The Influence of Mother Care on the relationship between Self-esteem and Neural Substrates in young men and women: A Neuroimaging Study.

Mehereen Wadiwalla Department of Neurology and Neuroscience, McGill University, Montreal, QC

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ACKNOWLEDGEMENTS	.III
COMMONLY USED ABBREVIATIONS	/III
ABSTRACT	1
RESUME	2
INTRODUCTION	3
MATERNAL CARE AND SELF-ESTEEM.	5
What is Self-esteem?	5
Why we do we need self-esteem?	7
Self-esteem Development and Mother Care	9
Self-esteem, Mother Care and Hippocampus (HC)	. 10
A case for an association between self-esteem, Mother care and the Prefrontal cortex	. 12
Prefrontal cortex and self-esteem have convergent ontogeny	. 14
Prefrontal cortex is also sensitive to maternal programming	. 15
HYPOTHESIS AND AIMS OF STUDY.	. 16
2 METHODS AND MATERIALS	18
2. METHODS AND MATERIALS	. 10
PARTICIPANTS	. 18
NEUROPSYCHOLOGICAL ASSESSMENT.	. 18
The Parental Bonding Inventory (PBI) (Parker et al 1979)	. 18
Rosenberg Self-esteem Scale (RSE) (Rosenberg, 1965):	. 19
Questionnaire for Competency and Control (QCC) (Krampen, 2001)	. 19
MRI ACQUISITION AND ANALYSIS	. 20
The Medial Prefrontal Cortex (MPFC) and the Dorsolateral Prefrontal Cortex (DLPFC) template.	. 22
Automated and semi automated segmentation	. 24
STATISTICAL ANALYSIS USING SEMI AUTOMATED DLPFC/MPFC VOLUME	. 25
ADDITIONAL AUTOMATED PROTOCOLS:	. 26
Voxel Based Morphometry (VBM):	. 26
Probabilistic maps	. 27
3. RESULTS	. 29
Participant's demographics	29
CORRELATION ANALYSIS	29
VOLUMETRIC DIFFERENCES RETWEEN MEN AND WOMEN IN LOW AND HIGH MOCA GROUPS	31
Correlation Analysis	. 32
MEDIATIONAL ANALYSIS	. 33
VBM RESULTS	.34
PROBABILISTIC MAPS (PB MAPS) RESULTS	. 34
4.DISCUSSION	. 36
THE BI-REGIONAL ASSOCIATION BETWEEN MEN AND WOMEN.	. 37
Self esteem different for men and women	. 37
Mother care contributes to sex difference in self-esteem	. 38
NEGATIVE ASSOCIATION BETWEEN SELF-ESTEEM AND DLPFC VOLUME IN WOMEN: A POSSIBLE EXPLANATION	. 40
THE SHAPE OF THINGS	. 41
LACK OF MPFC ASSOCIATION	. 43
5.LIMITATIONS AND FUTURE DIRECTIONS	. 45
Conclusions	. 48
6. BIBLIOGRAPHY	50
7. FIGURES	. 58
FIGURE 1: THE MEDIAL PREFRONTAL CORTEX (MPFC) TEMPLATE	58
· roote · · · me madelle i her homme conten i fin i cy i Enternette internette internette internette internette	

FIGURE 2: THE DORSOLATERAL PREFRONTAL CORTEX (DLPFC) TEMPLATE.	59
FIGURE 3: VOLUMETRIC GROUP DIFFERENCE BETWEEN LOW AND HIGH MOTHER CARE	60
FIGURE 4: ASSOCIATIONS BETWEEN DLPFC AND SELF ESTEEM IN HIGH AND LOW MOCA GROUPS	61
FIGURE 5: ASSOCIATION BETWEEN HC VOLUME AND SELF ESTEEM IN HIGH AND LOW MOCA GROUPS	
FIGURE 6: BAR GRAPH FOR DLPFC VOLUMES AS A FUNCTION OF SELF ESTEEM AND SEX IN HIGH MO	CA GROUP
	63
FIGURE 7: BAR GRAPH FOR HC VOLUMES AS A FUNCTION OF SELF ESTEEM AND SEX IN HIGH MOCA O	GROUP.64
FIGURE 8: ASSOCIATION BETWEEN SELF ESTEEM AND DLPFC IN MEN AND WOMEN ON LOW AND HIGH GROUPS	<i>MOCA</i>
FIGURE 9: ASSOCIATION BETWEEN SELF ESTEEM AND HC IN MEN AND WOMEN ON LOW AND HIGH MOO GROUPS	CA 66
FIGURE 10: VBM RESULTS	67
FIGURE 11: PROBABILISTIC MAPS	
Figurella. Probabilistic maps in the Low MOCA female groups	
Figure 11b: Probabilistic maps for just Mother care in women	
Figure 11c. A comparison of high self esteem women in both high and low mother care group	ps 70
8. TABLES	71
TABLE 1: DEMOGRAPHICS FOR THE WHOLE GROUP SPLIT BY MOTHER CARE	71
TABLE 2: PBI SCORES ON ALL FOUR QUADRANTS	72
TABLE 3: GROUP DEMOGRAPHICS FOR MEN AND WOMEN IN HIGH AND LOW MOCA GROUP	73
1.COMPLIANCE CERTIFICATE	74
2. QUESTIONNAIRES USED	74

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Commonly used Abbreviations

- I. ANOVA: Analysis of Variance
- II. BA: Brodmann Areas
- III. DLPFC: Dorsolateral Prefrontal Cortex
- IV. HC: Hippocampus
- V. MPFC: Medial Prefrontal Cortex
- VI. MOCA: Mother care
- VII. PBI: Parental Bonding Index
- VIII. PB Maps: Probabilistic Maps
 - IX. PFC: Prefrontal Cortex.
 - X. QCC: Questionnaire for Competency and Control
 - XI. RSE: Rosenberg Self esteem
- XII. SE: Self esteem
- XIII. VBM: Voxel Based Morphometry

Abstract

Introduction: Numerous studies have suggested that maternal care can influence the development and expansion of an individual's self-esteem. Yet the neural mechanisms of this relationship remain unexplored. Incidentally, it has already been demonstrated that a brain region, namely the Hippocampus (HC) is associated with both self-esteem and maternal care. Thus suggesting that there may be a three-way relationship. This also provided the impetus to speculate that a similar interaction could be observed in other brain regions like for example, the Dorsolateral Prefrontal cortex (DLPFC) and the Medial Prefrontal Cortex (MPFC). Therefore, the aim of this study is to scrutinize the possible relationship between mother care, self-esteem and neural correlates including the DLPFC, MPFC and HC, with emphasis on how normal variations in mother care could have consequences for the relationship between self-esteem and particularly the prefrontal cortices. Methods: Fifty-one subjects were recruited on the basis of their maternal scores, as assessed by the Parental Bonding Index and were consequently assigned to either a high mother care (MOCA) or low MOCA group. Their self-esteem was measured through various self-esteem scales including the Rosenberg self-esteem scale. The structural integrity of the regions was ascertained through the use of both manual and semi automated segmenting procedures. Results: Initial Bivariate correlations reported a negative association between DLPFC volumes and self-esteem in the high MOCA group while HC was positively associated with self-esteem in both high and low MOCA groups. There were no associations to report for the MPFC. Additional analysis revealed that the Biregional association was sex specific. Discussion: For the first time, we were successful in associating DLPFC volume with self-esteem. In addition, we successfully replicated the association between self-esteem and HC volume. This study could provide an indication how of maternal care could have a sex specific affect not only on the evolution of selfregions targeting. esteem, but also on the they may be

Resume

Plusieurs études ont suggéré que le soin maternel peut influencer le développement et l'accroissement de l'estime de soi. Pourtant, les mécanismes neuronaux sous-jacents demeurent encore inconnus. Par ailleurs, il a été démontré qu'une région du cerveau en particulier, l'hippocampe (HC), est associée à l'estime de soi et au soin maternel, suggérant ainsi une relation à trois voies. Ceci a également fait émerger l'hypothèse qu'on pourrait observer une interaction semblable dans d'autres régions du cerveau par exemple, le cortex préfrontal dorsolatéral (DLPFC) et le cortex préfrontal médian (MPFC). Ainsi, le but de cette étude est d'examiner la relation entre soin maternel, estime de soi et structures cérébrales comprenant le DLPFC, le MPFC et l'HC en mettant l'emphase sur comment les variations normen du soin maternel pourraient influencer la relation entre l'estime de soi et le cortex préfrontal. Méthodes: Cinquante et un participants ont été recrutés selon leurs scores au questionnaire sur les soins maternels, soit le «Parental Bonding Index». Les sujets ont ensuite été attribués aux groupes soin maternel (MOCA) faible ou élevé. L'estime de soi a été mesurée par diverses échelles, comprenant, entre autres, le questionnaire d'estime de soi de Rosenberg. L'intégrité structurale des régions cérébrales a été mesurée par des protocoles de segmentations manuelles et semi-automatisées. Résultats : Les corrélations bi-variées ont révélé une association négative entre les volumes du DLPFC et l'estime de soi dans le groupe MOCA élevé tandis qu'une association positive entre le volume de l'HC et l'estime de soi a été observée dans les 2 groupes (MOCA faible et élevé). Aucune association n'a été remarquée pour le MPFC. Des analyses additionnelles ont aussi indiqué que cette association bi-régionale était dépendante du sexe. Discussion : C'est la première fois que le volume du DLPFC est associé à l'estime de soi. De plus, nous avons répliqué l'association entre l'estime de soi et le volume de l'HC. Cette étude pourrait fournir une indication sur comment le soin maternel peut affecter un individu selon le sexe, non seulement dans l'évolution de l'estime de soi mais également sur les régions cérébrales impliquées dans l'estime de soi.

