes aproximadamente um e três meses após o parto. Esta tese pretende abordar resultados referentes aos dois primeiros encontros, portanto, apenas a metodologia destes será descrita.

Contato Inicial:

Para participantes provenientes do GHC, o contato inicial ocorria na maternidade até 72 horas após o parto. Já as participantes provenientes da UBS Santa Cecília eram convidadas em uma de suas consultas de rotina do pré-natal e do puerpério ou enquanto aguardavam para fazer o teste do pezinho de seus bebês.

Neste primeiro momento, os pesquisadores explicavam o projeto para a gestante e/ou puérpera (e possíveis acompanhantes) e a convidavam a participar do estudo, juntamente com seu filho. Havendo interesse, o TCLE era apresentado, possíveis dúvidas esclarecidas e, se de acordo, a puérpera assinava o Termo.

Após o aceite, era preenchida uma ficha com os contatos da participante, dados obstétricos e o Critério Brasil de Classificação Econômica (ABIPEME) versão 2014 (74).

Ao final, uma nova data era marcada com a puérpera para que a equipe realizasse uma visita domiciliar. A mesma era confirmada por telefone antes da data combinada. No caso das gestantes, era proposto para as mesmas que a equipe manteria contato telefônico para saber da evolução da gestação e data do parto e então marcar a data da visita domiciliar.

Originalmente foi proposto que os encontros fossem realizados no Centro de Pesquisa Clínica do Hospital de Clínicas de Porto Alegre (CPC-HCPA). Após 31 mães terem aceitado participar do projeto e apenas cinco comparecerem ao encontro do primeiro mês no CPC-HCPA, a estratégia de coleta foi modificada para visita domiciliar.

Encontro um mês após o parto:

O primeiro encontro domiciliar ocorria entre 25 e 40 dias após o parto no período da tarde (entre 14 e 18 horas). O encontro durava cerca de 1 hora e 30 minutos.

Ao chegar ao domicílio da participante, explicava-se como ocorreria o encontro. Tentava-se manter sempre a mesma ordem de acontecimentos, porém conforme a disponibilidade do bebê por vezes a rotina era modificada.

Iniciava-se com o preenchimento do questionário geral de quatro semanas após o parto. Este contém informações clínicas a respeito da mãe e do bebê.

Logo após, a puérpera realizava uma tarefa de processamento cognitivo com faces de adultos e bebês expressando diferentes emoções com duração de cerca de 15 minutos. A tarefa era realizada em computador portátil levado pela equipe de pesquisa.

Enquanto a puérpera realizava a tarefa de processamento cognitivo, o bebê era avaliado através do Roteiro de Avaliação do Comportamento Visuomotor do Lactente, para avaliação e qualificação das funções oculomotoras (fixação visual, contato ocular, exploração visual do ambiente, seguimento visual horizontal) e apendiculares (aumento da movimentação de membros superiores, estender o braço em direção ao objeto visualizado), com duração máxima de dez minutos (75).

Na sequência, mãe e filho eram filmados em interação livre por cinco minutos. A mãe era orientada a agir de forma mais natural possível com seu bebê. Após a filmagem da interação mãe-bebê, eram aplicadas a Entrevista Clínica Estruturada para o DSM-IV – Versão Clínica (SCID) e a escala de Hamilton para ansiedade (HAM-A) por psiquiatra treinada, e a participante respondia à Escala de Depressão Pós-natal de Edimburgo (EPDS).

A visita terminava com a coleta da saliva materna e do bebê, leite e sangue materno. Coletadores treinados realizavam a retirada de sangue. A amostra de leite era coletada pela própria participante.

3.3. Instrumentos e Medidas

<u>Tarefa de Processamento Cognitivo:</u>

A tarefa de processamento cognitivo empregada no projeto foi desenvolvida pelo grupo do Laboratório de Psicologia Experimental, Neurociência e Comportamento (LPNeC/UFRGS). Este grupo baseou-se na tarefa de processamento cognitivo utilizada por Pearson (51, 52, 55, 56) fazendo uso dos mesmos parâmetros para elaborar o instrumento com imagens de faces validadas para a população brasileira (76).

A tarefa consiste em um teste do tipo *go/no-go,* composto por dois blocos de treino e seis blocos-testes. Cada bloco-teste apresenta 30 imagens de estímulo. Os estímulos de interesse são imagens de faces de adultos e crianças expressando diferentes emoções; no caso de adultos, medo, neutralidade e alegria, e nos bebês, sofrimento (expressão de choro), neutralidade e alegria (bebê sorrindo). Entre cada bloco existe uma tela de intervalo na qual a participante decide quando retornar à tarefa.

O teste inicia com o aparecimento de uma cruz preta no centro da tela. Logo em seguida, no fundo da tela aparece uma imagem de estímulo por vez, sobreposta por uma cruz vermelha ou verde centralizada na imagem. Após o aparecimento dessas imagens surgirá uma linha vertical e uma horizontal na periferia da tela. As participantes são instruídas a ignorar a imagem atrás da cruz e responder se a linha vertical está à esquerda ou à direita da tela quando a cruz for verde (*go trial*) e a apenas apertar a tecla de espaço quando a cruz for vermelha (*no-go trial*). A imagem com a cruz à frente e as linhas apareceram por 240 milissegundos (ms). A seguir, uma tela branca surgirá aguardando a resposta da participante. O tempo de reação para cada estímulo é computado em milissegundos. A Figura 1 representa um modelo gráfico da tarefa de processamento cognitivo. Na figura se utilizou o desenho de um rosto, enquanto na tarefa foram utilizadas fotos de faces.

Quanto maior a atenção voltada para o estímulo atrás da cruz, mais tempo a pessoa leva para deslocar sua atenção deste para as linhas na periferia, ou seja, haverá maior tempo de reação computado pelo programa. A tarefa visa avaliar atenção não propositalmente dirigida ao estímulo.

A tarefa experimental é apresentada em um notebook da marca Dell, com monitor de 15 polegadas, e respostas são dadas por meio de duas telas de uma caixa de resposta serial do E-prime (Psychology Software Tools, Inc., EUA). O software E-prime é utilizado para o controle do tempo de exposição e registro das respostas. O software também controla a randomização das imagens.

Figura1. Modelo da Tarefa de Processamento Cognitivo

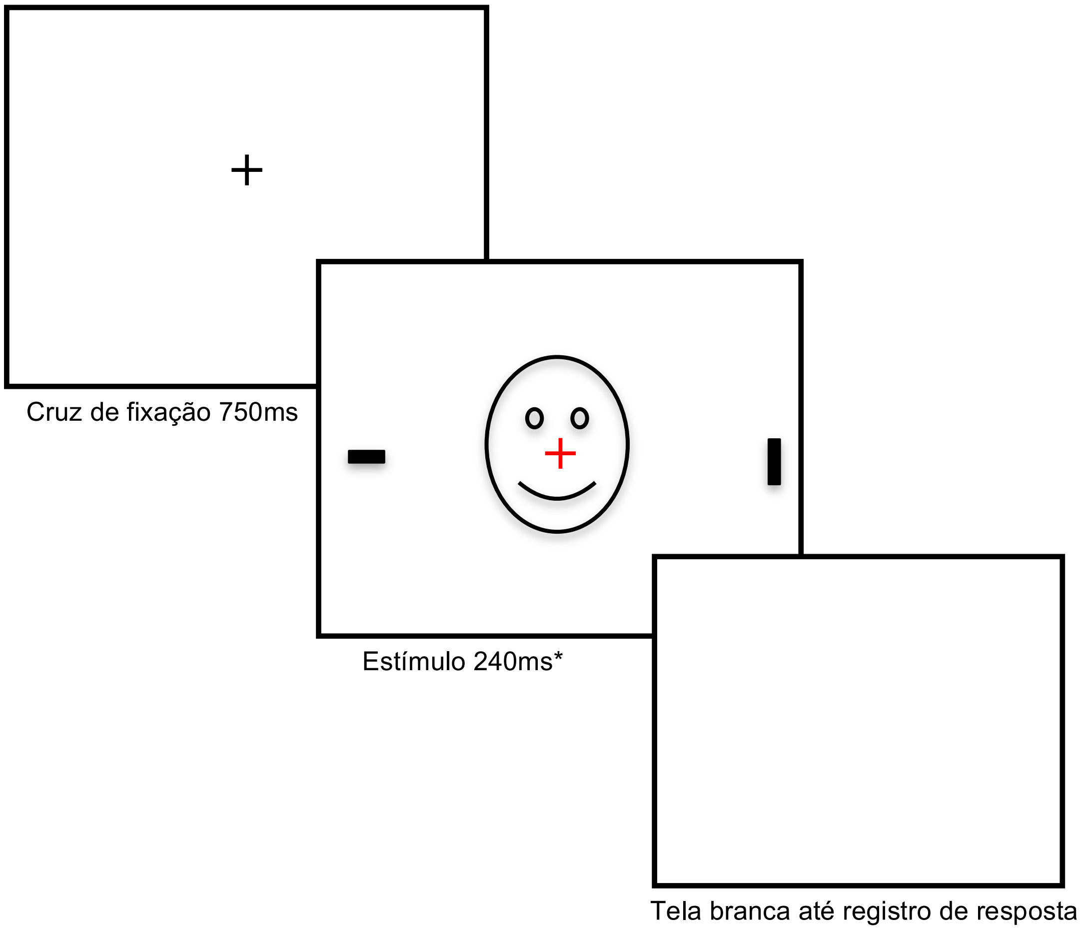

*Imagem de face meramente ilustrativa, a tarefa de processamento cognitivo utilizou fotos de adultos e bebês.

Relação Mãe-Bebê – *Coding Interactive Behavior*:

A avaliação da interação mãe-bebê é realizada através do *Coding Interactive Behavior* (CIB), utilizando a versão para recém-nascidos (77).

A codificação para recém-nascidos consiste em uma análise detalhada dos cinco minutos de interação livre entre a mãe e seu bebê. A cada dez segundos deve-se pontuar comportamentos maternos e do bebê que ocorreram naquele período.

São avaliados cinco comportamentos maternos, que podem ser categorizados da seguinte forma:

1. Olhar materno: olha para a face e o corpo do bebê, para o ambiente, para outra pessoa ou para um brinquedo, com atenção conjunta.
2. Afeto materno: positivo, neutro, negativo.
3. Vocalização materna: fala em “mamanhês” (voz frequentemente utilizada para se falar com bebês caracterizada pelo tom mais agudo), fala com o bebê como se falasse com um adulto, fala com outra pessoa, canta, permanece em silêncio.
4. Toque materno: toque afetuoso, manipulação das extremidades, toque proprioceptivo (por exemplo, trocar o bebê de posição), balançar, toque funcional (por exemplo, trocar fralda/roupa/limpar o bebê), toque com objeto, toque estimulatório, toque passivo, sem toque.
5. Posição mãe-bebê: embalando no colo, carregando contra o ombro, segurando no ar, no colo, sem ser segurado pela mãe (por exemplo, bebê está no berço).

E são pontuados três comportamentos do bebê:

1. Vocalização: choro/gemido, vocalizações neutras ou positivas, sem vocalização.
2. Estado de alerta: olha para a face da mãe, olha para o ambiente, olha para um brinquedo ou objeto, cansado/sonolento, dormindo.
3. Afeto: positivo, neutro ou negativo.

Ao final da codificação se tem a proporção de tempo que a mãe e o bebê realizaram cada comportamento. Em seus artigos referentes aos primeiros dois meses de vida, o grupo da Dra. Ruth Feldman frequentemente utiliza o termo *maternal affiliative behavior* como medida de sensibilidade materna. O *maternal* *affiliative behavior* é obtido pela soma dos tempos em que a mãe toca de forma afetuosa seu bebê, utiliza o "mamanhês" em sua fala, tem afeto positivo durante a interação e olha para a face do bebê.

Além da codificação, a cada dez segundos, três itens da atitude materna são pontuados durante os cinco minutos de interação mãe-bebê: *parental acknowledging*, *parental intrusiveness* e *parental affect*. Esses itens não são avaliados a cada dez segundos e sim ao se considerar toda a interação. Seu escore varia de um a cinco, sendo que um sugere que o comportamento avaliado ocorre muito pouco e cinco que ocorre em sua máxima intensidade. O *parental acknowledging* reflete a habilidade materna de estar atenta e receptiva aos sinais emitidos pelo seu bebê e de responder de forma adequada aos mesmos. O *parental intrusiveness* é caracterizado pelo comportamento da mãe de interromper a atividade do bebê, redirecionar a atenção do bebê para ações de interesse materno ou propostas por ela. *Parental affect* representa o afeto expresso pela mãe durante a interação.

A aplicação do Manual do CIB exige treinamento teórico e prático com os autores do instrumento. O mesmo foi realizado, obtendo escore de reabilidade interna de 81% e autorização para o uso do manual.

Entrevista Clínica Estruturada para o DSM-IV – Versão Clínica (SCID):

A SCID é uma escala baseada nos critérios diagnósticos do DSM-IV já amplamente validada para utilização em pesquisa como forma de aferir diagnósticos de transtornos psiquiátricos. A escala tem validação para uso no Brasil (78).

Escala de Depressão Pós-Natal de Edimburgo (EPDS):

A EPDS consiste em um instrumento de autorregistro composto de dez itens, referentes aos últimos sete dias, para avaliar a presença e a intensidade de sintomas depressivos.

Seus itens incluem sintomas psíquicos como humor depressivo (sensação de tristeza, autodesvalorização e sentimentos de culpa, ideias de morte ou suicídio), perda do prazer em atividades anteriormente consideradas agradáveis, fadiga, diminuição da capacidade de pensar, de concentrar-se ou de tomar decisões, além de sintomas fisiológicos (insônia ou aumento do sono) e alterações do comportamento (crises de choro). A somatória dos pontos perfaz escore de 30, sendo considerado de sintomatologia depressiva valor igual ou superior a 12, como definido na validação da escala em uma amostra brasileira (79).

Escala de Hamilton para Ansiedade:

A Escala de Hamilton para Ansiedade tem como finalidade avaliar sintomas ansiosos. A Hamilton é uma das escalas mais utilizadas e tem validação para uso em português (80). A escala é composta por 14 itens, e cada pergunta é dividida em cinco respostas que variam de zero (não presente) até quatro (gravemente presente). Sua graduação varia de acordo com o somatório dos escores: soma até 17 indica ausência de ansiedade ou ansiedade leve; de 18 a 24, ansiedade leve a moderada; e de 25 a 56 de moderada a grave (81, 82).

Critério Brasil de Classificação Econômica – ABIPEME:

O questionário ABIPEME na sua versão 2014 foi utilizado para definir o nível socioeconômico das participantes (74). O ABIPEME avalia o nível socioeconômico através de perguntas referentes ao imóvel que a família reside, posse de eletrodomésticos, veículos automotivos e nível educacional de quem apresenta maior renda na família. O ABIPEME 2014 é dividido em seis classes sociais. A Tabela 3.3.1 abaixo apresenta as classes e o valor de renda média bruta mensal para a respectiva classe.

Tabela 3.3.1. Referência de Classe e Renda mensal

Classes	Renda média bruta mensal em reais
Classe A	11.037
Classe B1	6.006
Classe B2	3.118
Classe C1	1.865
Classe C2	1.277
Classe DE	895

Medidas de Interleucinas:

As amostras de sangue foram coletadas por punção da veia cubital entre as 14 e 18 horas do dia da visita domiciliar. As amostras eram guardadas em ambiente refrigerado até serem processadas e estocadas na Unidade de Análises Moleculares e de Proteínas (UAMP). As amostras de sangue foram centrifugadas a -4°C por dez minutos. O soro foi aliquotado e congelado a -70°C até a data da análise.

As interleucinas foram analisadas utilizando o kit *Milliplex® Map Human High Sensitivity T Cell Magnetic Bead Panel*. O processamento do teste ocorreu conforme as instruções do kit e foi realizado em amostra nunca antes descongeladas. A sensibilidade mínima para cada interleucina é de: Il-6 = 0.11pg/ml; Il-10 = 0.56pg/ml; Il-1β = 0.14pg/ml; TNFα = 0.16pg/ml. Foram excluídas três medidas de TNFα e nove de Il-6 por não terem atingido contagem suficiente de *beads* de acordo com o manual.

4. PROCESSAMENTO E ANÁLISE DOS DADOS

4.1. Cálculo Amostral

O tamanho da amostra foi calculado considerando a possibilidade de detecção de diferença no viés atencional descrito por Pearson *et al.*, 2011 em relação ao viés atencional frente a faces de sofrimento versus neutra de bebês em mães com diferentes níveis de cuidado materno. Foi adotado um nível de significância de 5% e poder de 95%, obtendo 84 pares mãe-filho (51).

4.2. Análise Estatística

O banco de dados foi elaborado no programa Statistical Package for the Social Sciences (SPSS) 20.0 software (SPSS Inc., Chicago, IL, USA). Todos os dados passaram por dupla digitação e foram checados para detectar possíveis incongruências.

Para as análises, foi considerado um nível de significância de 5% ($p<0,05$) e um intervalo de confiança de 95%. Os dados foram analisados com os programas estatísticos Statistical Package for the Social Sciences (SPSS) 20.0 software (SPSS Inc., Chicago, IL, USA) ou com o Software Stata 14.0 (StataCorp LP, TX, USA).

Variáveis quantitativas foram descritas como médias, e o desvio padrão da média e variáveis categóricas foram por sua frequência relativa (porcentagem %).

A normalidade das variáveis utilizadas nas análises foi conferida através do teste de Shapiro–Wilk. No caso de variáveis com distribuição não normal fez-se a transformação da mesma em normal, realizando transformação em logaritmo, ou utilizou-se de teste estatístico não paramétrico, como a correlação de Spearman.

A associação entre variáveis contínuas normais foi realizada através de correlação bivariável de Pearson, e o Teste *t* de Student foi utilizado para comparar médias entre grupos.

No artigo 1, os tamanhos de efeitos foram calculados de acordo com Cohen, 1977.

No artigo 3, foi utilizado um modelo de equação estrutural incluindo nível socioeconômico, Il-6, tempo de reação na tarefa de processamento cognitivo e *maternal affiliative behavior* a fim de analisar essas variáveis em conjunto.

5. ASPECTOS ÉTICOS

O projeto foi aprovado pelos Comitês de Ética em Pesquisa do HCPA (número 13-0507) e do GHC (número CAAE: 24111113.3.0000.5327).

Foram garantidos o anonimato e a confidencialidade dos dados dos participantes, os quais foram utilizados apenas para os trabalhos relacionados ao projeto e serão guardados por no máximo cinco anos, sendo totalmente destruídos após esse prazo, conforme a Resolução 196/96 IX.2.

6. RESULTADOS

6.1. Artigo 1: "*Attentional Bias Toward Infant Faces – Review of the Adaptive and Clinical Relevance*"

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Review

Attentional bias toward infant faces – Review of the adaptive and clinical relevance

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ABSTRACT

Human survival depends on care received early in life. Infants need to capture adults' attention to have their basic needs met. Therefore, infant stimuli are prioritized by the attention system in adults, resulting in an attentional bias toward infant faces. We conducted a systematic review of the literature on behavioral measures of attentional bias toward infant faces. PubMed, PsycINFO, and ISI Web of Knowledge databases were used. The review suggests the existence of a measurable attentional bias toward infant faces and a positive correlation between attentional bias toward infant distress and the quality of mother-infant relationship. Depressive symptoms and breastfeeding modulate this behavior in women. Parental status and sex also influence the attentional prioritization of infant faces. Evidence indicates that differences in attentional bias are associated with clinical symptoms and variations in maternal behavior, reinforcing the potential use of attentional bias as a behavioral marker of clinical outcomes.

1. Introduction

The human brain has specialized for preferentially perceiving survival- and reproduction-related stimuli even in complex environments (Sander et al., 2005; Bernat et al., 2006; Anderson, 2013). Attention allocation toward specific stimuli is a natural outcome of human evolution. Stimuli that are considered emotionally significant by attentional mechanisms receive enhanced processing and are prioritized in the competition for selective attention (Compton, 2003). The emotional value of stimuli varies among individuals, but threatening stimuli, such as snakes and spiders, are of universal emotional significance, and so are human faces (Palermo and Rhodes, 2007).

The perception of human faces is a highly specialized area of visual processing in humans and requires the activation of visual, limbic, and prefrontal regions (Haxby et al., 2000; Ishai et al., 2005). The perception of infant faces is of particular interest because of its adaptive value in the survival of the human species: human newborns cannot survive without care. Caregivers should be able to meet their infants' needs in a proper way and learn to recognize their cues, since communication in infancy is essentially nonverbal (Bowlby, 1979; Brazelton and Cramer, 1992; Barrett and Fleming, 2011). In this context, infant facial expressions are an important mean of communication between parents and their infants. An early, sensitive caregivers' attunement to their infants is, therefore, a central determinant of positive parenting and contributes to the children's physiological, cognitive, and social-emotional growth (Feldman, 2006; Feldman, 2007a, 2007b).

Ethologist Konrad Lorenz proposed the concept of 'baby schema' (kindchenschema), a specific set of infantile physical characteristics that motivates caretaking behavior and acts as a "social releaser" (Lorenz, 1943). The 'baby schema' includes features such as round face, large head, large eyes, high and protruding forehead, chubby cheeks, small nose and mouth, short and thick extremities, and plump body shape. 'Baby schema' features elicit positive emotions and caregiving responses (Sternglanz et al., 1977; Alley, 1981), motivate caretaking

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behavior in adult parents and nonparents (Glocker et al., 2009a), and inhibit aggression, thus improving the chances of adults who are sensitive to the 'baby schema' effects of having their genes passed on to future generations. Some studies support the idea that women are more sensitive to the 'baby schema' effects than men (Fullard and Reiling, 1976; Hildebrandt and Fitzgerald, 1978; Berman, 1980; Maestripieri and Pelka, 2002; Glocker et al., 2009b; Sprengelmeyer et al., 2009).

The perception of infant faces, compared to adult faces, induces a specific pattern of activity in the medial prefrontal cortex, a region involved in reward processing (Kringelbach et al., 2008). Recent studies indicate that tenderness, elicited by cute images, is more than just a positive feeling. Stimuli characteristic of the 'baby schema' have been shown to activate another structure involved in reward processing: the nucleus accumbens (Glocker et al., 2009a). In addition, exposure to images of cute animals and babies has made people more careful about their motor behavior (Sherman et al., 2009; Nittono et al., 2012).

Attentional bias is an index of the difference in attention captured by two different stimuli. Greater cognitive engagement in a specific stimulus may be demonstrated by greater attentional bias toward the stimulus. The role of attentional biases has been extensively researched in the setting of addiction (Field et al., 2008; Field et al., 2013), anxiety (MacLeod and Mathews, 2012), and obesity (Castellanos et al., 2009; Renwick et al., 2013). Such studies provide evidence that individual differences in attentional bias are associated with clinically relevant behaviors. Interventions focusing on attentional bias modification have shown positive results in reducing anxiety and stress vulnerability (MacLeod and Mathews, 2012; Van Bockstaele et al., 2013).

