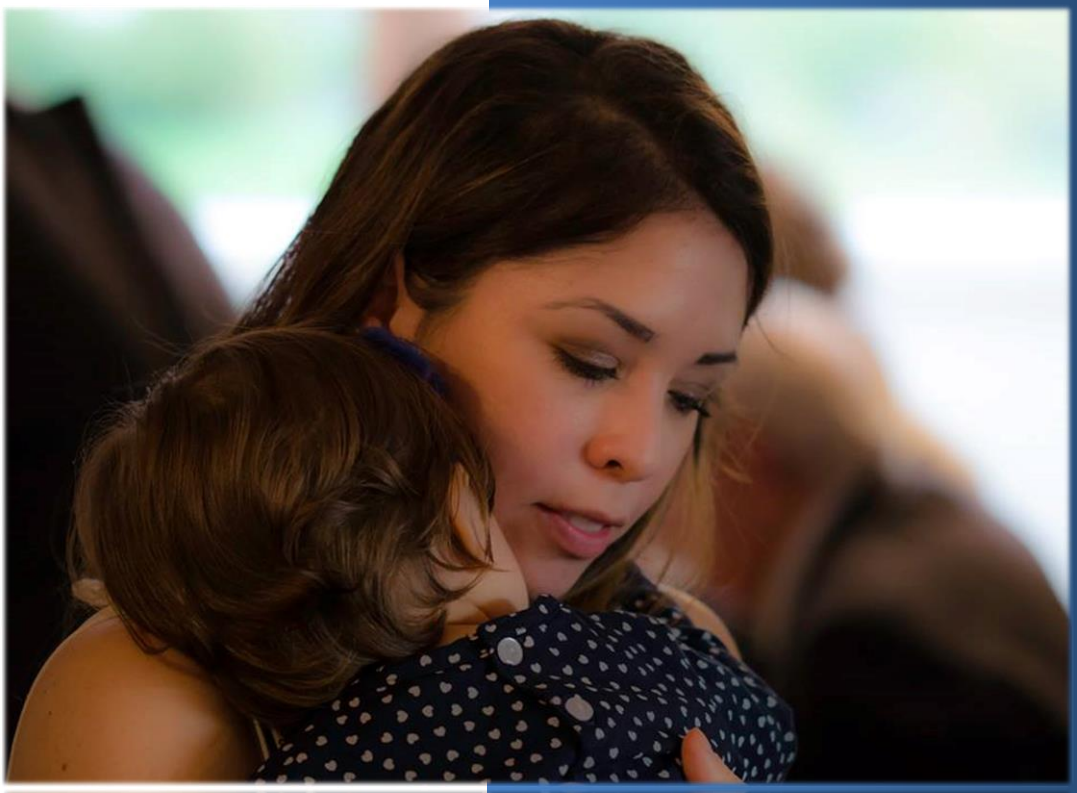
Mauro Serra

# Maternal Relationship, Social Skills and Parental Behavior Through Neuroimaging Techniques and Behavioral Studies



**DiPSCo**

Department of Psychology and Cognitive Science . University of Trento

UNIVERSITÀ DEGLI STUDI DI TRENTO
Dipartimento di Psicologia
e Scienze Cognitive

**Doctoral course in Psychological Science and Education**

# Maternal Relationship, Social Skills and Parental Behavior. Through Neuroimaging Techniques and Behavioral Studies

**Tutor** Paola Venuti

**PhD candidate** Mauro Serra

# Index

# Abstract

Mother child relationship is the first and the most important social relationship as it has implications on psychological and neural development of the individual. Here we investigated mother child relationship focusing on different aspects and using a combination of behavioural and neuroimaging techniques.

In the first study we addressed the association between brain connectivity and interpersonal competences which are at the basis of every social interaction including the ones involved in mother-child relationship. Several studies suggests that higher White Matter (WM) integrity - an index of increased brain connectivity - , is associated with better cognition and behavioural performance. To test the hypothesis that higher WM integrity is associated with higher interpersonal competence we used Diffusion Tensor Imaging (DTI), a neuroimaging technique which allows to study in vivo the anatomy of boundless of axons conveying information in the brain. Then we correlated this information with a self-reported measure of interpersonal competences: the Adolescent Interpersonal Competence Questionnaire (AICQ). Results indicate that Interpersonal competence is associate with higher WM integrity in several major tracts of the right hemisphere, in specific the uncinate fasciculus, the cingulum, the forceps minor, the infero-fronto occipital fasciculus, the inferior longitudinal fasciculus, and the superior longitudinal fasciculus. These results provide the first direct analysis of the neuroanatomical basis of interpersonal competencies and young adult self-reported skills in social contexts.

In the second work we used the same paradigm to test one of the main assumption of the attachment theory which states that social skills highly depends on the quality of attachment relationship. Results show higher integrity in four white matter association fibers in the left hemisphere: Uncinate Fasciculus, Cingulum, Superior Longitudinal Fasciculus and Inferior Fronto Occipital Fasciculus. This result supports the idea that the quality of the attachment relationship influences the emotional and social life of the individual from childhood to adulthood. Furthermore, the research represents an explorative approach to the study of mother-child relationship in healthy population, demonstrating the feasibility of using neuroimaging tools coupled with clinical investigations. Together those studies show that efficient structural connectivity is linked with secure attachment, improved social cognition and cognitive ability. Similarities and differences emerged in these studies will be discussed at the end of Chapter 3 in particular regarding left and right hemisphere specialization.

In the second part of the thesis we switched the focus on parenting behaviour. Evidence from the literature suggest an association between Axonal Integrity measured with FA and functional connectivity measured with TMS in two region involved in preparing ad executing actions: premotor and motor cortex. Moreover neuroimaging reveals that infant cries activate parts of the premotor cortical system. In line with this evidence we linked parenting and brain functional connectivity conducting a study on motor cortex excitability in response of infant cries. We used event-related transcranial magnetic stimulation (TMS) to investigated the presence and the time course of modulation of motor cortex excitability in young adults who listened to infant cries. TMS was delivered from 0 to 250 ms from sound onset in six steps of 50 ms in 10 females and 10 males. Motor Evoked Potentials (MEPs) were recorded from the biceps brachii (BB) and interosseus dorsalis primus (ID1) muscles. Results indicate an excitatory modulation

of MEPs at 100 ms from the onset of the infant cry specific to females and to the ID1 muscle. This modulation is considered as automatic response to natural cry as it was not present in response of control sounds and the effect is found at 100-ms latency which make this modulation not compatible with a voluntary reaction to the stimulus but suggests an automatic, bottom-up audiomotor association. These results indicate that the brains of adult females appear to be tuned to respond to infant cries with automatic motor excitation. This effect may reflect the greater and longstanding burden on females in caregiving infants.

The second part of the thesis continue with a study addressing the natural condition in which baby cries arise when the parent is not attending for infant stimulation. In this study we investigated how infant crying, compared to control sounds, captures adults' attentive resources. Participants were all nulliparous women and men, we investigated the effects of different sounds on cerebral activation of the default mode network (DMN) while listeners engaged in two different kind of tasks: one designed to activate the DMN ( self-referential decision task) and one designed to deactivate the DMN (syllabic counting tasks). We found a strong deactivation of DMN in woman during baby cry which suggest a shift of attention from self-referential thinking toward the baby cry stimuli. In men we found instead a weaker deactivation of DMN during woman cry while their attention was directed toward an external task and simultaneously a sudden woman crying arise. Gender differences found in our studies and in the literature will be discussed.

In the third part of the thesis we investigated the ability to discriminate synchrony and asynchrony during interaction between mother and child with typical or atypical development. We tested two kind of population: in the first study we compared parents of

children with Autism Spectrum Disorder (ASD) to parents of children with Typical Development (TD). In the second study we used the Autistic Quotient questionnaire to divide the sample in two groups according with their autistic traits. The relevance of this task is due to the extreme importance to promptly individuate cues of abnormal social behavior in those cases in which the child might shows deficit in the social development. We hypothesized that individual related with a child with ASD or an individual with high autistic traits, might show similar social difficulties as the individual with ASD finding more challenging to detect cue of appropriate or unappropriated social behavior. To test this hypothesis we asked parents of children with ASD and parents of children with TD to judge video of interactions between mothers and child with ASD and mothers and child with TD. Each video were 20s long and depicted either a synchrony or asynchrony interaction, as categorized by an expert clinician. Contrary to our initial hypothesis results indicate that parents of children with ASD are as accurate as parents of children with TD in discriminating synchrony and asynchrony interaction with ASD, however they are less accurate than parents of children with TD in judging interaction with TD.

In the second study by testing individual with higher autistic traits (HAQ group) versus lower autistic traits (LAQ group) we confirmed this trend. Using the same paradigm we found that both groups were less accurate during asynchrony interaction. However HAQ was more accurate in judging synchrony interaction with ASD while LAQ was more accurate in judging synchrony interaction with TD. This result indicate a facilitation effects in understanding interaction which include people that share similar characteristic with the observer disconfirming the hypothesis that people with higher autistic traits would have more difficulties in understanding social interactions and pointing the attention on other factors which might contribute during this process. A discussion on the need of further investigation using neuroimaging techniques to

understand similarities and differences on neural processing of social interactions is provided at the end of Chapter 4.

# 1. Mother-child relationship and social competences

## 2.1 General Introduction

The aim of this thesis is to address several aspects of mother child relationship investigating the neural underpinning of mother child relationship and parenting behaviour using different neuroimaging and behavioural techniques. In the first part I will present two studies on the association between brain connectivity and two fundamental factors that have an influence on the social life of the individual: the quality of mother child relationship and social competences which, according with extent literature, are closely linked with the quality of maternal relationship. In the second part of the thesis I will focus on parenting behaviour in particular on the behavioural and neural response elicited by cries. In the third part the concept of mother child relationship will be addressed considering the case in which the interaction include a child with social difficulties i.e. Autism Spectrum Disorder (ASD) and in particular I will focus on similarities and differences in recognizing quality in mother child interaction between parents of children with ASD and Typical Development (TD).

Both humans and animals since their birth exhibit behaviours which are aimed to promote proximity with the mother. The Australian zoologist Konrad Lorenz (Lorenz, 1952) called “Imprinting” the innate tendency of the newborn to follow the first moving things it sees, this evolutionary mechanism ensure the establishment of a relationship with the principal caregiver from which the new-born obtain the care and protection in order to

survive. A similar mechanism occurs in humans; at birth the infant is equipped with a repertoire of species-characteristic behaviours that promote proximity, for example, evidence in developmental psychology shows that human infants with no post-natal experience of the mother's voice are capable of discriminating the voice of their mother from the voice of a stranger since three hours after birth (Querleu et al., 1984). Other strategies that the child put in place to promote proximity with the caregiver include the production of signalling behaviours, the most conspicuous among these is crying which frequently operate to activate caregiving behaviours. At first, these emotional signals are simply emitted, rather than being directed toward any specific person, but gradually babies begin to discriminate one person from another. In such a way the child begin to establish what Bowlby called the "Attachment Relationship", a deep and enduring emotional bond between human beings in which the caregiver provide security and safety for the infant (Bowlby, 1969).

An important neurobiological assumption of the attachment theory suggests that the emotional regulation occurring during the interaction between mother and child influences the neuronal growth of the developing brain and the formation of a solid basis from which the mind develops (Ainsworth, 1982; Bowlby, 1969). In line with this hypothesis, the attachment theory also states that relationships in the earliest stages of life and their resulting mental representations - working models - indelibly shape the individual's construction of subsequent relationships from childhood to adulthood (Ainsworth, 1982; Bowlby, 1969; Bretherton & A Munholland, 1999). One purpose of this thesis is to assess those assumptions exploring the relationship between inter-individual differences in brain structure and, respectively, interpersonal competence and quality in mother child relationship. In the next chapter I will introduce the first empirical works aimed to address the association between brain structural connectivity and

interpersonal competences than I will present the second study in which we used a similar approach in order to test the association between brain connectivity and quality in maternal relationship. Afterwards a discussion on similarities and differences on the results from the two works will follow.