Introduction

Many studies have investigated the influence of Mother care on a child's social, emotional and cognitive development (Beers & De Bellis, 2002; Cicchetti & Rogosch, 2001; Cicchetti & Toth, 1995, 2000; De Bellis, 2005; Glaser, 2000; Hildyard & Wolfe, 2002; Keiley, Howe, Dodge, Bates, & Petti, 2001; Pelcovitz, Kaplan, DeRosa, Mandel, & Salzinger, 2000; Salzinger, Feldman, Ng-Mak, Mojica, & Stockhammer, 2001; Teicher et al., 2003; Teicher, Tomoda, & Andersen, 2006; Weber & Reynolds, 2004). In humans, there are critical periods in social development where the quality of mother care could result in different consequences (Cole et al., 2001). More specifically, Hildyard et al (2002) identified three key developmental periods during which variances in maternal care could have debilitating short-term and long-term effects on the child's socio-emotional, cognitive and behavioral development: infancy, young adolescence and older adolescence (Hildyard & Wolfe, 2002; Keiley et al., 2001).

A seminal study by Bowlby (1979) was the first to demonstrate the impact of early maternal-infant bonding, which sets the template for the child's future adult relationships. Interestingly, a 10-year follow-up on children whose initial level of care at infancy was classified as neglectful, revealed that they were more vulnerable to pathological life events in comparison to children with more adaptive maternal styles (Hildyard & Wolfe, 2002). In addition, during adolescence, they often exhibited compromised social adaptation and this trend continued all the way into adulthood where they were more distrustful of others, and often had negative self-representations (Cicchetti & Rogosch, 2002; Cicchetti & Toth,

2000; Hartner, 1999; Hildyard & Wolfe, 2002; Teicher, Andersen, Polcari, Anderson, & Navalta, 2002). Furthermore, neglected children are also more prone to delinquent behavior, running away from home and are four times at risk for elevated symptoms of anxiety and affective psychopathologies like depression, substance abuse and alcoholism (Clark, De Bellis, Lynch, Cornelius, & Martin, 2003; De Bellis et al., 2005; Hildyard & Wolfe, 2002). Besides the impact on the social and cognitive development of child, maternal neglect is also believed to affect the general health and mortality of the individual. These children are also at a greater risk for Type 2 diabetes and cardiovascular infractions (Barker, 2004).

Perhaps one of the best examples of how parental and mother care in particular, can have a significant impact on a child's social development is the Harvard Mastery of Stress Study. There, the investigators asked normal, healthy, collage students to rate their parental care by completing the Harvard parental care scale. Thirty-five years later, those students that used a higher degree of negative words to describe their mothers were more likely to suffer from physiological infractions like hypertension and coronal complications (Russek & Schwartz, 1996, 1997a, 1997b), as well as psychological pathologies like depression and alcohol abuse (Canetti, Bachar, Galili-Weisstub, De-Nour, & Shalev, 1997; Parker, 1990; Sato, Uehara, Narita, Sakado, & Fujii, 2000). It is important to keep in mind that these individuals were not severely neglected or abused as children. The only difference in these children was the parenting style that was securing and loving in some, and aloof and disciplinarian in others. Yet those with inadequate maternal care styles were considerably disadvantaged in the long-term follow-up. On a positive note, this study also validated the

fact that good parenting can serve as a source of resilience and a buffer, providing better coping skills and quality of life (J. Smith & Prior, 1995).

Maternal care and Self-esteem.

A key developmental milestone in socio-cognitive development is the management and expansion of self-esteem. Since it has been reliably established that mother care in fact, does influence the general social development trajectory, therefore, it stands to reason that it would similarly influence self-esteem development as well.

What is Self-esteem?

More than a century ago, William James (1890) was the first to formally define self-esteem as a value an individual places on themselves (James, 1890). Since then, many theories have attempted to explain the concept of self-esteem. However all of them ultimately differ on two major themes. The former is a teleological argument about the nature of selfesteem. More fundamentally, the question is if it is a personality trait or a psychological state. Most researchers tend to consider it as a relatively stable aspect of an individual, which one brings to a variety of situations, rather than as a dynamic state in response to them. On the other hand, many have conceptualized it as a state, which varies across situations and fluctuates in response to particular events.

The latter theme, in contrast seeks to investigate the influence of self-esteem in terms of whether it is a global all encompassing multimodal system or if it is restricted to a particular facets of ones life i.e. it seeks its conception and expansion from limited and self identified valuable domains of one's life. As a global measure, self- esteem adopts a top down approach (Crocker et al 2001). The self worth that an individual perceives for him or her self is not based on success in any particular domain but rather success in the course of life is attributed to the proper functioning of self-esteem in the first place. Others have conversely suggested that self-esteem could be a bottom up process where it is predominantly contingent on continuing success in few particular domains. This consequently translates into a general feeling of wellness and increase in positive self-evaluation, which is then generalized to every other facet of one's life (Crocker et al, 2001).

The general consensus in any case for the first theme seems to be in favor of self esteem being a stable personality trait that remains constant in most situations. However there is no such agreement with respect to the second theme, and to date the issue remains contentious.

As mentioned earlier, many studies over the years have tried to conceptualize self-esteem in novel and innovative ways, but ultimately all of them end up being variants of the original two fundamental issues. Some notable examples would be theories by Crocker and Wolfe (2001) where they make a case for self-esteem being more domain specific or "contingent vs. non contingent (Crocker & Wolfe, 2001). Or Pelham's (Pelham & Swann, 1989) stable vs. unstable self-esteem, which is starkly reminiscent of the state vs. trait argument. Nevertheless, there is an underlying assumption that all the theories subscribe too; that is, the need for self-esteem is universal and indeed people are motivated to maintain high levels of it and defend it when under threat (Pyszczynski, Greenberg, Solomon, Arndt, & Schimel, 2004).

Why we do we need self-esteem?

There has been an increasing interest in understanding the psychological need for selfesteem and its role in daily human interaction and growth. A possible explanation has been provided by the Terror management theory of self-esteem (Pyszczynski et al., 2004), which contends that self-esteem seeks to fundamentally mitigate the deep-rooted anxiety about an individual's mortality. It accomplishes this by enhancing an individual's personal value, which in turn, alleviates the apprehension one feels about their eventual demise. The sense of personal worth is obtained from believing in the validity and truth of one's own cultural views as well as the sense of living up to those cultural contingencies (Crocker & Wolfe, 2001). However while the cultural values are derived from the cultural milieu, they are largely integrated in individuals in purely subjective and thus create a uniquely individualized worldview. Hence self-esteem becomes an extremely personal experience where a person extracts what he or she considers valuable from the environment and that ultimately governs the course of the individual's life.

Another very influential theory is posited by Leary and Baumeister and is known as the "sociometer theory" (Leary, 2003). They speculate that self-esteem serves five fundamental needs; the maintenance of well being and positive effect, feedback for own coping and adequacy, reflection of individual status in social group, facilitation of self

determination and perhaps most importantly as providing vital information about individual's eligibility for social inclusion and exclusion.

The sociometer theory concludes that self-esteem "serves as a subjective monitor of ones own relational valuation" or the degree to which other individuals value their relationship with the person in question (R. F. Baumeister & Leary, 1995). It proposes that self-esteem acts an internal barometer that is sensitive to changes in one's relational value. While high self-esteem signifies an acceptance in the group, low self-esteem is associated with feelings of rejection and not feeling valuable to others (R. F. Baumeister & Leary, 1995).

Self-esteem therefore is a highly valued and imperative cognitive milestone whose proper functioning is required for the emotional and psychological wellbeing of an individual. Keeping in line with this, is the observation that high levels of self-esteem have subsequently been associated with both positive and negative life consequences. For example, positive self-esteem has been correlated with life affirming characteristics such as resilient coping styles, longevity, general happiness and satisfaction with oneself (R. F. Baumeister, Campbell, J.K., Krueger, J.I., Vohs, K.D., 2003), while low self-esteem has been causally implicated in substance abuse and affective disorders including depression, anxiety, antisocial behavior and eating disorders (Crocker & Wolfe, 2001; Hoyle, 1999; Leary, 2003).

8

Self-esteem Development and Mother Care.

Self-esteem development can be construed as an "experience dependent phenomenon" (Greenough, Black, & Wallace, 1987). The earliest environment a child experiences is contingent on the quality of parental care he or she is exposed to. While paternal care is important in mitigating a child's social development (Hall, Peden, Rayens, & Beebe, 2004; Heider, Matschinger, Bernert, Alonso, & Angermeyer, 2006), maternal influence is, more often than not, implicated in the management and expansion of the child's social self (Heinonen, 2003). Therefore, the initial environment can set the stage for future emotional, cognitive, and behavioral outcomes (Cole et al., 2001). Indeed, there is evidence that self-esteem ontogenesis is greatly dependent on the quality of maternal attachment the child receives (Bowlby, 1969). Interestingly, children of anxious/ambivalent and avoidant mothers often exhibit behavioral responses that are strangely reminiscent to responses that one expects from low self-esteem men and women (Bost et al., 2006; Domingo, Keppley, & Chambliss, 1997; Heider et al., 2006; Johnson, Gilbert, & Herdt, 1979; LeCuyer-Maus, 2000; Leifer, Kilbane, & Skolnick, 2002; McGarvey, Kryzhanovskaya, Koopman, Waite, & Canterbury, 1999; Uehara, Sato, Sakado, & Someya, 1998).

Furthermore, a child's ability to internalize feedback obtained during the course of their maturation plays a significant role in the construction of their self-esteem and self-defining characteristics (Block, 1993; Hartner, 1999; Mead, 1934). Additionally, adolescence is a

time where a child creates, develops and internalizes a worldview, which then assists in establishing their self worth in the scheme of things. Maternal influence at this point, serves as a catalyst in form of support and nurturing and also, as a source for internalizing world views (Pyszczynski et al., 2004). That is, a child looks to the maternal figure as a model for the creation of his or her own value system. Therefore maternal care can directly and indirectly impact the development of self-esteem.

Self-esteem, mother care and neural substrates.