The attention system plays an important role in eliciting appropriate parental behavior and, consequently, appropriate child development. Therefore, infant cues would be expected to have a high biological valence and be prioritized by the attention system in adults. The objective of this study is to review the existing evidence of behavioral measures of adults' attentional bias toward infant faces.

2. Method

We conducted a systematic review of the literature on behavioral measures of attentional bias toward infant faces. The literature search was conducted using MEDLINE/PubMed, PsycINFO, and ISI Web of Knowledge databases to locate all studies involving human subjects (search up to date January 20, 2016). The following search terms were used: "attentional bias" AND "infant". To broaden the scope of our findings, new searches were conducted using "attentional bias" AND "infant" OR "newborn" OR "toddler" OR "babies".

Two reviewers independently screened the title and abstract of each paper, and any discrepancies were resolved by consensus. A third reviewer was consulted if agreement could not be reached. In the second round of review, all selected articles were read in full by the two reviewers and independently assessed for eligibility. Any disagreements were resolved by consensus and, if necessary, a third reviewer was consulted.

Inclusion criteria were that eligible studies had to have used attention tasks to measure adults' attentional bias and had to have deployed infant faces as at least one of the stimuli. Studies focusing on infants' attentional bias toward stimuli were excluded. No date range or language restrictions were used. The reference lists of all selected articles were carefully reviewed for additional relevant studies. In addition, a last search was conducted using the name of the authors of all articles meeting the inclusion criteria for further identification of other potentially relevant studies.

3. Results

The searches yielded 193 citations in PubMed, 88 in PsycINFO, and 312 in ISI Web of Knowledge. A total of 403 articles had their title and abstract reviewed. Of these, only 10 articles were considered eligible for full-text review. The analysis of references in the literature obtained and additional search by authors' names yielded three additional publications for full-text review. Of those 13, three were excluded, totaling 10 articles on attentional bias and infant faces included in this review. Fig. 1 depicts the flowchart outlining the selection of studies included in the qualitative synthesis.

Of the 10 articles included, four were from the same first author, using the same attention task, and comparing attentional biases toward different infant emotions in pregnant women. Two studies compared attentional engagement in own-race vs. other-race infant and adult faces. The other four studies compared the attention retained by infant vs. adult faces using different tasks. Table 1 summarizes the main findings of each article.

Brosch et al. (2007) explored whether pictures of infant faces would have a facilitating effect on the attention system when compared to pictures of adult faces, and whether women and men would have different attentional bias toward infant faces (Brosch et al., 2007). For this purpose, they used a dot probe task including pictures of infants and adults with neutral facial expressions, kittens, adult cats, puppies, and adult dogs. Each trial started with the presentation of a fixation cross, followed by a pair of images that were randomly chosen and paired with others of the same "age" or same species. Then, a small dot appeared, replacing one of the images. Participants had to indicate whether the dot appeared in the left or right side of the screen. In a valid trial, the dot replaced the infant image; in an invalid trial, the dot replaced the adult image. When the target was presented in the left visual field, response times were statistically shorter in valid than in invalid trials only for human pictures. This result highlights that human infant faces capture more attention than adults and this has a species specificity, since other animal babies did not had the same effect on response times. This pattern of attention allocation was not observed when the target appeared in the right visual field. Another important finding of this study, is that attentional bias appears to be modulated by the arousal potential of a stimulus, since there was a very high correlation between arousal elicited by the image and the response time.

Hodsoll et al. (2010), in a later study, further investigated the influence of race on adults' attentional prioritization of infant faces. Also using a dot probe task, neutral infant faces were paired with neutral adult faces of the same race. Pictures of South Asian and Caucasian infants and middle-aged adults were used. Forty female undergraduate students participated in the study, half South Asian, and half Caucasian. The response time was shorter when the probe replaced infant pictures, but only when the infant's race was the same as that of the participant. The authors suggested that the attentional bias toward infant faces was race dependent.

Conversely, Proverbio et al. (2011) demonstrated that age impacts automatic allocation of attention, whereas ethnicity does not (Proverbio et al., 2011). The authors used as stimulus pictures of infant and adult faces of different ethnic groups, all of them showing a positive facial expression. Participants were asked to ignore the faces and answer whether the target (a picture of a tree) was presented upright or downward. The target was displayed on the screen right after the stimulus (face image) either in the same side of the stimulus (valid trial) or in the opposite side of the stimulus (invalid trial). Participants (30 undergraduate and graduate students) had shorter response times to targets preceded by infant than adult faces, suggesting greater attention allocation toward infant stimuli. Reinforcing this idea, participants committed more errors when the target was displayed on the other side of the infant face image, and the opposite occurred when adult faces were used as the stimulus. This suggests difficulty in disengaging attention from the infants' images. As opposed to Hodsoll et al. (2010) results, there was no effect of ethnic group on response times or error rates, suggesting that ethnicity did not influence attention allocation to infant faces.

In 2010, Pearson et al. (2010) published the first of a series of articles on attentional bias toward infant stimuli (Pearson et al., 2010; Pearson

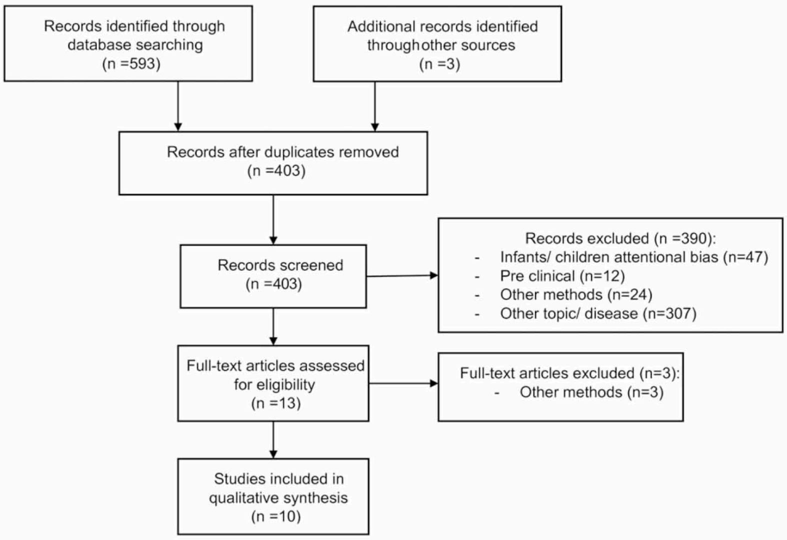

Fig. 1. PRISMA 2009 flow diagram.

et al., 2011b, 2011c; Pearson et al., 2013). The study aimed to investigate whether (a) pregnant women (in the first 12 weeks of pregnancy) would have an attentional bias toward infant faces vs. adult faces, (b) this bias would be related to the specific emotion expressed in the image, and (c) women with and without depressive symptoms would respond differently to distressed infant faces (Pearson et al., 2010). For this purpose, 101 women (51 multiparous, 31 with depressive symptoms) were recruited. The researchers developed an attention task with fearful, happy, or neutral adult faces and distressed, happy, or neutral infant faces as stimuli. The task involved go/no-go trials that required participants to focus on a central go/no-go signal (green/red cross, respectively) on the computer screen. Two lines, one horizontal and one vertical, were also presented at the screen's periphery. Participants were asked to ignore the pictures behind the cross and indicate the side where the vertical line appeared. Therefore, go trials required disengaging attention from the central signal to a peripheral target line. The results suggest that pregnant women take longer to respond to infant than adult face stimuli, regardless of depression status. In a further analysis, the difference in mean response time between distressed and nondistressed infant face trials was used as a marker of women's attentional bias toward distressed infant faces. Non-depressed women showed an attentional bias toward distressed infant faces, whereas women with depressive symptoms did not. In addition, multiparous women had greater attentional bias towards infant distress than primiparous women. Adjustment for possible confounders did not change the results, suggesting that depressive symptoms affect the cognitive processing of distressed infant faces.

Following the same sample during gestation, Pearson et al. (2011b) investigated the correlation between attentional bias toward infant distress in late pregnancy and the mother's ability to establish a relationship with her infant after birth (Pearson et al., 2011b, 2011c). Seventy-five women were seen during late pregnancy and again at 3 to 6 months after birth. In the first visit, participants completed the attention task (the same as described in the previous study), a questionnaire on demographics and pregnancy information, and the Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987). In the second visit, the EPDS and the Postpartum Bonding Questionnaire (PBQ) were administered (Brockington et al., 2006). Final PBQ scores were available only from 49 women because of loss to follow-up and bureaucratic issues. Consistent with their previous findings (Pearson et al., 2010), women's mean response times in the attention task were longer to distressed than nondistressed infant faces, suggesting that attentional bias toward infant distress persisted during pregnancy. Greater attentional bias toward infant distress was significantly associated with a more successful mother-infant relationship reported in the PBQ when extreme scores were compared. PBQ is a 25 items self-report instrument designed to detect early signs of problematic mother-infant relationship. Higher scores correlate with weaker mother-infant bonding and lower scores with stronger bonding. Limitations of the study included the loss of almost 35% of the initial sample and the fact that the PBQ is an indirect measure of the mother's behavior. Scores may signal maternal mental states other than bonding *per se*, such as hypervigilance and overprotection.

In a subsequent study, Pearson et al. (2011c) used data from the same sample as the previous two studies to investigate the impact of breastfeeding on mothers' attentional bias toward infant distress. The authors compared attentional bias towards infant distress after birth according to feeding method. The sample analyzed consisted in 51 women who have performed the attentional task at late pregnancy and after birth. There was no difference in attention bias towards infant distress before labor between breastfeeding and bottle-feeding groups. A simple linear regression analysis adjusted for potential confounders (postnatal mood, maternal age, social class, education level, parity, and infant age) showed that breastfeeding was associated with a higher index of maternal attentional bias toward infant distress after birth compared with formula feeding, suggesting that attentional bias toward infant distress after birth may be influenced by the act of breastfeeding. Women's attentional bias toward infant distress after birth was not associated with maternal mood after birth or parity differently of the results on first gestational trimester (Pearson et al., 2010). One possible limitation of this article is the smaller sample size compared to the previous ones.

In the last study of the series, Pearson et al. (2013) used a different sample of women and conducted a randomized trial to investigate whether cognitive behavioral therapy (CBT) would improve attentional bias toward infant distress in depressed pregnant women. Twenty-four pregnant women with a diagnosis of depression by the Clinical Interview Schedule- Revised (CIS-R) were recruited and equally divided into two groups to receive either CBT or usual care, and 51 nondepressed pregnant women served as the control group. All participants answered the CIS-R and EPDS and performed the previously described

Table 1
A summary of studies of adults' attentional bias toward infant stimuli.

Study	Objective	Task/stimuli	Duration of stimuli display	Sample (mean age)	Results
Brosch et al., 2007	Attentional capture by infant faces versus adult faces	Dot probe. Infant faces (human, kittens, puppies) vs Adults faces (human, cats and dogs) All neutral facial expressions	100 ms	20 men 20 women (24.5 years) (no information about parity)	- AB toward infant faces (ES: Cohen's d = 0.193 for differences in RT when image is presented on the left visual field, not significant for right visual field) - AB has a relation with image arousal - no differences between men and women.
Hodsoll et al., 2010	Influence of race in AB toward infant faces	Dot Probe. South Asian Infant × South Asian Adult White Infant × White Adult	200 ms	$N = 40$ [20 South Asian women (20.25 years) and 20 Caucasian women (19.63 years)]	- AB toward infant images only when participant has the same race as infant (ES: Cohen's d = 0.139 for RT differences in South Asian and 0.164 for Caucasians)
Proverbio et al., 2011	Influence of age and race in AB toward infant faces	Dot Probe. South Asian Infant × South Asian Adult White Infant × White Adult	200 ms	$N = 30$ (7 men and 23 women) (26.9 years)	- AB toward infant faces (ES: Cohen's d = 0.048 for RT differences) - AB toward infants images not influenced by race
Pearson et al., 2010	1-Difference in AB toward infant and adult images. 2-Difference of AB toward different expression of emotion of infant faces 3-Difference in AB toward infant distress in pregnant women with or without depressive symptoms	Go/no-go. Adult faces (happy, neutral, fearful) vs Infant faces (happy, neutral, distressed)	240 ms	101 pregnant women (29 years) Gestational age: 12 weeks.	- AB toward infant faces (ES: Cohen's d = 0.079) - Multiparous have higher AB toward infant distress than first time moms - Women without depressive symptoms have higher AB toward infant distress than women with depressive symptoms. (Non-depressive group: Cohen's d = 0.159 for difference in RT adult vs infant fearful, 0.088 for neutral and 0.028 for happy faces; Depressive group: Cohen's d = 0.116 for difference in RT adult vs infant fearful, 0.000 for neutral and 0.324 for happy faces.
Pearson et al. (2011b))	Correlation between AB toward infant distress and PBQ scores	Go/no-go. Adult faces (happy, neutral, fearful) vs Infant faces (happy, neutral, distressed)	240 ms	49 pregnant women (30 years) Gestational age: 37 weeks	- Pregnant women show AB toward infant distress in late pregnancy (ES: Cohen's d = 0.185 for difference in RT between distressed vs. non--distressed faces) - Lower PBQ scores (i.e. strongest M-I relationship) correspond to higher AB toward infant distress (ES for difference in RT between distressed vs. non-distressed faces: Cohen's d = 0.422 for low PBQ, 0.091 for mid PBQ and 0.014 for high PBQ scores)
Pearson et al. (2011c)	Difference in AB toward infant distress between breastfeeding and formula feeding mothers and	Go/no-go. Adult faces (happy, neutral, fearful) vs Infant faces (happy, neutral, distressed)	240 ms	51 women (30 years) Measured when women had 37 weeks of gestational age, and 18 weeks after birth. 27 breastfeeding 24 bottle feeding	- Similar AB toward infant distress between groups in late pregnancy - Breastfeeding mothers had higher AB toward infant distress than formula feeding ones. ES: Cohen's d = 0.488
Pearson et al., 2013	Investigate the impact of CBT on AB toward infant distress in depressed pregnant women	Go/no-go. Adult faces (happy, neutral, fearful) vs Infant faces (happy, neutral, distressed)	240 ms	24 depressed pregnant women - 12 UC arm - 12 CBT arm	- CBT improved AB toward infant distress compared to UC in late pregnancy. ES: Cohen's d = 0.910
Stein et al., 2012	Impact of 7 day use of reboxetine or citalopram in processing of infant stimuli	Dot probe Infant face (happy, neutral, sad) and Adult faces (happy, neutral, sad) Comparison was between neutral and emotion face from same group age.	1000 ms	20 male 23 female - 14 placebo group (23 years) - 13 reboxetine group (23 years) - 12 citalopram group (24 years) - probably none were parents	- No difference in AB between groups ES: f = 0.057 for happy faces when comparing all the groups. For sad faces, f = 0.295 (although the difference between the 3 groups is not statistically significant)
Cárdenas et al., 2013	Difference of attention toward infant in men and women	Free-viewing task using Eye tracking Neutral adult faces × neutral infant faces	6000 ms	32 men 31 women (19 years) One was pregnant, others weren't parents	- Men showed AB toward infant when image was paired with a male adult image. ES: Cohen's d = 0.489 - Women showed AB toward infant in all conditions.
Thompson-Booth et al., 2014	Processing of infant faces vs Parental Status	Irrelevant Feature Visual Search Paradigm Infant faces (content, neutral, distressed) vs	3000 ms	$N = 69$ (29 mothers, mean age 28.68 years, and 37 non-mothers, mean age 30.59 years)	- AB toward infants in both groups. (ES: Cohen's d for differences in RT between adult and infant faces ranging from 0.368 to 1.340 in mothers and from 0.343 to 1.058 in non-mothers in the

Table 1 (*continued*)

Study	Objective	Task/stimuli	Duration of stimuli display	Sample (mean age)	Results
		Adult faces (happy, neutral, sad)			different facial expressions - Parental status modulates AB toward infants. - AB toward emotional faces modulated by face age. - Greater parental distress associated with less interference of infant faces.

AB = attentional bias; PBQ = Postpartum Bonding Questionnaire; CBT = Cognitive Behavioral Therapy; RT = reaction time; EF = effect size; ms = miliseconds; s = seconds; UC = usual care. Effect sizes were calculated according to (Cohen, 1977), assuming a correlation of 0.5 in paired samples to estimate the standard deviation when information was not available for a particular comparison.

attention task (Pearson et al., 2010) in early pregnancy (at around 13 weeks of gestation). Of the 24 depressed women, only 17 completed the study. These women repeated the CIS-R and attention task at the end of the intervention period (around 15 weeks after the first visit). CBT included 9 to 12 one-on-one sessions with trained therapists. Patients randomized to receive usual care continued to receive assistance provided by midwives and general practitioners. While at baseline both CBT and usual care arms had similar attentional biases toward infant distress (showing a diminished attentional bias in relation to the healthy control group), attentional biases of women who received CBT increased, whereas attentional biases of women who received usual care further decreased after treatment. In addition, after treatment, attentional biases of women in the CBT arm no longer differed from attentional biases of nondepressed women. A reduction in depressive symptoms was also detected in the CBT arm after intervention compared with the usual care arm. Although the small sample size limited data interpretation, there was a correlation between the magnitude of change in depressive scores and attentional bias, in which the greater the reduction in depression after intervention, the greater the increase in attentional bias indices toward infant distress. Despite the limitations of the study, the results reinforced the idea that depressed women have a different attentional processing of distressed infant faces.

Later on, a double-blind, fixed-dose intervention conducted by Stein et al. (2012) investigated whether a 7-day treatment with either reboxetine or citalopram would influence how healthy volunteers process infant-related emotional information by using an attention task (Stein et al., 2012). The sample consisted of 43 healthy student volunteers with no psychiatric diagnosis (past or present). A dot probe task was performed to examine attentional vigilance toward stimuli. Pairs of photographs of adult or infant faces (one emotional – sad/happy – and one neutral expression of the same individual) were used as stimuli. On each trial, the face pair was presented and immediately followed by a probe (one or two dots on the screen replacing one of the faces). Participants were required to report the number of dots displayed on the screen as quickly and as accurately as possible. Reboxetine and citalopram did not influence attentional vigilance toward infant and adult faces of emotion in the dot probe task. Limitations of the study included sample size, duration of antidepressant administration and the design of the task used.

The influence of infant faces on attention in men and women was explored by Cárdenas et al. (2013) by examining whether their interest in infants would affect overt attentional bias toward infant faces (Cárdenas et al., 2013). Undergraduate students (32 male and 31 female) answered two questionnaires (Interaction-with-Infants and Infant-Job-Preference) as a measure of interest in infancy and a demographic questionnaire. The attention paradigm was a free-viewing, eye-tracking task with neutral adult faces and infant faces as stimuli. Stimuli were presented as paired face images, always one adult and one infant face, one above the other. During presentation, the eye-tracking system recorded the first fixation point, total viewing duration for each picture, and total number of fixations for each face. Results showed that the first fixation point was not influenced by age or sex, but by the screen position, as the participants looked first at images located on top. Viewing bias (total viewing time for infant faces subtracted from total viewing time for adult faces) and fixation bias (total number of fixations to infant faces compared to the number of fixations to adult faces) were considered components of overt attentional bias toward infant stimuli. Men had a viewing bias toward infant faces when the infant image was paired with a male image, but not when paired with a female image, whereas women had a viewing bias toward infant faces regardless of the image pair. A similar result was reported for the fixation bias: men fixated more often on the infant face when it was paired with a male face, and women had a fixation bias toward infant faces in all conditions. Women's interest-in-infant scores did not influence attentional bias toward infant faces. Conversely, men with above average interest-in-infant scores tended to have a greater attentional bias toward infant faces when the infant image was paired with an adult male image. The results of the study indicate a link between overt attention and self-reported interest in infants for men, and suggest that further research is warranted to determine the direct impact of this attentional bias on actual infant care. We wonder whether the overt attentional bias described in the study is a reliable indicator of attention modulation on its own or whether pairing it with automatic attentional bias measures would be a better arrangement in order to understand its pattern over time.

The most recently published study included in this review was conducted by Thompson-Booth et al. (2014), who investigated attention to infant emotional faces in mothers and non-mothers. The Irrelevant Feature Visual Search Paradigm, adapted from Theeuwes (1991, 1992, 1994) and Hodsoll et al. (2011), was used in the study and included an adult and an infant version of the attention task. In the task, a fixation cross was presented, followed by three faces presented on the screen until a response was given. Face images showed either neutral expressions or emotional faces (distressed/sad expression or content/happy expression). Participants were asked to find the blue-eyed face (which appeared in three conditions: all neutral faces, emotional face as target, and emotional face as distractor) and to indicate whether it was tilted to the right or left. The 66 women participating in the study showed slower response time to infant target stimuli than to adult target stimuli. This effect was modulated by parental status, as mothers had longer response times to infant compared with adult faces than did non-mothers. Both groups also had longer response times to emotional faces, with a greater effect on infant emotional faces. Appraisal theories of emotion predict that stimuli that are considered important or significant require increased allocation of attention and processing (Sander et al., 2005), and higher levels of arousal may be responsible for the engagement of attention (Lorenz, 1943; Brosch et al., 2007). In the preliminary study for image validation, infant faces were rated as more arousing than adult faces even when expressions were neutral. The authors argued that, if greater arousal ratings had been sufficient to drive greater attentional interference, then slower responses would have been observed for distressed vs. happy images, but no such difference was found.

Finally, the results of the study indicated that greater levels of mothers' self-reported parental distress were associated with less task interference when infant faces were presented. The results suggest that, for adult women, infant faces in general, especially infant emotional faces, preferentially engage attention compared with adult faces. And for mothers infant faces appear to be more salient in general.

4. Discussion

The 10 studies reviewed here have different objectives and methods. Except for the studies conducted by Pearson et al., which used the same attention task and same parameters, each study used a different type of attention task (dot probe, eye tracking), with different stimulus-onset asynchronies (SOA) and different stimulus comparisons.

In Brosch et al. (2007), Hodsoll et al. (2010) and Proverbio et al. (2011) the time frame used in the dot probe paradigm allows us to conclude that the attentional processing involved in those tasks is automatic (also referred to as reflex or exogenous) and mostly determined by bottom-up networks (Luck and Hillyard, 1994; Hopfinger and Mangun, 1998; Hopfinger et al., 2001). The go/no-go task used by Pearson et al. (2010, 2011b, 2011c, 2013) in all their studies also involved automatic attention processes. Due to the longer duration of cue display in Stein et al. (2012), we assume that the attentional processing involved in the task has already required some voluntary or top-down effort. In Cárdenas et al. (2013) and Thompson-Booth et al. (2014), a longer time frame clearly requires voluntary attentional processing.

Despite the methodological differences between studies and the different levels of attentional processing accessed, most findings point to the same direction. All studies have shown, in different populations, that adults have attentional biases toward infant faces (Brosch et al., 2007; Hodsoll et al., 2010; Pearson et al., 2010; Pearson et al., 2011b, 2011c; Proverbio et al., 2011; Cárdenas et al., 2013; Thompson-Booth et al., 2014). Thus, it is possible that infants have a biological valence capable of being prioritized by automatic and voluntary attention.