## 2.2 Interpersonal Competence in Young Adulthood and Right Laterality in White Matter

### *2.2.1. Introduction*

Human beings are highly social animals, and in complex societies where social interaction is pervasive, nuanced, and extremely diverse, maintaining effective and sensitive social ties places a heavy burden on cognitive and emotional capacities of the individual. For example, developing and sustaining social relationships require competent and flexible social cognition, including the ability to represent relationships between oneself and others and the capacity to apply those representations to effectively guide social behaviour (Adolphs, 2001). Indeed, these social cognitions are central to what Buhrmester (1990) referred to as "interpersonal competence," which encompasses the capacity to interact and communicate with others, to share personal views, to understand the emotions and opinions of others, and to cooperate with others or resolve conflict should it occur. Because these faculties constitute the building blocks of social relationships, inter-individual differences in interpersonal competence are linked to social rejection and isolation among both clinical and nonclinical samples of children (Kully-Martens, Denys, Treit, Tamana, & Rasmussen, 2012; Ladd, 1999) and adults (Anders &

Tucker, 2000; Phelps & Hanley-Maxwell, 1997). During the transition to adulthood, when young adults must navigate a vast and complex array of novel social contexts with sharply varying social protocols, deficiencies in interpersonal competence are likely particularly problematic. That is, transitioning adults are said to be caught "in between" childhood and adulthood (Maggs, Jager, Patrick, & Schulenberg, 2012; Shanahan, 2000), and as a result, they face the difficult challenge of transitioning into adult settings (e.g., work) and into adult roles (e.g., spouse and parent) while maintaining, if not renegotiating, existing social ties from settings that are remnants of childhood (e.g., school/college, peer groups, the family of origin). Thus, deficits in interpersonal competence during young adulthood are associated with greater difficulty transitioning into college (Mahoney, Cairns, & Farmer, 2003; Parker, Summerfeldt, Hogan, & Majeski, 2004) work (Fitzgerald, Brown, Sonnega, & Ewart, 2005), and lasting romantic relationships (Collins & van Dulmen, n.d.; Schneewind & Gerhard, 2002). Given the importance of interpersonal competence to young adult success and the fundamental roles that social and emotional cognition play in interpersonal competence, we were surprised to find that no social neuroscience studies have attempted to directly investigate brain mechanisms that underlie interpersonal competence. Because interpersonal competence entails the integration of cognitive and socioemotional resources, such as language processing, empathy, theory of mind, visual processing of socioemotional cues, and working memory, there is reason to believe that brain networks are involved in the development and maintenance of interpersonal competence. Brain regions link to each other through bundles of myelinated nerve cell processes (or axons), which carry nerve impulses between neurons and constitute the so-called white matter (WM). Associations of behavioral and personality traits with WM have received increasing attention (Kanai & Rees, 2011; Loui, Li, Hohmann, & Schlaug, 2011) WM integrity(Charlton et al., 2006;

Deary et al., 2006; Schmithorst, Wilke, Dardzinski, & Holland, 2002) or hyperconnectivity (Loui et al., 2011) are well-known key indicators of higher information-processing efficiency in cognition at every stage of human development. Therefore, in this study, we looked at WM correlates throughout the whole brain and examined whether individual differences in self reported interpersonal competence relate to WM connectivity in a sample of healthy young adults. More specifically, given that several distinct lines of research have linked socioemotional cognitions to WM integrity in the right hemisphere of the brain, our main hypothesis was that interpersonal competence would be specifically associated with WM integrity in the right hemisphere.

### *2.2.2 Socioemotional processing and right brain*

Individuals who are interpersonally competent are typically empathetic (Chow, Ruhl, & Buhrmester, 2013; de Wied, Branje, & Meeus, 2007) and display high levels of emotional intelligence, which includes the abilities to perceive, use, understand, and manage emotions (Brackett, Rivers, Shiffman, Lerner, & Salovey, 2006). Some components of empathy and emotional intelligence appear to reflect functioning of the human mirror neuron system (Iacoboni & Dapretto, 2006; Parkinson & Wheatley, 2014), and these aspects have been associated with the right hemisphere portion of the mirror neuron system (Cattaneo & Rizzolatti, 2009; Uddin, Iacoboni, Lange, & Keenan, 2007), which is believed to be central to understanding of self in relation to others. Additionally, social cognition has long been linked to right laterality (Decety & Lamm, 2007; Devinsky, 2000; Frith & Frith, 2012; Semrud-Clikeman, Goldenring Fine, & Zhu, 2011; Winner, Brownell, Happé, Blum, & Pincus, 1998). Several comparative studies—some

even involving phylogenetically distant species—indicate right hemispheric dominance in recognition of familiar social partners in processing information relative to other individuals as well as in the development of social competencies (Vallortigara, 1992). More specifically, abnormal WM integrity in the right hemisphere of the human brain has been linked to abnormalities in processing socioemotional information. For example, lesions in the right hemisphere are associated with deficits in social perception and understanding, such as recognition and expression of facial emotion , affective prosody (Breitenstein, Daum, & Ackermann, 1998), and sarcasm (Shamay-Tsoory, Tomer, & Aharon-Peretz, 2005). Right hemisphere damage is also associated with impaired communication (Bartels-Tobin & Hinckley, 2005), lack of empathy (Rankin et al., 2006), and the inability to attribute mental states, such as desires, intentions, and beliefs, to oneself and to others (Happé, Brownell, & Winner, 1999; Lombardo, Chakrabarti, Bullmore, & Baron-Cohen, 2011; Weed, McGregor, Feldbaek Nielsen, Roepstorff, & Frith, 2010). Moreover, there is evidence to suggest that the interpersonal impairments associated with Asperger's syndrome are the result of developmental abnormalities within the right cerebral hemisphere (Gunter, Ghaziuddin, & Ellis, 2002; McKelvey, Lambert, Mottron, & Shevell, 1995). With respect to social cognition, several studies have identified the special role of the right pFC. For example, showing participants pictures of eyes expressing friendly or hostile emotions activates the right OFC (Wicker, Perrett, Baron-Cohen, & Decety, 2003). Additionally, Tranel, Bechara, & Denburg (2002) reported that patients with lesions in the right ventromedial pFC displayed impairments in interpersonal behaviour, but that patients with similar contralateral left lesions displayed no such impairments in social behaviour. Guided by the extant literature, we hypothesized that interpersonal competence is associated with the integrity of WM tracts in the right hemisphere of healthy young adults. The methodology we adopted accords with lines of

research that link complex information about personality or attitudes measured off-line with brain structures measured with neuroimaging (Kanai & Rees, 2011). Of course, complex functions associated with social cognition cannot be understood solely in terms of localization of specialized brain areas working in isolation. Rather, a fundamental aspect in neural networks is connectivity between components, which determines the efficiency of the network as a whole. This basic concept is reflected in brain anatomy in terms of integrity of WM fibers connecting cerebral regions. To test our main hypothesis, we evaluated interindividual differences in WM integrity using fractional anisotropy (FA), which provides information about the directionality of the diffusion of water molecules in the whole brain, and we then correlated this neuroanatomical information with an index of selfreported interpersonal competence as measured by the Adolescent Interpersonal Competence Questionnaire (AICQ; Buhrmester, 1990).

### *2.2.3 Methods*

Participants Thirty-one healthy, right-handed young adults (20 men) participated. They ranged in age from 19 to 29 years 1258 Journal of Cognitive Neuroscience Volume 26, Number 6 (M = 22.93 years, SD = 2.66 years). The study was approved by the University of Trento Ethical Committee, and all participants gave written informed consent. Procedures and Measures Image Acquisition MR images were acquired with a 4T Bruker Medspec scanner (Bruker Medical, Ettlingen, Germany) using a birdcage transmit, eight-channel receive head coil (USA Instruments, Inc., Aurora, OH). Each participant underwent a T1-weighted structural image (3-D MP-RAGE, 1 × 1 × 1 mm3 , repetition time = 2700 msec, echo time = 4 msec, flip angle = 7°, GRAPPA [generalized

auto calibrating partially parallel acquisition] factor 2, inversion time = 1020 msec, bandwidth = 150 Hz/pixel, acquisition time = 5 min) optimized for maximal contrast to noise ratio between gray matter and WM at 4 T (Papinutto & Jovicich J., 2008). In each session, a diffusion weighted image data set was also acquired with a twice refocused 2-D SE-EPI sequence (Reese, Heid, Weisskoff, & Wedeen, 2003) and the following acquisition parameters: repetition time = 7000 msec, echo time = 85 msec, GRAPPA factor 2, voxel size = 2.5 × 2.5 × 2.5 mm3 , b value = 1000 sec/mm2 . Five images without any sensitizing diffusion gradient applied (b0) and 30 diffusion weighted images with diffusion gradients applied along unique directions that were defined by an electrostatic repulsion algorithm (Jones, Horsfield, & Simmons, 1999; Jones, 2004) were acquired, with an axial slice acquisition along the x–y plane of the static magnetic field reference frame. A field of view of 240 mm2 and 50 contiguous slices enabled our covering the whole brain. A full Fourier acquisition was used to reduce cardiac pulsation artifacts (Robson & Porter, 2005).The total scan time lasted 270 sec per acquisition. Diffusion Tensor Imaging Preprocessing All diffusion-weighted images were processed using tools from the FMRIB software library (FSL, version 4.1.5; www.fmrib.ox.ac.uk/fsl) running on a Linux operating system.

First, the DICOM files were converted to the nifti format using an open source DICOM-to-nifti converter (www.mccauslandcenter.sc.edu/mricro/mricron/index. html). Then, each data set was corrected for head movement and eddy current distortions using an affine transformation of each diffusion weighted image and b0 image to the first b0 image, used as reference. Second, a binary brain mask was generated from the non-diffusion weighted image by using the BET brain extraction tool (Smith, 2002). Following these steps, a diffusion tensor model was fitted independently for each voxel within the brain mask, and images of FA were generated for each participant. FA

describes the degree of anisotropy of the water diffusion within a voxel and is considered a reliable index of microstructural integrity of WM and a measure of directional strength of the local tract structure. FA values range from 0 (minimum coherence in the WM structures) to 1 (maximum coherence in WM structures).

As an additional test for the relative contribution of parallel diffusivity and radial diffusivity (RD) to FA, for each participant we separately computed mean diffusivity (MD), RD, and axial diffusivity (AD) globally in the whole brain. Additionally, we computed RD and AD locally in small ROIs selected around the central coordinates of the first five clusters reported in Table 1, and we summed the results. Voxelwise statistical analysis of the diffusivity data was carried out using tract-based spatial statistics (TBSS; Smith et al., 2006). TBSS is a technique that aims to improve the sensitivity, objectivity, and interpretability of analysis in multiparticipant diffusion imaging studies. TBSS has been proposed to reduce problems related to possible misalignment of different participants' coregistered data through an optimized nonlinear registration followed by projection onto an alignment-invariant tract representation. In this way, the TBSS method allows for valid conclusions to be drawn from the subsequent voxelwise analysis. Briefly, TBSS for FA consists of the following steps: (1) identification of the most typical participant in the group as target for all the nonlinear registration. This participant is selected minimizing the amount of warping required for all other participants to be coregistered with the target. (2) Alignment of all participants' FA images to the target using both linear and nonlinear transformations(Andersson, Jenkinson, & Smith, 2007a, 2007b) and subsequent affine transformation to the standard Montreal Neurological Institute (MNI) space. (3) Averaging of the aligned individual FA image and generation of a skeleton representing WM tracts common to all participants. In our case, the mean skeleton image was created using an inferior FA threshold of 0.2. (4) Projection of each

participant's aligned FA data onto the skeleton. (5) Group comparison using voxelwise cross-participant statistic. Statistical Analysis We performed cross-subject analyses to relate voxelwise measures of diffusivity values (FA, MD, AD, RD) to interpersonal competence using the general linear model tool in FSL in conjunction with permutation-based tests using Randomise (5000 permutations). The cluster size analysis results were corrected for multiple comparisons across space ( $p < .05$) using threshold-free cluster enhancement. Clusters where local diffusivity measures differed as a function of scores in interpersonal competence were labeled using a stereotaxic WM atlas (Mori et al., 2008). Interpersonal Competence Interpersonal competence was assessed with the AICQ (Buhrmester, 1990), which has been widely used in young adult samples (Daley & Hammen, 2002; Lopes et al., 2004). The AICQ is a 40-item measure with five subscales: self-disclosure, providing emotional support to friends, management of conflicts, negative assertion, and initiation of friendships. Items were rated on a 5-point scale (1 = Poor at this, would be so uncomfortable and unable to handle this situation that it would be avoided if possible; 5 = Extremely good at this, would feel very comfortable and could handle this situation very well). The total scale as well as the subscales all displayed excellent reliability (e.g., in each case, the Cronbach alpha was .85 or higher). We used a composite measure of interpersonal competence that incorporated all five AICQ subscales. After calculating mean scores for each subscale, we conducted a confirmatory factor analysis within Mplus (Muthén & Muthén, 1998/2009) that loaded each of the five subscale means onto a single latent factor. Using the FSCORE command within Mplus, we then outputted the latent factor scores so that they could be used in subsequent analyses. This latent factor approach for calculating a composite AICQ measure is superior to merely calculating a global mean score (i.e., the mean of AICQ's 40 items), because only the latent factor approach adjusts for measurement error and thereby

increases both power and measurement reliability (Kline, 2011). Identification of WM Tracts Identification of WM tracts in which there was a correlation between AICQ and diffusivity measures (FA, MD, AD, RD) was based on the Johns Hopkins University WM tractography probabilistic atlases, available within the FSL toolboxes (Hua et al., 2008; Wakana et al., 2007). These atlases allow voxel-by-voxel categorization to different major WM tracts within certain probabilities.