In short, it is apparent that mother care directly contributes to the development of selfesteem. There is an existing body of literature, which has studied the behavioral ramifications of how mother care can influence self-esteem. More recently, however, the focus has shifted to the arena of neural and biological substrates and as a result, there has been an increasing interest in studying this relationship through the context of neurobiological substrates. Two main regions of interest include the Hippocampus (HC) in the Medial temporal lobe, and the Prefrontal cortex (PFC) in the frontal lobes.

Self-esteem, Mother Care and Hippocampus (HC).

To date, there is some evidence that both mother care and self-esteem are linked to the morphology of the hippocampus (HC). The first paper to disentangle the influence of mother care on the hippocampal volume was by Buss et al (2007). They posited that higher

levels of postnatal maternal care could mitigate the influence of prenatal adversity on the hippocampus. More specifically, higher mother care resulted in higher HC volume in a group of participants who were designated as a high prenatal stress group. It is important to keep in mind that this group reported higher levels of prenatal stress that included emotional and financial distress during pregnancy as well as birth complications. Despite the disadvantaged beginnings, those individuals who had high levels of post natal maternal care, were considerably better off than their counterparts whose levels of maternal care was less than stellar. These individuals reported lower than average hippocampal volumes. Thus suggesting that good postnatal maternal care could in fact, serve as a buffer against the debilitating effects of early prenatal insults. Furthermore, animal studies have provided evidence of a similar phenomenon in rodents where higher levels of maternal care has been known to affect the neurogenesis of the HC (Bredy, Grant, Champagne, & Meaney, 2003; Liu, Diorio, Day, Francis, & Meaney, 2000; Liu et al., 1997; Weaver, Meaney, & Szyf, 2006).

With respect to the link between self-esteem and hippocampal volumes, Pruessner et al (2005) were first to discover this association. They demonstrated that higher levels of self-esteem were significantly associated with higher hippocampal volumes and more interestingly, this association was consistent across the lifespan. This paper was the first to show a link between self-esteem and the structural integrity of a brain region and thus raised the possibility that this relationship could also be realized in other regions of the brain as well.

A case for an association between self-esteem, Mother care and the Prefrontal cortex

This being said, another region that should also be investigated is the Prefrontal cortex (PFC). The PFC has a well established roles in the domain of the self (Eslinger, Flaherty-Craig, & Benton, 2004; Eslinger, Grattan, Damasio, & Damasio, 1992; C. D. Frith & Frith, 1999; Gallagher, 2000) as well has been known to be vulnerable to mother care (Teicher et al., 2002). Evidence below will be provided to make a case for investigating the Prefrontal cortex in relation to self-esteem and mother care.

The Prefrontal Cortex.

The PFC is a heterogeneous area, which is most developed in primates and it is an area that has afferents to cortical sensory, motor and sub-cortical structures (Miller & Cohen, 2001). It is situated in the frontal lobe and can be divided into four subdivisions: Medial, Orbital, Dorsal and Dorsolateral. In humans and non-human primates, the PFC includes areas rostral to the premotor cortices. It also includes part of the anterior Cingulate cortex including Brodmann (BA) areas 24a, 24b, 23a and 23b. Each of these areas have their own vigorous connections with the amygdala, HC, entorhinal and parahippocampal cortices (Carmichael & Price, 1995). It also has direct connections with the inferior parietal lobe, the amygdala and the occipital cortex (Fossati et al., 2004). For the purposes of our study the two areas of special interest within the PFC, are the Dorsolateral Prefrontal Cortex (DLPFC) and the Medial Prefrontal Cortex (MPFC).

The Dorsolateral Prefrontal cortex (DLPFC)

The DLPFC is the most lateral portion of the prefrontal cortex and has been featured prominently in the working memory literature (Mitelman, Buchsbaum, Brickman, & Shihabuddin, 2005; Petrides, 2000a, 2000b), as well as schizophrenia (Mitelman et al., 2005; Prasad, Sahni, Rohm, & Keshavan, 2005). Its primary role is the cognitive assessment and decision-making using visceral emotional and environment cues for the process of executive functioning. It accomplishes this by initiating a triangular circuitry between HC, thalamus and itself (Barbas, 1995; Carmichael & Price, 1995; Petrides & Pandya, 1999). Thus making this area integral to the functioning of emotional and cognitive decision-making.

The Medial Prefrontal cortex (MPFC).

The MPFC, in concert with the DLPFC is involved in the integration and processing of sensory information from the external world, (Barbas, 1995; Carmichael & Price, 1995). It is colloquially referred to as the "area of the self" (C. Frith & Frith, 2005; U. Frith & Frith, 2003) and one of the areas that shows high neural activity at rest that is, it is functionally active at baseline (Gusnard, 2005; Gusnard, Akbudak, Shulman, & Raichle, 2001; Gusnard, Raichle, & Raichle, 2001). In addition, it also has the highest amount of activity when the task at hand is self-relevant (Raichle & Gusnard, 2005; J. R. Simpson, Jr., Drevets, Snyder, Gusnard, & Raichle, 2001; J. R. Simpson, Jr., Snyder, Gusnard, & Raichle, 2001).

Together these two subdivisions of the prefrontal cortex are responsible for the monitoring of self-relevant information and higher order cognitive processes such as decision-making, perception and emotional regulation (D'Argembeau et al., 2005; DeYoung, Peterson, & Higgins, 2005; C. D. Frith & Frith, 1999; Gusnard, Akbudak et al., 2001; Northoff & Bermpohl, 2004; Ochsner et al., 2005; Petrides, 2005; Schmitz, Kawahara-Baccus, & Johnson, 2004; J. R. Simpson, Jr., Snyder et al., 2001) and therefore, are perfectly poised to contribute to the evolution and maintenance of self-esteem.

Prefrontal cortex and self-esteem have convergent ontogeny

Perhaps the most significant factor in considering a relationship between self-esteem and DLPFC and MPFC in particular, is that these regions experience exponential growth during early adolescence, which coincides with the maturing of social cognition in children (Andersen, 2003; Teicher et al., 2003; Teicher et al., 1997). Early puberty is a time where a child develops a sense of social order and an understanding of societal rules (Nelson et al 2005). Incidentally, right around this time, the young adolescents also learns to actively and quite expertly engage in theory of mind processes (Gallagher et al 2003) that is, the ability to perceive an other's state of mind. Furthermore, during this period there is an eventual cognitive shift, which enables them to regulate their emotions and engage in necessary inhibitory responses (Nelson et al 2005). The social evolution continues right unto the second decade of one's life where these early social experiences assist in molding and consolidating the individual's basic self worth (Hildyard 2002). So far the neural underpinnings of these burgeoning social networks have not been studied. This is quite

surprising considering that along with this dramatic period of social growth, there are concurrent changes occurring in the prefrontal cortex, as a result of extensive neurogenesis and pruning (Teicher et al., 2002). The mirroring of these two processes, precisely at the same time is intriguing to say the least. In short, the convergent ontogeny of these two processes suggests a possible link that cannot simply be attributed to chance.

Prefrontal cortex is also sensitive to maternal programming

In addition to having theoretical reasons for being associated with self-esteem, there are also waves of studies, which have demonstrated that a gross lack of maternal care at least, can affect the morphology and integrity of these neuro-anatomical structures as well. Abused children tend to have smaller volumes in different sub regions of the prefrontal cortex(Bremner, 2002; Glaser, 2000; Teicher, 2002; Teicher et al., 2002; Teicher et al., 2003).

In brief it is possible that key limbic structures, including HC and PFC, are vulnerable to variations in mother care. While it is certainly true that in most cases, the effect on the integrity of neural structures can be attributed to a lack of maternal care, it cannot be ignored that normal deviations in mother care have also been known to exert a tremendous influence on the social and cognitive development of an individual and therefore, by extension can be equally important for the development and integrity of key morphological structures.

Hypothesis and aims of study.

The literature reviewed above suggests that mother care can be linked to self-esteem. In addition, evidence has been put forth showing a link between quality of mother care and neurodevelopment of brain regions. Furthermore, results from our lab indicate that there is a relationship between integrity of brain structures (HC in particular) and self-esteem. Interestingly, ample background literature suggests that such an interaction could also exist in regions of the prefrontal cortex. However, this relationship remains unexplored, particularly, in the PFC regions of the DLPFC and MPFC.

Considering that mother care is the one variable that seems to influence the development and maintenance of both self-esteem and neural substrates, a case can be made for suggesting that variation in both self-esteem and neural substrates are a consequence of variations in maternal care. We hypothesize that higher levels of maternal care would be more likely to contribute to a positive association between self esteem and Hippocampal volume and given the precedence in the hippocampus, we expect to see a similar positive association in the prefrontal cortex as well. The main reason for investigating the volumes of these structures is that it can be taken as a proxy measure for cellular processing. In fact, recent studies have suggested that volumes might reflect differential neuronal and glial packing density, as well as differences in neuronal soma sizes which could be indicative of proper functioning (Miguel-Hidalgo et al., 2002; Stockmeier, 2004). Nevertheless, the one thing that is beyond the scope of this study is to establish directionality in the association between self-esteem and neural substrates. This is a considerably problematic venture, especially in the case of the Prefrontal cortex. Given that both self-esteem and prefrontal development share convergent growth periods, it is therefore unclear which one is the causal variable. On the other hand, there is controversy about the directionality of the association between self-esteem and hippocampus. There has been speculation that a pre-existing abnormality in its morphology could serve as a vulnerability factor for future affective and cognitive disturbances (Gilbertson et al., 2002). Furthermore, the early maturity of the HC makes it principally sensitive to early maternal programming (Akers et al., 2006; E. Gould & Tanapat, 1999; McEwen, 2003). So it is unclear if a personality variable could be contributing to the morphological variances or if pre-existing abnormalities may cause the individual to embrace certain personality characteristics. Thus, our question is simply to investigate if maternal care can influence the association between self-esteem and neural substrates.