The studies reviewed here are in line with research using electrophysiological and neuroimaging techniques. Studies by Thompson-Booth et al. (2014) and Cárdenas et al. (2013) reinforce the findings of Proverbio et al. (2006), who showed by electrophysiological analyses that men and women, parents and nonparents, respond differently to unknown infant face pictures (Proverbio et al., 2006). Parents had increased cortical responses compared with nonparents to infant facial expressions, showing that parenthood increases both attention and neural responses. Sex differences were expressed by higher arousal and more consistent attention allocation toward infant stimuli by women than men (Proverbio et al., 2006; Cárdenas et al., 2013)

A relationship between the type of infant emotional expression and the degree of response activation in parents has also been previously reported. Similar to the findings of Pearson et al., other authors have identified that distress produces a greater response than do neutral or happy expressions. In Proverbio et al. (2006), while nonparents tended to respond similarly to expressions of intense distress and mild discomfort, parents (especially mothers) showed greater sensitivity to very sad infant faces. Seifritz et al. (2003) demonstrated higher sensitivity of parents to distress signals by showing that the sound of an unfamiliar infant crying, but not the infant's laughter, induced greater activation of the amygdala and interconnected limbic regions in parents than in nonparents (Seifritz et al., 2003). Furthermore, Stein et al. (2012), in a sample of nonparents, found no attentional bias toward a specific infant emotion. Therefore, responding to infant faces expressing distress may be considered important for the survival of the species.

There might be multiple reasons why parents have higher attention bias towards infant faces, specially towards their own infant, since parenting provokes changes in hormones, neuropeptides, brain function and behavior on both men and women (Pereira and Ferreira, 2016). Oxytocin may play a role on these changes as attention allocation towards infant is higher in situations associated higher circulating oxytocin levels such as parenting, breastfeeding, better mother-infant relation and being in love (Feldman, 2007a, 2007b; Grasso et al., 2009; Kim et al., 2010; Kim et al., 2011; Pearson et al., 2011b, 2011c; Weisman et al., 2012). Moreover, oxytocin is linked to the activation of areas involved in socio-cognition abilities (e.g. dorsolateral prefrontal cortex) and reward, which can promote a perpetuation of the interest for the stimuli (Atzil et al., 2012; Pereira and Ferreira, 2016). It is important to highlight that changes in neurotransmission and brain activation occur also in fathers and adoptive parents, indicating that the contact with an infant is also key to promote differences between parents and non-parents (Grasso et al., 2009; Pereira and Ferreira, 2016)

The high relevance of a stimulus strongly correlates with its rewarding properties and power to alter attentional prioritization. Attentional priority changes according to the reward intensity (greater reward has greater influence on the attention system) (Anderson et al., 2011; Anderson, 2013). The influence on attention allocation persists even after the reward has ceased and occurs even without conscious awareness (Seitz et al., 2009; Anderson et al., 2011). Childbearing behavior usually activates the reward system (Leibenluft et al., 2004; Swain et al., 2007; Kringelbach et al., 2008).

Although data on the role of the reward system in postpartum depression are scarce, this system is known to be altered during depression in other periods of life (Henriques and Davidson, 2000; Foti and Hajcak, 2009). Depressive symptoms alter attention toward reward-related stimuli, extinguishing the attentional bias toward these stimuli (Anderson et al., 2014). This is, perhaps, one possible explanation for the lower attention bias toward infant distress observed in Pearson's sample of pregnant women with depressive symptoms.

Correspondence can also be found between the studies of Pearson et al. (2011c) and Kim et al. (2011), as both investigated the impact of breastfeeding on maternal behavior. The first study focused on attentional processing, while the second study explored the association between neuroimaging and behavioral analyses. Kim et al. (2011) suggested that nursing positively influences maternal sensitivity because breastfeeding mothers show higher amygdala, putamen, globus pallidus, and superior frontal gyrus activation than formula-feeding mothers in response to their infants' cry. These brain areas are important in caregiving behavior and empathy (Swain et al., 2007; Kim et al., 2010). Additionally, breastfeeding mothers show a trend towards higher maternal sensitivity during mother-infant interactions when compared with formula-feeding mothers.

Studying automatic attention and its biases toward different stimuli allows a better understanding of the exogenous drive of attention that often occurs at the beginning of many processes involved in perception and decision-making. Attentional biases toward stimuli such as food, erotica, predators, and human emotional facial expressions hold a possible key to unveiling what has contributed to the survival of our species and what has been perceived as universally relevant to humans to date. Describing reflexive attention, as well as its neurobiological bases and behavioral patterns, is also important for understanding the development and maintenance of addictions and compulsive and anxious behaviors.

Beyond the scope of this review but worth mentioning, there are other methods to explore adults' attention to infant cues, such as event-related potentials (ERP) on electroencephalograms (EEG) and neuroimaging studies. These are useful and interesting research tools that provide an understanding on how the infant cues are processed at a neurobiological level.

As it happens in behavioral measures of attentional bias towards infant faces, there are not many studies with ERP using infant faces as stimuli. One advantage of ERP is the ability to differentiate components of cue processing. The first waves after the stimuli onset (N170) are related to visual processing with visual cortex activation. Attention allocation initiates around 200 ms after the stimuli onset (e.g. P200 and P300) and progresses towards a more elaborate engagement and stimuli processing during late positive potential (LPP) (Vuilleumier and Pourtois, 2007; Maupin et al., 2015).

Confirming some of the behavioral findings, ERP studies demonstrate that images of infant distress generate higher attention processing with larger wave amplitudes 200 ms after the stimuli onset compared to neutral and happy faces (Proverbio et al., 2006; Rodrigo et al., 2011; Doi and Shinohara, 2012; Peltola et al., 2014; Malak et al., 2015). This finding is replicated in different sets of samples: mothers, non-mothers, fathers, and neglectful or highly anxious mothers. Although the last two conditions interfere with infant face processing, the effect of infant distress stimuli persists (Rodrigo et al., 2011; Malak et al., 2015). Findings also indicate that infant stimuli generate larger responses than adults, and the picture of a parent's own infant also produces larger responses than an unfamiliar one (Proverbio et al., 2006; Weisman et al., 2012; Peltola et al., 2014).

Neuroimaging studies using functional magnetic resonance imaging (fMRI) have demonstrated that infant faces trigger responses in different brain areas, including parietal and prefrontal cortices, both involved in attention and cognitive processing (Strathearn et al., 2008; Shomstein, 2012; Luo et al., 2015).

Most of the fMRI and magnetoencephalography (MEG) studies that were designed to evaluate brain responses to infant faces used a stimuli exposure time that requires voluntary attention, and compared responses to own parents' child picture versus an unfamiliar infant picture. Results suggest that infant faces activate more attention and reward areas than images of adults and other animals in parents and non-parents (Kringelbach et al., 2008; Caria et al., 2012). In addition, images depicting the subjects' own children's faces, especially happy ones, promote higher activation than unknown infants in areas related to cognitive and emotion processing of stimuli such as the anterior cingulate, insula, medial and dorsolateral prefrontal cortex (Strathearn et al., 2008; Luo et al., 2015). Conditions such as depressive symptoms and substance abuse negatively impact the activation of areas related to emotion processing on mothers (Landi et al., 2011; Laurent and Ablow, 2013)

5. Conclusions and Future directions

Attentional bias toward certain types of stimuli reflects their evolutionary relevance to our species. Once automatic attention is captured, the subsequent processing of salient stimuli will take place and direct behavior. The presence, reduction or absence of an attentional bias toward infant faces highlights the caregiver's availability to respond to the infant's signals, particularly to those that convey urgency or danger, such as emotional expressions of distress. Measures of attentional bias toward infant faces, in terms of response time, provide objective data on important processes previously assessed only by self-report and observation. Given the great adaptive value shown in the different studies reviewed here, attentional bias toward infant stimuli appears to be a promising field of research with potential for clinical application. Pearson's studies, for instance, focused on a major health concern: postpartum depression. Considering the major impact that the quality of maternal care has on child development and risk for future psychopathology (Murray et al., 1996; Feldman, 2007a, 2007b; Stein et al., 2009; Pearson et al., 2011a), recognition of disturbances in maternal mood and/or mother-infant relationship should be one of the focuses for concern in public health. The assessment of at-risk families would benefit greatly from a practical and objective index such as the behavioral measure of attentional bias toward infant faces, especially toward distress signals. The application of this knowledge may include potential strategies related to a more successful mother-infant relationship. Although the findings by Stein et al. should be interpreted with caution, the effect of antidepressants on mothers' positive perception of infants' expression may contribute to positive interactions. Further studies should investigate the association between altered attentional bias toward infant faces and breastfeeding difficulties and/or feeding behavior alterations, so that this tool may be potentially used for identification of problematic dyads. Similarly, as the quality of maternal care influences neuroendocrine responses (McGowan et al., 2009) and seems especially important for vulnerable populations (Escobar et al., 2014), early screening for possible deviations in maternal-infant relationship may be relevant to prone interventions.

An increase in research on attentional bias toward infants is needed to further understand the influence of behavioral and biological mechanisms of the infant, the caregivers, their relationship, and their environment on caregivers' attention to infant signals. Possible correlations between attentional bias and future child cognitive, social and emotional development should also be further explored. Larger studies with adequate methodology are necessary so that the potential clinical applications of such tool can be understood and optimized.

References

Alley, T.R., 1981. Head shape and the perception of cuteness. Developmental Psychology 17 (5), 650.

Anderson, B.A., 2013. A value-driven mechanism of attentional selection. J Vis 13 (3).

Anderson, B.A., Laurent, P.A., Yantis, S., 2011. Value-driven attentional capture. Proc Natl Acad Sci U S A 108 (25), 10367–10371.

Anderson, B.A., Leal, S.L., Hall, M.G., Yassa, M.A., Yantis, S., 2014. The attribution of value-based attentional priority in individuals with depressive symptoms. Cogn. Affect. Behav. Neurosci.

Atzil, S., Hendler, T., Zagoory-Sharon, O., Winetraub, Y., Feldman, R., 2012. Synchrony and specificity in the maternal and the paternal brain: relations to oxytocin and vasopressin. J Am Acad Child Adolesc Psychiatry 51 (8), 798–811.

Barrett, J., Fleming, A.S., 2011. Annual research review: all mothers are not created equal: neural and psychobiological perspectives on mothering and the importance of individual differences. J Child Psychol Psychiatry 52 (4), 368–397.

Berman, P.W., 1980. Are women more responsive than men to the young? A review of developmental and situational variables. Psychological Bulletin 88 (3), 668.

Bernat, E., Patrick, C.J., Benning, S.D., Tellegen, A., 2006. Effects of picture content and intensity on affective physiological response. Psychophysiology 43 (1), 93–103.

Bowlby, J., 1979. The making and breaking of affectional bonds. Tavistock, London.

Brazelton, T.B., Cramer, B.G., 1992. As primeiras relações. São Paulo, Martins Fontes.

Brockington, I.F., Fraser, C., Wilson, D., 2006. The Postpartum Bonding Questionnaire: a validation. Arch. Womens Ment. Health 9 (5), 233–242.

Brosch, T., Sander, D., Scherer, K.R., 2007. That baby caught my eye... attention capture by infant faces. Emotion 7 (3), 685–689.

Cárdenas, R.A., Harris, L.J., Becker, M.W., 2013. Sex differences in visual attention toward infant faces. Evolution and Human Behavior 34, 280–287.

Caria, A., Falco, S., Venuti, P., Lee, S., Esposito, G., Rigo, P., Birbaumer, N., Bornstein, M.H., 2012. Species-specific response to human infant faces in the premotor cortex. Neuroimage 60 (2), 884–893.

Castellanos, E.H., Charboneau, E., Dietrich, M.S., Park, S., Bradley, B.P., Mogg, K., Cowan, R.L., 2009. Obese adults have visual attention bias for food cue images: evidence for altered reward system function. Int J Obes (Lond) 33 (9), 1063–1073.

Cohen, J., 1977. The t Test for means. Statistical Power analysis for the Behavioral Sciences, revised ed. A. Press, New York, Harcourt Brace Jovanovich, pp. 19–74.

Compton, R.J., 2003. The interface between emotion and attention: a review of evidence from psychology and neuroscience. Behav. Cogn. Neurosci. Rev. 2 (2):115–129. http://dx.doi.org/10.1177/1534582303255278.

Cox, J.L., Holden, J.M., Sagovsky, R., 1987. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry 150, 782–786.

Doi, H., Shinohara, K., 2012. Event-related potentials elicited in mothers by their own and unfamiliar infants' faces with crying and smiling expression. Neuropsychologia 50 (7), 1297–1307.

Escobar, R.S., O'Donnell, K.A., Colalillo, S., Pawlby, S., Steiner, M., Meaney, M.J., Levitan, R.D., Silveira, P.P., Team, M.S., 2014. Better quality of mother-child interaction at 4 years of age decreases emotional overeating in IUGR girls. Appetite 81, 337–342.

Feldman, R., 2006. From biological rhythms to social rhythms: physiological precursors of mother-infant synchrony. Dev Psychol 42 (1), 175–188.

Feldman, R., 2007a. Mother-infant synchrony and the development of moral orientation in childhood and adolescence: direct and indirect mechanisms of developmental continuity. Am J Orthopsychiatry 77 (4), 582–597.

Feldman, R., 2007b. Parent–infant synchrony: biological foundations and developmental outcomes. 16 (6), 340–345.

Field, M., Schoenmakers, T., Wiers, R.W., 2008. Cognitive processes in alcohol binges: a review and research agenda. Curr. Drug Abuse Rev. 1 (3), 263–279.

Field, M., Marhe, R., Franken, I.H., 2013. The clinical relevance of attentional bias in substance use disorders. CNS Spectr. 1–6.

Foti, D., Hajcak, G., 2009. Depression and reduced sensitivity to non-rewards versus rewards: Evidence from event-related potentials. Biol Psychol 81 (1), 1–8.

Fullard, W., Reiling, A.M., 1976. An investigation of Lorenz's babyness. Child Development 1191–1193.

Glocker, M.L., Langleben, D.D., Ruparel, K., Loughead, J.W., Gur, R.C., Sachser, N., 2009a. Baby schema in infant faces induces cuteness perception and motivation for caretaking in adults. Ethology 115 (3), 257–263.

Glocker, M.L., Langleben, D.D., Ruparel, K., Loughead, J.W., Valdez, J.N., Griffin, M.D., Sachser, N., Gur, R.C., 2009b. Baby schema modulates the brain reward system in nulliparous women. Proceedings of the National Academy of Sciences 106 (22), 9115–9119.

Grasso, D.J., Moser, J.S., Dozier, M., Simons, R., 2009. ERP correlates of attention allocation in mothers processing faces of their children. Biol Psychol 81 (2), 95–102.

Haxby, J.V., Hoffman, E.A., Gobbini, M.I., 2000. The distributed human neural system for face perception. Trends Cogn. Sci. 4 (6), 223–233.

Henriques, J.B., Davidson, R.J., 2000. Decreased responsiveness to reward in depression. Cognition & Emotion 14 (5), 711–724.

Hildebrandt, K.A., Fitzgerald, H.E., 1978. Adults' responses to infants varying in perceived cuteness. Behavioural Processes 3 (2), 159–172.

Hodsoll, J., Quinn, K.A., Hodsoll, S., 2010. Attentional prioritization of infant faces is limited to own-race infants. PLoS One 5 (9).

Hodsoll, S., Viding, E., Lavie, N., 2011. Attentional capture by irrelevant emotional distractor faces. Emotion 11 (2):346–353. http://dx.doi.org/10.1037/a0022771.

Hopfinger, J.B., Mangun, G.R., 1998. Reflexive attention modulates processing of visual stimuli in human extrastriate cortex. Psy. Sci. 9 (6), 441–447.

Hopfinger, J.B., Woldorff, M.G., Fletcher, E.M., Mangun, G.R., 2001. Dissociating top-down attentional control from selective perception and action. Neuropsychologia 39 (12), 1277–1291.

Ishai, A., Schmidt, C.F., Boesiger, P., 2005. Face perception is mediated by a distributed cortical network. Brain Res. Bull. 67 (1), 87–93.

Kim, P., Leckman, J.F., Mayes, L.C., Feldman, R., Wang, X., Swain, J.E., 2010. The plasticity of human maternal brain: longitudinal changes in brain anatomy during the early postpartum period. Behav Neurosci 124 (5), 695–700.

Kim, P., Feldman, R., Mayes, L.C., Eicher, V., Thompson, N., Leckman, J.F., Swain, J.E., 2011. Breastfeeding, brain activation to own infant cry, and maternal sensitivity. J Child Psychol Psychiatry 52 (8), 907–915.

Kringelbach, M.L., Lehtonen, A., Squire, S., Harvey, A.G., Craske, M.G., Holliday, I.E., Green, A.L., Aziz, T.Z., Hansen, P.C., Cornelissen, P.L., Stein, A., 2008. A specific and rapid neural signature for parental instinct. PLoS One 3 (2), e1664.

Landi, N., Montoya, J., Kober, H., Rutherford, H.J., Mencl, W.E., Worhunsky, P.D., Potenza, M.N., Mayes, L.C., 2011. Maternal neural responses to infant cries and faces: relationships with substance use. Front Psychiatry 2, 32.

Laurent, H.K., Ablow, J.C., 2013. A face a mother could love: depression-related maternal neural responses to infant emotion faces. Soc Neurosci 8 (3), 228–239.

Leibenluft, E., Gobbini, M.I., Harrison, T., Haxby, J.V., 2004. Mothers' neural activation in response to pictures of their children and other children. Biol Psychiatry 56 (4), 225–232.

Lorenz, K., 1943. Die angeborenen formen möglicher erfahrung. Zeitschrift für Tierpsychologie 5 (2), 235–409.

Luck, S.J., Hillyard, S.A., 1994. Spatial filtering during visual search: evidence from human electrophysiology. Journal of Experimental Psychology: Human Perception and Performance 20 (5), 1000.

Luo, L., Ma, X., Zheng, X., Zhao, W., Xu, L., Becker, B., Kendrick, K.M., 2015. Neural systems and hormones mediating attraction to infant and child faces. Front Psychol 6, 970.

MacLeod, C., Mathews, A., 2012. Cognitive bias modification approaches to anxiety. Annu Rev Clin Psychol 8, 189–217.

Maestripieri, D., Pelka, S., 2002. Sex differences in interest in infants across the lifespan. Human Nature 13 (3), 327–344.

Malak, S.M., Crowley, M.J., Mayes, L.C., Rutherford, H.J., 2015. Maternal anxiety and neural responses to infant faces. J Affect Disord 172, 324–330.

Maupin, A.N., Hayes, N.J., Mayes, L.C., Rutherford, H.J., 2015. The application of electroencephalography to investigate the neural bases of parenting: a review. Parent Sci. Pract. 15 (1), 9–23.

McGowan, P.O., Sasaki, A., D'Alessio, A.C., Dymov, S., Labonte, B., Szyf, M., Turecki, G., Meaney, M.J., 2009. Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. Nat Neurosci 12 (3), 342–348.

Murray, L., Fiori-Cowley, A., Hooper, R., Cooper, P., 1996. The impact of postnatal depression and associated adversity on early mother-infant interactions and later infant outcome. Child Dev 67 (5), 2512–2526.

Nittono, H., Fukushima, M., Yano, A., Moriya, H., 2012. The power of kawaii: Viewing cute images promotes a careful behavior and narrows attentional focus. PloS one 7 (9), e46362.

Palermo, R., Rhodes, G., 2007. Are you always on my mind? A review of how face perception and attention interact. Neuropsychologia 45 (1), 75–92.

Pearson, R.M., Cooper, R.M., Penton-Voak, I.S., Lightman, S.L., Evans, J., 2010. Depressive symptoms in early pregnancy disrupt attentional processing of infant emotion. Psychol Med 40 (4), 621–631.

Pearson, R.M., Heron, J., Melotti, R., Joinson, C., Stein, A., Ramchandani, P.G., Evans, J., 2011a. The association between observed non-verbal maternal responses at 12 months and later infant development at 18 months and IQ at 4 years: a longitudinal study. Infant Behav Dev 34 (4), 525–533.

Pearson, R.M., Lightman, S.L., Evans, J., 2011b. Attentional processing of infant emotion during late pregnancy and mother-infant relations after birth. Arch Womens Ment Health 14 (1), 23–31.

Pearson, R.M., Lightman, S.L., Evans, J., 2011c. The impact of breastfeeding on mothers' attentional sensitivity towards infant distress. Infant Behav. Dev. 34 (1), 200–205.

Pearson, R.M., O'Mahen, H., Burns, A., Bennert, K., Shepherd, C., Baxter, H., Chauhan, D., Evans, J., 2013. The normalisation of disrupted attentional processing of infant distress in depressed pregnant women following Cognitive Behavioural Therapy. J. Affect. Disord. 145 (2), 208–213.

Peltola, M.J., Yrttiaho, S., Puura, K., Proverbio, A.M., Mononen, N., Lehtimäki, T., Leppänen, J.M., 2014. Motherhood and oxytocin receptor genetic variation are associated with selective changes in electrocortical responses to infant facial expressions. Emotion 14 (3), 469–477.

Pereira, M., Ferreira, A., 2016. Neuroanatomical and neurochemical basis of parenting: Dynamic coordination of motivational, affective and cognitive processes. Horm. Behav. 77, 72–85.

Proverbio, A.M., Brignone, V., Matarazzo, S., Del Zotto, M., Zani, A., 2006. Gender and parental status affect the visual cortical response to infant facial expression. Neuropsychologia 44 (14), 2987–2999.

Proverbio, A., De Gabriele, V., Manfredi, M., Adorni, R., 2011. No Race Effect (ORE) in the automatic orienting toward baby faces: when ethnic group does not matter. Psychology 2 (9), 931–935.

Renwick, B., Campbell, I.C., Schmidt, U., 2013. Review of attentional bias modification: a brain-directed treatment for eating disorders. Eur. Eat. Disord. Rev. 21 (6), 464–474.

Rodrigo, M.J., Leon, I., Quinones, I., Lage, A., Byrne, S., Bobes, M.A., 2011. Brain and personality bases of insensitivity to infant cues in neglectful mothers: an event-related potential study. Dev. Psychopathol. 23 (1), 163–176.

Sander, D., Grandjean, D., Scherer, K.R., 2005. A systems approach to appraisal mechanisms in emotion. Neural Netw. 18 (4), 317–352.

Seifritz, E., Esposito, F., Neuhoff, J.G., Lüthi, A., Mustovic, H., Dammann, G., von Bardeleben, U., Radue, E.W., Cirillo, S., Tedeschi, G., Di Salle, F., 2003. Differential sex-independent amygdala response to infant crying and laughing in parents versus nonparents. Biol. Psychiatry 54 (12), 1367–1375.

Seitz, A.R., Kim, D., Watanabe, T., 2009. Rewards evoke learning of unconsciously processed visual stimuli in adult humans. Neuron 61 (5), 700–707.

Sherman, G.D., Haidt, J., Coan, J.A., 2009. Viewing cute images increases behavioral carefulness. Emotion 9 (2), 282.

Shomstein, S., 2012. Cognitive functions of the posterior parietal cortex: top-down and bottom-up attentional control. Front. Integr. Neurosci. 6, 38.