**Table 1.** Clusters Where FA and Interpersonal Competence Correlated Significantly ($p < .05$)

| *Cluster No.* | *Size (Voxels)* | *Corrected p Value* | *Peak x* | *Peak y* | *Peak z* | *Hemisphere and Lobe* | *Tract Location* |
|---|---|---|---|---|---|---|---|
| 1 | 10786 | .016 | 8 | 36 | 47 | R frontal | CM |
| 2 | 1123 | .021 | 28 | −89 | −7 | R occipital | ILF |
| 3 | 864 | .018 | 47 | −50 | 0 | R temporal | SLF |
| 4 | 351 | .028 | 35 | −28 | −23 | R temporal | ILF |
| 5 | 143 | .028 | 54 | −20 | 1 | R temporal | ILF |
| 6 | 115 | .028 | 44 | −17 | −17 | R temporal | ILF |
| 7 | 80 | .028 | 44 | −32 | 10 | R temporal | ILF |
| 8 | 64 | .029 | 58 | −36 | 17 | R temporal | SLF |
| 9 | 50 | .021 | 15 | 6 | −19 | R frontal | UF |
| 10 | 14 | .03 | 18 | −102 | 8 | R occipital | FMa |
| 11 | 11 | .03 | 45 | 5 | −34 | R temporal | ILF |
| 12 | 9 | .03 | 10 | −83 | 30 | R occipital | FMa |

**Table 1:** Larger clusters have smaller numbers (1–12). The column Size (Voxels) indicates how many voxels are contained in each cluster. The column Corrected p Value refers to the p value associated with the maximum "intensity" voxel within the cluster after correction for multiple comparisons using threshold-free cluster enhancement. The columns x, y, and z indicate the MNI coordinates of the maximum intensity voxel in each cluster; coordinates are expressed in standard space (mm). The last column reports the WM labels taken from the Johns Hopkins University WM tractography atlas. According to the atlas, the clusters contain voxels belonging to six WM tracts: UF, CM, forceps major (FMa), IFOF, ILF, and SLF.

### *2.2.4 Results*

Voxelwise analysis in TBSS revealed significant differences within participants in mean FA indicating that higher interpersonal competence—as measured by the AICQ (Buhrmester, 1990)—is correlated with higher WM integrity ( $p < .05$, corrected). We

hypothesized that the difference in WM integrity should be localized exclusively in the right hemisphere (*Figure 1*). Specifically, higher FA values were found in voxels belonging to six major WM tracts of the right hemisphere: the uncinate fasciculus (UF), the cingulum (CM), the forceps minor (FM), the infero-fronto occipital fasciculus (IFOF), the inferior longitudinal fasciculus (ILF), and the superior longitudinal fasciculus (SLF). The significant voxels obtained from the voxelwise TBSS analysis were grouped in clusters and are reported in *Table* 1. The global TBSS analysis of MD, AD, and RD showed no significant correlation with AICQ ( $p < .05$, corrected). Without the correction for multiple comparisons, too conservative to evidence effects on the three metrics, RD showed a significant correlation with the AICQ in many voxels ( $p < .05$, uncorrected). An additional local analysis of relative contributions of parallel diffusivity and RD to FA within the first five clusters reported in *Table 1* showed that AD and RD values were both anticorrelated to the AICQ measure (see *Figure 1*). This result was more evident for RD ($r = -0.62$, $p = .00019$) than for AD ($r = -0.31$, $p = .093$).

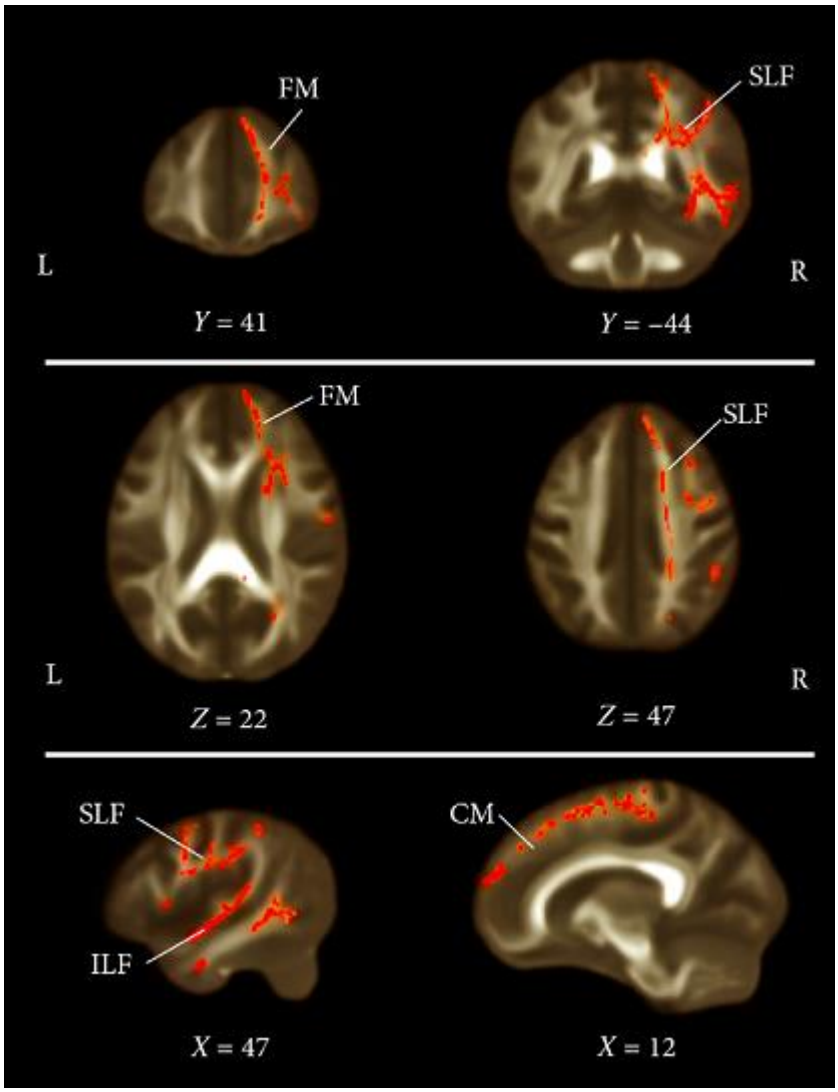



**Figure 1:** Coronal, axial, and sagittal views (from top to bottom) of the t statistics map of FA comparison between participants ( $p < .03$ corrected). The background image is the MNI template. Red voxels represent regions in which higher FA values are associated with higher scores in AICQ. The images are reported in the neurological orientation (left side of the brain is on the left of the coronal and axial views). Some of traits include FM, SLF, ILF, and CM, all in the right hemisphere. x, y, and z coordinates are based on the atlas of the MNI.

### *2.2.5. Discussion*

The main goal of this study was to investigate associations between interpersonal competence of healthy young adults and their WM structural connectivity. Given that interpersonal competence depends on the integration of cognitive, affective, and social competencies, it is presumably served by distant brain regions working in concert. We hypothesized that interpersonal competence would be associated with higher integrity of WM pathways connecting distant brain regions in the whole brain. Specifically, in line with other behavioural, neuroimaging, and lesion studies that identify right laterality in social competence, we expected to find more pronounced associations of social competence with WM integrity in the right hemisphere. Here we found that increased FA was associated with greater social competence in specific clusters identified using probabilistic atlases. Additional local RD and AD diffusivity analyses in the first five clusters reported in Table 1 suggest that this result is primarily driven by a negative correlation between RD and the AICQ. RD, like FA, is a parameter that is generally linked to myelination and axonal packing, whereas AD can vary with fiber diameter and axon coherence (Beaulieu, 2002; Song et al., 2005; Takahashi, Ono, Harada, Maeda, & Hackney, 2000). Thus, in several studies (Lebel & Beaulieu, 2011; Lebel, Walker, Leemans, Phillips, & Beaulieu, 2008), longitudinal increases of FA, paired with reductions of RD and AD remaining constant, have been interpreted in terms of an increase in myelination from childhood into adolescence and young adulthood. Therefore, our results suggest that interpersonal competence might be associated to greater integrity of WM pathways connecting distant brain regions in the whole brain, possibly because of more complete maturation of WM in terms of increased myelination into young adulthood. In particular, we found that AICQ correlated with several major tracts of the

right hemisphere, including the UF, the CM, the forceps minor, the IFOF, the ILF, and the SLF. The anatomical structure of these tracts connects several regions, which form the neural basis of several cognitive, emotional, and social functions, such as perception, language, modulation of social stimuli, auditory and visual association cortices, executive functions, and emotion regulation, all of which are of great relevance to interpersonal competence. We discuss these WM tracts and their functions in greater detail and how efficiency in these pathways indicates prioritized information processing of interpersonal and social competence. The UF connects the OFC, the hippocampus, and the amygdala (Mori et al., 2008). Given that the UF is a part of the limbic system (Catani, Howard, Pajevic, & Jones, 2002; Hasan et al., 2009), its major purpose is believed to lie in emotional functioning, in particular sharing affective states, which typically characterizes empathy (Jackson, Brunet, Meltzoff, & Decety, 2006). Disruption of the UF tract in people affected by autism spectrum disorder (Ameis et al., 2011) has further confirmed its association with socioemotional behaviour. The CM connects the cingulate gyrus to the entorhinal cortex, facilitating communication between sections of the limbic system (Mori et al., 2008). It has been identified with processing emotional information as well as performing error monitoring in the service of cognitive control (Metzler-Baddeley et al., 2012). Specific right CM lesions have been found to relate to impaired social functioning in children (Angelini, Mazzucchi, Picciotto, Nardocci, & Broggi, 1981) The FM is a part of the anterior region of the corpus callosum. In particular, it connects—via the most anterior part of the corpus callosum (the genu)—orbitofrontal areas involved in emotional and executive control (Park et al., 2008), which is a fundamental function in socioemotional competence. IFOF and ILF jointly connect occipital and temporal cortices, and IFOF also connects with the frontal lobe and the posterior part of the parietal lobe (Mori et al., 2008). Thus, they are two of the largest and longest association fiber

bundles in the human brain. Damage to these long association fibers has been linked to impairment in processing visual emotional cues (Bauer, 1982) and facial expressions of emotions (Philippi, Mehta, Grabowski, Adolphs, & Rudrauf, 2009). Damaged ILF has also been associated with autism spectrum disorder (Cheung et al., 2009). The SLF is one of the major intrahemispheric pathways that connects parietal, temporal, and frontal lobes and is effectively a bundle of fibers carrying most high level processing of information taking place in the human brain (Mori et al., 2008). The right SLF has been determined to be involved in processing tones and melodic information, particularly in pitch-based grammar learning (Loui et al., 2011)thus suggesting a major role of these connections in processing emotion and communication during language learning, development, and understanding others. Our study shows that WM integrity in several key tracts of the right hemisphere correlate with self-assessed interpersonal competence. Such individual differences might arise for a variety of reasons. They might be the effect of repeated behavioral patterns that favor interpersonal competence, as in continuous practice of those skills. This view is supported by several cognitive and affective neuroscience studies showing that the brain is highly plastic and that its interactions with the environment preserve gray matter from decaying (A. Pascual-Leone, Amedi, Fregni, & Merabet, 2005) and promote the formation of new and more efficient connections in WM (Scholz, Klein, Behrens, & Johansen-Berg, 2009). Alternatively, such individual differences in WM integrity might reflect genetic causes that predispose people to more effective interpersonal competencies. Finally, they might result from both experiences that simultaneously promote more effective interpersonal competencies and right hemisphere development (e.g., parenting or favorable economic circumstances). Interpersonal competence is not an isolated function, but it is linked to a number of other cognitive and socioemotional skills, such as language processing, empathy, theory of mind, visual

processing of relational cues, and working memory. Thus, our finding that several major brain WM tracts are correlated with high levels of interpersonal competence should not be taken as indicative that these connections are specific or exclusive to this function; on the contrary, these are key fiber bundles, which play fundamental roles in other domains. Additionally, given the complexity of interpersonal interactions and the number of different factors that play important parts in them (biological, cognitive, emotional, and social), further assessments of associations between interpersonal competence and brain structure call for longitudinal, multicultural, and additional functional neuroimaging investigations.

In overview, finding of this study highlight a right lateralization in WM integrity which emerge in association with interpersonal competence. This finding supports evidence in the literature that points to the fundamental role of the right hemisphere in social cognition (e.g., Frith & Frith, 2012). Those socioemotional competencies according with a large extent of literature heavily rely on right brain function (Schore, 2001). Our results support this hypothesis, highlighting the association between WM in the right hemisphere and interpersonal competence. Shore (2001) also suggested that dysfunction in the development of the right hemisphere might affect infant mental health and lead to psychosis and social difficulties in later stages of development. This suggestion might explain the large literature, which associates right hemisphere underconnectivity with personality disorder, and it is supported by evidence of reduced WM connectivity of the right hemisphere in animal and human studies with early deprivation of maternal care (Helmeke, Ovtscharoff, Poeggel, & Braun, 2001) and orphanage care (R M. Govindan, Behen, Helder, Makki, & Chugani, 2010). In addition, the finding may have implications for theories claiming that the right hemisphere plays a major role in modulating emotion and nonverbal communication during the first interpersonal relationship that every human

being experiences, namely the infant– mother relationship (Schore, 1997, 2000, 2009). According to this line of research, the development of emotional and social intelligence in the individual — from childhood to adulthood — depends on the quality of their relationship with a principal caregiver. In light of this results and given the importance of the mother child relationship for the development of the individual, we aimed to pursue the goal of exploring the relationship between brain connectivity and quality in maternal relationship with a further study presented in the next chapter

## 2.3. Secure Attachment Status is associated with White Matter Integrity in Healthy Young Adults

### *2.3.1.Introduction*

Attachment describes the tendency of a child to seek protective proximity in relationship to a caregiver (Bowlby, 1969). Attachment theory states that maternal sensitivity to a child's needs – emotional attunement – likely influences organization of the child's brain (Bornstein, 2013). In an attempt to clarify how, at the biological level, the interaction between mother and child facilitate the maturation of the brain systems involved in the attachment relationship (Schore, 2000) proposed that during emotional non-verbal communication the caregiver acts as a regulator of the child's arousal levels, which are associated with metabolic energy (Schore, 1994, 1997, 2000). This regulation of energetic metabolism occurs in a critical period, in which the baby's immature brain is easily adapted and coupled to the regulation of the caregiver's brain. In other words, when the members of the dyadic relationship are emotionally attuned, the stimulation from the mother might affect the child's organization of his/her brain systems (Bornstein, 2013).