Therefore, the aim of this study is to scrutinize the possible relationship between mother care, self-esteem and neural correlates including the DLPFC, MPFC and HC, with emphasis on how normal variations in mother care could have consequences for the relationship between self-esteem and particularly the prefrontal cortices. Furthermore, since previous studies have already documented a link between self-esteem and HC, we would also like to replicate that finding in our own sample.

2. Methods and materials

Participants

Fifty-one (26 women) healthy university students between the ages of 20-32 (mean age =23.14 years ± 3.04) were recruited on and around McGill university campus Written consent was obtained from each subject prior to entering the study. The Douglas Hospital Research Centre Ethics Board and the Montreal Neurological Institute Ethics Board approved the study. Each respondent was specially selected based on the Mother care score (G. Parker, Tupling, H., Brown, L.D., 1979) and were consequently assigned to either a high or low Mother care (MOCA) group.

Neuropsychological assessment.

Psychological assessment included the following questionnaires:

The Parental Bonding Inventory (PBI) (Parker et al 1979)

The PBI is a standard instrument to retrospectively measure parental style (Parker 1979). The 48-items questionnaire assesses care and overprotection children received independently from mother and father during their first 16 years of life, resulting in four subscales: mother care, mother overprotection, father care, and father overprotection. We used the Mother care variable as our discerning variable of choice. We employed the mean split method to create two groups: Low Maternal care (Low MOCA) and High Maternal care (high MOCA) groups.

Rosenberg Self-esteem Scale (RSE) (Rosenberg, 1965):

RSE is a 10 scale self report that assesses global self-esteem levels. It was designed to be a Guttmann scale, which means that its items were to represent a continuum of self-worth statements. Rosenberg (1965) scored his 10-question scale that was presented with four response choices, ranging from strongly agree to strongly disagree. The 10 items RSE has been translated into many languages and has been used worldwide as measure of global self-esteem.

Questionnaire for Competency and Control (QCC) (Krampen, 2001)

The QCC is a 32 item questionnaire that uses the four primary scales: global self-concept, chance, control of others and internality. It combines aspects of locus of control, self-concept and self- esteem (Krampen 2001). The internality sub scale was used as a mean to validate our results as previous findings from our lab have shown that Rosenberg self-esteem is highly correlated with internal locus of control as well as the global self-concept (Pruessner et al 2005).

Additional battery of questionnaires included NEO Personality Inventory (Costa, Busch, Zonderman, & McCrae, 1986), Mastery (Pearlin & Schooler, 1978) and Ways of coping (Vitaliano, 1985).

MRI Acquisition and analysis

Structural scans for all subjects were acquired using the protocol of the international consortium of brain mapping (ICBM) initiative to create a statistical atlas of the normal adult brain(Mazziotta, Toga, Evans, Fox, & Lancaster, 1995). This protocol generates T1, T2 and PD weighted images. For the purpose of this analysis, only T1 weighted images were used. Several algorithms were applied in order to prepare the images for manual segmentation. This included non uniformity corrections (Sled, Zijdenbos, & Evans, 1998). They correct for MRI intensity inhomogenieties due to individual anatomical variability, or poor Radio Frequency (RF) coil uniformity that generates signal drift.

The second process is linear stereotaxic transformation (Collins, Neelin, Peters, & Evans, 1994) into coordinates based on the talairach atlas (Talairach, 1988). This process allows for comparison across groups and large subjects by insuring that the results are as coordinates in a standardized space. This is accomplished through affine linear registration using the ICBM 152 average model. The affine registration protocol transforms the file by rotating, translating, scaling and skewing the file in all three x, y and z dimensions, in order to ensure that the brain is as standardized as possible.

After the registration the file undergoes non-intensity normalization, which makes the signal range comparable between subjects. In addition, the files were subjected to an automated tissue classifying protocol created by Zijdenbos (1994) which specifically generates individual subject grey matter (GM), white matter (WM) and Cerebro-spinal fluid (CSF) maps. It accomplishes this by classifying every voxel in the file as either grey

white or CSF. The process can be split into two parts. The first is a fully automated "prior probability method" which based on an existing template deduces the probability of a voxel belonging to any of the three categories. The second step of this process is more intuitive as it recalculates the probability of a voxel being a grey matter voxel, for example by conducting a k-neighbor clustering interpolation where it assesses the likelihood of a particular voxel based on the category its neighbor belongs to (Cocosco, Zijdenbos, & Evans, 2003).

The Volumetric analysis was performed with the interactive software package DISPLAY developed at the Brain Imaging Centre of the Montreal Neurological Institute in Montreal, QC, Canada.

Hippocampal volume was assessed using a highly validated and widely used protocol developed in our laboratory (For more details please refer to Pruessner et al (2000)). Structural segmenting of the hippocampus was conducted by Dr. Claudia Buss and was validated by Dr. Jens Pruessner.

Since there were no pre-existing protocols on the assessment of volumetric difference in the PFC, we developed a new segmentation protocol to specifically evaluate the MPFC and the DLPFC regions.

The Medial Prefrontal Cortex (MPFC) and the Dorsolateral Prefrontal Cortex (DLPFC) template.

The labels were created on an average brain map of all the subjects to ensure the best fit possible. The author undertook the creation of the two labels manually.

MPFC label

The MPFC label includes Brodmann Area (BA) 9m, 10m, 24 and 32. BA 9 has a lateral and medial component and 9M encompasses the most rostral portion of the medial longitudinal fissure. BA 10 refers to the frontal pole and 24 and 32 are part of the anterior cingulate cortex.

When segmenting the MPFC regions, a precise way to orient your self is to paint primarily in the coronal view, which proves to be the most reliable indicator of boundaries. Therefore, in this view in particular, the most rostral part of the frontal pole (10) acts as its anterior boundary. The posterior boundary is evident on the most caudal slice in which the anterior commisssure is visible. The ventral border is the most caudal slice in which the inner curvature of the corpus collusum is visible. In the sagittal view the anterior border was defined as the first deep sulcus measured form the genu of CC and is usually the cingulate sulcus (See figure 1).

DLPFC label

The DLPFC cortex is the most lateral portion of the prefrontal cortex and includes BA 8,9 and 46. These regions are encapsulated in the superior and middle frontal gyri.

BA 8, which is also known as intermediate frontal region, and 9, which is known as the granular frontal, has a lateral and medial component. BA 46 is located primarily in the middle frontal gyrus.

With respect to the borders, the best option is to segment in the coronal and sagittal views as they allow the most optimal view for segmenting. Therefore, in the coronal and sagittal views, the ventral lateral border is the inferior frontal sulcus .The Posterior Border is the precentral sulcus and the anterior border is demarcated by the frontal pole region which Tisserand et al (2002) designated as all anterior slices before Y=44. Anatomically after this slice the inferior frontal sulcus starts to become visible in the coronal view. The rostral medial border is the most rostral part of the medial longitudinal sulcus. In the sagittal view the anterior border was the paracingulate sulcus, which is dorsal to the cingulate cortex. In case the paracingulate was not discernible, the most caudal slice was designated as the slice in which the curvature of the corpus collusum was visible (See Figure 2).

Automated and semi automated segmentation

With the prefrontal labels created the next step was superimposing the labels unto the individual subject grey matter map files (Cocosco et al., 2003). The files are in MINC (medical imaging net CDF) format, which is a medical imaging file format. The MINC format was created by Peter Neelin in 1993 and is based on the UNIX platform. In order to work with the files a series of MINC tools were employed to initiate the necessary changes.

The first was 'minclookup- discrete which performs lookup table operations on each voxel in the classified files. The most common use of the lookup table is to convert intensity values into RGB colors and where all input values range from 0 to 1(therefore instead of 3 separate labels for GM, WM and CS there are only two labels 0 and 1). This method achieves this by employing discrete look up tables, where the classified files are remapped and each input value, (in this case the grey matter, white matter and CSF classified voxels) is compared to a look up table and if the input value is found, a corresponding output value is prescribed. If it is not found then a null value is indicated for that particular voxel. The algorithm is specifically designed to select the GM by assigning the integer value of 1 to it, while the while matter and CSF are consequently discarded as they are automatically assigned a null value.

Furthermore, the dimensions of the DLPFC and MPFC labels were resized with the intention of making them more compatible with classified files. The MINC command that is used is "Mincreshape". This command initiates a series of conversions including

changing type, range and normalization of the pixel values, expanding or contracting images to give a specified image size. It achieves this by normalizing the image to a real value in this case the minimum being 0 and the maximum being 255.

The next step of this procedure involves resampling the individual files to be in the same spatial dimensions as the label template file therefore ensuring that the individual classified file is resampled in the same voxel positions as the template. After correcting for file dimensions, label template was superimposed on the individual on individual's files to ascertain an approximate estimate of volume (for both MPFC and DLPFC), for each subject. However, in order to account for the interindividual variability found in these regions, manual correction of each individual file was subsequently undertaken.

The volume difference before and after the manual correction was significant for both the DLPFC (t $_{(45)}$ = 14.08 p =<. 001) and MPFC (t $_{(46)}$ = 26.75 p = <. 001). All statistical analyses were therefore conducted only on the manually corrected volumes.

Statistical analysis using Semi Automated DLPFC/MPFC Volume

The subjects were divided into low and high Mother care (MOCA) groups using the mean split method. The Mean score (Mean $=26\pm8$) was used as a cut off point in order to facilitate the creation of the groups in this sample as it represents a better estimate of the population. Since our sample was normally distributed, the mean, median and mode were

not significantly different thus the mean was deemed to be a good estimate for our sample in general. Analysis of variance (ANOVA) and student t tests were employed in order to assess mean differences between our groups, where suitable.

Bivariate Pearson Correlational Analysis was employed to assess an association between self-esteem and regions of interests in our groups. In course of our analysis we also conducted Mediation analysis using hierarchical regression analysis approach in order to see if mother care mediated the relationship between self-esteem, hippocampus and the PFC. The dependent variable was either PFC volume or HC and the independent variable was entered as Rosenberg self-esteem score and mother care. All statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS) 11.0.