Sprengelmeyer, R., Perrett, D., Fagan, E., Cornwell, R., Lobmaier, J., Sprengelmeyer, A., Aasheim, H., Black, I., Cameron, L., Crow, S., 2009. The cutest little baby face: ahormonal link to sensitivity to cuteness in infant faces. Psychol. Sci. 20 (2), 149–154.

Stein, A., Lehtonen, A., Harvey, A.G., Nicol-Harper, R., Craske, M., 2009. The influence of postnatal psychiatric disorder on child development. Is maternal preoccupation one of the key underlying processes? Psychopathology 42 (1), 11–21.

Stein, A., Murphy, S., Arteche, A., Lehtonen, A., Harvey, A., Craske, M.G., Harmer, C., 2012. Effects of reboxetine and citalopram on appraisal of infant facial expressions and attentional biases. J. Psychopharmacol. 26 (5), 670–676.

Sternglanz, S.H., Gray, J.L., Murakami, M., 1977. Adult preferences for infantile facial features: an ethological approach. Anim. Behav. 25, 108–115.

Strathearn, L., Li, J., Fonagy, P., Montague, P.R., 2008. What's in a smile? Maternal brain responses to infant facial cues. Pediatrics 122 (1), 40–51.

Swain, J.E., Lorberbaum, J.P., Kose, S., Strathearn, L., 2007. Brain basis of early parent-infant interactions: psychology, physiology, and in vivo functional neuroimaging studies. J. Child Psychol. Psychiatry 48 (3–4), 262–287.

Theeuwes, J., 1991. Cross-dimensional perceptual selectivity. Percept. Psychophys. 50 (2), 184–193.

Theeuwes, J., 1992. Perceptual selectivity for color and form. Percept. Psychophys. 51 (6), 599–606.

Theeuwes, J., 1994. Stimulus-driven capture and attentional set: selective search for color and visual abrupt onsets. J. Exp. Psychol. Hum. Percept. Perform. 20 (4), 799.

Thompson-Booth, C., Viding, E., Mayes, L.C., Rutherford, H.J., Hodsoll, S., McCrory, E.J., 2014. Here's looking at you, kid: attention to infant emotional faces in mothers and non-mothers. Dev. Sci. 17 (1), 35–46.

Van Bockstaele, B., B. Verschuere, H. Tibboel, J. De Houwer, G. Crombez and E. H. Koster (2013). "A Review of Current Evidence for the Causal Impact of Attentional Bias on Fear and Anxiety." Psychol. Bull.

Vuilleumier, P., Pourtois, G., 2007. Distributed and interactive brain mechanisms during emotion face perception: evidence from functional neuroimaging. Neuropsychologia 45 (1), 174–194.

Weisman, O., Feldman, R., Goldstein, A., 2012. Parental and romantic attachment shape brain processing of infant cues. Biol. Psychol. 89 (3), 533–538.

6.2. Artigo 2: "*Correlation between Automatic Attention Engagement to Infant Faces and Behavioral Components of Maternal Sensitivity*"

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Correlation between automatic attention engagement to infant faces and behavior components of maternal sensitivity

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Abstract

Sensitive maternal behavior in the first months after birth impacts child development. Our aim was to investigate the association between maternal automatic attention towards emotional infant faces and components of maternal sensitive behavior. Eighty-two mother-child dyads were filmed in free interaction one month post-partum, and mothers performed an cognitive processing task with infant expressing different emotions (happy, distress and neutral) as stimuli. Enhanced attention engagement towards infant distress stimuli on the attentional task correlated with the maternal ability to acknowledge her infant needs during the interaction.

Key words: mother-infant; attention, maternal sensitivity, emotion processing

Introduction

The quality of mother-infant interaction impacts child development (Barrett & Fleming, 2011). Maternal sensitivity is a key component of good mother-infant relationships. It is associated with secure attachment and better cognitive/social development (Feldman, 2010). During sensitive periods, children's neurobehavioral development is more susceptible to be influenced by the environment, especially by the interaction with parents and peers. The first months after birth are a sensitive period where maternal behavior persistently impacts infant development (Feldman, 2015) .

Infant stimuli provoke greater activation and arousal than adult stimuli in brain areas related to attention (parietal regions and posterior cingulate cortex), emotion processing (Orbitofrontal Cortex, insula), reward, empathy and motor behavior (e.g Striatum and Superior Frontal Gyrus) (Luo et al., 2015). Therefore, activation of these areas elicited by the emotion processing of infant faces might be a precursor of maternal behavior. Infant stimuli capture more attention from adults than adult stimuli, this effect is stronger in mothers than non-mothers(Lucion et al., 2017) . Pearson et al. 2011 showed that pregnant women with higher attentional bias towards infant distress report themselves as having a better bonding with their babies after birth through the postpartum bonding questionnaire (PBQ) (Pearson, Lightman, & Evans, 2011). However, the possible correlation between measures of automatic attention allocation towards different infant emotions faces and the actual observed quality o the mother-infant relationship was never investigated, and this was our objective.

Materials and methods

Mother-infant pairs fulfilling the inclusion and exclusion criteria (living in Porto Alegre-RS, Brazil, >= 18 years of age, no current or past history of drug abuse, singleton gestation of at least 37 weeks' duration, no more than four previous gestations, newborn without congenital disease and not requiring hospitalization) were recruited during prenatal visits or immediately after giving birth, from February/2015 to January/2016.

The project received approval from Grupo Hospitalar Nossa Senhora da Conceição and Hospital de Clinicas de Porto Alegre Ethics boards (GPPG/HCPA 13-0507). After signing the informed consent and providing baseline information, dyads were visited at home 25-40 days after birth for the cognitive processing task and mother-infant relationship assessment.

The cognitive processing task was based on the computerized paradigm established by Pearson (Pearson, Cooper, Penton-Voak, Lightman, & Evans, 2010), with a set of pictures validated for the Brazilian population in a previous study (Arteche, Vivian, Dalpiaz, & Salvador-Silva, 2016; Rodrigues, 2015; Oliveira et al., 2017). This task consists in go/no go trials having images of babies and adults faces with 3 types of emotions expressed for each age (baby-distress, baby-neutral, baby-happy, adult-fear, adult-neutral and adult-happy) as stimuli. The trial started with a black cross at the center of a blank screen for 750ms. Next, a face image with a superimposed green or red cross appeared for 240ms at the center of the screen; red crosses indicated no-go trials, and green crosses meant go trials. Mothers were oriented to ignore the face images, and to press the space bar from the computer keyboard in ‘no go’ trials; in ‘go’ trials, they were asked to identify in which corner (left or right) a vertical line was placed, by pressing the keyboard right or left arrows. The task was designed to measure attention engagement by the stimuli, being longer reaction time representative of higher attention engagement toward stimuli. The task run on E-prime 2.0 (PST Inc., USA), which was designed to randomly assign the blocks order and to compute the reaction time. E-prime computed the reaction time in milliseconds (ms). Data was extracted from E-prime to a spreadsheet and subsequently to the statistical software for analysis.

Mother-infant interaction was scored based on 5 minutes filmed free interaction. Dyadic behavior was analyzed with the use of Coding Interactive Behavior (CIB) for newborns. CIB is widely used instrument to code mother-infant interaction throughout child life. It has been used in cohorts, proving to have behavior constructs related to child development. Coding Interactive Behavior (CIB) for newborns includes the evaluation of maternal gaze, affect, vocalization, touch, mother-infant positioning, child affect, alertness and vocalization every 10 seconds; global evaluation of maternal acknowledging, intrusiveness and affect are also scored in a 1 to 5 scale, being 1 minimum of specific behavior occurring and 5 the maximum possible to occur (Feldman, 1998). A Psychiatrist trained on the coding system, and blinded for the attentional task results, performed CIB. There were 5 behaviors of special interest in this study: maternal gaze to infant face, maternal positive affect, ‘motherese’ speech, affectionate touch and parental acknowledging due their importance for bonding and child development (Feldman & Eidelman, 2003;

Feldman, Weller, Zagoory-Sharon, & Levine, 2007). The first four behaviors were computed as a proportion of time that they happened during the interaction, therefore they vary from 0 to 100%. Parental acknowledging is considered the mother's ability to read, understand, and respond to infant signs in a sensitive manner, and is scored from 1 (no acknowledging) to 5, in 0.5 increments.

Data were entered and analyzed in the Statistical Package for the Social Sciences (SPSS) 20.0 software (SPSS Inc., Chicago, IL, USA). Quantitative variables were described as mean ± standard deviation of the mean (SD), whereas categorical data were described using relative (%) frequencies. Non-parametric test Spearman's correlation (r_s) analyses were performed to investigate possible correlations between the attention processing and maternal behavior components, since most variables did not reach normal distribution. Significance levels for all measures were set at $p<0.05$.

Results

Eighty-two dyads joined the study. Data from 3 mothers were excluded due to problems in filming the mother-infant interaction or performing the attentional task. Mean maternal age was 27 years (SD=5.48 years), 12.7% had less than 8 years of education and 19% were single (not living with partner). Mean gestational age was 39.15 weeks (SD=1.1 weeks), 47,5% were primiparous, 44.3% of the infants were female, and 70.1% of the sample was on exclusive breastfeeding, average baby age during visits was 29.8 days (SD= 3.75).

Table 1 shows the mean reaction time on the attentional task per block type. On average, mothers spent 80.21% (SD=21.37) of the time looking at their infants' face. Mean positive maternal affect comprised 41.19% of the time (SD=27). Motherese occurred on average 25.73% of the time (SD=26.25) and affectionate touch happened in 14.76% of the time (SD=14.9). Mean parental acknowledging score was 2.88 (SD=0.99).

When analyzing the attentional engagement by each set of infant stimuli (infant distress, happy and neutral face), we observed a statistically significant correlation between the reaction time on the infant distress block and parental acknowledging (r_s=0.244 p=0.030). The correlations with other components of maternal behavior were not significant (gaze infant face r_s=0.138, p=0.226; positive affect r_s=0.120, p=0.292; motherese speech r_s=0.169, p=0.136; affectionate touch r_s=-0.26, p=0.818).

There were no statistical significant correlations between mean reaction time on happy (gaze infant face r_s=0.072, p=0.529; positive affect r_s=0.039, p=0.736; motherese speech r_s=0.102, p=0.373; affectionate touch r_s=-0.091, p=0.424 and acknowledgement r_s=0.180, p=0.113) and neutral infant blocks (gaze infant face r_s=0.104, p=0.362; positive affect r_s=0.115, p=0.315; motherese speech r_s=0.094, p=0.410; affectionate touch r_s=-0.086, p=0.453 and acknowledgement r_s=0.147, p=0.197) and behavioral components of maternal sensitivity.

Discussion

To our knowledge this is the first study to analyze patterns of automatic attention allocation towards infant emotion and behavioral measures of mother-infant relationship after birth. Longer reaction time towards infant distress was positively correlated with higher scores of parental acknowledging. This finding agrees with previous results described by Pearson et al.(Pearson et al., 2011) where greater engagement with infant distress was associated to better reported bonding with infant. However, here we extended this to observed maternal behaviour. Although evidence for the relationship is relatively subtle, it is notably that a simple automatic task like the measurement of attention engagement to infant distress can somewhat predict specific aspects of maternal behavior. Acknowledging is described as the mothers' ability to detect, understand and respond to infant signs. This is an important feature of sensitive parenting according to CIB which is related to child development(Feldman, 2010). Pending replication, results described here have a strong potential for clinical application in detecting vulnerable dyads for poor mother-infant bonding and understanding the cognitive basis of sensitive maternal behaviour.

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Arteche, A., Vivian, F., Dalpiaz, B., & Salvador-Silva, R. (2016). Effects of Sex and Parental Status on the Assessment of Infant Faces. *Psychology & Neuroscience, 9*(2), 176-187. doi:http://dx.doi.org/10.1037/h0101552

Barrett, J., & Fleming, A. S. (2011). Annual Research Review: All mothers are not created equal: neural and psychobiological perspectives on mothering and the importance of individual differences. *J Child Psychol Psychiatry, 52*(4), 368-397. doi:10.1111/j.1469-7610.2010.02306.x

Feldman, R. (1998). Mother–newborn coding system manual. In. Tel Aviv, Israel: Bar-Ilan University University Press.

Feldman, R. (2010). The relational basis of adolescent adjustment: trajectories of mother-child interactive behaviors from infancy to adolescence shape adolescents' adaptation. *Attach Hum Dev, 12*(1-2), 173-192. doi:10.1080/14616730903282472

Feldman, R. (2015). Sensitive periods in human social development: New insights from research on oxytocin, synchrony, and high-risk parenting. *Dev Psychopathol, 27*(2), 369-395. doi:10.1017/S0954579415000048

Feldman, R., & Eidelman, A. I. (2003). Direct and indirect effects of breast milk on the neurobehavioral and cognitive development of premature infants. *Dev Psychobiol, 43*(2), 109-119. doi:10.1002/dev.10126

Feldman, R., Weller, A., Zagoory-Sharon, O., & Levine, A. (2007). Evidence for a neuroendocrinological foundation of human affiliation: plasma oxytocin levels across pregnancy and the postpartum period predict mother-infant bonding. *Psychological Science, 18*(11), 965-970. doi:10.1111/j.1467-9280.2007.02010.x

Lucion, M. K., Oliveira, V., Bizarro, L., Bischoff, A. R., Silveira, P. P., & Kauer-Sant'Anna, M. (2017). Attentional bias toward infant faces - Review of the adaptive and clinical relevance. *Int J Psychophysiol*. doi:10.1016/j.ijpsycho.2017.01.008

Luo, L., Ma, X., Zheng, X., Zhao, W., Xu, L., Becker, B., & Kendrick, K. M. (2015). Neural systems and hormones mediating attraction to infant and child faces. *Front Psychol, 6*, 970. doi:10.3389/fpsyg.2015.00970

Oliveira, V., Goulart, M., Nobre, J., Lucion, M., Silveira, P., & Bizarro, L. (2017). Emotional interference of baby and adult faces on the automatic attention in parenthood. *Psychology & Neuroscience, 10*(2), 144-153. doi:http://psycnet.apa.org/doi/10.1037/pne0000085

Pearson, R. M., Cooper, R. M., Penton-Voak, I. S., Lightman, S. L., & Evans, J. (2010). Depressive symptoms in early pregnancy disrupt attentional processing of infant emotion. *Psychological Medicine, 40*(4), 621-631. doi:10.1017/S0033291709990961

Pearson, R. M., Lightman, S. L., & Evans, J. (2011). Attentional processing of infant emotion during late pregnancy and mother-infant relations after birth. *Arch Womens Ment Health, 14*(1), 23-31. doi:10.1007/s00737-010-0180-4

Rodrigues, M. (2015). *Composição de um banco de expressões faciais brasileiro: um estudo de validação e comparação transcultural.* . (Master's Degree), Universidade Federal da Paraíba, João Pessoa,

Table 1. Reaction time per block type

Block Type	Reaction Time (ms)
Happy infant	689.2 (188)
Neutral infant	703.3(191)
Distress infant	677.6(198)
Happy adult	691.4(189)
Neutral adult	696.5(179)
Fear adult	688.5(193)

Values are given in mean (standard deviation)

6.3. Artigo 3: *“Cognitive Processing, Inflammation, Environment and Maternal Behavior in Early Postpartum”*

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Cognitive Processing, Inflammation, Environment and Maternal Behavior in Early Postpartum

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Abstract

Background: Cognitive processing of stimuli is important for activating proper behavior. Different aspects can alter cognitive processing, as inflammatory marker interleukin 6 (Il-6). Our objective was to analyse correlations between cognitive processing, interleukin-6 and maternal behavior. Methods: Fifty-one mother-infant dyads were visited at home 1 month postpartum. In this visit mothers performed a go/no-go cognitive processing task with infant and adult faces expressing different emotions as a measure of cognitive processing, maternal blood was collected for interleukin-6 level measure, and dyads were filmed during 5 minutes free interaction. Data about familiar income was also acquired. Results: There was positive correlation between reaction time on cognitive processing task and Il-6 levels; negative correlation between Il-6 and maternal affiliative behaviour; and participants with lower-income had less amount of maternal affiliative behaviour and higher Il-6 levels. All 4 variables were set in a Structural Equation model resulting in a more integrative approach. In this model differences on Il-6 and maternal behavior according to income, Il-6 correlation with maternal affiliative behavior and reaction time persisted; and reaction time on go/no-go task became positively correlated to maternal affiliative behavior. Conclusion: Cognitive processing of faces expressing emotion during early postpartum seems to be related to Il-6 levels. Our data suggest the importance of economic status and inflammatory processes for modulating the quality of maternal care.

Keywords: maternal behaviour; cognitive processing; inflammation; poverty; postpartum; mother-infant relationship, socioeconomic

Introduction

Human faces are salient stimuli capable of activating several brain regions (amygdala, insula, cingular cortex, prefrontal cortex) (Brosch, Sander, and Scherer 2007, Luo et al. 2015, Haxby, Hoffman, and Gobbini 2002, Kim, Strathearn, and Swain 2016, Vuilleumier and Pourtois 2007). Mothers have a distinct cognitive processing of infant emotional cues when compared to non-mothers (Moses-Kolko et al. 2014, Lucion et al. 2017, Kim, Strathearn, and Swain 2016). Parents have higher responses to infant stimuli than non-parents(Oliveira et al. 2017). The heightened salience of infant signals to mothers might have been an evolutionary adaptation since nonverbal communication is predominant on the first months after birth (Parsons et al. 2010). Moreover, differences in cognitive processing of infant emotional stimuli are related to differences in maternal care. Indeed, synchronic mothers (i.e. those who show sensitive interaction with their children in a time-coordinated manner) process infant stimuli in a different manner than non-synchronic ones, as well as good caregivers do in comparison to neglectful parents (Kim et al. 2011, Moses-Kolko et al. 2014, Rodrigo et al. 2011, Pearson, Lightman, and Evans 2011).

As in other animals, studies have shown that specific sets of maternal behavior and attunement towards infant signals during sensitive periods impact child hypothalamic–pituitary–adrenal axis (HPA), oxytocin levels and signalling, as well as cognitive and psychosocial developments (Feldman 2010, Feldman and Eidelman 2006, Feldman et al. 2013, Tarullo and Gunnar 2006, Raby et al. 2015, Feldman 2015). Maternal positive affect, gaze towards infant's face, affectionate touch (e.g. caressing) and motherese speech in the first months after birth have been considered behaviors related to caring mothers, the first 3 being related to higher oxytocin levels in infants. Those behaviors should be coordinated with infant signs in order to develop sensitive parenting (Feldman 2015, Granat et al. 2016, Feldman et al. 2002, Feldman et al. 2007). For that, mothers need to have their attention engaged to infant cues and be able to process them.

Some environmental adversities such social disadvantages and maternal diseases (i.e mood disorders and drug abuse) have been related to alterations in both maternal behavior and cognitive processing, and also to raised levels of inflammatory cytokines (Kim et al. 2017, Landi et al. 2011, Morozink et al. 2010, Petersen et al. 2008, John-Henderson et al. 2016, Araos et al. 2015, Moreira et al.

2016, de Britto Rosa et al. 2011, Fraga et al. 2015, Pearson et al. 2010, Köhler et al. 2017, Kim and Bianco 2014). More specifically, interleukin 6 (Il-6) has been consistently linked to alterations in cognitive processing. Higher levels of peripheral Il-6 are related to cognitive dysfunction in drug users, cirrhotic and cardiovascular patients, and depression (Trapero and Cauli 2014, Levandowski et al. 2016, Athilingam et al. 2013, Sukoff Rizzo et al. 2012). Induced neuroinflammation, with the rise of Il-6 levels, promotes a blunted reaction to reward in ventral striatum, an important brain region for motivating maternal caregiving behavior (Eisenberger et al. 2010, Kim, Strathearn, and Swain 2016).

Another important relation of Il-6 is with socioeconomic status. Disadvantaged socioeconomic status (SES) has been linked to higher levels of Il-6 in different populations (Petersen et al. 2008, de Britto Rosa et al. 2011, Morozink et al. 2010). Life stressors and social support modulate the relationship between Il-6 levels and socioeconomic disadvantage, in such a way that exposure to adverse life events is correlated to higher levels of Il-6, but availability of social support dampens Il-6 reactivity in stressful situations (John-Henderson et al. 2015, John-Henderson et al. 2016).

Given the importance of maternal cognitive processing of emotion and the apparent role of inflammatory interleukin 6 in disorders with cognitive impairment, we hypothesized that this biological marker would be related to maternal cognitive processing in the first month postpartum. To our knowledge there is no study investigating the possible role of inflammatory cytokine in maternal cognitive processing of infant and adult facial stimuli expressing emotions. Therefore, the aim of the present study was to analyze the relation of Il-6 with cognitive processing on first postpartum month. Moreover, we used an integrated approach to investigate possible relations between cognitive processing, Il-6, family income and maternal behavior. We hypothesized that higher Il-6 would be correlated with altered cognitive processing and maternal behavior. As supported by literature we predicted that Il-6 levels and maternal behavior would be influenced by family income.

Methods

Participants and Design

Mothers eligible for the study were invited in their primary care facility visit prior to childbirth or in the hospital after they gave birth to join the study. Inclusion criteria were having at least 18 years old, singleton gestation, no more than 4 previous gestations, no current or past history of drug abuse, and normal or corrected eye vision. Exclusion criteria were preterm birth (less than 37 weeks), and baby with congenital disease or required hospitalization on intensive care unit after birth. Results presented in this article consist in data of part of a bigger sample. For this article woman who did not had Il-6 measures were excluded.

During the first interview, mothers answered to a Brazilian validated questionnaire about family income (named *Criterio Brasil de Classificaçao Econômica*-ABIPEME)(ABEP) and a questionnaire with general data about family formation, education, family support, and mother and child's health. Dyads were visited at home 25 to 40 days after labour (M= 29.5 SD=4.02). Three dyads were seen at the research institute. All visits occurred between 2 and 6 p.m. This visit comprised an attentional task, a questionnaire about mother and infant health, a five-minute filmed free interaction, and a maternal blood sample collection (see details below).

Invitation and visits occurred from February 2015 to January 2016. Fifty-three participants joined the study and had Il-6 measured. Table 1 shows sample characteristics. One participant did not perform the go/no-go task and one recorded interaction was excluded due to lack of recording quality that precluded further coding.

The project was reviewed and approved by Hospital de Clínicas de Porto Alegre and Grupo Hospitalar Nossa Senhora da Conceição Ethic boards (GPPG/HCPA 13-0507) and all participants provided written assigned consent.

Measures

Family income

ABIPEME is a standardized instrument used to evaluate family income in Brazil (ABEP). It considers housing characteristics, home appliances and car possession, and educational level. It is divided in classes, being A representative of the highest income and D the lowest. For the sake of the analysis, we grouped into a binary variable: high income, representing A and B classes, and low income comprising C and D.