Nevertheless, in addition to periods of positive exchange, the mother also regulates moments of stressful negative affect such as separation and other stressful experiences (Chapple, 1970). The mother's emotional modulation plays a crucial role in the child's mental development even during such unpleasant periods. In fact, a period of positive exchange -restored by the mother- following a time of stress, provides a "recovery" period that allows the infant to deal with stressful situation while maintaining positively charged affects (Chapple, 1970; Schore, 1994). This idea is supported by animal studies showing that negative emotional experience during mother-infant interaction may create a permanent trace in the still developing neural network and in the immature synaptic connections of the new-born (Helmeke et al., 2001). Interestingly, these changes were still present several weeks after the animals were reintegrated under normal conditions (Helmeke et al., 2001). Also evidence from human studies supports the idea that early mother deprivation affects the anatomy of White Matter (WM) showing reduced WM diffusivity in children with history of orphanages compared with controls (Rajkumar Munian Govindan, Behen, Helder, Makki, & Chugani, 2010). These findings - consistent with the attachment theory (Ainsworth, 1989; Bowlby, 1969) - indicate that neural changes attributable to early postnatal experience may have a legacy into later stages of life, extending or limiting the functional capacity of the brain in the balance of the lifespan (Bornstein, 2014). By contrast, exposure to a socially rich environment is associated with changes in WM microstructure and improved social cognition (De Pisapia et al., 2014; Molesworth, Sheu, Cohen, Gianaros, & Verstynen, 2014; Rigon, Duff, & Voss, 2015) .

### *2.3.2. WM an maternal relationship*

WM is composed of fibers (axons) which carry information between the neurons (Mori et al., 2008). One important component of the WM microstructure is myelin, a dielectric membrane surrounding the axon that increases the velocity of transmitted information down the axon body (Mori et al., 2008). Longitudinal studies point to increased myelination from childhood to adolescence (Lebel & Beaulieu, 2011), a period in the human lifespan during which the immature brain is sensitive to environmental stimulation. It follows that maternal stimulation could affect myelination of the child's developing brain and thereby facilitate neural connections among brain structures key to emotional and social information processing such as connection within structures in the link limbic system and between limbic system and distant brain regions. Accordingly. evidence indicates that decreased functional and structural connectivity of in the amygdala is linked with attachment avoidance (Rigon et al., 2015), and increased WM integrity in multiple fiber pathways including cingulum and hypothalamic paths is associated with social network diversity in humans (Molesworth et al., 2014). A biobehavioural model proposed by Porges & Furman, (2011) suggest that increased myelination in vagal fibers improve neuro regulation of the autonomic nervous system supporting the infants to express appropriate social engagement behaviour, in turn facilitating development of social skills. On this argument, a recent study by De Pisapia et al. (2014) reported that higher Fractional Anisotropy (FA), a product of myelination, was associated with greater social competence. FA is an index of directionality of diffusion, whose values change according to the structure of the axonal cell membranes and myelin sheath (Pierpaoli & Basser, 1996). These findings informed the present study in that, according to attachment theory, social abilities are predicted by quality of attachment (Bowlby, 1969) which shape construction of the individual's subsequent relationships

from childhood to adulthood (Bowlby, 1969). However, no studies have yet explored associations between security in the maternal relationship and WM connectivity in healthy young adults. Except for Whittle et al. (2009) on adolescents' changing gray matter volume in association with maternal behavior, our knowledge of effects of parenting in the normal range and neural development in the child remains limited.

Based on the extant literature, showing positive association between FA and social skills driven by increased myelination (De Pisapia et al., 2014; Molesworth et al., 2014) as well as decreased WM connectivity associated in with attachment avoidance (Rigon et al., 2015)we hypothesized that efficient WM connectivity within and between limbic regions would be associated with security in the maternal relationship experienced during childhood. We therefore expected to find positive associations between FA and attachment security in WM tracts previously associated with interpersonal competence by De Pisapia and colleagues (2014), namely: Uncinate Fasciculus (UF), Cingulum (CM), the Forceps Minor (FM), Infero-Fronto Occipital Fasciculus (IFOF), Inferior Longitudinal Fasciculus (ILF), and Superior Longitudinal Fasciculus (SLF). These same tracts have been reported to be associated with adverse childhood experiences (Benedetti et al., 2014), emotional processing and attachment avoidance (Rigon et al., 2015; Woolley, Zhang, Schuff, Weiner, & Katz, 2011), and so they are likely also influenced by the quality of the person's attachment relationship history from childhood.

### *1.3.3. Method*

*Participants*

Fifty-three healthy right-handed young adults (31 males; M age = 23.56 years, SD = 2.68) took part. The study was approved by the University of Trento Ethical Committee, and all participants gave written informed consent. The procedure consisted in two parts. First participants underwent Diffusion Tensor Imaging (DTI) and then completed the Kerns Security Scale (SS) on the basis of the relationship they had with their mother during childhood.

*Security Measure*

The SS is a self-reported measure of perceived childhood attachment security. It is a well-established psychometrically valid measure used to evaluate attachment status after childhood (Main, Kaplan, & Cassidy, 1985). It addresses children's perceptions of security in a specific parent-child relationship, such as the degree to which children believe the caregiver to be responsive and available, the children tendency to rely on the attachment figure in time of stress, the children's reported ease and interest in communication with the attachment figure. Here, we asked participants to rate their maternal relationship by thinking back to when they were children. The test is structured as a 15-item questionnaire; the participants have to rate whether one of two statements is sort of true for them or really true for them. The two statements are presented as one item in a forced-choice format developed by (Harter, 1982) to minimize response bias due to perceptions of social desirability (e.g., "Some kids find it easy to trust their mom BUT other kids are not sure if they can trust their mom"). Each item is scored from 1 to 4. Items are averaged ($\alpha$ = .87), with larger scores indicating greater security with their mother. In initial testing performed by Kerns and colleagues (1996) scores on the Security

Scale showed adequate range (1.62-4.00) and internal consistency (Cronbach's = .84). The sample mean was 3.24 (SD = 0.57), (Kerns, Klepac, & Cole, 1996) the scores demonstrated high test-retest stability (r = .75, Median duration =14 days). The validity of the SS as a measure of perceived attachment security in adolescence was assessed by Van Ryzin and Leve (2012). For the present study, we conducted a confirmatory factor analysis with Mplus (Muthén & Muthén, 2009) and modeled a single latent factor to obtain an SS score on a continuous dimension of security. Then, we used the FSCORE command within Mplus to obtain latent factor scores for subsequent analysis. The latent factor approach is superior to the calculation of mean scores as it adjusts for measurement error, increasing both power and measurement reliability (Kline, 2011).

*Image Acquisition and DTI processing*

DTI was used to acquire images of WM structures with a 4T Bruker Medspec scanner (Bruker Medical, Ettlingen, Germany) using a birdcage-transmit, eight-channel receive head coil (USA Instruments, Inc., Ohio, USA). The image acquisition protocol followed exactly De Pisapia et al., (2014). All diffusion weighted images were processed using tools from the FMRIB software library (FSL, version 4.1.5; http://www.fmrib.ox.ac.uk/fsl) running on a Linux operating system. First, DICOM files were converted to the nifti format, using the DICOM-to-nifti converter (by Chris Rorden, Delphi: http://www.mccauslandcenter.sc.edu/mricro/mricron/index.html).

Then, each dataset was corrected for head movement and eddy current distortions using an affine transformation of each diffusion weighted image and b0 image to the first b0 image, used as reference. Next, a binary brain mask was generated from the non-diffusion weighted image using the BET brain extraction tool (Song et al., 2002). Diffusion tensor model was fitted independently for each voxel within the brain mask,

and maps of Fractional Anisotropy (FA), Mean Diffusivity (MD), and Axial Diffusivity (AD) were generated for each participant. A Radial Diffusivity (RD) map was also generated averaging the second and the third eigenvalues (RD = (l2 + l3)/2). FA describes the degree of anisotropy of the water diffusion within a voxel and is a reliable index of micro-structural integrity of WM and so a measure of how strongly directional the local tract structure is. Its value ranges from 0 (minimum coherence in the WM structures) to 1 (maximum coherence in WM structures). MD is expected mainly to reflect tissue damage in pathological conditions. RD and AD are sub-components of FA and are related to myelination and axonal integrity, respectively (Beaulieu, 2002).

*DTI analysis*

To inspect regional associations with the SS, we conducted a Region Of Interest (ROI) analysis based on the results in De Pisapia et al. (2014). We used Tract-Based Spatial Statistics (TBSS; Smith et al., 2006) to acquire the group level WM structure from which FA, MD, RD, and AD images were extracted. TBSS is a technique that aims to improve the sensitivity, objectivity, and interpretability of multi-subject diffusion imaging studies and has been proposed to reduce the problems related to possible misalignment of different subjects' co-registered data through the use of an optimized non-linear registration followed by projection onto an alignment-invariant tract representation. TBSS allows for valid conclusions to be drawn from the subsequent voxelwise analysis (for details on the TBSS steps, see Andersson, Jenkinson, & Smith, 2007). Bilateral tracts ROIs were defined using the probabilistic Johns Hopkins University White Matter Atlas (Hua et al., 2008) provided by "fslview". A threshold of 10 was applied at each tract, and the results binarized to obtain masks that were used to crop the group-wise WM skeleton generated by the TBSS. Finally, for each ROI mean FA, MD, RD, and AD was calculated

and, as FA was not normally distributed, correlated using Spearman correlation coefficient against the SS scores. (*Figure* 2) shows a graphical representation of the tracts included in the ROI.

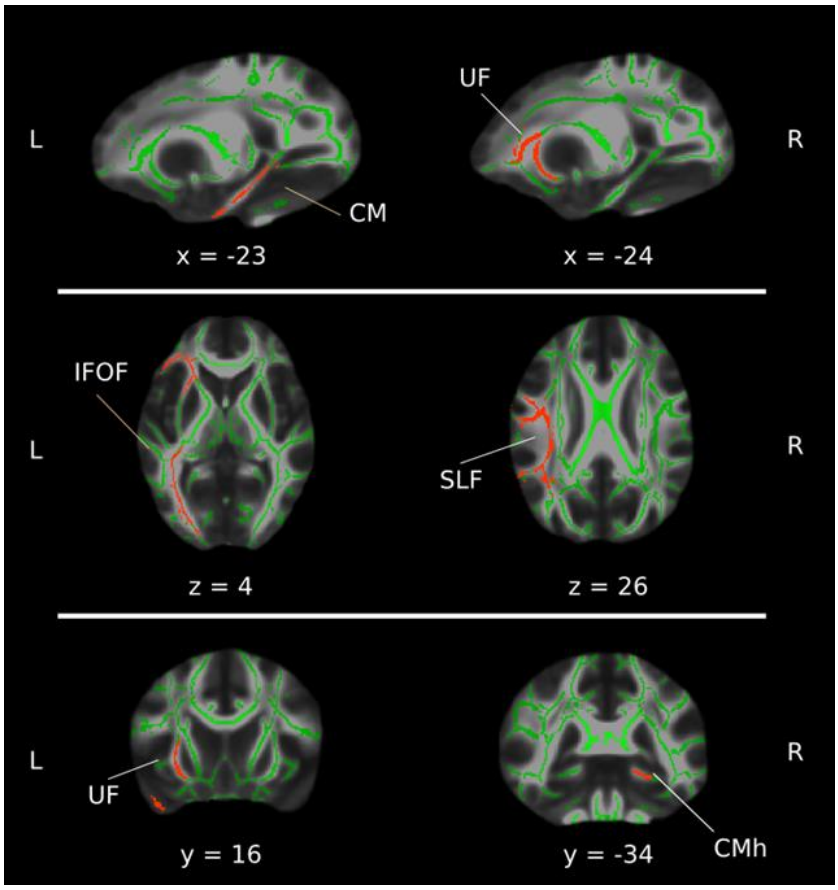



**Figure 2:** Graphical representation of the tracts included in the ROI analysis: from top to bottom: coronal, axial and sagittal views of the ROI, including CMh, UF, IFOF, SLF. The background image is the mean FA mask of the sample fitted in the MNI template. Shown in red are the tract included in the ROIs cropped on the FA skeleton map (in green). The image is reported in the neurological orientation, x, y, and z, coordinates are based on the MNI atlas.