Additional automated protocols:

Voxel Based Morphometry (VBM):

As an initial exploration, Voxel Based Morphometry (Ashburner & Friston, 2000) was used in order to confirm if there was an association present between self-esteem and the prefrontal cortex quite early in the project and this provided the basis for our future explorations. It is a computational neuroanatomy method to assess anatomical differences throughout the brain. It is usually used for a voxel wise comparison of local content of grey matter between two groups. It essentially looks for differences in local composition of brain tissue after macroscopic shape differences have been accounted for. VBM analysis
was conducted after spatially normalizing the native brains in standard stereotaxic space and partitioning grey matter, white matter and cerebrospinal fluid. This process, which is known as segmentation, is primarily used so that grey matter and white matter regions can be correctly identified for future analysis. The next step of preprocessing involves smoothing the regions with a Gaussian kernel called full width half maximum (FWHM). Smoothing allows VBM to be comparable to region of interest analysis as each voxel in the smoothed image contains an average concentration of grey matter around the voxel (Ashburner, Andersson, & Friston, 2000; Ashburner & Friston, 1999, 2005; Friston & Ashburner, 2004). Statistical analysis involved the use of general linear modeling (GLM)(Worsley, Taylor, Tomaiuolo, & Lerch, 2004) to identify regions for grey matter concentration that were related to the specific parameters of the study.

Probabilistic maps

Probabilistic maps (PB maps) were computed from the manually corrected individual structural files in order to check for the probability that the difference may be attributed to the homogeneity of the structure. PB maps indicate the probability for each voxel to be included in the volume of the structure in one subject across all subjects of a prescribed group. For each voxel the probability is indicated ranging from 0 to 1. A high probability indicates that for many subjects in the group that particular voxel is a part of the structure examined. This implies that if there are any shape differences the map will show voxels with lower probability scores. Consequently, if the shape is homogenous the map will show less voxels but each with higher probability (Corbo, Clement, Armony, Pruessner, &

Brunet, 2005). Three separate sets of analysis were conducted with our respondents being grouped according to their self-esteem and mother care affiliation.

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3. Results

Participant's demographics.

There were 27 participants in the High MOCA group and 24 in the Low MOCA groups. There was a significant difference between low and high MOCA groups in their Mother care scores (t $_{(49)}=11.11 \text{ p} <.001$). There was also a difference in Rosenberg self esteem scores (t $_{(49)}=2.572 \text{ p} <.01$. Neither age nor QCC internality scores were significantly different between both groups. (See table 1). Additionally there were no significant volumetric differences observed between low or high MOCA groups for either the left (*t* $_{(45)}=1.2$, p >.05) or right (t $_{(45)}=.774 \text{ p} >.05$) DLPFC, left (t $_{(47)}=.25$, p>.05) or right (t $_{(47)}=.81$, p >.05) or right (t $_{(47)}=.25$, p>.05) Hippocampal volume (See figure 3).

Correlation Analysis.

In order to assess if there was an association between the morphological integrity of brain regions and self-esteem, we conducted Pearson correlation analysis in low and high MOCA groups separately. It is important to note here that, in our sample, higher mother care coincided with higher levels of father care as well as, lower levels on maternal and paternal overprotection; therefore, higher mother care can also be construed as a proxy for optimal parenting styles (See table 2).

In the high MOCA group, our initial analysis revealed a negative association between selfesteem and left (r=-.409, p= .05) and right (r=-.399, p= .05) DLPFC (See figure 4). There was no significant association with MPFC (p >.05) or HC volume (p >.05) in both hemispheres. With respect to the internality subscale of the QCC, we observed a similar pattern of association with both left (r=-.494, p= .02) and right (r= -.439, p= .03) DLPFC. There were no significant associations to report for either MPFC or HC volumes.

In the low MOCA group, there was no association observed between self-esteem and neither DLPFC (p > .05), nor MPFC (p > .05) volumes. Interestingly, there was a strong positive association observed between right HC volume and self-esteem (r=.486, p=.02) (see figure 5). There were no significant associations reported in the left HC (p > .05). Furthermore, there were no significant associations evident for the Internality subscale and all three volumetric measures. In addition there was no association between total gray matter volume and self esteem in either groups (p>.05) as well.

To summarize, while we observed a negative association between left and right DLPFC volume, Rosenberg self-esteem (RSE) and the internality subscale of the QCC in the high MOCA group, the only significant association in the low MOCA group was found between right Hippocampal volume and Rosenberg self-esteem.

The next question that we wanted to investigate was if sex differences could be a contributing factor in the associations described above; especially since there is evidence that there are sex differences found in the prefrontal cortex. (Gur et al., 2000; Tisserand et al., 2002). With respect to the hippocampus, we also had reason to believe that we could be seeing a similar sex difference especially since the association between self-esteem and Hippocampal volume has so far only been evident only in men (Pruessner et al 2005). Therefore lending credence to the possibility that sex differences could be an important variable to consider for further analysis.

As a result, we decided to perform all subsequent analysis with sex as a grouping variable in addition to mother care. We consequently had 13 men and 11 women who reported high MOCA scores and 11 men and 12 women who reported low MOCA scores. (See table 3). With respect to personality measures, there were significant differences in PBI Mother care, as expected, between low and high MOCA men $t_{(23)}$ =7.373 p .001 and women $t_{(24)}$ =8.398 p= <. 001.

Volumetric differences between Men and Women in Low and High MOCA groups.

Additional analysis revealed that there was an 11% difference between right DLPFC volume and a 12% difference in Left DLPFC volume between low and high self-esteem groups in the high mother care group only in women but not in men ($f_{(1,20)} = 4.485 \text{ p} = .047$ (DLPFC X RSE X SEX), mixed design ANOVA) (see figure 6) which revealed that

women with higher self-esteem has lower DLPFC volumes in the high MOCA group. There were no significant effects to report in the Low MOCA group.

Intriguingly in the hippocampus, we discovered that there was a volumetric difference between low and high self-esteem men That is, there was 12% difference in the right, and a 13% difference in the left Hippocampal volumes between men with low and high selfesteem in the high MOCA group ($f_{(1, 19)}=3.049$ p=. 05, Mixed design ANOVA (RSE x HC) (Figure 7). There were no significant effects to report in the Low MOCA group. There were no significant volumetric differences in MPFC volumes in either the High or Low MOCA groups.

Correlation Analysis

After rerunning the correlational analysis, we noticed that the association between DLPFC volume and Rosenberg self-esteem was still significant. However it was present only in women for both the right (r= -.64, p =. 04) and partially for the left (r= -.544 p =. 07) DLPFC. (See figure 8). That is, this association was observed only in women and was subsequently absent in the men. Therefore indicating that the women in our sample could have driven the initial association. This was accordingly substantiated in the case of the Internality subscale as well, where once again left (r=-.626, p=. 04) and right (r= -.613, p=. 05) DLPFC were associated with internality in women, but not in men (p >.05).

There were no significant associations to report for men or women with respect to MPFC volumes for both Rosenberg self-esteem scale and the internality subscale of the QCC.

For the hippocampus, we observed a robust association between right HC and Rosenberg self-esteem in the high MOCA group, which was present only in men (r=.58, p=.03) (see figure 9) but was completely absent in women (p > .10). With the internality subscale, the earlier association between right HC and internality was once again evident, but only in men (r=.566 p=. 06). In the low MOCA group, the only significant association was between RSE and right HC (r=.711, p .02) only in men. There was no significant relationship between hippocampal volume and self esteem in women in both high and Low MOCA groups. There was no significant relationship between total gray matter volume and self esteem, in neither men nor women for both MOCA groups.

To summarize once again, we found an association between both measures of self-esteem and DLPFC in women, only in the High MOCA group, and HC volumes and self esteem in men in both Maternal care groups.

Mediational analysis.

Since our initial statistical analysis revealed a strong association between DLPFC regions and self-esteem, we chose to include only the DLPFC volume for the subsequent Mediational analysis. In our first set of analysis using DLPFC as the dependent variable, and RSE and MOCA subsequently entered as independent variables, we found that there were no significant associations in either men or women (p>.05) Using hippocampal volume as the dependent variable and RSE and MOCA subsequently entered as the independent variables, it was revealed that mother care contributed considerably to the relationship between self-esteem and HC (F $_{(1,22)}$ = 4.166 p=. 03) only in men, but not in women (p=>.05)

VBM results

Preliminary VBM results indicated a trend towards lower self-esteem, higher grey matter density in the area of BA 10 or the frontal pole region (t= -3.43, x=27, y=60,z=18) (see figure 10) in women. There were no significant grey matter density differences evident neither in the frontal lobes nor in the hippocampus for men.

Probabilistic maps (PB Maps) results

We wanted to investigate the reason for the lack of any significant associations between Prefrontal volume and self-esteem in the Low MOCA group. Hence the decision was made to examine if there were any possible shape discrepancies instead of volumetric scale measurements, which could be affected. Standardized segmenting protocols do not allow us to assess variability in shape and therefore we employed automated probabilistic maps method to identify any discrepancies. In the low MOCA group, specifically for women, we observed that the high self-esteem group had a more homogenous shape relative to the low self-esteem group (see figure 11a). There were no differences between high and low mother care women per se (see figure 11b). Furthermore, we also chose to compare the high mother care, high self-esteem women with low mother care, high self-esteem women and we observed that once again the optimal case of high mother care and high self-esteem resulted in a shape that was much more homogenous as indicated by the presence of voxels with higher probability in this group (See figure 11c).

4.Discussion

Our aim was to investigate if variances in mother care could influence the relationship between self-esteem and three specific regions: the hippocampus in the medial temporal lobe, and the Dorsolateral and Medial prefrontal cortex in the frontal lobes. This of course assumes that a relationship exists between self-esteem and neural substrates and indeed in the case of the hippocampus this was shown to be the case (Pruessner et al 2005). Furthermore, a review of literature proved to reliably indicate that a similar relationship would be plausible in the frontal lobes as well. However, given the implicit association between mother care and self-esteem, an important question on whether mother care could influence this relationship was raised.