Attentional Task

The attentional task applied was based on the computerized paradigm established by Pearson (Pearson et al. 2010), with a set of pictures validated for the Brazilian population (Oliveira et al. 2017). This task consists in go/no go trials having images of infants and adults faces with 3 types of emotions expressed for each age: happy infant, neutral infant, distress infant, happy adult, neutral adult, and fear adult . The trial started with a black cross shown at the center of a blank screen for 750ms. Next, a face image (stimulus) with a superimposed green or red cross flanked by a vertical and a horizontal bar appeared for 240ms at the center of the screen; red crosses indicated no-go trials, and green crosses meant go trials. Mothers were oriented to ignore the face images, to press the space bar from the computer keyboard in ‘no go’ trials; in ‘go’ trials, they were asked to identify in which corner (left or right) a vertical line was placed, by pressing the right or left arrows of the keyboard. There were two trial blocks for participants adapt to the task, one without images behind the green and red cross, and one with objects images behind the color cross. The task run on E-prime 2.0 (PST Inc., USA), which was designed to randomly assign face stimuli, type of trial (go or no-go) and bar combination, as well as the blocks’ order, and to compute reaction time. E-prime computed the reaction time in milliseconds (ms). Data was extracted from E-prime to a spreadsheet and subsequently to the statistical software for analysis. Babies would be under the supervision of an adult family member or one of the two research assistants while the mother was executing the task.

Maternal Behavior

Maternal behavior was analyzed with the use of Coding Interacting Behavior (CIB) for newborns. Mothers were oriented to interact freely with their baby for 5 minutes. The interaction was recorded for posterior coding. A Psychiatrist that completed training program on CIB and was blinded for the attentional task and interleukin results performed the coding. CIB for newborns includes the evaluation of maternal gaze, affect, vocalization, touch, mother-infant positioning, child affect, alertness and vocalization every 10 seconds (Feldman 1998). In this study, we focused on maternal behaviors that are considered as caring behaviors and related to child development: maternal gaze to infant face, maternal positive affect, motherese speech, and affectionate touch (Feldman and Eidelman 2007, Feldman et al. 2007, Feldman and Eidelman 2003). These behaviors were computed as a proportion of time that they happened during the five minutes interaction, therefore they vary from 0 to 100%. As in other articles that used CIB, we computed the sum of these 4 behaviors as an indices of Maternal Affiliative Behavior (MAB), and this sum was used in the analyses (Feldman and Eidelman 2007, Feldman et al. 2007). CIB is a widely used method of evaluating mother-infant interaction with cohorts from birth until adolescence showing relation between its constructs and child development (Feldman 2015).

Interleukin-6

Blood was collected between 2 and 6 p.m. and kept in cold transportation until centrifuged for 10 minutes in the research facility. Serum was aliquoted and stored in -80°C. Il-6 was measured with the use of Milliplex® Map Human High Sensitivity T Cell Magnetic Bead Panel on first time-thawed samples. Minimum assay sensitivity for Il-6 is 0.11pg/ml by an experienced laboratory technician according to the manufacturer instructions.

Statistical analysis

Variables' distributions were analyzed by Shapiro–Wilk test. All reaction times were log transformed to fit a normal distribution. Repeated measures ANOVA was performed to compare mean reaction time according to block type. Bivariate correlations were used to analyze the relationship between two continuous variables, Student's *t* Test was used to compare means between groups, and Chi-square test to compare categorical variables between low and high income groups. Structural Equation Model was performed including the variables of interest considering the complex relation between variables. Data were analyzed in the Stata 14.0 software (StataCorp LP, TX, USA).

Results

Table 1 describes the socio-demographic characteristics of the total sample, and compares high and low income groups. As expected, low and high income differ on maternal education. All other socio-demographic variables did not differ between groups. The results of the Attentional Task show the following mean reaction time and standard deviation according to stimuli block type: happy infant 682.4 ms (SD=192.29), neutral infant 680.0 ms (SD=168.85), distress infant 666.6 ms (SD=199.72), happy adult 675.8 ms (SD=181.10), neutral adult 689.9 ms (SD=179.05) and fear adult 682.8 ms (SD=192.42). A repeated measures ANOVA, performed to investigate differences in reaction time according to the age and emotion expressed by the stimulus, shows that there was no statistically significant difference between reaction times on the different emotions for both infant images (p=0.548) and adult images (p=0.542). Therefore, two new variables were created: Infant Trials, mean reaction of all infant faces trials (mean=682.03, SD=182.12), and Adult Trials mean reaction times for all adult ones (mean=689.70, SD=173.71).

The coding of maternal behavior revealed that mothers spent an average 83.5% of the time looking at their infant's face, 40.2% of the time demonstrating positive affect during the interaction, 26.9% of the time performing "motherese" vocalization and 17.2% of the total time showing affectionate touch (note: these behaviors are not mutually exclusive). Maternal affiliative behavior (MAB) values vary from 42 to 320 on this sample, mean=167.8(SD=59.39). Il-6 mean level was 1.32pg/ml (SD=0.63). Two participants were considered outliers (Il-6 levels were above 3 SD of the mean) and were excluded from further analyses.

Table 2 shows the correlations between reaction times in adult and infant trials, Il-6 and maternal affiliative behavior. Il-6 level was positively correlated with both adult trial (r=0.443, p=0.001) and infant trial (r=0.432, p=0.002) and negatively correlated with maternal affiliative behavior (r=-0.313, p=0.027). Maternal behavior was not correlated with any reaction time. Table 3 presents a comparison of reaction time on infant and adult trials, Il-6 levels and maternal affiliative behavior measure according to income. Low-income group had less quantity of maternal affiliative behaviors and higher levels of serum Il-6. There was no difference on reaction time to infant and adult trials according to income.

Considering the results above, a Structural Equation model was set to analyze the correlation between those variables. Two models were created, one considering reaction time on Infant Trials and another on Adult Trials due to possible higher significance of infant processing for mothers.

Table 4 and Figure 1 contains the results and path model of Structural Equations on the Infant Trials. Lower family income group was related to higher levels of Il-6 and less amount of maternal affiliative behavior. Il-6 level was positively correlated with reaction time on cognitive processing task, and negatively correlated to maternal affiliative behavior. Higher reaction time was positively correlated to maternal affiliative behavior. Table 5 and Figure 2 express results and path model considering the Adult Trial, showing a similar pattern of variables correlation that was seen in Infant Trial model.

Discussion

The present study integrated four different aspects of motherhood: maternal behavior, cognitive processing, maternal social environment via family income, and a biological marker of inflammation. These elements are complex per se and the analysis of their interaction creates an integrative picture more related to the reality than their individual analysis, but still a rather challenging to be interpreted. First, we will discuss the bivariate relations (Il-6 and reaction time, maternal affiliative behavior and reaction time, income and Il-6, income and maternal affiliative behavior), and later the structural equation model.

Our results showed positive correlations between serum Il-6 levels in postpartum mothers and cognitive processing of infant and adult faces expressing different emotions, as women with higher levels of Il-6 had longer reaction times on the go/no-go task. To our knowledge this is the first study that correlated higher levels of serum Il-6 with cognitive processing in women during the postpartum period. The go/no-go task was a behavior test in which the reaction time to press a specific key was measured. The stimuli presented in the task are considered distractors, and longer reaction time is supposed to be a measure of attention engagement towards the stimuli (Pearson et al. 2010). However, there is no assurance that the reaction time would only represent a measure of attention engagement. The longer reaction time could also represent poorer cognitive function. It is possible that higher Il-6 levels could impair cognitive flexibility altering maternal ability to execute the multiple task commands (identify cross color, and locate peripheral target). In fact, higher levels of Il-6 have been linked to poorer executive function and worse cognitive flexibility in women with a history of drug abuse (Levandowski et al. 2016). Brydon *et al.* 2008 also described the relation between higher levels of Il-6 and worse executive function(Brydon et al. 2008). Therefore, we could interpret the positive correlation between higher serum Il-6 and longer reaction time as a negative effect of neuroinflammation on cognitive processing. Moreover, as discussed below, Il-6 was negatively correlated with maternal affiliative behavior. A balanced cognitive processing between attentional engagement and cognitive flexibility seems to be crucial for the establishment of sensitive maternal behavior (Barrett and Fleming 2011, Moses-Kolko et al. 2014, Pereira and Ferreira 2016). Behavioral tests of cognitive processing are interesting research tools with possible clinical application due to their low cost and relative easiness to be performed. However, they are non-specific measurements of cognitive processing.

Results also showed negative correlations between serum Il-6 and maternal affiliative behavior. A previous study demonstrated that inflammation, with increased levels of Il-6, causes anhedonia and alters reward processing(Eisenberger et al. 2010). Modification on rewards circuitry can negatively impact maternal behavior (Kim et al. 2010, Kim, Strathearn, and Swain 2016). Several lines of investigation have shown that the reward system is critical for the establishment and maintenance of maternal care (Barrett and Fleming 2011, Kim, Strathearn, and Swain 2016, Moses-Kolko et al. 2014, Pereira and Ferreira 2016). This system changes during gestation and postpartum. Some stimuli that are usually aversive to non-mothers, as baby distress, become salient and even rewarding to mothers to engage affective maternal behavior (Barrett and Fleming 2011, Kim, Strathearn, and Swain 2016, Swain, Kim, and Ho 2011, Brunton and Russell 2008). Ahn and Corwin 2015 demonstrated lower Il-6 levels in breastfeeding mothers compared to bottle feeding ones at 6 moths postpartum (Ahn and Corwin 2015). Considering that maternal sensitivity has been related to breastfeeding (Kim et al. 2011, Jonas et al. 2015, Tharner et al. 2012, Papp 2014), this study seem to agree to our results, in which lower levels of Il-6 were correlated with more maternal affiliative behavior. In our sample the majority of mothers were breastfeeding, therefore we could not test if Il-6 levels were different between breastfeeding and bottle-feeding mothers.

Results from the unadjusted analysis showed no significant correlation between maternal affiliative behavior and the reaction times on infant and adult trials. It was expected a positive correlation between reaction time to infant faces and maternal affiliative behavior, since Pearson et al. 2011 using the same cognitive task correlates maternal bonding in postpartum period to higher attention engagement (longer reaction time) towards infant distress during pregnancy (Pearson, Lightman, and Evans 2011). No difference in reaction time according to the emotional stimuli was detected in our sample. A possible reason to explain the discrepancies is the use of pictures of unfamiliar infants in a study with mothers who already knew their infant’s faces, differing from Pearson’s sample that had only pregnant women. Both variables are complex, depending on several components. They can be better interpreted when a more integrated approach is used, as analyzed later. When other variables were controlled for, a positive correlation between reaction time and maternal affiliative behavior was observed.

Our study demonstrated that postpartum mothers in disadvantage economic situation had higher levels of serum Il-6 than participants of high-income group. The immune system appears to be permeable to environment characteristics and social support (Morozink et al. 2010, John-Henderson et al. 2015, John-Henderson et al. 2016, Carroll, Cohen, and Marsland 2011, Fagundes, Glaser, and Kiecolt-Glaser 2013, Slopen et al. 2015). Difference in Il-6 peripheral levels according to socioeconomic status has been shown in other studies (de Britto Rosa et al. 2011, Fraga et al. 2015, Morozink et al. 2010), but, to our knowledge, this is the first time that it was identified in early postpartum. Economic conditions seem to have long lasting effects on Il-6 levels, and it secretion during stressful events (Miller and Chen 2007, Miller, Chen, and Parker 2011, John-Henderson et al. 2015, John-Henderson et al. 2016). A noteworthy study describes that lower socioeconomic status during childhood is related to a differential immune reactivity when exposed to a stressful situation in adulthood, which is modulated by social support (John-Henderson et al. 2015). Another aspect to be considered in our results is that the levels of Il-6 might be a marker of harsher past childhood environment for the mothers. Unfortunately, we do not have information about maternal past socioeconomic status.

Family income was highly related with maternal affiliative behaviors, independently of other variables. Socioeconomic disadvantage was related to less maternal behavior as early as the first postpartum month, reinforcing the vulnerability of economically disadvantaged populations. Other studies have also pointed to altered maternal behavior associated with income (Evans and Kim 2010, Siqveland, Smith, and Moe 2012, Sturge-Apple, Jones, and Suor 2017, Kim and Bianco 2014). Economic status influences multiple aspects of a person life, low-income is often related with lower educational level, less social support, violence, worse housing condition, less access to medical care and worse alimentary quality in a cumulative way (Evans and Kim 2010, Kim and Bianco 2014). All those items can be involved in higher inflammation, stress response and also impact cognitive processing. In a neuroimaging study, Kim et al. 2017 reports different activation of the neural reward system (amygdala and insula) between mothers with different socioeconomic status while processing infant stimuli, altering maternal sensitive behavior (Kim et al. 2017). The finding of less quantity of maternal sensitive behavior in the lower-income group is particularly important for us, since Brazil is a country in development, with the majority of its population belonging to C and D classes (group considered low income is this study). The data presented here reinforces the importance of public intervention to better support mothers and their children in economic disadvantage situation.

When the four variables were set in a structural equation model, the correlations among income, Il-6, and maternal affiliative behavior persisted. The persistence of the correlation, when variables were controlled, reinforces the importance of Il-6 and income on maternal affiliative behavior. Even controlled for income, Il-6 negatively correlated with maternal affiliative behavior, thus Il-6 per se seems important for maternal behavior. The identification of aspects that individually impact maternal behavior is an important but challenging task. The finding of those aspects helps the recognition of higher risk dyads and the development of intervention strategies.

Once integrating the four variables, longer reaction time positively correlated with maternal affiliative behavior, differently than what was observed using bivariate correlations. As discussed previously, the cognitive task was designed to measure attention engagement (Pearson et al. 2010). The hypothesis was that mothers with higher attention engagement towards infant emotional stimuli would also display more maternal affiliative behavior. Possibly the adjustment for Il-6 and income reduced the interference of these aspects have on cognitive processing and maternal behavior. One possible explanation, is that Il-6 interferes with maternal cognitive flexibility (a mother's ability to shift attention and perform multiple tasks, as needed on the go/no-go task) inducing longer reaction time. Indeed, a previous study have linked worst cognitive flexibility with higher Il-6 levels (Levandowski et al. 2016). Cognitive flexibility is correlated with better maternal behavior and sensitivity (Chico et al. 2014). Therefore, we may infer that Il-6 interferes with cognitive flexibility promoting longer reaction time on the cognitive processing task, which is not related to more maternal affiliative behaviour.

Although this study presents some interesting findings and strong points, as being able to gather different aspects of maternity in one model, it has some limitations. This was a cross-sectional study, therefore no causality can be inferred from the results. The attentional task uses pictures of unfamiliar infants to mothers who already know their babies. Most studies of neuroimaging show a different pattern of brain activation when visualizing own infant versus unfamiliar (Luo et al. 2015, Laurent and Ablow 2013, Atzil, Hendler, and Feldman 2011). The use of unfamiliar infants may have lowered the difference on processing of both groups. Even though, it is interesting to find relation between the cognitive processing task and maternal behavior, not measured by self-report questionnaires. Another limitation was that we measured peripheral levels of Il-6, this may not correspond to higher levels in the brain and does not identify in which brain areas this possible neuroinflammation occurs. Although animal model suggests relation between neuroinflammation and rises in peripheral Il-6 (Yang et al. 2013).

The study highlights the importance of an integrative approach to simultaneously address the different aspects involved in maternal behavior. There might be an interesting link between maternal sensitive behavior, Il-6 levels and income since there was a correlation between these variables and all are beneficiate by social support. Furthermore, studies show that maternal caring behavior has a protective role for child development in harsher economic environment (Evans and Kim 2010, Odgers et al. 2012, Fagundes, Glaser, and Kiecolt-Glaser 2013, Meins et al. 2013). Rodent models have shown that a better quality of maternal care on the first 10 days after birth impacts neurodevelopment through persistent epigenetic changes in the pup. In rats, this period would roughly correspond to 1 month in humans (Curley and Champagne 2016, Champagne et al. 2006, Peña, Neugut, and Champagne 2013, Weaver et al. 2004). As mentioned, the immune system seems to be modified by the environment, and this influence may be particularly important early in life(Carroll, Cohen, and Marsland 2011). May be maternal affiliative behavior could lower the impact of disadvantage economic situation on the children immune system. In the current study, an integrative approach involving the environment, the cognitive function, and an inflammation marker unravels possible effects on maternal affiliative behavior in a very early period of infant development. Future studies associating other experimental techniques such as neuroimaging and longitudinal approach may contribute further to the inference of causal relations among those variables.

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ABEP, Associação Brasileira de Empresas de Pesquisa -. "O Novo Critério Padrão de Classificação Econômica Brasil – Critério Brasil de Classificação Economica. 2014.". http://www.abep.org.

Ahn, S., and E. J. Corwin. 2015. "The association between breastfeeding, the stress response, inflammation, and postpartum depression during the postpartum period: Prospective cohort study." *Int J Nurs Stud* 52 (10):1582-90. doi: 10.1016/j.ijnurstu.2015.05.017.

Araos, P., M. Pedraz, A. Serrano, M. Lucena, V. Barrios, N. García-Marchena, R. Campos-Cloute, J. J. Ruiz, P. Romero, J. Suárez, E. Baixeras, R. de la Torre, J. Montesinos, C. Guerri, M. Rodríguez-Arias, J. Miñarro, R. Martínez-Riera, M. Torrens, J. A. Chowen, J. Argente, B. J. Mason, F. J. Pavón, and F. Rodríguez de Fonseca. 2015. "Plasma profile of pro-inflammatory cytokines and chemokines in cocaine users under outpatient treatment: influence of cocaine symptom severity and psychiatric co-morbidity." *Addict Biol* 20 (4):756-72. doi: 10.1111/adb.12156.

Athilingam, P., J. Moynihan, L. Chen, R. D'Aoust, M. Groer, and K. Kip. 2013. "Elevated levels of interleukin 6 and C-reactive protein associated with cognitive impairment in heart failure." *Congest Heart Fail* 19 (2):92-8. doi: 10.1111/chf.12007.

Atzil, S., T. Hendler, and R. Feldman. 2011. "Specifying the neurobiological basis of human attachment: brain, hormones, and behavior in synchronous and intrusive mothers." *Neuropsychopharmacology* 36 (13):2603-15. doi: 10.1038/npp.2011.172.

Barrett, J., and A. S. Fleming. 2011. "Annual Research Review: All mothers are not created equal: neural and psychobiological perspectives on mothering and the importance of individual differences." *J Child Psychol Psychiatry* 52 (4):368-97. doi: 10.1111/j.1469-7610.2010.02306.x.

Brosch, T., D. Sander, and K. R. Scherer. 2007. "That baby caught my eye... attention capture by infant faces." *Emotion* 7 (3):685-9. doi: 10.1037/1528-3542.7.3.685.

Brunton, P. J., and J. A. Russell. 2008. "The expectant brain: adapting for motherhood." *Nat Rev Neurosci* 9 (1):11-25. doi: 10.1038/nrn2280.

Brydon, L., N. A. Harrison, C. Walker, A. Steptoe, and H. D. Critchley. 2008. "Peripheral inflammation is associated with altered substantia nigra activity and psychomotor slowing in humans." *Biol Psychiatry* 63 (11):1022-9. doi: 10.1016/j.biopsych.2007.12.007.

Carroll, J. E., S. Cohen, and A. L. Marsland. 2011. "Early childhood socioeconomic status is associated with circulating interleukin-6 among mid-life adults." *Brain Behav Immun* 25 (7):1468-74.

Champagne, F. A., I. C. Weaver, J. Diorio, S. Dymov, M. Szyf, and M. J. Meaney. 2006. "Maternal care associated with methylation of the estrogen receptor-alpha1b promoter and estrogen receptor-alpha expression in the medial preoptic area of female offspring." *Endocrinology* 147 (6):2909-15. doi: 10.1210/en.2005-1119.

Chico, E., A. Gonzalez, N. Ali, M. Steiner, and A. S. Fleming. 2014. "Executive function and mothering: challenges faced by teenage mothers." *Dev Psychobiol* 56 (5):1027-35. doi: 10.1002/dev.21185.

Curley, J. P., and F. A. Champagne. 2016. "Influence of maternal care on the developing brain: Mechanisms, temporal dynamics and sensitive periods." *Front Neuroendocrinol* 40:52-66. doi: 10.1016/j.yfrne.2015.11.001.

de Britto Rosa, N. M., B. Z. de Queiroz, D. S. Pereira, M. L. di Sabatino Santos, D. M. Oliveira, F. M. Narciso, and L. S. Pereira. 2011. "Interleukin-6 plasma levels and socioeconomic status in Brazilian elderly community-dwelling women." *Arch Gerontol Geriatr* 53 (2):196-9. doi: 10.1016/j.archger.2010.10.022.

Eisenberger, N. I., E. T. Berkman, T. K. Inagaki, L. T. Rameson, N. M. Mashal, and M. R. Irwin. 2010. "Inflammation-induced anhedonia: endotoxin reduces ventral striatum responses to reward." *Biol Psychiatry* 68 (8):748-54. doi: 10.1016/j.biopsych.2010.06.010.

Evans, G. W., and P. Kim. 2010. "Multiple risk exposure as a potential explanatory mechanism for the socioeconomic status-health gradient." *Ann N Y Acad Sci* 1186:174-89. doi: 10.1111/j.1749-6632.2009.05336.x.

Fagundes, C. P., R. Glaser, and J. K. Kiecolt-Glaser. 2013. "Stressful early life experiences and immune dysregulation across the lifespan." *Brain Behav Immun* 27 (1):8-12. doi: 10.1016/j.bbi.2012.06.014.

Feldman, R. 1998. Mother–newborn coding system manual. Tel Aviv, Israel: Bar-Ilan University University Press.

Feldman, R. 2010. "The relational basis of adolescent adjustment: trajectories of mother-child interactive behaviors from infancy to adolescence shape adolescents' adaptation." *Attach Hum Dev* 12 (1-2):173-92. doi: 10.1080/14616730903282472.

Feldman, R. 2015. "Sensitive periods in human social development: New insights from research on oxytocin, synchrony, and high-risk parenting." *Dev Psychopathol* 27 (2):369-95. doi: 10.1017/S0954579415000048.

Feldman, R., and A. I. Eidelman. 2003. "Direct and indirect effects of breast milk on the neurobehavioral and cognitive development of premature infants." *Dev Psychobiol* 43 (2):109-19. doi: 10.1002/dev.10126.

Feldman, R., and A. I. Eidelman. 2006. "Neonatal state organization, neuromaturation, mother-infant interaction, and cognitive development in small-for-gestational-age premature infants." *Pediatrics* 118 (3):e869-78. doi: 10.1542/peds.2005-2040.

Feldman, R., and A. I. Eidelman. 2007. "Maternal postpartum behavior and the emergence of infant-mother and infant-father synchrony in preterm and full-term infants: the role of neonatal vagal tone." *Dev Psychobiol* 49 (3):290-302. doi: 10.1002/dev.20220.

Feldman, R., A. I. Eidelman, L. Sirota, and A. Weller. 2002. "Comparison of skin-to-skin (kangaroo) and traditional care: parenting outcomes and preterm infant development." *Pediatrics* 110 (1 Pt 1):16-26.

Feldman, R., I. Gordon, M. Influs, T. Gutbir, and R. P. Ebstein. 2013. "Parental oxytocin and early caregiving jointly shape children's oxytocin response and social reciprocity." *Neuropsychopharmacology* 38 (7):1154-62. doi: 10.1038/npp.2013.22.