### *2.3.4.Results*

We found positive relations between FA and SS in four WM tracts of the left hemisphere: UF ($\rho$ = .31 p = .02), IFOF ($\rho$ = .30 p = .03), SLF ($\rho$ = .37 p = .005), and the hippocampal region of Cingulum: CMh ($\rho$ = .29 p = .03) (*Figure* 3). In no tracts was MD

correlated with SS. Additional analyses established the relative associations of AD and RD with FA. Negative correlations emerged between RD and SS in all tracts: UF (ρ = -.29 p = .03), IFOF (ρ = -.32 p = .02), SLF (ρ = -.30 p = .03), and CMh (ρ = -.30 p = .02). In no tracts was AD correlated with SS.

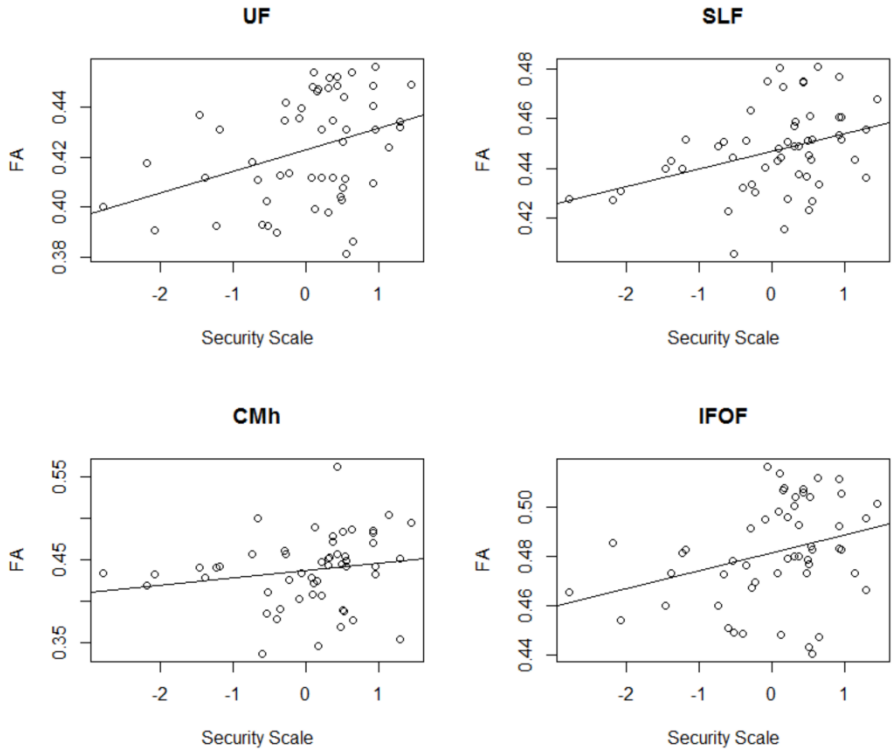



**Figure 3:** From left to right: scatter plot of the correlation between Fractional Anisotropy (FA) and the Security Scale in (a) Uncinate Fasciculus (UF) (ρ = .31 p = .02), Superior Longitudinal Fasciculus (SLF) (ρ = .37 p = .005), Cingulum (CMh) (ρ = .29 p = .03) and Inferior Fronto Occipital Fasciculus (IFOF) (ρ = .30 p = .03). All the tracts belong to the left hemisphere.

### *2.3.5. Discussion*

The present study was designed to investigate associations between security in the young adult's maternal attachment relationship and WM structural connectivity in the young adult's brain. We found correlations between WM integrity and security in the maternal relationship in four WM association fibers: CM, UF, IFOF, and SLF. CM and

UF are components of the limbic system. CM conveys communication between structures in the limbic system and facilitates prefrontal, parietal, and temporal interactions (Mori et al., 2008) and is known for its function in human emotion processing, memory, and language. The UF connects components of the limbic system (amygdala, hippocampus) with frontal regions. UF fibers have been associated with processes related to emotional and social cognition, and their disruption has been linked with specific pathologies. In particular, the CM is related to apathy (Woolley et al., 2011) and cognitive control (Metzler-Baddeley et al., 2012). Underconnectivity in the UF is associated with autism spectrum disorder (Aoki, Abe, Nippashi, & Yamasue, 2013). Notably, a recent meta-analysis revealed a significant FA reduction in the left UF in autistic compared to typically developing individuals (Aoki et al., 2013). IFOF and SLF are large bundles of fibers interconnecting brain regions involved in high-level cognitive functions (Mori et al., 2008). The SLF connects frontal, parietal, and temporal lobes (Mori et al., 2008), and its disruption is also linked to autism (Aoki et al., 2013). The IFOF connects the frontal lobe with parietal and temporal lobes, it intermingles with UF (Mori et al., 2008), and its functions include integration of visual and auditory cortex with prefrontal cortex.

Our findings linking these specific WM fibers to maternal security extend those of De Pisapia et al. (2014), who reported an association between the same tracts and interpersonal competence in young adults. Moreover, our findings are consistent with the results of Govndan and colleagues (2010), who observed reduced integrity of UF and SLF in children with a history of early social deprivation. Together, these findings support a tenet of attachment theory which states that the quality of the mother-infant relationship affects the construction of children's socioemotional abilities and future adult relationships (Bowlby, 1969).

In the present work, the positive correlation between FA and maternal security was driven by a negative correlation between RD and the SS. Like FA, RD is generally linked to myelination and axonal packing, whereas AD can vary with fiber diameter and axon coherence (Song et al., 2002). This result is consistent with previous longitudinal studies in which increases of FA, paired with reductions of RD and AD remaining constant, have been interpreted in terms of an increase in myelination from childhood into adolescence and young adulthood (Lebel & Beaulieu, 2011)

In contrast with De Pisapia and colleagues (2014) and with Schore's (2000) hypothesis regarding the role of the right hemisphere (RH) in affect regulation, we found that no tract in the RH correlated with attachment security. The RH has previously been associated with emotional and social cognition (Spence, Shapiro, & Zaidel, 1996) and likely plays a role in attachment formation. However, findings regarding a right-left hemisphere distinction in emotional cognition are actually mixed in the literature, bringing this strict dichotomy into question (see Abbott, Cumming, Fidler, & Lindell, 2013). Moreover, attachment measured in childhood, as well as interpersonal competence measured in young adults, refer to the ongoing situation of the individual; in contrast, here we asked young adults to rate the relationship they had with their mother during childhood. This task likely involves cognitive processes of self-referential thinking and retrieval of autobiographical memory, both of which typically recruit left hemisphere involvement (Maguire, 2001). However, evidence indicates that the left hemisphere might also be involved in the formation of internal working models. For example Benetti et al., (2010) found that high attachment-related anxiety in healthy adults was associated with decreased gray matter volume in the right anterior temporal pole and increased gray matter in the left lateral orbital gyrus (Benedetti et al., 2014). This result supports the idea that the attachment relationship might affect the development of brain structures involved

in social and emotional processing and that this influence is not limited to the right hemisphere.

The cross-sectional nature of the present study only indicates a correlation between a psychological measure (attachment) and a biological measure (structural connectivity of the brain) and thus does not establish any causal relation. Given the complexity of the parent-child relationship, and the number of different factors that play important roles in relationship development and expression, further assessment of the impact of attachment on brain development requires additional study. That said, this study constitutes an important first step in attempts to find experimental evidence for regulatory theories of attachment.

This research also contributes to the neuroscience of mother-child interaction. Our aim was to investigate possible relations between attachment relationships and brain connectivity in young adults, demonstrating the feasibility of applying neuroimaging methods – in this case DTI - to the field of social developmental neuroscience. This approach affords clinicians novel tools to couple clinical investigations with neuroanatomical information and thereby overcome limitations of sole reliance on self-reports.

## 2.4. General discussion on similarities and differences in the results

In contrast with both the result of the previous works and with Schore's hypothesis regarding the role of the right hemisphere in affect regulation (Schore, 2000),

in the present study we found that no tract of the right hemisphere correlated with security in maternal relationship. This result is surprising because, as mentioned above, the right hemisphere is extensively associated with emotional and social cognition (Fournier, Calverley, Wagner, Poock, & Crossley, 2008; Heberlein, Adolphs, Pennebaker, & Tranel, 2003; Spence et al., 1996) and certainly has a role in the formation of the attachment relationship. However, it is worth considering more closely findings regarding the right and left hemisphere dichotomy in emotional cognitions. As in our case, there have been mixed results in recent literature (Abbott et al., 2013). Whereas some studies support the right hemisphere hypothesis (Hagemann, Hewig, Naumann, Seifert, & Bartussek, 2005), indicating a dominance of the right hemisphere for the whole emotional processing, other studies support the valence hypothesis (Brüne, Nadolny, Güntürkün, & Wolf, 2012) indicating that the right hemisphere processes negative emotions, while the left hemisphere process positive emotions. However a recent meta-analysis on the topic shows that the involvement of the two hemispheres in emotion processing might be more complex, with the right hemisphere processing negative emotions and the left hemisphere processing negative and positive emotions (Abbott et al., 2013). Recent work points instead to the level of emotional processing rather than its valence. For example, Shobe and colleagues (2014), propose that the right hemisphere detects the emotional valences of stimuli, while the left hemisphere contributes to higher level processing of the information received by the right hemisphere (Shobe, 2014). Considering that the contribution of the right and left hemisphere in social and emotional processing is more complex than a mere dichotomy, a possible explanation for our results is that the left lateralization might be due to the specific construct examined with the Kerns's Security Scale, namely the internal model of the maternal relationship in adults. In fact both the attachment relationship measured in childhood and the interpersonal competence

measured in young adults refers to the present situation of the individual, in contrast in this study we asked young adults to rate the relationship they had with their mother during childhood. This task involves cognitive processing such as self-referential thinking and retrieval of autobiographical memories which are typically associated with the left hemisphere (Maguire, 2001). In line with this hypothesis, left hippocampal activation is known to be involved in the retrieval of autobiographical memory, even when using visual rather than verbal stimulation - more likely to involve left hemisphere activity - (Burgess, Maguire, Spiers, & O'Keefe, 2001; Gilboa, Winocur, Grady, Hevenor, & Moscovitch, 2004). In another neuropsychological study, which used a virtual reality paradigm to study autobiographical memory, the authors found that patients with right temporal lobectomy were more impaired on navigation tasks, while patients with left temporal lobectomy were more impaired on retrieving aspects of autobiographical events (Spiers et al., 2001).

Moreover, experimental evidence point out that also the left hemisphere might be involved in this process. For example, Benetti et al., (2010), who aimed to study the association between grey matter volumes and attachment styles in healthy adults, found high attachment-related anxiety to be associated with decreased grey matter volumes in the right anterior temporal pole and increased grey matter in the left lateral orbital gyrus (Benetti et al., 2010). This study supports the idea that the attachment relationship might affect the development of brain structure involved in social and emotional processing and that this influence is not limited on the right hemisphere. Taking into account the similarities and differences, our first two studies highlight the importance of considering the construct assessed by behavioural measures which is as important as the choice of an appropriate methodological technique in determining direction of results. In our case our result suggest that the Kerns Security Scale might rely on cognitive functions, such as

referential thinking and retrieval of autobiographical memory, in which the connectivity between structures of the left hemisphere plays a major role.

# 2. Parenting response to infant cries

Studies suggest that a secure mother child relationship starts when the infant craving for adult care finds a responsive and emotionally attuned caregiver (Bowlby, 1969; Esposito, Venuti, De Falco, 2009). An important step stone in the attachment relationship might therefore depend on inter-individual differences in the neural and behavioural response of adults to infant signals. In this chapter I will focus on specific behavioural and neural parenting responses elicited by baby cries as it represent the evolutionary most important signalling behaviour from the child, I will then discuss on gender differences emerging from these studies and why this might represent an evolutionary advantage.

## 3.1 Sex Specific increases in motor evoked potentials in response of baby cries in females: a Transcranical Magnetic Stimulation study.

(Messina, Cattaneo, De Pisapia, **Serra**,, Farneti, Rigo, Esposito, Bornstein, Venuti , under revision)

Transcranical Magnetic Stimulation (TMS) is a non-invasive method used to stimulate region of the brain, this technique can be used to trace the timing at which activity in a particular cortical region contributes to a given task, and to manipulate the functional connectivity between brain regions (Pascual-Leone, Walsh, & Rothwell,

2000). In the previous chapter we saw that an efficient structural connectivity is linked with secure attachment, improved social cognition and cognitive ability in general. Evidence from the literature suggest an association between Axonal Integrity measured with FA and functional connectivity measured with TMS in two region involved in preparing ad executing actions: premotor and motor cortex (Boorman, O'Shea, Sebastian, Rushworth, & Johansen-Berg, 2007). In line with this evidence, Messina et al., (in submission) linked parenting and brain functional connectivity conducting a study on motor cortex excitability in response of infant cries.