Our results revealed that indeed, mother care did contribute to the relationship between self-esteem and structural correlates. Most interestingly, this relationship was sex specific.

While these results are extremely exciting, they raise more questions; the most pertinent one is incontestably the presence of a sex difference in the first place. More specifically, that the relationship between self esteem and neural substrates was found for the DLPFC in women, but not in men; while for men but not women, that relationship was predominant in the HC. Another interesting question involves the negative association between selfesteem and DLPFC in high MOCA women, which implies that bigger is not necessarily better. Lastly, the lack of any associations between the Medial prefrontal cortex and self esteem was certainly surprising, given the role that medial prefrontal cortex plays in self referencing and self monitoring of social information (Fossati et al., 2003; C. D. Frith & Frith, 1999; U. Frith & Frith, 2003; Ochsner et al., 2005).

The Bi-regional association between men and women.

With reference to the first question about self esteem's bi-regional association in men and women, it has been observed that self esteem in general is different for men and women and this in itself could provide some clues about why different regions could be targeted.

Self esteem different for men and women

Men in general seem to base their levels of self-esteem on more achievement oriented goals, whereas women are more inclined to modulate their levels of self-esteem through more socially relevant means (Vohs & Heatherton, 2003).

Vohs et al (2003) contend that when men are in a socially threatened environment they are more likely to appear competitive and antagonistic. Incidentally, the authors also noticed that men with higher levels of self-esteem generally chose to highlight their unique competencies, while low self-esteem men were more inclined to emphasize their positive social qualities as a defense mechanism against the perceived insults to their self. Conversely, high self-esteem women when threatened, focused more on qualities, which signified their value to a group whereas low self-esteem women chose to rely on their social affiliations as a validation of their worth. Additional evidence in women points to the fact that women are more likely than men to focus on social acceptance and therefore are more preoccupied by body image. The need to belong seems to be stronger in women relative to men, and thus ties into the concept that different "selves" may be relevant in self-esteem (Biro, Striegel-Moore, Franko, Padgett, & Bean, 2006).

Mother care contributes to sex difference in self-esteem

Interestingly enough, it has also been found that maternal control often directly contributes to the sex differences in self-evaluative development (Pomenrantz, 1998). Mothers are more likely to inculcate the concept of socialization and social responsibility in their daughters and conversely give greater autonomy to their sons while mitigating societal constraints. This could be one of the mechanisms by which women develop a self-esteem that is more socially defined while men chose to define it through achievement-based goals (Vohs et al, 2003).

Moreover, since their primary avenue to gain maternal approval is though means where they get rewarded, this is what defines their value. This may drive them to adopt coping mechanisms, which facilitate this achievement-driven reward system. Intriguingly, the coping style of men is usually more sensory focused coping (Keogh & Herdenfeldt, 2002) which seeks to contextualize the problem with the least amount of abstraction. This form of direct contextualization and information processing is the hallmark of the hippocampus and therefore the increasing dependence on the hippocampus seems more plausible (D. M. Smith & Mizumori, 2006; Somerville, Wig, Whalen, & Kelley, 2006).

On the other hand female self-esteem is much more multifaceted and seeks approval for a number of sources beyond the mother. It caters to societal expectations (Stroink, 2004) and depending on their levels of self-esteem will either invoke their belonging to their social group or will highlight facts that signal their valued worth in the group (Vohs et al 2003). This complicated form of informational processing complete with the requisite monitoring of social cues and emotional regulation (Schmitz et al., 2004), is indeed the domain of the DLPFC and therefore the impact of self-esteem in this context is once again not surprising.

Interestingly, one of the major consequences of the sex differences in self –esteem is that they also seem to have an impact on how men and women respond to stress. It has been demonstrated that men seem to respond more to stressors which the challenges are more achievement based in comparison to women who would report higher levels of stress when faced with paradigms in which they encountered social rejection (Stroud, Salovey, & Epel, 2002). Thus it highlights the need to examine the role of sex differences in greater detail, as it is apparent their influence is not limited to just differences in self-esteem, but can also have a significant impact on how men and women conduct their lives and cope in stressful situations.

Negative association between self-esteem and DLPFC volume in women: a possible explanation.

The negative association that we observed seems to suggest that that in women, lower levels of self-esteem may correspond with higher DLPFC volume. This could imply a number of things. Firstly, it could be indicative of abnormal or inefficient pruning. As mentioned earlier, prefrontal development undergoes exponential synaptic remodeling during puberty. Right before puberty there is an increase in grey matter volume, which then precipitates a post adolescence decline (Sowell et al., 2001). Grey Matter decline in the prefrontal cortex is exclusively achieved through the process of pruning that results in synaptic remodeling of existing networks. The maturing neural networks are extremely sensitive to environmental manipulations (Andersen, 2003; Teicher et al., 2003), so at this critical point, the trajectory of normal development can easily be compromised by the lack of a nourishing environment. Maternal care, especially during puberty could have a tremendous influence by ensuring that the child is exposed to an environment that encourages the proper trajectory of development. To give a drastic example of how important maternal care could be in dictating the environment, is a study by Gould et al (2005) which revealed that one of the reasons for adolescence suicide were problems with maternal figure of authority. If discrepancies in maternal care can have an influence on the mortality of an individual it is thus entirely possible that it could influence general brain development as well.

An alternate explanation may be that the individuals with lower self esteem are more prone to higher levels of self reflection and rumination and given the role of PFC in self-relevant information, it maybe a developmental safeguard that allows for allocation of more resources for vigilance required to assess a situation. For example, a study by Magnini et al (2004) demonstrated that the frontal and occipital lobes experienced an incremental change in neuronal density in parallel with the progression of hypertension in rats. Thus, along the same lines, a bigger DLPFC may be a necessary adaptation in order to better process the information to assign socially relevant contexts.

The shape of things.

However in case of women, this still does not explain why we only saw the association in the high MOCA group. Since we were relatively assured that there were no volumetric differences in our Low MOCA group, we chose to explore the possibility that perhaps along with the size, the shape too may be similarly affected. In addition, our exploratory VBM analysis had previously indicated that there was a gray matter discrepancy in all women with respect to their Rosenberg self esteem scores. Since VBM does not provide any further information with respect to the nature of the gray matter discrepancies, (Bookstein, 2001; Corbo et al., 2005) we wanted to investigate the possibility that we may encounter shape discrepancies which may perhaps be especially prominent in the LOW MOCA group. Shape differences are not necessarily visible through contemporary volumetric assessment measures, thus we decided to adopt the fully automated probabilistic maps. What we discovered was an extremely interesting observation that in the low MOCA group those women who indicated higher levels of self-esteem had a relatively more homogenous structure than those whose levels of self-esteem was less than optimal.

At this point one can speculate that perhaps self-esteem may very well have a protective influence on the shape of the DLPFC. While proper maternal care may be instrumental in contributing to the robust development of gross size, having a high self-esteem level can at least insure that there is less variability in the shape. This is not surprising considering that puberty is a time where there is shift from parental authority to peer group (Nelson, Leibenluft, McClure, & Pine, 2005). Women are more sensitive to social pressures (Pine, 2002) and seem to be better equipped to negotiate in the changing social environment (Pomenrantz, 1998). Therefore one can additionally surmise that those who manage to successfully make the cognitive set shift to friends develop a higher self-esteem are consequently better off than those whose inadequate mother care impedes on their ability to succeed in the social domain. Thus making it difficult for them to develop stable social networks, which could have a mitigating effect.

Nevertheless, we were still extremely keen to understand why the volumetric DLPFC association was only evident in the in high MOCA group, especially considering that the HC association was apparent in both groups. The answer perhaps lies once again in the fact that self-esteem it self could be profoundly affecting this relationship. Especially since we already know that it seems to have a different definition depending on the sex of the

individual. Self-esteem in men is primarily maintained through achievement based success (Vohs et al 2003) and the earliest source of validation for any success in most cases is the maternal figure (Pomenrantz et al 1998). This suggests that perhaps, the link between self esteem and maternal care may be considerably more relevant in men than in women (Matsuoka et al., 2006). Our own Mediational analysis confirmed that maternal care contributed significantly in the variance in HC volume only in men. Thus perhaps providing a possible explanation as to why HC could be principally sensitive to both maternal care and self-esteem.

Women's, self-esteem on the other hand, is more socially oriented which provides them with more avenues to develop it independent of the mother's input. Plus in the case of the DLPFC, one can additional surmise that perhaps the DLPFC is not as sensitive to maternal care as it is to self-esteem. The only way this could truly be validated is through a longitudinal study and that is unfortunately beyond the scope of this study. However it is urged to investigate how gender could significantly affect the relationship between mother care and self esteem.

Lack of MPFC association

The last question that we wanted to examine in detail was the unexpected absence of an effect in the MPFC. However, this could be an indication that the difference may be functional. Gusnard and Raichle (2001) constantly found that the MPFC often showed

increases and decreases specifically in areas BA 8, 9 and 10 (Gusnard, Akbudak et al., 2001). However, most of the increases have often been observed in studies where the experimental condition demanded monitoring or reporting one's own mental state or recollection of personal life events (Castelli, Happe, Frith, & Frith, 2000). The decreases were once again seen when the experimental task relied on cognitively challenging tasks. This prompted Frith et al (2003) to consider the medial prefrontal to be concerned primarily with "explicit representation of states of self".

This has been validated by various studies which have consistently found increases especially when the attention is specifically directed toward self-referential material (Fossati et al., 2004; Gusnard, Akbudak et al., 2001; Gusnard & Raichle, 2001; J. R. Simpson et al., 2000). Moreover, it is also active during the so-called "theory of mind" i.e. the reading of the mental states of others. This inferring ability can also be translated into being aware of what the other person thinks about the self (C. Frith & Frith, 2005).

This gives an added confirmation that the MPFC may be linked to subtle functional differences rather than structural abnormalities and in our future studies we will definitely re-examine our initial hypothesis that the MPFC may be intrinsically associated with self-esteem.