Feldman, R., A. Weller, O. Zagoory-Sharon, and A. Levine. 2007. "Evidence for a neuroendocrinological foundation of human affiliation: plasma oxytocin levels across pregnancy and the postpartum period predict mother-infant bonding." *Psychol Sci* 18 (11):965-70. doi: 10.1111/j.1467-9280.2007.02010.x.

Fraga, S., P. Marques-Vidal, P. Vollenweider, G. Waeber, I. Guessous, F. Paccaud, H. Barros, and S. Stringhini. 2015. "Association of socioeconomic status with inflammatory markers: a two cohort comparison." *Prev Med* 71:12-9. doi: 10.1016/j.ypmed.2014.11.031.

Granat, A., R. Gadassi, E. Gilboa-Schechtman, and R. Feldman. 2016. "Maternal Depression and Anxiety, Social Synchrony, and Infant Regulation of Negative and Positive Emotions." *Emotion*. doi: 10.1037/emo0000204.

Haxby, James V, Elizabeth A Hoffman, and M Ida Gobbini. 2002. "Human neural systems for face recognition and social communication." *Biological psychiatry* 51 (1):59-67.

John-Henderson, N. A., A. L. Marsland, T. W. Kamarck, M. F. Muldoon, and S. B. Manuck. 2016. "Childhood Socioeconomic Status and the Occurrence of Recent Negative Life Events as Predictors of Circulating and Stimulated Levels of Interleukin-6." *Psychosom Med* 78 (1):91-101. doi: 10.1097/PSY.0000000000000262.

John-Henderson, N. A., J. E. Stellar, R. Mendoza-Denton, and D. D. Francis. 2015. "Socioeconomic Status and Social Support: Social Support Reduces Inflammatory Reactivity for Individuals Whose Early-Life Socioeconomic Status Was Low." *Psychol Sci* 26 (10):1620-9. doi: 10.1177/0956797615595962.

Jonas, W., L. Atkinson, M. Steiner, M. J. Meaney, A. Wazana, A. S. Fleming, and MAVAN research team. 2015. "Breastfeeding and maternal sensitivity predict early infant temperament." *Acta Paediatr* 104 (7):678-86. doi: 10.1111/apa.12987.

Kim, P., C. G. Capistrano, A. Erhart, R. Gray-Schiff, and N. Xu. 2017. "Socioeconomic disadvantage, neural responses to infant emotions, and emotional availability among first-time new mothers." *Behav Brain Res*. doi: 10.1016/j.bbr.2017.02.001.

Kim, P., R. Feldman, L. C. Mayes, V. Eicher, N. Thompson, J. F. Leckman, and J. E. Swain. 2011. "Breastfeeding, brain activation to own infant cry, and maternal sensitivity." *J Child Psychol Psychiatry* 52 (8):907-15. doi: 10.1111/j.1469-7610.2011.02406.x.

Kim, P., J. F. Leckman, L. C. Mayes, R. Feldman, X. Wang, and J. E. Swain. 2010. "The plasticity of human maternal brain: longitudinal changes in brain anatomy during the early postpartum period." *Behav Neurosci* 124 (5):695-700. doi: 10.1037/a0020884.

Kim, P., L. Strathearn, and J. E. Swain. 2016. "The maternal brain and its plasticity in humans." *Horm Behav* 77:113-23. doi: 10.1016/j.yhbeh.2015.08.001.

Kim, Pilyoung, and Hannah Bianco. 2014. "How Motherhood and Poverty Change the Brain." *ZERO TO THREE* 34 (4):29-36.

Kim, Y. S., K. J. Lee, and H. Kim. 2017. "Serum tumour necrosis factor-α and interleukin-6 levels in Alzheimer's disease and mild cognitive impairment." *Psychogeriatrics*. doi: 10.1111/psyg.12218.

Köhler, C. A., T. H. Freitas, M. Maes, N. Q. de Andrade, C. S. Liu, B. S. Fernandes, B. Stubbs, M. Solmi, N. Veronese, N. Herrmann, C. L. Raison, B. J. Miller, K. L. Lanctôt, and A. F. Carvalho. 2017. "Peripheral cytokine and chemokine alterations in depression: a meta-analysis of 82 studies." *Acta Psychiatr Scand*. doi: 10.1111/acps.12698.

Landi, N., J. Montoya, H. Kober, H. J. Rutherford, W. E. Mencl, P. D. Worhunsky, M. N. Potenza, and L. C. Mayes. 2011. "Maternal neural responses to infant cries and faces: relationships with substance use." *Front Psychiatry* 2:32. doi: 10.3389/fpsyt.2011.00032.

Laurent, H. K., and J. C. Ablow. 2013. "A face a mother could love: depression-related maternal neural responses to infant emotion faces." *Soc Neurosci* 8 (3):228-39. doi: 10.1080/17470919.2012.762039.

Levandowski, M. L., A. R. Hess, R. Grassi-Oliveira, and R. M. de Almeida. 2016. "Plasma interleukin-6 and executive function in crack cocaine-dependent women." *Neurosci Lett* 628:85-90. doi: 10.1016/j.neulet.2016.06.023.

Lucion, M. K., V. Oliveira, L. Bizarro, A. R. Bischoff, P. P. Silveira, and M. Kauer-Sant'Anna. 2017. "Attentional bias toward infant faces - Review of the adaptive and clinical relevance." *Int J Psychophysiol*. doi: 10.1016/j.ijpsycho.2017.01.008.

Luo, L., X. Ma, X. Zheng, W. Zhao, L. Xu, B. Becker, and K. M. Kendrick. 2015. "Neural systems and hormones mediating attraction to infant and child faces." *Front Psychol* 6:970. doi: 10.3389/fpsyg.2015.00970.

Mansur, R. B., G. R. Cunha, E. Asevedo, A. Zugman, M. Zeni-Graiff, A. C. Rios, S. Sethi, P. K. Maurya, M. L. Levandowski, A. Gadelha, P. M. Pan, L. Stertz, S. I. Belangero, M. Kauer-Sant' Anna, A. L. Teixeira, J. J. Mari, L. A. Rohde, E. C. Miguel, R. S. McIntyre, R. Grassi-Oliveira, R. A. Bressan, and E. Brietzke. 2016. "Socioeconomic Disadvantage Moderates the Association between Peripheral Biomarkers and Childhood Psychopathology." *PLoS One* 11 (8):e0160455. doi: 10.1371/journal.pone.0160455.

Meins, E., L. C. Centifanti, C. Fernyhough, and S. Fishburn. 2013. "Maternal mind-mindedness and children's behavioral difficulties: mitigating the impact of low socioeconomic status." *J Abnorm Child Psychol* 41 (4):543-53. doi: 10.1007/s10802-012-9699-3.

Miller, G., and E. Chen. 2007. "Unfavorable socioeconomic conditions in early life presage expression of proinflammatory phenotype in adolescence." *Psychosom Med* 69 (5):402-9. doi: 10.1097/PSY.0b013e318068fcf9.

Miller, G. E., E. Chen, and K. J. Parker. 2011. "Psychological stress in childhood and susceptibility to the chronic diseases of aging: moving toward a model of behavioral and biological mechanisms." *Psychol Bull* 137 (6):959-97. doi: 10.1037/a0024768.

Moreira, F. P., J. R. Medeiros, A. C. Lhullier, L. D. Souza, K. Jansen, L. V. Portela, D. R. Lara, R. A. da Silva, C. D. Wiener, and J. P. Oses. 2016. "Cocaine abuse and effects in the serum levels of cytokines IL-6 and IL-10." *Drug Alcohol Depend* 158:181-5. doi: 10.1016/j.drugalcdep.2015.11.024.

Morozink, J. A., E. M. Friedman, C. L. Coe, and C. D. Ryff. 2010. "Socioeconomic and psychosocial predictors of interleukin-6 in the MIDUS national sample." *Health Psychol* 29 (6):626-35. doi: 10.1037/a0021360.

Moses-Kolko, E. L., M. S. Horner, M. L. Phillips, A. E. Hipwell, and J. E. Swain. 2014. "In search of neural endophenotypes of postpartum psychopathology and disrupted maternal caregiving." *J Neuroendocrinol* 26 (10):665-84. doi: 10.1111/jne.12183.

Odgers, C. L., A. Caspi, M. A. Russell, R. J. Sampson, L. Arseneault, and T. E. Moffitt. 2012. "Supportive parenting mediates neighborhood socioeconomic disparities in children's antisocial behavior from ages 5 to 12." *Dev Psychopathol* 24 (3):705-21. doi: 10.1017/S0954579412000326.

Oliveira, V, M Goulart, JC Nobre, MK Lucion, PP Silveira, and L Bizarro. 2017. "Emotional interference of baby and adult faces on the automatic attention in parenthood." *Psychology & Neuroscience* 10 (2):144-153. doi: http://psycnet.apa.org/doi/10.1037/pne0000085.

Papp, L. M. 2014. "Longitudinal associations between breastfeeding and observed mother-child interaction qualities in early childhood." *Child Care Health Dev* 40 (5):740-6. doi: 10.1111/cch.12106.

Parsons, C. E., K. S. Young, L. Murray, A. Stein, and M. L. Kringelbach. 2010. "The functional neuroanatomy of the evolving parent-infant relationship." *Prog Neurobiol* 91 (3):220-41. doi: 10.1016/j.pneurobio.2010.03.001.

Pearson, R. M., R. M. Cooper, I. S. Penton-Voak, S. L. Lightman, and J. Evans. 2010. "Depressive symptoms in early pregnancy disrupt attentional processing of infant emotion." *Psychol Med* 40 (4):621-31. doi: 10.1017/S0033291709990961.

Pearson, R. M., S. L. Lightman, and J. Evans. 2011. "Attentional processing of infant emotion during late pregnancy and mother-infant relations after birth." *Arch Womens Ment Health* 14 (1):23-31. doi: 10.1007/s00737-010-0180-4.

Pereira, M., and A. Ferreira. 2016. "Neuroanatomical and neurochemical basis of parenting: Dynamic coordination of motivational, affective and cognitive processes." *Horm Behav* 77:72-85. doi: 10.1016/j.yhbeh.2015.08.005.

Petersen, K. L., A. L. Marsland, J. Flory, E. Votruba-Drzal, M. F. Muldoon, and S. B. Manuck. 2008. "Community socioeconomic status is associated with circulating interleukin-6 and C-reactive protein." *Psychosom Med* 70 (6):646-52. doi: 10.1097/PSY.0b013e31817b8ee4.

Peña, C. J., Y. D. Neugut, and F. A. Champagne. 2013. "Developmental timing of the effects of maternal care on gene expression and epigenetic regulation of hormone receptor levels in female rats." *Endocrinology* 154 (11):4340-51. doi: 10.1210/en.2013-1595.

Raby, K. L., J. M. Lawler, R. J. Shlafer, P. S. Hesemeyer, W. A. Collins, and L. A. Sroufe. 2015. "The interpersonal antecedents of supportive parenting: a prospective, longitudinal study from infancy to adulthood." *Dev Psychol* 51 (1):115-23. doi: 10.1037/a0038336.

Rodrigo, M. J., I. Leon, I. Quinones, A. Lage, S. Byrne, and M. A. Bobes. 2011. "Brain and personality bases of insensitivity to infant cues in neglectful mothers: An event-related potential study." *Development and Psychopathology* 23 (1):163-176. doi: 10.1017/s0954579410000714.

Siqveland, T., L. Smith, and V. Moe. 2012. "The impact of optimality on maternal sensitivity in mothers with substance abuse and psychiatric problems and their infants at 3 months." *Infant Behav Dev* 35 (1):60-70. doi: 10.1016/j.infbeh.2011.09.004.

Slopen, N., E. B. Loucks, A. A. Appleton, I. Kawachi, L. D. Kubzansky, A. L. Non, S. Buka, and S. E. Gilman. 2015. "Early origins of inflammation: An examination of prenatal and childhood social adversity in a prospective cohort study." *Psychoneuroendocrinology* 51:403-13. doi: 10.1016/j.psyneuen.2014.10.016.

Sturge-Apple, M. L., H. R. Jones, and J. H. Suor. 2017. "When stress gets into your head: Socioeconomic risk, executive functions, and maternal sensitivity across childrearing contexts." *J Fam Psychol* 31 (2):160-169. doi: 10.1037/fam0000265.

Sukoff Rizzo, S. J., S. J. Neal, Z. A. Hughes, M. Beyna, S. Rosenzweig-Lipson, S. J. Moss, and N. J. Brandon. 2012. "Evidence for sustained elevation of IL-6 in the CNS as a key contributor of depressive-like phenotypes." *Translational Psychiatry* 2 (12):e199. doi: 10.1038/tp.2012.120.

Swain, J. E., P. Kim, and S. S. Ho. 2011. "Neuroendocrinology of parental response to baby-cry." *J Neuroendocrinol* 23 (11):1036-41. doi: 10.1111/j.1365-2826.2011.02212.x.

Tarullo, A. R., and M. R. Gunnar. 2006. "Child maltreatment and the developing HPA axis." *Horm Behav* 50 (4):632-9. doi: 10.1016/j.yhbeh.2006.06.010.

Tharner, A., M. P. Luijk, H. Raat, M. H. Ijzendoorn, M. J. Bakermans-Kranenburg, H. A. Moll, V. W. Jaddoe, A. Hofman, F. C. Verhulst, and H. Tiemeier. 2012. "Breastfeeding and its relation to maternal sensitivity and infant attachment." *J Dev Behav Pediatr* 33 (5):396-404. doi: 10.1097/DBP.0b013e318257fac3.

Trapero, I., and O. Cauli. 2014. "Interleukin 6 and cognitive dysfunction." *Metab Brain Dis* 29 (3):593-608. doi: 10.1007/s11011-014-9551-2.

Vuilleumier, P., and G. Pourtois. 2007. "Distributed and interactive brain mechanisms during emotion face perception: evidence from functional neuroimaging." *Neuropsychologia* 45 (1):174-94. doi: 10.1016/j.neuropsychologia.2006.06.003.

Weaver, I. C., N. Cervoni, F. A. Champagne, A. C. D'Alessio, S. Sharma, J. R. Seckl, S. Dymov, M. Szyf, and M. J. Meaney. 2004. "Epigenetic programming by maternal behavior." *Nat Neurosci* 7 (8):847-54. doi: 10.1038/nn1276.

Yang, S. H., M. Gangidine, T. A. Pritts, M. D. Goodman, and A. B. Lentsch. 2013. "Interleukin 6 mediates neuroinflammation and motor coordination deficits after mild traumatic brain injury and brief hypoxia in mice." *Shock* 40 (6):471-5. doi: 10.1097/SHK.0000000000000037.

Table 1. Sample Characteristic

Characteristic	Mean (SD) or Frequency (%)			
	Total Sample n 53	High SES n 17	Low SES n 36	p
Maternal age in years	26.5(5.64)	28.53(5.38)	26.67(5.60)	0.084
Educational level				0.001*
Incomplete School Education (below 12 years)	26(49.1%)	4(23.5%)	22(61.1%)	
School Education Complete (≥12years)	22(41.5%)	8(47.0%)	14(38.9%)	
University degree or higher	5 (9.4%)	5(29.4%)	0	
Marital Status				0.198
Married/ Cohabiting	45(84.9%)	16(94.1%)	29(80.5%)	
Number of people living in the same house				0.889
2-4	33	10	23	
5-7	18	6	12	
8 or more	2	1	1	
Ethnicity				0.659
Caucasian	30 (56.6%)	10 (58.8%)	20(55.6%)	
Others	23(43,4%)	7(41.2%)	16(44.4%)	
Income				
A (highest)	1(1.9%)			
B	16(30.2%)			
C	31(58.5%)			
D (lowest)	5(9.4%)			
Planned gestation	27(50.9%)	8(47.0%)	16(44.4%)	0.711
Primiparous	23(43.4%)	9(52.5%)	14(38.9%)	0.335
Gestational age in weeks at delivery	39.2(1.19)	39.29(1.31)	39.19(1.16)	0.781
Caesarean delivery	21(39.6%)	8(47.7%)	13(36.1%)	0.447
Female infant	27 (50.9%)	7(41.2%)	20(55.6%)	0.328
Feeding method				0.287
Exclusive breastfeeding	38(71.7%)	12(70.6%)	26(72.2%)	
Breast and bottle feeding	11(20.8%)	5(29.4%)	6(16.6%)	
Exclusive bottle feeding	4(7.5%)	0	4(11.1%)	

Values expressed as mean and standard deviation or absolute frequency and percentage.

Table 2: Bivariate correlations among all study variables

	1.	2.	3.	4.
1. Interleukin 6	--	0.443*	0.432*	-0.313*
2. Adult Trial		--	0.959*	0.064
3. Infant Trial			--	0.094
4. MAB				--

*p < 0.05; Adult Trial= reaction time on adult trial; Infant Trial= reaction time on infant trial; MAB = maternal affiliative behavior

Table 3. Reaction Time, Il-6 and Maternal Behavior according to Income

	High Income mean(sd)	Low Income mean(sd)	p
TR Adult trial	656.98(138.30)	699.96(187.59)	.418
TR Infant trial	646.04(161.80)	693.33(194.01)	.395
Il-6 level	1.11(0.42)*	1.43(0.69)	.045
MAB	207.10(62.89)**	144.22(45.07)	.001

*p< 0.05; **p<0.001. Values expressed in means and standard values (sd)

Table 4. Coefficients (B), standardized errors (SE) and 95% confidence intervals (95%IC) for the structural models considering the Infant Trials.

	B	SE	p	95% IC
Interleukin 6				
Low income	0.346	0.160	0.031	(0.031; 0.662)
Reaction time on Infant Trials[a]				
Interleukin 6	0.076	0.022	0.001	(0.031; 0.121)
MAB				
Interleukin 6	-30.040	9.461	0.001	(-48.585; -11.495)
Reaction time on Infant Trials[a]	160.682	58.609	0.006	(45.810; 275.555)
Low income	-60.478	16.012	<0.001	(-91.862; -29.095)

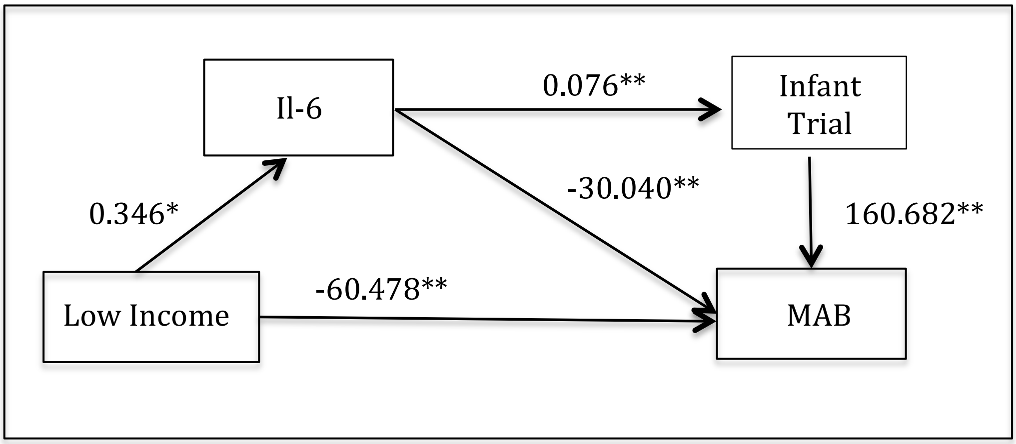
[a] logarithm of reaction time in Infant Trial was used due to non-normal distribution;, MAB = Maternal affiliative Behavior.

Table 5. Coefficients (B), standardized errors (SE) and 95% confidence intervals (95%IC) for the structural equation models considering the Adult Trials.

	B	SE	p	95% IC
Interleukin 6				
Low income	0.346	0.160	0.031	(0.031; 0.662)
Reaction time on Adult Trial[a]				
Interleukin 6	0.074	0.022	0.001	(0.030; 0.118)
MAB				
Interleukin 6	-28.486	9.526	0.003	(-47.157; -9.815)
Reaction time on Adult Trials[a]	142.010	64.846	0.029	(14.914; 269.106)
Low income	-59.555	16.741	<0.001	(-92.368;-26.743)

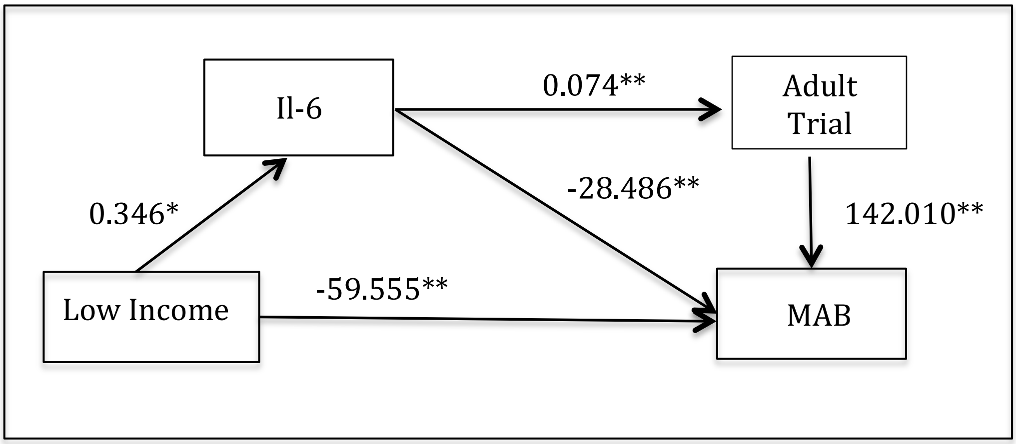
[a] logarithm of reaction time in Adult Trial was used due to non-normal distribution; MAB = Maternal affiliative Behavior

Figure 1. Path Model of Structural Equation for Infant Trial



Path model for structural equation for Infant Trial shows that lower income is related to 0.346 increase in Il-6 and, -60.478 points decreased of maternal affiliative behavior. A rise in Il-6 represents an increase of 0.076 points on logarithm of reaction time on Infant Trial, and a decrease of -30.040 on maternal affiliative behavior. While an increase on 1 point of logarithm of reaction time a increase of 160.682 on maternal affiliative behavior. $*p<0.05$; $**p<0.001$; Il-6= interleukin 6; Infant Trial = logarithm of reaction time on infant trial blocks; MAB= maternal affiliative behavior

Figure 2. Path Model of Structural Equation for Adult Trial



Path model for structural equation for Adult Trial shows that lower income is related to 0.346 increase in Il-6 and, -9.555 points decreased of maternal affiliative behavior. A rise in Il-6 represents an increase of 0.074 points on logarithm of reaction time on Adult Trial, and a decrease of -28.486 on maternal affiliative behavior. While an increase on 1 point of logarithm of reaction time a increase of 142.010 on maternal affiliative behavior. *p<0.05; **p<0.001; Il-6= interleukin 6; Adult Trial = logarithm of reaction time on infant trial blocks; MAB= maternal affiliative behavior

6.4 Resultados Complementares Não Submetidos à Publicação

Das 82 mães que participaram da pesquisa, 62 tiveram uma amostra de sangue coletada. Os níveis periféricos de interleucinas 1 beta (Il-1β), interleucinas 10 (Il-10) e fator de necrose tumoral alfa (TNFα) estão expressos na Tabela 6.4.1 como média e desvio padrão. Foram excluídas da análise medidas que não preencheram critérios de qualidade necessários para validade das medidas (todos os casos foram por menor contagem mínima de *beads* pelo equipamento do que aquilo preconizado pelo teste). Desta forma, 62 mães tiveram valores válidos de Il-1β e Il-10 e 59 de TNFα.