Infant stimulation automatically grasp adult attention eliciting a physiological, neural and behavioural state that prepare the caregiver to act (Brosch, Sander, & Scherer, 2007). For example listening infant cries modulate hormone levels (Fleming, Corter, Stallings, & Steiner, 2002; Swain, Kim, & Ho, 2011) and autonomic activity (Boukydis & Burgess, 1982; Frodi, Lamb, & Wille, 1981). It increase hand gripping force, improve speed and accuracy in intentional movement (Bakermans-Kranenburg, van IJzendoorn, Riem, Tops, & Alink, 2012; Parsons, Young, Parsons, Stein, & Kringelbach, 2012) and it elicit motor response including activation in the premotor cortex (De Pisapia et al., 2013; Montoya et al., 2012; Venuti et al., 2012). However given the limited temporal resolution of functional Magnetic Resonance Imaging (fMRI) is not possible to determine whether this activation is automatic or not. In the work of Messina et al., (in submission) Transcranical Magnetic Stimulation (TMS) was used to test the hypothesis that infant cries automatically evoke motor patterns as this technique allows investigations with high temporal resolution overcoming the low temporal limitation of fMRI.

When an infant cries, the most common behavioural response is picking and holding pattern (Gustafson & Harris, 1990). Accordingly we have investigated two muscles involved in such behaviour: an harm flexor: the biceps branchi (BB) and a finger flexor: the interosseous dorsalis primus (ID1). TMS was applied to participants motor cortex time locked with the presentation of the infant cries and Motor Evoked Potentials (MPSs) produced by TMS were recorded. To test the hypothesis of an automatic response ,single pulse TMS was delivered from 0 to 250ms, in six step of 50ms, where 0 represent a baseline in which the brain could not possibly have access to auditory stimulation. With this design we were able to distinguish top down from bottom up processing. When investigating neural response to baby cries two factor might play an important role: gender difference and actual specificity of the response to cries as opposed to any kind of sounds. In the work of Messina et al., (in submission) we have addressed these factor comparing a sample of 10 male and 10 female in the main experiment and through the use of scrambled infant cries in a control experiment. Participants were non-parents and right handed (age 25-28). The control sounds was realized following the procedure of Colignon et al (2013) which maintain all the physical features of the original sound in spite of being unrecognizable as baby cry (Collignon et al., 2013).

Results shows a facilitation effect, for adults non parent in a distal muscle, the ID1, this effect is present only for native cry sounds and only in females. Importantly as it was expected its latency (100ms) indicate an automatic audio-motor association (*Figure* 4

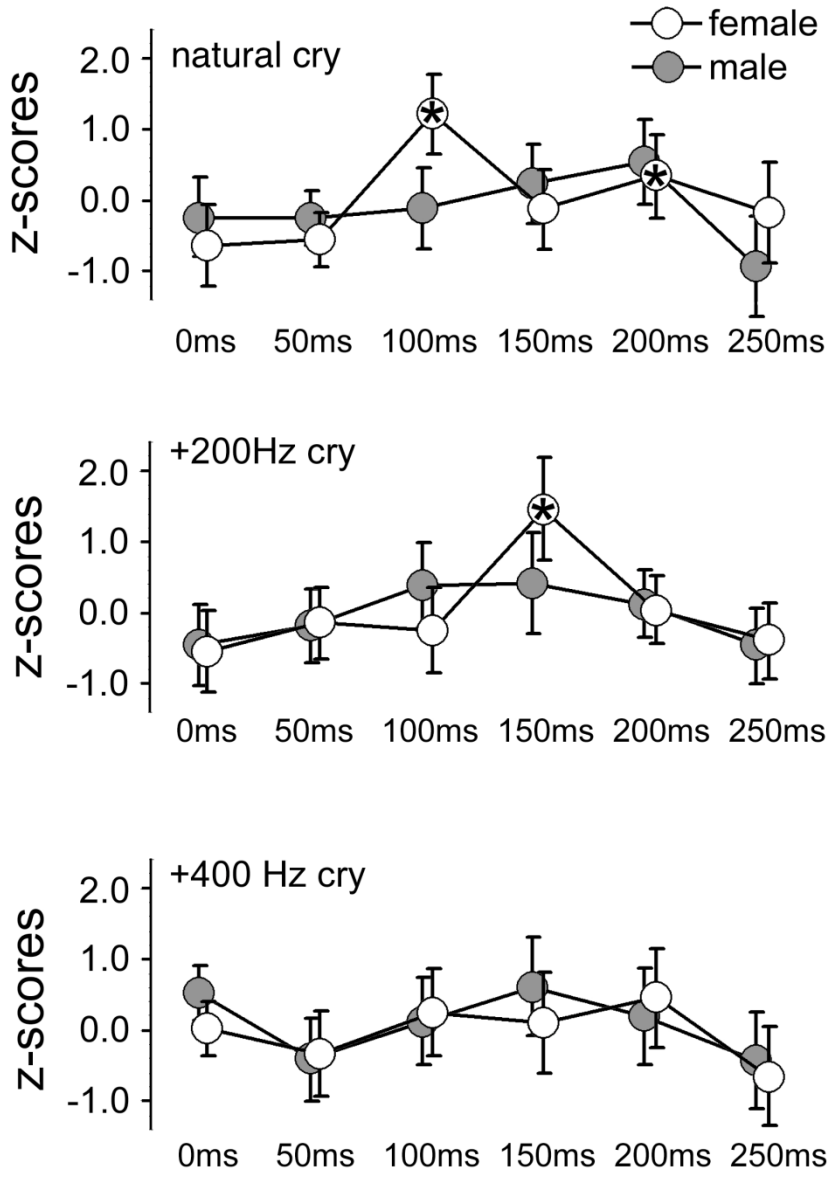



**Figure 4**: Mean z-scores for each cry type and each ISI for females and males. Error bars indicate 95% CIs. Asterisks indicate ISIs at which a significant difference was found with data obtained at 0 ms (baseline).

It is worth noting that the facilitation is found only in female non parents, indeed most of evidence on sex differences are found in non-parents participant whereas in several cases no sex differences are found in physiological measures in parents (Frodi & et al, 1978; Messina et al., in submission) indicating that behavioural and physiological changes occur with experiences of becoming parents (Delahunty, McKay, Noseworthy, & Storey, 2007; Storey, Delahunty, McKay, Walsh, & Wilhelm, 2006).

Limitation of this work include the small sample size, which is at the lower limit for between-subjects investigations of sex differences. Moreover we have no information about our participant's previous experience with children caring however we ruled out the possibility that some of participants were professionally exposed to young children (kindergarten educators, teachers, professional baby-sitters). Cultural aspect also could have influenced the results as typically women are more involved in direct child care than men. Similarly, we have no information on other important variables such as mood, empathy, or menstrual phase which could possibly have an influence in the neural response to baby cry, future studies are needed to address these issues. In addition Because the response was recorded only from two muscles the results cannot be interpreted as a specific motor pattern activated by infant stimulation, however it indicates biological marker of a stimulus-response association which can be evolutionary advantageous to provide a prompt help in response of a child signal (Messina et al., in submission) especially in female which have not yet parental experiences.

Another fundamental factor that has to be considered when investigating the parental behaviour is that in the everyday life, baby cries dos not normally occur when adults are waiting to assist the infant, and ready to react. On the contrary crying erupts more probably while adults are normally engaged in external tasks or simply immersed in their own thoughts. Nonetheless, caregivers need to respond appropriately regardless of the situation. During spontaneous cognition or self-referential mental state (i.e. when the individual is mind wandering) the brain shows a pattern of activation called Default Mode Network (DMN). This network includes structures such as Medial Prefrontal Cortex (MPFC) and Posterior Cingulate Cortex (PCC) that are active during self-referential thinking, taking another person's perspective mental imagery o envisioning the future (Buckner, Andrews-Hanna, & Schacter, 2007; Fox & Raichle, 2007; Raichle & Snyder,

2007). Conversely the DMN is deactivated when the individuals attention is externally oriented. A recent study indicated that women shows greater deactivation than men when probed with infant cry during resting state (De Pisapia et al., 2013). This result accords with the finding of Messina et al (in submission) pointing for a facilitation effect for women which would show a more prompt disengagement from an internal cognitive state to direct the attention toward the baby. However De Pisapia et al., (2013) did not control for the specificity of the infant sound. In addiction as we mentioned above when a baby cry arise, the caregiver could either be in a self-oriented cognitive state or his/her attention could already be engaged in an external task from which the caregiver have to disengage to direct attention toward the baby. These scenario have been simulated in an elegant work of Rigo et al., (in submission) that I'm going to describe in the next paragraph.

## 3.2. Neurocognitive processes in women and men to emotive sounds

(Rigo, De Pisapia, Bornstein, Putnick, **Serra**, Esposito, Venuti; in submission)

In order to recreate a realistic everyday life situation in a fMRI environment, two cry-unrelated tasks were developed. The participants were required to perform the tasks inside the scanner during stimuli presentation. The tasks were: a Self-Oriented Task (SOT) in which the participant had to decide if an adjective describes the his/her own personality and a Goal Oriented Task (GOT) to decide whether the adjective has three or four syllables. The two tasks were designed to respectively activate and deactivate the DMN Figure 5. We expected that woman would be more readily engaged by infant crying, deactivating DMN more than men in correspondence of infant cry . To test for specificity of the results we used control stimuli including baby laugh and adult cries and

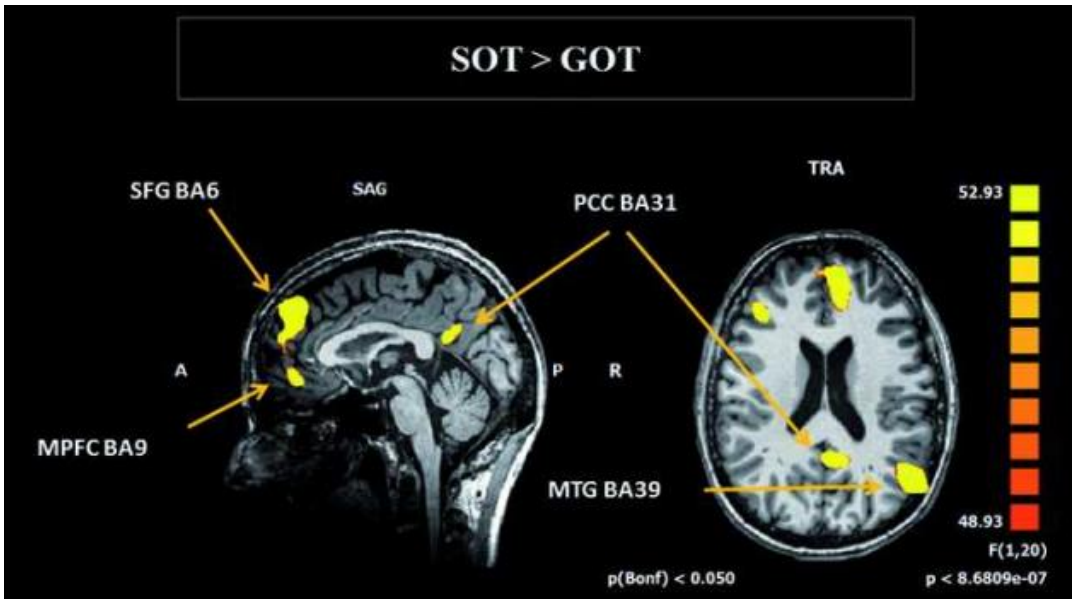



**Figure 5**:Brain regions that showed greater activation in the SOT in contrast in contrast to the GOT (P(Bonf) < .05). Self-oriented task involved a cerebral network which was compatible with the DMN. Abbreviations: SOT= self-oriented task, GOT= goal-oriented task, MPFC= medial prefrontal cortex, SFG= superior frontal gyrus, PCC= posterior cingulate cortex, MTG= middle temporal gyrus.

a white noise matched with the baby cries in order to have a noise control sound which replicate the physical characteristic of the cries. Participants included 22 nulliparous adult (11 females, M age 20.05 years, 11 males, M age 25.25). The results partly confirmed the expectation. During SOT –designed to activate the DMN- woman deactivate the PCC more than men when listening infant crying in contrast to adult crying and infant laughing . During GOT instead, -designed to deactivate the DMN- lesser deactivation in men than women is found both in PCC and MPFC in association with female adult crying (compared to baby cry).

The women deactivation during SOT suggest a shift of attention from the self-referential task to the cry (Di & Biswal, 2014; Sridharan, Levitin, & Menon, 2008). During GOT instead men showed weaker deactivation of DMN indicating that female crying more than other sound induce in men self-relevant processing (associated with the partial activation of the DMN) which can contribute to mentally understand others (De Pisapia et al., 2013). Taking together the results of Rigo et al., (in submission) indicate

that infant crying distracted women when their attention was directed in a self-oriented task, whereas female crying induced an activation of DMN in men while their where focusing in a goal oriented task. In the next paragraph I'm going to discuss the gender differences found in this study and in the work of Messina et al., (in submission) as well as other work which indicate different behavioral and neural functioning in male and female.