5.Limitations and Future Directions

There are certain limitations in this study the primary being that we did not have any measure for depression. Given the higher incidence of depression in women (Piccinelli & Wilkinson, 2000) we suspect that particularly, in the low mother care group, and especially those individuals with low self-esteem, there could be additional confounds that could be contributing to the effects we observed.

Another aspect limitation is that our study hinges on the strength of two questionnaires; the PBI and the Rosenberg Self esteem scale. In case of the PBI specially, there have been many questions that have been raised about its validity and consistency. However, it has proven to be quite resistant to these allegations and in fact, it has shown robust test- retest reliability for extended periods up to 10 years (Parker et al 1990). It has also been quite resistant to assertions that it may be susceptible to individual mood states and personality variables. Indeed, Parker (1990) failed to find any significant impact of a response bias on the answers when they re-administered the test to the same set of individuals after a time lag. Perhaps the best example in the PBI immunity from current mood states would be that when it was administered to depressed individuals prior to, and after treatment, their response frequency remained unchanged (G. Parker, 1979). Thus implying that parental care recollections remained unaffected by mood or emotional regulation. Furthermore,

there is also evidence that it reflects true parenting styles rather than subjective assessments. When independently conducted in siblings, monozygotic and di-zygotic twins, there was a remarkable consistency of answers between siblings as well (Parker et al 1990).

The Rosenberg self-esteem scale is widely considered to be an extremely reliable measure of global self-esteem. In fact, when it administered to over 52 nations it showed a consistent cross cultural and internal validity (Schmitt & Allik, 2005). The theoretical midpoint of the scale is designated at M=25.00 (Rosenberg et al 1965). This being said, in our samples we seemed to have an unusually high mean of (M =32 \pm 5) and this could potentially be a problem and our inflated scores could perhaps be artificially contributing to results. Fortunately, a review by Schmitt and Allik (2005) confirmed that in several countries including England, Switzerland and the United States of America the mean score for self-esteem tends be higher, especially in the 18-35 age bracket. For instance, the mean value for the United States is higher than 30 (Schmitt and Allik 2005). Therefore our mean seems to fit well within this schema.

With respect to having two dichotomous groups for mother care, we acknowledge that it would have perhaps afforded us a greater degree of precision if we had chosen to treat mother care as a continuous variable. However, our basic premise was to examine how mother care could influence the relationship between self-esteem and neural substrates, we believed that the best course of action would be to first examine the impact in two extreme groups.

Nonetheless, while we were very particular in terms of selecting people who fit within our to discrete mother care groups, we did not deem it necessary to also select them on the basis of their self-esteem scores as well. Given the variability of self-esteem scores in a normal population, we were relatively certain that we would get a normal distribution. In the future, however, more precaution will be taken to ensure that along with Mother care; self-esteem measures are also included in the specific recruitment criteria.

Perhaps another shortcoming of our study is that it is only a structural study and to complete the picture there needs to be a functional component through which structure and form can be seen in the context of functional neuronal changes. While we can speculate about the gross impact that mother care and consequently self-esteem can have, the story remain incomplete unless we can see behavioral manifestations than can be correlated with the prerequisite morphological aberrations. Therefore the next step would be a functional study, which examines the neural differences along with the underlying mechanistic changes.

An interesting direction would be to observe the circuitry changes rather than changes in individual structures. The hippocampus and prefrontal cortex are part of the emotional circuit (Gusnard et al., 2003; Posner & Rothbart, 1998; Vermetten & Bremner, 2002) and therefore changes in one region would undoubtedly influence the functioning of the other as well. Two possible avenues through which this could be plausible would be to utilize Diffusion Tensor Imaging (DTI) for white matter tracts and functional connectivity

analysis for investigating the functional involvement of the entire circuit. It stands to reason that changes in one could influence changes in other. Therefore, it is imperative that future studies see the system in its entirety.

While we are extremely excited about the unique nature of our result and the fact that this would be the first time an association between self esteem and the DLPFC will be reported, it also gives us reason to proceed with caution. The lack of any prior scientific evidence in the burgeoning field of social neuroscience makes it necessary for us to state that at this point our explanation should be treated as speculation and not fact.

Conclusions

To our knowledge, this is the first study to examine how mother care influences the relationship between Prefrontal volume and self-esteem in a sample of healthy young adults. In addition it is also the first study to successfully demonstrate a specific association between self-esteem and DLPFC volume. In addition, these associations are new in nature, as they seem to suggest that larger DLPFC volumes are associated with lower scores on the Rosenberg self-esteem scale, which is in contrast to what one would normally observe. This data is particularly intriguing considering that the correlations between DLPFC volume and low self-esteem were only found in women. In addition to the theoretical contribution this study also provided us with the opportunity to create two new templates, especially for the MPFC, which has as yet, never been attempted. Future fMRI data will examine functional significance of the associations found between self-esteem the

prefrontal cortex. This project, which has thus far embraced the structural complexities of self-esteem, could shed new light on the widespread impact of self-esteem on neural correlates and thus help us better understand a multifaceted trait which is a vulnerability factor for most, if not all chronic diseases and state of being.

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7. FIGURES

Figure 1: The Medial Prefrontal Cortex (MPFC) template



Figure 2: The Dorsolateral Prefrontal Cortex (DLPFC) Template.



Figure 2: A and B show the inferior frontal sulcus that acts as its ventral lateral border. You can also see its rostral medial border, which is BA 9m or anatomically the most rostral part of the medial longitudinal sulcus. Figure 2C shows the posterior border, which is the precentral sulcus.

Figure 3: Volumetric Group Difference Between Low and High Mother care



Figure 3: There were no volumetric differences observed between groups in (A): Total DLPFC, (B): total MPFC and (C): total HC volumes. D is the total mean volumes in both groups and the Standard deviation.

Figure 4: Associations between DLPFC and self esteem in high and low MOCA groups.



High MOCA group

Figure 4: In the high MOCA group (A & C), there is an association between self esteem and DLPFC volume in both Right DLPFC (A) (r=-.399, p<.05) and left DLPFC (C) (r=-.409, p=<.05). This association is not present in the Low MOCA group (B &D)

Low MOCA Group

Figure 5: Association between HC volume and self esteem in High and Low MOCA groups



Figure 5: (A& C) are the associations between right and left HC and Rosenberg self esteem, in the high MOCA group. Both were non significant. In case of the Low MOCA group (B & D), there was a positive association observed in the Right HC = (r=. 486, p=.02) (B). The association between the left HC and Rosenberg self esteem was insignificant (D).
Figure 6: Bar graph for DLPFC volumes as a function of self esteem and sex in High MOCA group



Figure 6: There was an 11% difference in the right DLPFC volume and 12% difference in the left DLPFC volume *only* in women as a function of self-esteem in the high MOCA group.

Figure 7: Bar Graph for HC volumes as a function of self esteem and sex in High MOCA group



Figure 7: There was a 12% difference in the right DLPFC volume and 13% difference in the left HC volume *only* in men as a function of self-esteem in the high MOCA group.

High MOCA Low MOCA A. B. 70000 (mm) (uuu), volume 6000 a 701 volume S000 RDLPFC 20 25 30 35 40 500 Women 30 35 20 25 40 Rosenberg Self esteem Rosenberg Self Esteem C. D. 80006 LDLPFC volume (mm) 20000 00000 00000 70000 <u>m</u> volum 101PFC 50000 25 30 35 20 25 Rose 30 35 40 4 Rosenberg self esteem ra Self esteem E. F. 70 800 RDLPFC volume(mm) mm - 7000 7000 6000 RDLPFC 5000 40000| 20 50000 + 25 30 35 40 25 30 35 40 Rosenberg Self Esteem Rosenberg Self esteem Men G. H. 7000 (mm)³ (EE EE volume LDLPC 5000 Ú.

Figure 8: Association between self esteem and DLPFC in men and women on low and high MOCA groups

Figure 8: (A & C): In the high MOCA group there was a negative association between Rosenberg self esteem and right (A) (r=-.644, p= .04,) and partially in the left (C) DLPFC (r=-.544, p=.07). (B & D): There was no significant association between Rosenberg selfesteem and DLPFC volumes in Low MOCA women. (E-H): There were no significant associations to report in either high or low MOCA men.

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Figure 9: (A-D): represents women in high and low MOCA groups and there were no significant associations to report in either group. (E & G): show the correlation in High MOCA men between right(E) and left (G) hippocampus and Rosenberg self esteem. In the right there was a positive association reported (r=.57, p= .04) this association was non significant in the left (p >.05). (F & H) represent associations in low MOCA men. The only significant association was between right HC volume (F) and Rosenberg (r-.71, p = .02).

Figure 10: VBM results



Initial VBM results for women suggesting a possible link between self-esteem a prefrontal cortex at t = -3.43, x = 27, y = 60, z = 18.

Figure 11: Probabilistic Maps

Figure11a. Probabilistic maps in the Low MOCA female groups.

Higher self-esteem women (left hand column) had relatively homogenous structure in comparison to low self esteem individuals. This is denoted by the color of the voxel, that is, the whiter the voxels the more homogenous the structure is, or in detail, there is a 100% probability that these voxels are present in all subjects. Thus the column of the left has a higher number of voxels which are white in comparison to the 2^{nd} column which has a preponderance of green voxels which in turn suggests that the structure is homogenous in only 75% of all subjects.





Figure 11b: Probabilistic maps for just Mother care in women.

Figure 11c. A comparison of high self esteem women in both high and low mother care groups.

At 75% confirmed that the optimal combination of high mother care high self esteem has more homogenous shape.