Os níveis de Il-1β, Il-10 e TNFα não se correlacionaram com *maternal affiliative behavior*, nem com *parental acknowledging,* com tempo de reação na tarefa de processamento cognitivo, ou com nível socioeconômico. A Tabela 6.4.2 expressa a correlação entre os níveis séricos das interleucinas acima e os componentes do comportamento materno e tempos de reação para faces infantis e de adulto. Foram comparados os níveis séricos de interleucinas entre o grupo de alto nível socioeconômico (classes A e B) versus baixo nível socioeconômico (classes C e D), com resultados expressos na tabela 6.4.3.

Tabela 6.4.1. Nível sérico das interleucinas

	N	Média (dp) em pg/ml
Il-1β	62	1.2(0.76)
Il-10	62	6.0 (4.06)
TNFα	59	4,4(1.14)

Resultados expressos em picogramas por mililitros (pg/ml).
dp = desvio padrão da média

Tabela 6.4.2. Correlações entre interleucinas, comportamento materno e tempo de reação.

		MAB	*Parental acknowledging*	TR bebê	TR adulto
Il-1β	Spearman's rho	-0.156	-0.168	0.008	0.066
	Sig.(2-tailed)	0.229	0.197	0.949	0.609
Il-10	Spearman's rho	-0.086	0.001	-0.075	-0.063
	Sig.(2-tailed)	0.508	0.993	0.563	0.627
TNFα	Spearman's rho	-0.096	-0.092	0.099	0.164
	Sig.(2-tailed)	0.473	0.494	0.457	0.214

MAB = *maternal affiliative behavior*; TR bebê= tempo de reação materno nos blocos de faces de bebês; TR adulto= tempo de reação materno nos blocos de faces de bebês.

Tabela 6.4.3 Níveis de interleucinas conforme nível socioeconômico.

	Classes A e B	Classes C e D	
Il-1β	1,0(0.49)	1,3(0.85)	p 0.110
Il-10	5,4(4.22)	6,3(3.99)	p 0.442
TNFα	4,3(1.35)	4,5(1.02)	p 0.448

Resultados expressos em média e desvio padrão.

7. DISCUSSÃO

Nesta tese, observamos que a qualidade do comportamento maternal é influenciada por uma série de fatores, entre eles fatores intrínsecos como a cognição materna, seu estado de saúde mental e metabolismo, assim como fatores extrínsecos como o nível socioeconômico. A análise conjunta dos três artigos elaborados para esta tese reforça a ideia de que exista uma interação entre processamento cognitivo e comportamento materno.

O artigo de revisão "*Attentional Bias Toward Infant Faces – Review of the Adaptive and Clinical Relevance*" aponta a relevância de estímulos infantis para o sistema atencional materno e sugere que a parentalidade modifica o processamento cognitivo de estímulos infantis. Vimos que, aprofundando-se na análise do processamento cognitivo materno a estímulos infantis, a Dra. Rebecca Pearson realizou uma sequência de estudos que acompanhou mulheres ao longo da gestação. Nessas pesquisas, ela reforça a importância da priorização de faces infantis expressando sofrimento pelo sistema atencional materno em comparação a faces neutras e alegres. Em seus estudos ela demonstra que gestantes com sintomas depressivos não apresentam priorização do processamento cognitivo para faces de sofrimento infantil, e que gestantes que não apresentam essa priorização referem pior vínculo mãe-bebê no pós- parto (51, 52, 56).

Seguindo ideias levantadas na revisão, e principalmente pelos estudos da Dra. Pearson, esta tese se desenvolveu para aprofundar a análise da relação entre o processamento cognitivo de faces infantis expressando diferentes emoções e o comportamento materno. Diferentemente de estudos anteriores, nosso trabalho optou por avaliar o processamento cognitivo durante o puerpério e não durante o período gestacional. O puerpério, apesar de bruscamente iniciado após o parto, é um intenso período de transição em aspectos fisiológicos e socioemocionais femininos, sendo um momento caracterizado por maior vulnerabilidade para o surgimento de transtornos psiquiátricos (16, 24). Além disso, optamos por avaliar o comportamento materno através de filmagens da interação da mãe com seu bebê em vez de apenas aplicar questionários sobre o vínculo. Apesar de alguns questionários sobre vínculo mãe-bebê terem boa correlação com medidas comportamentais, preferimos utilizar filmagens a fim de ter uma análise ampla do comportamento da díade, em especial sobre a sensibilidade materna, e minimizar o componente da percepção materna sobre a relação que ocorre quando a mãe responde a questionários (51).

É interessante perceber que diferentes componentes do constructo de sensibilidade materna estão relacionados a diferentes aspectos do processamento cognitivo. No artigo "*Correlation between Automatic Attention Engagement to Infant Faces and Behavior Components of Maternal Sensitivity*", o tempo de reação das mães para faces de bebês expressando sofrimento teve correlação positiva com o *parental acknowledging*, um comportamento que exige reflexão e interpretação materna dos sinais emitidos do bebê. Por outro lado, no artigo *"Cognitive Processing, Inflammation, Environment and Maternal Behavior in Early Postpartum"*, quando utilizando o modelo de equação estrutural, os tempos de reação para faces de bebês e adultos expressando as três emoções propostas (sofrimento/medo, neutralidade e alegria) se correlacionavam com o *maternal affiliative behavior*. Este componente da sensibilidade materna pode ser descrito como um conjunto de comportamentos afetivos: o toque afetuoso (por exemplo, fazer carinho, abraçar), o modo de falar com o bebê em tom mais agudo e direcionado para ele, o afeto positivo expresso por faces de alegria e tranquilidade por parte da mãe e o olhar da mãe para o seu bebê. Tanto o *parental acknowledging* quanto o *maternal affiliative behavior* expressam características de comportamento materno sensível, segundo o modelo da Dra. Ruth Feldman, porém são comportamentos distintos e que se complementam. Não basta a mãe falar de forma afetuosa com seu bebê, acariciá-lo, olhá-lo se isso não é feito em sintonia com os sinais emitidos pelo bebê naquele momento. Vale destacar que também foi analisada a possível correlação entre o tempo de reação para faces de sofrimento infantil e o *maternal affiliative behavior*, sendo que não houve correlação. Essa constatação sugere que o processamento cognitivo do sofrimento infantil pela mãe durante o puerpério seja especificamente correlacionado ao *parental acknowledging* e não a vários componentes do comportamento materno.

Ainsworth (1985) não incluiu o afeto materno em sua definição de sensibilidade materna, porém autores posteriores passaram a considerar o afeto como mais um componente importante para uma maternagem sensível (83). De fato, talvez essas diferentes características de sensibilidade materna influenciem o desenvolvimento do bebê de maneira distinta. Por exemplo, Davidov *et al.,* 2006 sugerem que o maternal *warmth* (descrito nesse artigo como o prazer da mãe em interagir com seu filho, a admiração que tem por ele, o afeto expresso – como carinho e elogios) prediz a habilidade da criança de regular afetos positivos. A maneira como a mãe reage a momentos de frustração e sofrimento prediz a habilidade da criança de empatizar com o sofrimento de outros e de regular afetos negativos (84).

Conforme dito na Introdução, *parental acknowledging* consiste na habilidade materna de perceber os sinais emitidos por seu(ua) filho(a) e sinalizar esse entendimento de forma adequada para ele(a). É um comportamento fundamental para o desenvolvimento da sintonia entre a mãe e o bebê, e mesmo ao longo da vida dos indivíduos. O *parental acknowledging* é um dos componentes principais da sensibilidade materna no modelo da Dra. Ruth Feldman. Existem discussões sobre a definição de sensibilidade materna e como caracterizá-la (83, 85). O *Coding Interactive Behavior* é uma tentativa de objetivar tais medidas (77).

Além disso, a definição do *parental acknowledging* se aproxima do conceito de sensibilidade materna de Ainsworth (86) e do *mind mindeness* de Meins *et al.,* 2001 (85), já que nos três conceitos a ideia-chave é que a mãe consiga perceber o estado mental do bebê e responder de maneira apropriada; que possa perceber o bebê como um indivíduo separado dela, sendo capaz assim de se adaptar a suas demandas. Os três conceitos ressaltam a importância de que a demanda/necessidade do bebê norteie a interação.

A correlação positiva entre processamento cognitivo diferenciado para faces infantis expressando sofrimento com características favoráveis da relação mãe-bebê assemelha-se aos resultados da literatura em gestantes (51). No entanto, diferentemente desses estudos, em nossa análise utilizamos os tempos brutos de reação para cada expressão de emoção infantil (alegre, neutro e sofrimento). Pearson *et al.* utilizam um índice de viés atencional obtido através da subtração do tempo de reação para faces de não sofrimento (alegre e neutro) infantil pelo tempo de reação para faces expressando sofrimento. O uso de tempos brutos de reação, em vez de índices, permite que haja identificação de qual emoção está promovendo maior engajamento do sistema atencional. No caso de índices, como o de viés atencional para sofrimento infantil, não sabemos se para aquele participante houve uma diferença por ela apresentar um tempo de reação alto para faces de sofrimento ou só por ter tempo de reação baixo para faces neutras ou alegres. Pearson e seus colaboradores citam o uso de índice de viés atencional como uma das limitações de seus resultados. Pearson *et al.,* 2011a relatam ter investigado a associação entre os tempos de reação bruto para sofrimento infantil e a qualidade da relação mãe-bebê sem achar correlação estaticamente significativa. O artigo 2 foi escrito em parceria com a Dra. Pearson, sendo recomendação da mesma o uso dos tempos brutos em vez do índice de viés atencional. Contudo, o uso de tempos brutos também traz limitações, já que outros fatores, além do engajamento atencional, podem alterar o tempo de reação na tarefa (51).

É interessante perceber que a forma como a mãe processa e reage a uma imagem apresentada por 240 milissegundos se correlaciona com a forma como ela interage com seu bebê. A tarefa utilizada no presente estudo e naqueles de Pearson envolve provavelmente o processamento automático dos estímulos apresentados, assim o tempo de exposição ao estímulo induz uma reposta que possivelmente não atinja nível consciente.

Uma das hipóteses para explicar a relação entre o tempo de reação a faces de sofrimento e o *parental acknowledging* se refere ao caráter adaptativo da comunicação do sofrimento pelo bebê, e no seu imediato reconhecimento pela mãe. Bebês com um mês apresentam um repertório restrito de expressão e comunicação. O sorriso social, por exemplo, é descrito por se estabelecer no segundo mês. Por outro lado, o choro/sofrimento é uma expressão primitiva, existente desde o nascimento. Durante os primeiros dias/meses após o parto, a mãe aprende a ler os sinais do bebê, e interpretar suas demandas. Com a evolução da relação, as mães passam a identificar e diferenciar os sinais específicos dos seus bebês (geralmente sabem qual choro significa fome, frio, dor, sono e outras angústias). Talvez a priorização do sofrimento pelo sistema atencional da mãe seja um facilitador na comunicação entre a mãe e o bebê, e a não aversão do sistema de recompensa materno a esse estímulo pode ser um componente importante na formação do vínculo materno-infantil nos primeiros meses. Assim, o maior engajamento do sistema atencional para faces de sofrimento pode ser essencial para o desenvolvimento do *parental acknowledging*.

Outro ponto desta tese consistiu em identificar potenciais fatores que influenciassem o processamento cognitivo e o comportamento materno. No artigo *“Cognitive Processing, Inflammation, Environment and Maternal Behavior in Early Postpartum”* utilizamos um modelo de equação estrutural que relacionava processamento cognitivo materno, níveis periféricos de Il-6, nível socioeconômico e comportamento materno. Nesse modelo, o grupo com baixo nível socioeconômico apresentou níveis séricos mais elevados de Il-6 e menos *maternal affiliative behavior* do que o grupo de alto nível socioeconômico. A Il-6 também se correlacionou positivamente com o tempo de reação das mães na tarefa de processamento cognitivo (tanto para faces de bebês quanto para faces de adultos independentemente da emoção expressa) e negativamente com o *maternal affiliative behavior*. O tempo de reação na tarefa de processamento cognitivo se correlacionou positivamente com o *maternal affiliative behavior* no modelo de equação estrutural, mas não quando as duas variáveis foram analisadas sem os demais fatores (correlação bivariável).

Ainda no artigo 3, os tempos de reação para cada bloco de faces infantis (bebê alegre, neutro e em sofrimento) foram considerados conjuntamente na análise, diferentemente do artigo 2, por dois motivos: 1) a correlação com o tempo de reação para cada emoção foi analisada com as outras variáveis de interesse (Il-6, nível socioeconômico, comportamento materno): Considerando que os tempos apresentaram a mesma correlação com as variáveis, se investigou se havia diferença estatística entre os tempos de reação de cada emoção. Na ausência de diferenças, se optou por utilizar a média de reação de todos os blocos em conjunto, conforme a idade do estímulo (adulto ou bebê); e 2) o comportamento materno avaliado é diverso entre os dois trabalhos: no artigo 2 utilizamos o *parental acknowledging,* e no artigo 3 o *maternal affiliative behavior*. Nos dois trabalhos testamos a correlação das variáveis com ambos os comportamentos, porém só houve correlação com o comportamento descrito em cada artigo. Vale apontar que a correlação entre *maternal affiliative behavior* e o *parental acknowledging* é significativa (0.530, $p<0.001$), sugerindo que fazem parte de um mesmo constructo (a sensibilidade materna).

Avaliamos também (item 6.4) se outros marcadores inflamatórios estavam correlacionados ao comportamento materno, processamento cognitivo e nível socioeconômico. Diferentemente da Il-6, os níveis séricos de Il-1β, Il-10, TNFα não apresentaram correlação com *maternal affiliative behavior*, com *parental acknowledging,* com tempos de reação na tarefa de processamento cognitivo ou com nível socioeconômico. Esse achado fortalece a especificidade da correlação do Il-6 com as variáveis em estudo.

Trabalhos prévios já haviam correlacionado a Il-6 com alterações cognitivas e baixo nível socioeconômico (59, 63-66, 71, 72, 87), porém não no primeiro mês pós-parto.

Brydon *et al.*, 2008 também demonstraram associação entre aumento de Il-6 e maior tempo de reação em tarefa de processamento cognitivo. Nesse estudo, homens jovens e saudáveis receberam vacina para febre tifoide que induziu um quadro inflamatório leve. Posteriormente realizaram o *Color-Word Stroop Task* e os níveis sanguíneos de Il-6, TNFα e do antagonista do receptor da interleucina 1 (IL-1Ra) foram medidos. A tarefa de processamento cognitiva utilizada neste estudo avalia o processo atencional e controle executivo. Assim como em nosso estudo, apenas o Il-6 se correlacionou com o tempo de reação na tarefa de processamento cognitivo. Os participantes que tiveram maior aumento de Il-6 apresentaram maior tempo de reação na *Stroop Task.* Sintomas clínicos relacionados à vacina e sintomas de humor não se correlacionaram com o tempo de reação (59).

É interessante pontuar que os valores de Il-6 pós-indução inflamatória no estudo acima (Il-6 = 1.66±0.86pg/ml) são próximos aos valores de Il-6 do nosso grupo de baixo nível socioeconômico (Il-6 = 1.83±0.69pg/ml). Os valores de Il-6 pré-vacinação no estudo de Brydon *et al.,*2008 (Il-6 = 0.66±0.38pg/ml) são mais baixos que valores de Il-6 no nosso grupo de alto nível socioeconômico (Il-6 = 1.11±0.42pg/ml). Assim, os altos níveis de Il-6 observados devido ao processo inflamatório induzido pela vacinação são semelhantes aos observados nas mães de baixo nível socioeconômico durante o puerpério. Analisando de forma conjunta, os resultados aqui descritos e aqueles dados da literatura permitem sugerir que a adversidade socioeconômica atuaria como indutor de inflamação durante o puerpério.

A relação entre Il-6 e adversidade socioeconômica tem sido relatada em diferentes populações (idosos, homens, mulheres, de países diferentes) e por diferentes grupos de pesquisa (68, 69, 71, 88). A adversidade econômica não parece apenas aumentar o Il-6 momentaneamente. Estudos têm sugerido que a adversidade socioeconômica durante a infância atue na modulação do sistema imune (89, 90). Miller *et al.*, 2007 evidenciou que o nível socioeconômico entre o segundo e terceiro ano de vida prediz a expressão leucocitária de mRNA do receptor de glicocorticoide (GR) e do *toll-like receptor* 4 (TLR4) em adolescentes canadenses, sendo que ambos os genes estão envolvidos na regulação inflamatória de forma oposta: os glicocorticoides tem ação anti-inflamatória (91), enquanto a atividade nos *toll-like receptors* está relacionada à ativação da cadeia inflamatória na presença de produtos microbianos (92). Desta forma, o estudo acima sugere que o baixo nível socioeconômico cria um ambiente pró-inflamatório por diminuir a expressão do mRNA de GR e aumentar a expressão de TLR4 (93).

Carroll *et al.,* 2011 também ressaltam os primeiros anos de vida como período crítico para a modulação do sistema imune por condições econômicas da infância. Neste estudo, o nível sérico de Il-6 de homens e mulheres de meia-idade se correlaciona com o nível socioeconômico destas ao longo da infância, independentemente do nível socioeconômico atual, sendo que a correlação foi mais forte com as condições existentes nos primeiros anos de vida, propondo que o nível socioeconômico nos dois primeiros anos de vida se correlaciona ao nível de Il-6 na meia-idade (67).

Assim, a demonstração que o baixo nível socioeconômico está associado ao aumento de uma citocina inflamatória durante o puerpério e a um comportamento materno menos afetivo reforça a importância de ações sociais na primeira infância. Nesse sentido, é relevante ressaltar a permeabilidade de reações inflamatórias ao suporte social (71, 72). Mais do que isso, Chen *et al.,* 2011 sugerem que o afeto materno (*maternal warmth*) reduz a ação pró-inflamatória do baixo nível social. Uma amostra de adultos que teve baixo nível socioeconômico na infância foi dividida em grupo de alto e baixo *maternal warmth* avaliado pelo *Parental Bonding Instrument* (PBI). O grupo que recebeu menos afeto materno na infância apresentou perfil de expressão gênica pró-inflamatória, e suas células mononucleares sanguíneas, ao serem estimuladas com ligantes para *toll-like receptors* (TLR), produziram mais Il-6 do que o grupo que recebeu mais afeto materno na infância. Não houve diferença entre os grupos quanto aos valores de proteína C reativa (CRP). O cuidado materno foi capaz de induzir diferenças de expressão gênica e responsividade inflamatória celular em indivíduos que tiveram baixo nível socioeconômico na infância (94).

De forma extrapolativa, podemos pensar que os achados desta tese, principalmente a correlação negativa entre o componente de comportamento afetuoso materno (*maternal affiliative behavior)* e o processo pró-inflamatório, complementam os de Chen et *al*., 2011, já que ambos sugerem interação entre o comportamento afetuoso materno e o sistema inflamatório. Inclusive alguns itens do PBI que avaliam o *maternal warmth* se assemelham ao conceito de *maternal* *affiliative behavior*, por exemplo, os itens: “Falava comigo com uma voz meiga e amigável”; “Parecia emocionalmente frio(a) comigo”; “Era carinhoso(a) comigo”; “Frequentemente sorria para mim”; “Não conversava comigo”.

Não temos dados sobre o nível socioeconômico das participantes da pesquisa durante a infância. Esses dados seriam importantes para analisar a origem da alteração imune e o impacto do nível socioeconômico e do cuidado materno que essas mães teriam recebido durante seu período neonatal. Porém, com base na literatura e em nossos resultados podemos supor que os bebês das díades de nível socioeconômico mais baixo apresentam maior vulnerabilidade em seu desenvolvimento, tanto pelo risco social como pelo risco de receber um cuidado materno menos sensível. Esses fatores podem ser perpetuados para gerações seguintes. Em nossa amostra, potencialmente esses dois fatores podem interferir na modulação do sistema imune dessas crianças: o nível socioeconômico e o baixo suporte pela sensibilidade materna. De fato, na literatura há evidências de que o nível socioeconômico influencia o cuidado materno (95-99).

A pesquisadora Pilyoung Kim vem propondo em alguns de seus artigos que a dificuldade socioeconômica prejudica a adaptação ao puerpério das redes neurais relacionadas à regulação emocional e motivação materna, assim influenciando o comportamento materno sensível. Mais especificamente, a autora ressalta alterações de ativação em amígdala e áreas do córtex pré-frontal (por exemplo, giros médio, medial e temporal superior) para estímulos de sofrimento infantil (choro e faces de sofrimento) (98, 100, 101). Assim como nós, Kim *et al.,* 2017 tentam integrar padrão de processamento de estímulos infantis por parte da mãe (através de ressonância magnética), nível socioeconômico e comportamento materno com resultados próximos aos nossos. Os autores correlacionam nível socioeconômico materno a padrões distintos de ativação amigdaliana durante a visualização de imagens infantis expressando alegria e sofrimento. O nível socioeconômico mais baixo esteve correlacionado a menor atividade amigdaliana ao visualizar fotos de bebês alegres e maior atividade para faces expressando sofrimento. No puerpério é esperado que haja uma diminuição da ativação amigdaliana a estímulos aversivos (como faces de sofrimento ou choro) a fim de facilitar a aproximação materna a esses estímulos por diminuir a reatividade ao estresse e facilitar a regulação emocional (38, 98). De fato, em Kim *et al.*, 2017, a maior atividade amigdaliana durante a visualização de faces de bebê em sofrimento esteve correlacionada a comportamento materno mais intrusivo, portanto menos sensível durante a interação mãe-bebê. Porém, não houve correlação direta entre nível socioeconômico analisado de forma contínua e o comportamento materno, diferentemente do nosso estudo que mostra esta correlação direta. Outro diferença entre os estudos é o fato de Kim *et al.,* 2017 terem identificado que grupos de menor nível socioeconômico apresentavam maior atividade amigdaliana ao visualizar faces de sofrimento, e menor ao visualizar faces alegres, enquanto em nossa amostra não houve diferença entre tempos de reação dos grupos de baixo e alto nível socioeconômico. Existem vários fatores que podem gerar a diferença entre os dois estudos, em destaque diversidades do método para avaliar o processamento do estímulo (tarefa de processamento cognitivo apresentando a imagem por 240ms versus exame de imagem com visualização passiva do estímulo por 2000ms) e a diferença da avaliação da relação mãe-bebê. Kim *et al.*, 2017 também avaliaram sensibilidade materna, mas apenas obteve resultados significativos com a medida de intrusão (100). Um ponto de destaque de nossos resultados é serem fruto de uma pesquisa feita em um país em desenvolvimento, diferentemente de muitos dos estudos que avaliam impacto da pobreza no comportamento maternal em locais com menor privação ou menor desigualdade social em relação ao Brasil.