## 3.3. Gender difference in parenting

Caring a baby is a fundamental task for the parents, it gives support to the infant, allows his/her correct development and in certain cases survival as well. However it is also an incredible challenge for the parents, a challenge that require a diverse set of skills and cognitive abilities which parents have to quickly develop and improve. Given its importance, it is likely that evolution would have shaped parental cognition in such a way to ensure the most comprehensive care for the infant. In addition, the role of male and female in a community differs in terms on how much time the caregiver spend with the infant and on specific duty that usually they holds. These differences are reflected in the familiar environment and in the parenting behavior. In both studies discussed above, we found a gender differences in response to infant cries. This does not indicate that women are better than men in parenting a child, conversely it seems to indicate differences between men and women in how an infant stimulation versus other noises can grasp the attention of the caregiver and in the way in which the brain responds and prepare the body to react. This difference could be the result of an advantageous evolutionary strategy which reflect the different role of male and female in a family. Accordingly, recent

physiological studies suggest that men shows higher physiological reaction to violent sound than baby cries (Tkaczyszyn et al., 2013), On this view in the result of Rigo et al., (in submission) woman cries might be interpreted as environmental danger more than baby crying and therefore elicit greater responsiveness in men.

It is worth noting that several findings in the literature indicate a general attentional bias for humans toward infant stimulation that in both male and female grasp attention more than other kind of stimulation (Brosch et al., 2007), however, when it comes to fatherhood, evidence indicate gender differences in parental investment with the paternal involvement varying depending on the degree to which it contribute to offspring survival, certainty of paternity and the cost of loss of mating opportunities with other females (Geary,2008). In support of these results a study of Cárdenas et al., (2013), showed that during simultaneous presentation of infant and adult faces, men prefer to fixate an infant face only if the concurrent adult face is a male, but not when the counterpart is a female (Cárdenas et al., 2013). Interestingly this tendency in men was linked with inter-individual differences in self-reported interest in infant.

A further point to consider is that the majority of finding on gender difference in parenting come from nulliparous sample, whereas in several cases no sex-differences have been found between male and female parents (Frodi & et al, 1978). Longitudinal studies might help to clarify this trend as evidence shows that physiological and neural response to infant stimulation changes with the experiences (James E Swain, 2011) . Comparing neural activation from a sample of mother and father at 2-4 weeks post-partum and 3-4 months the activation shifted from anxiety related brain areas such as amygdala and insula, to region linked with regulatory brain activity and executive function such as hypothalamic and prefrontal cortex highlighting the effect of experience

on brain response as parents start to associate the infant signaling behavior with more flexible social behavior and mature attachment(James E Swain, 2011). These results accords with a recent physiological study from Esposito, Valenzi, Islam, & Bornstein, (2015) in which fathers were calmer and acted more promptly than non-fathers to typical baby cry.

Thanking together, those results highlight gender differences when experience is missing. In this case females seems to be provided with a more ready raw toolbox to face the parenting challenge. However  both men and women can face the parenting care challenge and quickly improve their skills through experience balancing the gender differences typically found in non-parents.

# 4. Understanding mother-child interaction and broader autism phenotype

In the third part of this thesis we were interested in addressing accuracy in understanding social interactions in parents of children with Autism Spectrum Disorder (ASD) and in non-affected populations that might presents particularly high autistic trait. In particular we were interested in the delicate task of observing and judging the quality of mother-infant interactions. The relevance of this task is due to the extreme importance to promptly individuate cues of abnormal social behavior in those cases in which the child might shows deficit in the social development.

## 4.1 Differences in judging mother-infant interaction in parents of children with ASD and parents of children with TD

### *4.1.1 Introduction*

Individuals social skills vary tremendously within the population ranging from highly social individuals to pathological populations such as in Autism Spectrum Disorder (ASD). ASD is defined as a complex neurodevelopmental disorder characterized by difficulties in social interaction and communication as well as the presence of restricted, repetitive patterns of behavior, interests, or activities (American Psychiatric Association, 2013). Recent clinical and epidemiological studies have suggested that autistic disorders might not be limited to the affected population, they would rather be an

extreme manifestation of a range of deficits continuously distributed in nature (Constantino & Todd, 2003; Piven, Palmer, Jacobi, Childress, & Arndt, 1997; Spiker, Lotspeich, Dimiceli, Myers, & Risch, 2002; Waterhouse et al., 1996). Those sorts of evidence define a Broader Autism Phenotype (BAP) that is the expression of similar, yet less severe autistic traits in not affected individuals (Bolton et al., 1994). In particular, according with BAP studies, family members of autistic probands shows an increased probability to manifest autistic symptoms often under the threshold for a diagnosis of Autism Spectrum Disorder (Constantino & Todd, 2003). The possibility that the BAP poses limits on the social skills of individual related with a child with ASD is extremely relevant for the child itself. Accordingly the ability to detect social information from observed behaviors is crucial for an early diagnosis of autism; every child before being diagnosed is simply a child showing unusual behaviors, however if the person close to a child with ASD share with him/her some autistic traits they might as well show difficulties in detecting cue of unappropriated social behaviors. Or conversely they might be more expert in such task because of their daily exposition to problematic social interaction. In line with this suggestion we believe it is important to investigate in more details whether parents of children with ASD are fit to promptly understand the quality in a mother-child interaction and possible difference which might exist with parents of children with TD. Moreover it is important to take into account the influence that the BAP might have on this ability. Although extensive research has been carried out on the incidence of the BAP and on similarities between family member with autism phenotype and individual with autism (Dawson et al., 2002; Piven et al., 1997), to our knowledge no single study exists which attempt to compare differences between mother of TD and ASD in understanding the quality of mother child relationship and their accuracy in detecting relevant social cues during social interaction using ecological stimulation.

The main goal of the this work was to compare parents of children with ASD and parents of children with TD in terms of their ability in understanding the quality of mother-child interaction which includes children with TD and their mother, and children with ASD and their mother. Our hypothesis is that differences exist between those groups, in particular Parents of children with ASD might show either more difficulty in detecting problem in social interaction due to their familiar relationship with an individual with ASD or conversely they might show an experience effect due to their daily exposition to such problematic social interactions. If parents of children with ASD will result to be disadvantaged to detect cue of abnormal social behavior in mother child interactions then more weigh should be given to opinion of people external to the family unit of the child such as pediatrician and school educator which, might play a fundamental role in paving the way for further investigations that may lead to a diagnosis of autism.

### *4.1.2. Methods:*

*Participants:*

Forty-two participants, 30 mother of children with TD mean (Mage: 35.24; SD 6.35) and 12 mother of children with ASD (M age: 42.69; SD 6.67) took part in the experiment. None of the participants exceeded the Autistic Quotient (AQ) cut-off score. Mother of children with ASD had no other sons with TD as well as mother of children with TD had no other sons with ASD

*Construction of experimental stimuli*

Video depicting 15 minutes free play session interaction between mother and child were recorded in the Observation, Diagnosis and Education Lab at the University of Trento (ODFlab), Italy. Dyads of children with ASD or TD and their own mothers were recorded using the same room and a standardized set of toy previously used by De Falco, and colleagues,(2008). The child age ranged between 2 and 4 years mean (33.13 months TD; 38.30 months ASD). Subsequently the interactions were microcoded for synchrony by a trained clinician using ObsWin32 software (Martin, N., Oliver, C., & Hall, 2001). Each video was divided in several fragment lasting 20 seconds each. The fragments depicted either synchronous or asynchronous interactions. However in order to include in the experimental stimulation only the videos that were perceived as either synchronous or asynchronous by a naive viewers all the fragments were included in a pre-test in which participants were asked to rate in a 5 points Likert scale (Likert, 1932) the quality of the interaction ranging from 1 (totally not succesful) to 5 (totally succesful). The word successful/not successful has been used because it is the same word in which typically parents of children with ASD describe the interaction with their own child. Moreover, since our focus lies in the perception of non-verbal interaction and in order to avoid variability introduced by differences in verbal communication skills between TD and ASD, the interactions were shown without audio. This also reduce source of variability for a future fMRI follow up. After the pre-test, only the video that obtained a median score equal or higher than 3 and lower or equal then 3 has been chosen to be part of the synchrony and asynchrony stimulation respectively. The resultant four categories were: synchTD (Md=4.16), SynchASD (Md=4.66), AsynchTD (Md=1.52) and AsinchASD (Md=1.54), each category included twenty video. The behavioural task was designed using Eprime 2 (Schneider, Eschman, & Zuccolotto, 2007).

*Measures*

The Autism Spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) is a self-reported measure of autistic traits it is based on 50 items identifying high-functioning autism in individuals with normal intelligence. Each item is rated on a 4-point scale, “definitely agree”, “slightly agree”, “slightly disagree”, and “definitely disagree.” Items are scored dichotomously as “0” or “1”, with “1” representing answers in the direction of autism thus the scoring does not depend from any interpretation. In the original paper addressed for Test-retest reliability and self vs parents report showing that scores from the first and second measurement did not differ statistically ($t = 0.3$, $df = 16$, $p = 0.75$) and were strongly correlated ($r = 0.7$, $p = 0.002$). Whereas the self-reported scores were more conservative than the parent’s report with a mean 2.8 points increase for the parents report ($sd = -0.6$)

*Procedure*

The study is divided into two sections. In the first section each participant was placed in front of the screen and observe the videos of interactions. All videos were shown in a randomized order using E-prime 2 (Schneider et al., 2007). Each video (20 seconds) was followed by a phase in which participants rated the quality of the interaction based on a 5 points likert. The points on the Likert scale are indicated by boxes varying with a color gradient that goes from light grey to dark grey with only the extreme boxes marked with labels: “totally not successful” and “totally successful”. All videos are shown without any auditory feature. In the second section, participants will be administered with the questionnaire.

*Data analysis*

Given that the data were not normally distributed and to account for the different sample size of the groups we performed Wilcoxon tests considering Bonferroni multiple comparison correction. As such we address the effect of the interaction type (synchronous/asynchronous) and the diagnosis (interaction with TD/interaction with ASD) on the ratings, accuracy and reaction time. Even though none of the participants exceeded the AQ cut-off correlation between AQ and participants ratings were calculated to account for the association between BAP and the evaluation of the interaction.

### *4.1.3. Results:*

*AQ:*

None of the measures (accuracy, rating, and reaction time) were correlated with AQ scores, indicating that the autistic traits of our participants were not associated with the evaluation of the interactions.

*Accuracy:*

As showed in *Figure 6*, no differences between groups have been found in judging interaction with ASD. Parents of children with TD were more accurate (Mdn = 0.75) than parents of children with ASD (Mdn = 0.50) in judging asynchronous interaction with TD (W = 167.0, p = .002). Parents of children with TD were also more accurate (Mdn = 08.0) than parents of ASD (Mdn = 0.65) in judging synchrony in the interaction with TD (W = 175, p = .004).

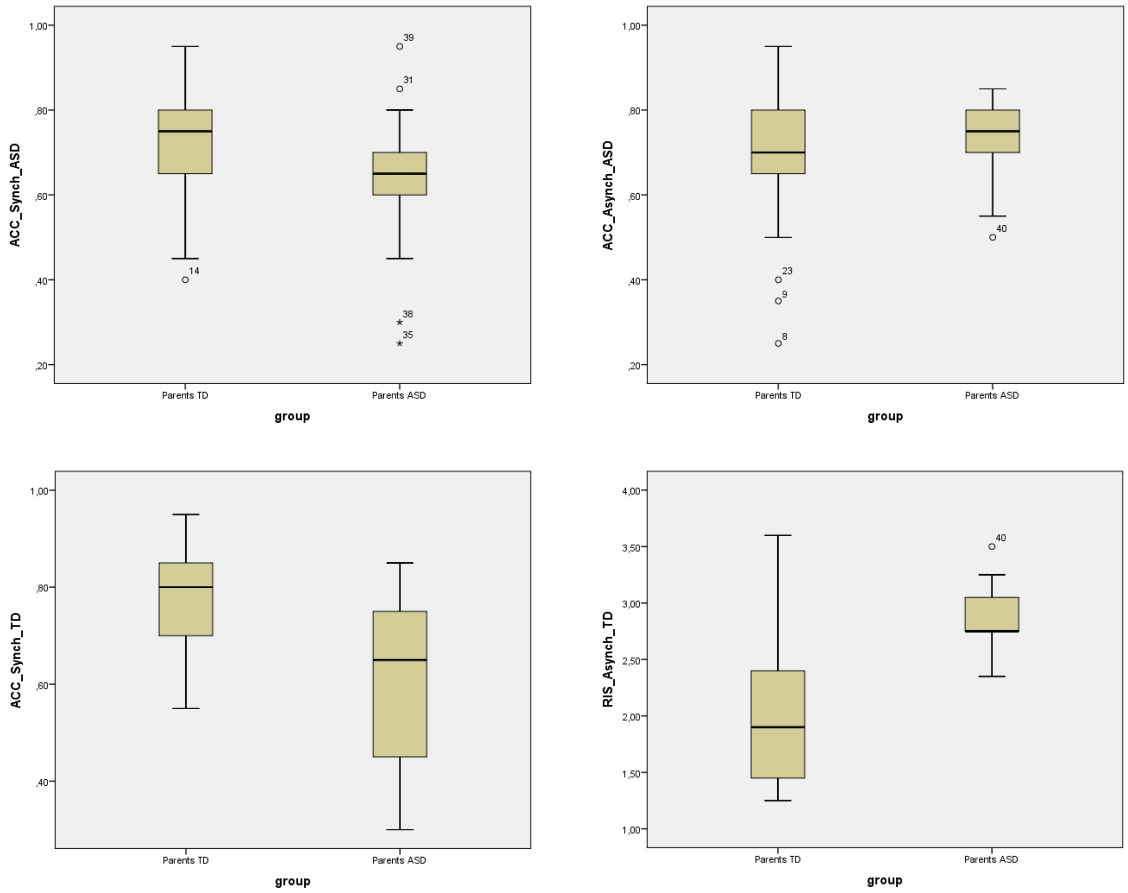



**Figure 6**: The two upper squares show accuracy results in synchrony interaction (left) and asynchrony interaction (right) in which children with ASD were filmed. The two lower squares shows accuracy results in synchrony interaction (left) and asynchrony interaction (right) in which children with TD were filmed.