Table 1: Demographics for the whole group split byMother care

	High MOCA	Low MOCA	Significance
Mother care	32 (3)	19 (6)	T ₍₄₉₎ = 11.11 p <. 001
Age	22 (2)	24 (4)	P >.05
RSE	33 (6)	29 (3)	T ₍₄₉₎ = 2.57 p <. 05
Internality	32 (4)	31 (4)	P >.05
	N= 27	N= 24	

Table 1: Indicates the mean scores with the standard deviation denoted by the parenthesis. The last column indicates that the two main variable of interest, that is mother care and Rosenberg self esteem were significantly different between our two groups.

Table 2: PBI scores on all four quadrants.

	High Mother Care group	Low Mother Care group	Statistical significance
Mother care	32 (3.2)	19(5.5)	t ₍₄₂₎ =9.9; p=.000
Mother over protection	10(5.8)	19 (6.6)	$t_{(42)} = -4.9; p = .000$
Father care	27(7.1)	20(7.1)	$t_{(41)} = 2.8 p = .000$
Father Overprotection	7.2 (4.1)	12(4.2)	$t_{(42)} = 3.5 \text{ p} = .000$

Table 2: Indicates that along with mothercare, the two groups were also significantly different in the mean scores in the subscales of Mother over protection, father care and father overprotection, thus ensuring that we did indeed have two discreet groups. The Parenthesis denotes the standard deviation.

Table 3: Group demographics for men and women in highand low MOCA group

	High MOCA Males	Low MOCA Males	Stat Sig.	High MOCA Females	Low MOCA Females	Stat Sig.	Stat Sig. high moca males- females	Stat Sig. Low Moca males- females
Right HC(mm)	4255±389 N=13	4353±328 N=11	>.05	4331±647 N=11	4421±617 N=12	>.05	>.05	.05*
Left HC(mm)	4260±518 N=13	4203±213 N=10	>.05	4370±636 N=12	4356±350 N=13	>.05	>.05	>.05
LMPFC(mm)	24436±2090 N=14	23676±2337 N=10	>.05	24488±2070 N=11	23958±1741 N=13	>.05	>.05	>.05
RMPFC(mm)	23389±1992 N=14	22826±2121 N=10	>.05	24272±1833 N=11	23346±2213 N=13	>.05	>.05	>.05
LDLPFC(mm)	59468±3600 N=14	57709±6247 N=10	>.05	63271±7094 N=11	60400±4764 N=12	>.05	<.05*	>.05
RDLPFC(mm)	61275±3988 N=14	59800±7196 N=10	>.05	63939±6068 N=11	62324±5253 N=12	>.05	>.05	<.05*
РВІ МОСА	31±3 N=14	19±6 N=11	<.001*	33±3 N=13	19±5 N=13	<.001*	<.05	>.05
RSE	35±5 N=14	29±4 N=11	<.001*	32±7 N=13	31±4 N=13	>.05	>.05	>.05
Age	22±2 N=14	25±4 N=11	<.05*	22±2 N=13	24±4 N=12	>.05	>.05	>.05

Table 3: is the demographics for the group split by mother care and sex. The statistical significance as ascertained by *t*-values is a comparison between high and low MOCA men and women and within group men and women on the neural substrates, age as well as the parameters of self-esteem and Mother care. As indicated, in the low MOCA group there is a difference between men and women in left HC volume. Similarly there is a difference in the mean volume of the Right DLPFC between low MOCA men and women as well. On the other hand, there seems to be gender difference between High MOCA men and women in the Left DLPFC. As expected, there is considerable difference between low and high mother care on both men and women, but no difference within the group is noticed.

9.Appendices

1.compliance certificate

2. Questionnaires used.

2a:Parental Bonding index (Parker et al 1979)2b: Rosenberg self esteem (Rosenberg 1965)2c: Questionnaire for competency and control (Krampen 2001)

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PBI

This questionnaire lists various attitudes and behaviours of parents. As you remember your **mother** in the **first 16 years of your life**, please mark the most appropriate response to each statement.

		Very true	Rather true	Rather untrue	Very untrue
1	Spoke to me with a warm and friendly voice.				
2	Did not help me as much as I needed.				
3	Let me do those things that I liked to do.				
4	Seemed emotionally cold to me.				
5	Appeared to understand my problems and worries.				
6	Was affectionate to me.				
7	Wanted me to make my own decisions.				
8	Did not want me to grow up.				
9	Tried to control everything I did.				
10	Invaded my privacy.				
11	Enjoyed talking things over with me.				
12	Frequently smiled at me.				
13	Tended to baby me.				
14	Did not seem to understand what I needed or wanted.				
15	Let me decide things for myself.				
16	Made me feel I wasn't wanted.				
17	Could make me feel better when I was upset.				
18	Did not talk to me very much.				
19	Tried to make me dependent on her.				
20	Felt I could not look after my-self unless she was around.				
21	Gave me as much freedom as I wanted.				
22	Was overprotective of me.				
23	Did not praise me.				
24	Let me dress in any way I wanted.				

As you remember your **father** in the **first 16 years of your life**, please mark the most appropriate response to each statement.

		Very true	Rather true	Rather untrue	Very untrue
25	Spoke to me with a warm and friendly voice.				
26	Did not help me as much as I needed.				
27	Let me do those things that I liked to do.				
28	Seemed emotionally cold to me.				
29	Appeared to understand my problems and worries.				
30	Was affectionate to me				
31	Wanted me to make my own decisions.				
32	Did not want me to grow up.				
33	Tried to control everything I did.				
34	Invaded my privacy.				
35	Enjoyed talking things over with me.				
36	Frequently smiled at me.				
37	Tended to baby me.				
38	Did not seem to understand what I needed or wanted.				
39	Let me decide things for my-self.				
40	Made me feel I wasn't want-ed.				
41	Could make me feel better when I was upset.				
42	Did not talk to me very much.				
43	Tried to make me dependent on him.				
44	Felt I could not look after my-self unless he was around.				
45	Gave me as much freedom as I wanted.				
46	Was overprotective on me.				
47	Did not praise me.				
48	Let me dress in any way I wanted.				Ţ

ROSENBERG SCALE OF SE

Below is a list of statements dealing with your general feelings about yourself. If you STRONGLY AGREE, circle 1. If you AGREE with the statement, circle 2. If you DISAGREE, circle 3. If you STRONGLY DISAGREE, circle 4.

		1	2	3	4
		Strongly	Agree	Disagree	Strongly
		Agree			Disagree
1	I feel that I am a person of				1
	worth, at least on an equal	1	2	3	4
	plane with others.				
2	I feel that I have a number of				
ł	qualities.	1	2	3	4
3	All in all, I am inclined to				1
	feel that I am a failure.	. 1	2	3	4
4	I am able to do things as well	1			
	as other people.	1	2	3	4
5	I feel I do not have much to)	
	be proud of.	1	2	3	4
6	I take a positive attitude				
	towards myself.	1	2	3	4
7	On the whole, I am satisfied				
	with myself.	1	2	3	4
8	I wish I could have more				
	respect for myself.	1	2	3	4
9	I certainly feel useless at				
	times.	1	2	3	4
10	At times I think I am no				
	good at all.	1	2	3	4

Questionnaire of Competence and Control

The following thirty-two questions deal with the way you perceive situations and events. Please answer each question by deciding whether the statement is

- 1 totally wrong
- 2 wrong
- 3 more wrong than right
- 4 more right than wrong
- 5 right
- 6 totally right

and circle the appropriate number next to the question. Please answer all questions, even if some of them will appear very similar to you.

1.	It mainly depends on me whether other people do what I want.	1	2	3	4	5	6
2.	A good proportion of my life is determined by coincidental events.	1	2	3	4	5	6
3.	I feel that a lot of things in my life depend on other people.	1	2	3	4	5	6
4.	Sometimes I feel passive and not creative.	1	2	3	4	5	6
5.	Whether I have an accident only depends on me and my behavior.	1	2	3	4	5	6
6.	When I make plans I am sure that they will come true.	1	2	3	4	5	6
7.	I often don't have the possibilities to protect myself from misfortune.	1	2	3	4	5	6
8.	l often do not know what to do in ambiguous situations.	1	2	3	4	5	6

9.	When whishes come true, good fortune plays a role.	1	2	3	4	5	6
10.	Other people often prevent the fulfillment of my plans.	1	2	3	4	5	6
11.	I have ways to protect myself from getting ill.	1	2	3	4	5	6
. 12	I often do not know how to make my dreams come true.	1	2	3	4	5	6
13.	A lot of things in my life happen by chance.	1	2	3	4	5	6
14.	Other people influence my everyday life in many ways.	1	2	3	4	5	6
15.	Whether I have an accident depends on how fortunate I am.	1	2	3	4	5	6
16.	I know a lot of ways to protect myself from illnesses.	1	2	3	4	5	6
17.	I only have little possibility to defend my interests against others.	1	2	3	4	5	6
18.	It is not a good idea to plan things in advance because of destiny.	1	2	3	4	5	6
19.	Being nice and friendly helps in being successful.	1	2	3	4	5	6
20.	I always know what to do when I am in danger.	1	2	3	4	5	6
21.	It is pure coincidence if other people do what I want.	1	2	3	4	5	6
22.	Other people impose on how I feel.	1	2	3	4	5	6
23.	I can determine a lot of things that happen in my life.	1	2	3	4	5	6
24.	I sometimes feel very helpless and don't know what to do.	1	2	3	4	5	6

25. I usually follow my interests and reach my goals.	1	2	3	4	5	6
26 Other people determine whether I have an accident or not.	1	2	3	4	5	6
27. Reaching my goals is a consequence of my personal effort and ambition.	1	2	3	4	5	6
28. Even in difficult situations I know what to do.	1	2	3	4	5	6
29. In order to have a greater chance of reaching my goals, I adjust them to the wishes of other people.	1	2	3	4	5	6
30. My life is determined entirely by me and my wishes.	1	2	3	4	5	6
31. Destiny determines whether I get sick.	1	2	3	4	5	6
32. I always find ways for solving my problems.	1	2	3	4	5	6

Mehereen Wadiwalla (2007) The Influence of Mother Care on the relationship between Self-esteem and Neural Substrates in young men and women: A Neuroimaging Study.