A identificação de fatores que influenciam a relação mãe-bebê é importante para a proposta de medidas preventivas que possam beneficiar o desenvolvimento do bebê a longo prazo. Estudos sugerem que intervenções durante a gestação e nos primeiros três anos após o parto são mais efetivas e de menor custo do que intervenções aplicadas quando a criança atinge idade escolar (102-104). O efeito benéfico parece ser ainda maior em populações de risco como mães adolescentes, sem parceiros, baixo nível socioeconômico e para crianças com baixo peso ao nascer (102).

Limitações

Apesar desta tese ter gerado informações interessantes que auxiliam na construção de hipóteses sobre o desenvolvimento da relação mãe-bebê, não é livre de limitações. Os dados apresentados aqui são transversais, representando apenas correlações sem identificar causalidade. Além disso, grande parte dos estudos de neuroimagem e processamento cognitivo comparam fotos, vídeo e/ou som do próprio bebê da díade com estímulos de bebês desconhecidos. O fato de termos utilizado fotos de bebês desconhecidos, e não do próprio bebê, na tarefa de processamento cognitivo talvez seja um dos motivos pelos quais não encontramos diferenças entre tempos de reação para faces infantis e faces de adulto no artigo "*Cognitive Processing, Inflammation, Environment and Maternal Behavior in Early Postpartum"***.**

Outra limitação referente à tarefa de processamento cognitivo consiste na falta de controle de possíveis distratores do ambiente (como ruídos da rua) durante a execução da tarefa, tendo em vista que essa era realizada na residência das participantes. No entanto, é compreensível que mães de bebês com um mês de vida tenham dificuldade de locomoção com seus bebês, e a opção pelas visitas domiciliares foi decisiva para a realização desta tese.

8. CONCLUSÃO

Esta tese destaca a complexidade do comportamento materno, reforçando a ideia de que múltiplos fatores interagem para o desenvolvimento de uma maternagem sensível. Identificou-se que faces infantis são um estímulo importante para o sistema atencional materno, assim como foi observado que o maior engajamento atencional em faces de sofrimento infantil se correlaciona diretamente ao *parental acknowledging*, uma característica de maternagem sensível.

Resultados dessa tese também permitem sugerir que os diferentes componentes da sensibilidade materna exigem processamentos cognitivos distintos, um sendo guiado por identificar sofrimento infantil, enquanto o outro por um maior engajamento atencional para estímulos de face humanas independente da emoção expressa. Sugere-se o Il-6 como um possível marcador de alterações do processamento cognitivo e menor sensibilidade materna, associados a um ambiente adverso como o baixo nível socioeconômico.

9. REFERÊNCIA BIBLIOGRÁFICA

1. Ainsworth MD. Object relations, dependency, and attachment: a theoretical review of the infant-mother relationship. Child Dev. 1969;40(4):969-1025.
2. Bowlby J. The making and breaking of affectional bonds. London: Tavistock; 1979.
3. Winnicott D. O Papel da Mãe e da Família no Desenvolvimento Infantil. . O Brincar & a Realidade. Rio de Janeiro: Imago Editora Ltda.; 1975. p. 153 a 62.
4. Tinbergen N. The study of instinct. New York, NY, US: Clarendon Press/Oxford University Press; 1951. xii, 237 p.
5. Lorenz K. *King Solomon's Ring*. London: Methuen; 1961. 202 p.
6. Brazelton TB, Cramer BG. As primeiras relações. São Paulo: Martins Fontes; 1992.
7. Raby KL, Lawler JM, Shlafer RJ, Hesemeyer PS, Collins WA, Sroufe LA. The interpersonal antecedents of supportive parenting: a prospective, longitudinal study from infancy to adulthood. Dev Psychol. 2015;51(1):115-23.
8. Feldman R, Masalha S. Parent-child and triadic antecedents of children's social competence: cultural specificity, shared process. Dev Psychol. 2010;46(2):455-67.
9. Feldman R. The relational basis of adolescent adjustment: trajectories of mother-child interactive behaviors from infancy to adolescence shape adolescents' adaptation. Attach Hum Dev. 2010;12(1-2):173-92.
10. Feldman R, Gordon I, Influs M, Gutbir T, Ebstein RP. Parental oxytocin and early caregiving jointly shape children's oxytocin response and social reciprocity. Neuropsychopharmacology. 2013;38(7):1154-62.
11. Murray L, Hipwell A, Hooper R, Stein A, Cooper P. The cognitive development of 5-year-old children of postnatally depressed mothers. J Child Psychol Psychiatry. 1996;37(8):927-35.
12. Murray L, Halligan SL, Adams G, Patterson P, Goodyer IM. Socioemotional development in adolescents at risk for depression: the role of maternal depression and attachment style. Dev Psychopathol. 2006;18(2):489-516.
13. Bigelow AE, MacLean K, Proctor J, Myatt T, Gillis R, Power M. Maternal sensitivity throughout infancy: continuity and relation to attachment security. Infant Behav Dev. 2010;33(1):50-60.
14. Landry SH, Smith KE, Swank PR. Responsive parenting: establishing early foundations for social, communication, and independent problem-solving skills. Dev Psychol. 2006;42(4):627-42.
15. Murray L, Fiori-Cowley A, Hooper R, Cooper P. The impact of postnatal depression and associated adversity on early mother-infant interactions and later infant outcome. Child Dev. 1996;67(5):2512-26.
16. Stein A, Pearson RM, Goodman SH, Rapa E, Rahman A, McCallum M, et al. Effects of perinatal mental disorders on the fetus and child. Lancet. 2014;384(9956):1800-19.
17. Barrett J, Fleming AS. Annual Research Review: All mothers are not created equal: neural and psychobiological perspectives on mothering and the importance of individual differences. J Child Psychol Psychiatry. 2011;52(4):368-97.
18. Feldman R. Sensitive periods in human social development: New insights from research on oxytocin, synchrony, and high-risk parenting. Dev Psychopathol. 2015;27(2):369-95.
19. Mäntymaa M, Puura K, Luoma I, Latva R, Salmelin RK, Tamminen T. Predicting internalizing and externalizing problems at five years by child and parental factors in infancy and toddlerhood. Child Psychiatry Hum Dev. 2012;43(2):153-70.

20. van der Waerden J, Galéra C, Larroque B, Saurel-Cubizolles MJ, Sutter-Dallay AL, Melchior M, et al. Maternal Depression Trajectories and Children's Behavior at Age 5 Years. J Pediatr. 2015.
21. Santos IS, Matijasevich A, Barros AJ, Barros FC. Antenatal and postnatal maternal mood symptoms and psychiatric disorders in pre-school children from the 2004 Pelotas Birth Cohort. J Affect Disord. 2014;164:112-7.
22. Apter-Levy Y, Feldman M, Vakart A, Ebstein RP, Feldman R. Impact of maternal depression across the first 6 years of life on the child's mental health, social engagement, and empathy: The moderating role of oxytocin. Am J Psychiatry. 2013;170(10):1161-8.
23. Jones I, Chandra PS, Dazzan P, Howard LM. Bipolar disorder, affective psychosis, and schizophrenia in pregnancy and the post-partum period. Lancet. 2014;384(9956):1789-99.
24. Howard LM, Molyneaux E, Dennis CL, Rochat T, Stein A, Milgrom J. Non-psychotic mental disorders in the perinatal period. Lancet. 2014;384(9956):1775-88.
25. Silveira PP, Portella AK, Goldani MZ, Barbieri MA. Developmental origins of health and disease (DOHaD). J Pediatr (Rio J). 2007;83(6):494-504.
26. Curley JP, Champagne FA. Influence of maternal care on the developing brain: Mechanisms, temporal dynamics and sensitive periods. Front Neuroendocrinol. 2016;40:52-66.
27. Champagne FA, Weaver IC, Diorio J, Dymov S, Szyf M, Meaney MJ. Maternal care associated with methylation of the estrogen receptor-alpha1b promoter and estrogen receptor-alpha expression in the medial preoptic area of female offspring. Endocrinology. 2006;147(6):2909-15.
28. Peña CJ, Neugut YD, Champagne FA. Developmental timing of the effects of maternal care on gene expression and epigenetic regulation of hormone receptor levels in female rats. Endocrinology. 2013;154(11):4340-51.
29. Weaver IC, Cervoni N, Champagne FA, D'Alessio AC, Sharma S, Seckl JR, et al. Epigenetic programming by maternal behavior. Nat Neurosci. 2004;7(8):847-54.
30. Champagne F, Meaney MJ. Like mother, like daughter: evidence for non-genomic transmission of parental behavior and stress responsivity. Prog Brain Res. 2001;133:287-302.
31. Neppl TK, Conger RD, Scaramella LV, Ontai LL. Intergenerational continuity in parenting behavior: mediating pathways and child effects. Dev Psychol. 2009;45(5):1241-56.
32. Miller WB, Feldman SS, Pasta DJ. The effect of the nurturant bonding system on child security of attachment and dependency. Soc Biol. 2002;49(3-4):125-59.
33. Feldman R. Parent–Infant Synchrony : Biological Foundations and Developmental Outcomes 2007;16(6):340-5.
34. Granat A, Gadassi R, Gilboa-Schechtman E, Feldman R. Maternal Depression and Anxiety, Social Synchrony, and Infant Regulation of Negative and Positive Emotions. Emotion. 2016.
35. Feldman R, Eidelman AI, Sirota L, Weller A. Comparison of skin-to-skin (kangaroo) and traditional care: parenting outcomes and preterm infant development. Pediatrics. 2002;110(1 Pt 1):16-26.
36. Feldman R, Weller A, Zagoory-Sharon O, Levine A. Evidence for a neuroendocrinological foundation of human affiliation: plasma oxytocin levels across pregnancy and the postpartum period predict mother-infant bonding. Psychol Sci. 2007;18(11):965-70.

37. Pereira M, Ferreira A. Neuroanatomical and neurochemical basis of parenting: Dynamic coordination of motivational, affective and cognitive processes. Horm Behav. 2016;77:72-85.
38. Kim P, Strathearn L, Swain JE. The maternal brain and its plasticity in humans. Horm Behav. 2016;77:113-23.
39. Anderson BA, Laurent PA, Yantis S. Value-driven attentional capture. Proc Natl Acad Sci U S A. 2011;108(25):10367-71.
40. Anderson BA. A value-driven mechanism of attentional selection. J Vis. 2013;13(3).
41. Bindemann M, Burton AM, Hooge IT, Jenkins R, de Haan EH. Faces retain attention. Psychon Bull Rev. 2005;12(6):1048-53.
42. Lucion MK, Oliveira V, Bizarro L, Bischoff AR, Silveira PP, Kauer-Sant'Anna M. Attentional bias toward infant faces - Review of the adaptive and clinical relevance. Int J Psychophysiol. 2017.
43. Parsons CE, Young KS, Murray L, Stein A, Kringelbach ML. The functional neuroanatomy of the evolving parent-infant relationship. Prog Neurobiol. 2010;91(3):220-41.
44. Luo L, Ma X, Zheng X, Zhao W, Xu L, Becker B, et al. Neural systems and hormones mediating attraction to infant and child faces. Front Psychol. 2015;6:970.
45. Strathearn L, Li J, Fonagy P, Montague PR. What's in a smile? Maternal brain responses to infant facial cues. Pediatrics. 2008;122(1):40-51.
46. Kim P, Feldman R, Mayes LC, Eicher V, Thompson N, Leckman JF, et al. Breastfeeding, brain activation to own infant cry, and maternal sensitivity. J Child Psychol Psychiatry. 2011;52(8):907-15.
47. Atzil S, Hendler T, Feldman R. Specifying the neurobiological basis of human attachment: brain, hormones, and behavior in synchronous and intrusive mothers. Neuropsychopharmacology. 2011;36(13):2603-15.
48. Elmadih A, Wan MW, Downey D, Elliott R, Swain JE, Abel KM. Natural variation in maternal sensitivity is reflected in maternal brain responses to infant stimuli. Behav Neurosci. 2016;130(5):500-10.
49. Strathearn L, Fonagy P, Amico J, Montague PR. Adult attachment predicts maternal brain and oxytocin response to infant cues. Neuropsychopharmacology. 2009;34(13):2655-66.
50. Atzil S, Touroutoglou A, Rudy T, Salcedo S, Feldman R, Hooker JM, et al. Dopamine in the medial amygdala network mediates human bonding. Proc Natl Acad Sci U S A. 2017;114(9):2361-6.
51. Pearson RM, Lightman SL, Evans J. Attentional processing of infant emotion during late pregnancy and mother-infant relations after birth. Arch Womens Ment Health. 2011;14(1):23-31.
52. Pearson RM, Cooper RM, Penton-Voak IS, Lightman SL, Evans J. Depressive symptoms in early pregnancy disrupt attentional processing of infant emotion. Psychol Med. 2010;40(4):621-31.
53. Leon I, Rodrigo MJ, Quinones I, Hernandez JA, Lage A, Padron I, et al. Electrophysiological Responses to Affective Stimuli in Neglectful Mothers. Plos One. 2014;9(1).
54. Rodrigo MJ, Leon I, Quinones I, Lage A, Byrne S, Bobes MA. Brain and personality bases of insensitivity to infant cues in neglectful mothers: An event-related potential study. Development and Psychopathology. 2011;23(1):163-76.

55. Pearson RM, Lightman SL, Evans J. The impact of breastfeeding on mothers' attentional sensitivity towards infant distress. Infant Behav Dev. 2011;34(1):200-5.
56. Pearson RM, O'Mahen H, Burns A, Bennert K, Shepherd C, Baxter H, et al. The normalisation of disrupted attentional processing of infant distress in depressed pregnant women following Cognitive Behavioural Therapy. J Affect Disord. 2013;145(2):208-13.
57. Najjar S, Pearlman DM, Alper K, Najjar A, Devinsky O. Neuroinflammation and psychiatric illness. J Neuroinflammation. 2013;10:43.
58. Köhler CA, Freitas TH, Maes M, de Andrade NQ, Liu CS, Fernandes BS, et al. Peripheral cytokine and chemokine alterations in depression: a meta-analysis of 82 studies. Acta Psychiatr Scand. 2017.
59. Brydon L, Harrison NA, Walker C, Steptoe A, Critchley HD. Peripheral inflammation is associated with altered substantia nigra activity and psychomotor slowing in humans. Biol Psychiatry. 2008;63(11):1022-9.
60. Song C, Merali Z, Anisman H. Variations of nucleus accumbens dopamine and serotonin following systemic interleukin-1, interleukin-2 or interleukin-6 treatment. Neuroscience. 1999;88(3):823-36.
61. Pourtois G, Schettino A, Vuilleumier P. Brain mechanisms for emotional influences on perception and attention: what is magic and what is not. Biol Psychol. 2013;92(3):492-512.
62. Eisenberger NI, Berkman ET, Inagaki TK, Rameson LT, Mashal NM, Irwin MR. Inflammation-induced anhedonia: endotoxin reduces ventral striatum responses to reward. Biol Psychiatry. 2010;68(8):748-54.
63. Trapero I, Cauli O. Interleukin 6 and cognitive dysfunction. Metab Brain Dis. 2014;29(3):593-608.
64. Levandowski ML, Hess AR, Grassi-Oliveira R, de Almeida RM. Plasma interleukin-6 and executive function in crack cocaine-dependent women. Neurosci Lett. 2016;628:85-90.
65. Athilingam P, Moynihan J, Chen L, D'Aoust R, Groer M, Kip K. Elevated levels of interleukin 6 and C-reactive protein associated with cognitive impairment in heart failure. Congest Heart Fail. 2013;19(2):92-8.
66. Gimeno D, Kivimäki M, Brunner EJ, Elovainio M, De Vogli R, Steptoe A, et al. Associations of C-reactive protein and interleukin-6 with cognitive symptoms of depression: 12-year follow-up of the Whitehall II study. Psychol Med. 2009;39(3):413-23.
67. Carroll JE, Cohen S, Marsland AL. Early childhood socioeconomic status is associated with circulating interleukin-6 among mid-life adults. Brain Behav Immun. 2011;25(7):1468-74.
68. Morozink JA, Friedman EM, Coe CL, Ryff CD. Socioeconomic and psychosocial predictors of interleukin-6 in the MIDUS national sample. Health Psychol. 2010;29(6):626-35.
69. Fraga S, Marques-Vidal P, Vollenweider P, Waeber G, Guessous I, Paccaud F, et al. Association of socioeconomic status with inflammatory markers: a two cohort comparison. Prev Med. 2015;71:12-9.
70. de Britto Rosa NM, de Queiroz BZ, Pereira DS, di Sabatino Santos ML, Oliveira DM, Narciso FM, et al. Interleukin-6 plasma levels and socioeconomic status in Brazilian elderly community-dwelling women. Arch Gerontol Geriatr. 2011;53(2):196-9.
71. John-Henderson NA, Marsland AL, Kamarck TW, Muldoon MF, Manuck SB. Childhood Socioeconomic Status and the Occurrence of Recent Negative Life Events as

Predictors of Circulating and Stimulated Levels of Interleukin-6. Psychosom Med. 2016;78(1):91-101.
72. John-Henderson NA, Stellar JE, Mendoza-Denton R, Francis DD. Socioeconomic Status and Social Support: Social Support Reduces Inflammatory Reactivity for Individuals Whose Early-Life Socioeconomic Status Was Low. Psychol Sci. 2015;26(10):1620-9.
73. Nunes CCA, Tânia Alves Heineck, Isabela. O medicamento na rotina de trabalho dos agentes comunitários de saúde da unidade básica de saúde Santa Cecília, em Porto Alegre, RS, Brasil. Saude e Sociedade. 2008;17(1):85-94.
74. ABEP ABdEdP-. O Novo Critério Padrão de Classificação Econômica Brasil – Critério Brasil de Classificação Economica. 2014. http://www.abep.org/criterio-brasil [Available from: http://www.abep.org.
75. Gagliardo HG, Gonçalves VM, Lima MC. [A method to evaluate visual ability in infants]. Arq Neuropsiquiatr. 2004;62(2A):300-6.
76. Oliveira V, Goulart M, Nobre J, Lucion M, Silveira P, Bizarro L. Emotional interference of baby and adult faces on the automatic attention in parenthood. Psychology & Neuroscience. 2017;10(2):144-53.
77. Feldman R. Mother–newborn coding system manual. Tel Aviv, Israel: Bar-Ilan University University Press1998.
78. Del-Ben C, Vilela J, Crippa J, Hallak J, Labate C, Zuardi A. Test-retest reliability of the Structured Clinical Interview for DSM-IV – Clinical Version (SCID-CV) translated into portuguese. Revista Brasileira de Psiquiatria. 2001;23:156-9.
79. Santos IS, Matijasevich A, Tavares BF, Barros AJ, Botelho IP, Lapolli C, et al. Validation of the Edinburgh Postnatal Depression Scale (EPDS) in a sample of mothers from the 2004 Pelotas Birth Cohort Study. Cad Saude Publica. 2007;23(11):2577-88.
80. Moreno R, Moreno D. Escalas de depressão de Montgomery & Asberg (MADRS) e de Hamilton (HAM-D) Revista Psiquiatria Clínica 1998.
81. Gorenstein C, Andrade L, Zuardi A. Escalas de avaliação Clínica em Psiquitaria e Psicofarmacologia. Lemos, editor. São Paulo2000.
82. HAMILTON M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960;23:56-62.
83. Mesman J, Emmen RA. Mary Ainsworth's legacy: a systematic review of observational instruments measuring parental sensitivity. Attach Hum Dev. 2013;15(5-6):485-506.
84. Davidov M, Grusec JE. Untangling the links of parental responsiveness to distress and warmth to child outcomes. Child Dev. 2006;77(1):44-58.
85. Meins E, Fernyhough C, Fradley E, Tuckey M. Rethinking maternal sensitivity: mothers' comments on infants' mental processes predict security of attachment at 12 months. J Child Psychol Psychiatry. 2001;42(5):637-48.
86. Ainsworth MD. Attachments across the life span. Bull N Y Acad Med. 1985;61(9):792-812.
87. Kim YS, Lee KJ, Kim H. Serum tumour necrosis factor-α and interleukin-6 levels in Alzheimer's disease and mild cognitive impairment. Psychogeriatrics. 2017.
88. Petersen KL, Marsland AL, Flory J, Votruba-Drzal E, Muldoon MF, Manuck SB. Community socioeconomic status is associated with circulating interleukin-6 and C-reactive protein. Psychosom Med. 2008;70(6):646-52.
89. Fagundes CP, Glaser R, Kiecolt-Glaser JK. Stressful early life experiences and immune dysregulation across the lifespan. Brain Behav Immun. 2013;27(1):8-12.

90. Miller GE, Chen E, Parker KJ. Psychological stress in childhood and susceptibility to the chronic diseases of aging: moving toward a model of behavioral and biological mechanisms. Psychol Bull. 2011;137(6):959-97.
91. Sorrells SF, Sapolsky RM. An inflammatory review of glucocorticoid actions in the CNS. Brain Behav Immun. 2007;21(3):259-72.
92. O'Neill LA. TLRs: Professor Mechnikov, sit on your hat. Trends Immunol. 2004;25(12):687-93.
93. Miller G, Chen E. Unfavorable socioeconomic conditions in early life presage expression of proinflammatory phenotype in adolescence. Psychosom Med. 2007;69(5):402-9.
94. Chen E, Miller GE, Kobor MS, Cole SW. Maternal warmth buffers the effects of low early-life socioeconomic status on pro-inflammatory signaling in adulthood. Mol Psychiatry. 2011;16(7):729-37.
95. Siqveland T, Smith L, Moe V. The impact of optimality on maternal sensitivity in mothers with substance abuse and psychiatric problems and their infants at 3 months. Infant Behav Dev. 2012;35(1):60-70.
96. Evans GW, Kim P. Multiple risk exposure as a potential explanatory mechanism for the socioeconomic status-health gradient. Ann N Y Acad Sci. 2010;1186:174-89.
97. Meins E, Centifanti LC, Fernyhough C, Fishburn S. Maternal mind-mindedness and children's behavioral difficulties: mitigating the impact of low socioeconomic status. J Abnorm Child Psychol. 2013;41(4):543-53.
98. Kim P, Bianco H. How Motherhood and Poverty Change the Brain. ZERO TO THREE. 2014;34(4):29-36.
99. Sturge-Apple ML, Jones HR, Suor JH. When stress gets into your head: Socioeconomic risk, executive functions, and maternal sensitivity across childrearing contexts. J Fam Psychol. 2017;31(2):160-9.
100. Kim P, Capistrano CG, Erhart A, Gray-Schiff R, Xu N. Socioeconomic disadvantage, neural responses to infant emotions, and emotional availability among first-time new mothers. Behav Brain Res. 2017.
101. Kim P, Capistrano C, Congleton C. Socioeconomic disadvantages and neural sensitivity to infant cry: role of maternal distress. Soc Cogn Affect Neurosci. 2016;11(10):1597-607.
102. Doyle O, Harmon CP, Heckman JJ, Tremblay RE. Investing in early human development: timing and economic efficiency. Econ Hum Biol. 2009;7(1):1-6.
103. Campbell F, Conti G, Heckman JJ, Moon SH, Pinto R, Pungello E, et al. Early childhood investments substantially boost adult health. Science. 2014;343(6178):1478-85.
104. Heckman JJ. Schools, Skills, and Synapses. Econ Inq. 2008;46(3):289.