*Ratings*

In order to understand the origin of the difference in accuracy we examined the ratings (*Figure 7*) highlighting that mother of children with ASD gave higher response (Mdn = 2.7) than mother of children with TD (Mdn = 1.9) in judging asynchrony interaction with TD (W= 465.5, p =.0001) indicating that they detected more synchrony in the interaction with TD compared to parents of TD. Moreover parent of children with ASD gave lower scores (Mdn = 3.85) then parent of TD (Mdn = 4.15) in judging

synchrony interaction with TD (p = .006) meaning that they detected less synchrony in the interaction with TD.

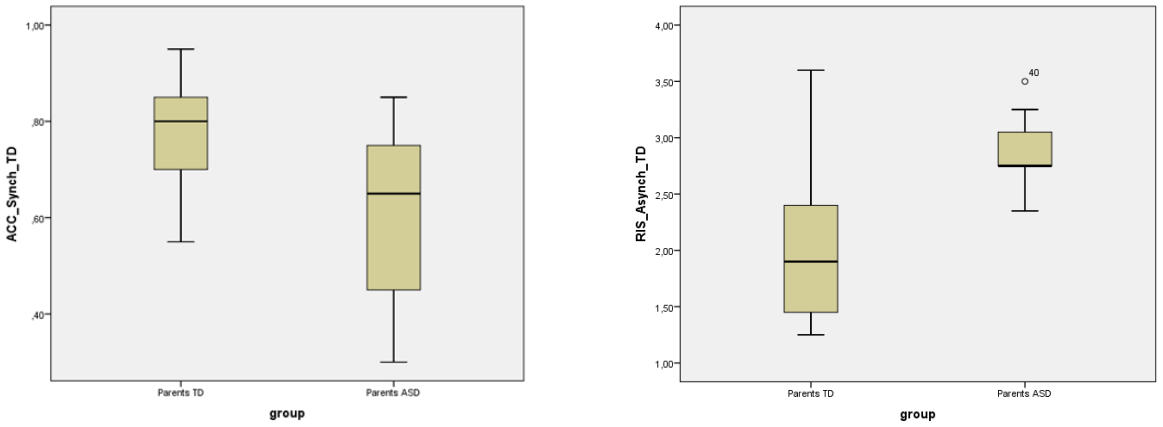



**Figure 7:** The left square shows ratings results in synchrony interaction with TD, the right square shows ratings results in asynchrony interaction with TD.

*Reaction times*

As shown in *Figure* 8, parents of children with ASD (Mdn = 2108.62 ms) were faster, and as accurate as parents of TD (Mdn = 3831.80 ms) in judging synchrony in the interaction with ASD (W = 196.00; p = .004). Same result is found in judging asynchrony in the interaction with ASD. Parents of children with ASD (Mdn = 2122.40 ms), are faster and as accurate of parents of children with TD (Mdn = 3005.70 ms) (W = 182.0; p = .008). Moreover, parents of children with ASD were faster (Mdn = 2124.45 ms), but less accurate than parents of TD (3232.70) in judging asynchrony in the interaction with TD (W = 142.0; p = .003). No difference is found between parents of children with ASD (Mdn = 2178.32 ms) and TD (Mdn = 3372.10 ms) in judging synchrony in the interaction with TD as it does not survive Bonferroni correction (W =190.0; p = .02)

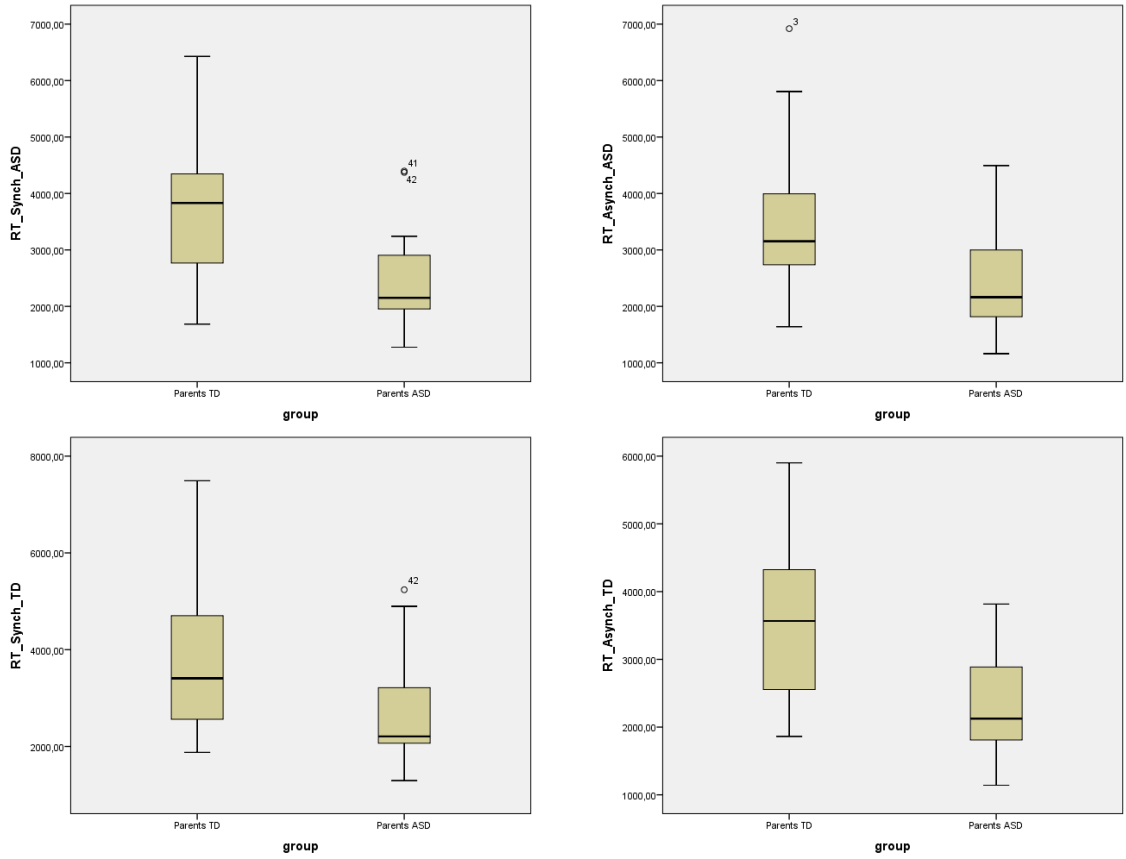



**Figure 8:** The two upper squares show reaction time results in synchrony interaction (left) and asynchrony interaction (right) in which children with ASD were filmed. The two lower squares shows reaction times results in synchrony interaction (left) and asynchrony interaction (right) in which children with TD were filmed.

*Video TD vs video ASD*

As shown in *Figure* 9, parents of children with TD were more accurate in judging synchrony in the interaction with TD (Mdn = 0.80; SD = 0.12) than synchrony interaction with ASD (Mdn = 0.75; SD = 0.13), (Z = -2.736; p = .006). No differences was found between judgment of asynchrony interaction with ASD (Mdn = 0.70; SD = 0.16) and TD (Mdn = 0.75; SD = 0.23). Parents of children with ASD did not differ in judging synchrony interaction with TD (Mdn = 0.65; SD = 0.17) and ASD (Mdn = 0.65; DS = 0.17) while they judged more accurately asynchrony interaction with ASD (Mdn = 0.75; SD = 0.11) than asynchrony interaction with TD (Mdn = 0.50; SD = 0.12), (Z = -3.074; p = .002).

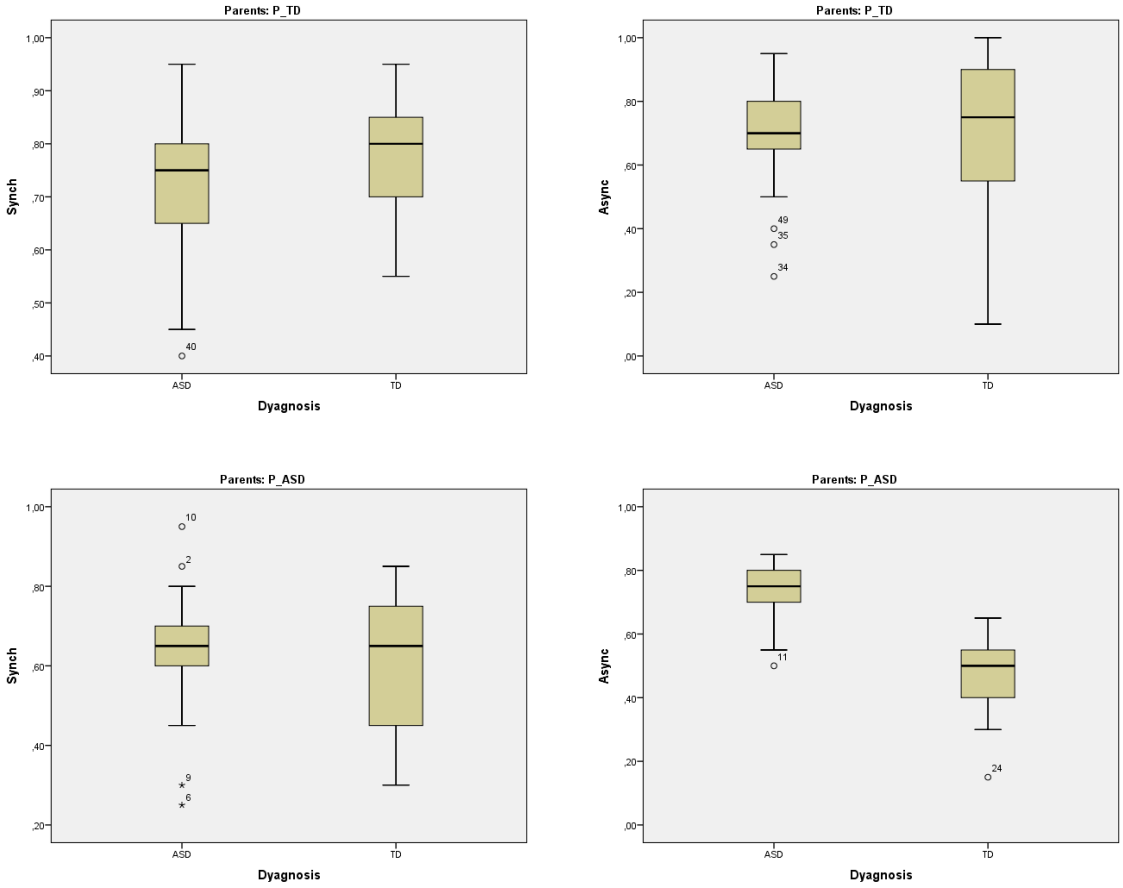



**Figure 9**: Upper squares shows accuracy in parents of children with TD in judging synchrony(left) interaction with TD and ASD and asynchrony (right) interaction with TD and ASD. Lower squares shows accuracy in parents of children with ASD in judging synchrony (left) interaction with TD and ASD and asynchrony (right) interaction with TD and ASD.

### *4.1.4. Discussion*

Our main goal with this project is to address whether parents of children with ASD are fit to promptly understand the quality of an interpersonal interaction. That is if they are able to detect cue of abnormal social behavior in children with ASD and children with TD. We address this issue analyzing the performance in rating social interaction between mother and child. Taking together the result of this work indicate that Parents of

ASD are as accurate as parents of TD in judging interaction with ASD and also faster in this task which might reflect the effect of their experience. However parents of ASD are less accurate than parents of TD in judging both synchrony and asynchrony in the interactions with TD. This lack of accuracy was due to an overestimation of the quality of the interaction with TD during asynchrony and an overestimation of asynchrony during synchrony interaction with TD. Parent of ASD are generally exposed to more problematic interaction with their child in their daily life, therefore it is reasonable to expect that they perceive an asynchrony interaction between a child with TD and his/her mother as more synchronic than it actually is. However the reason why they judged less successful a synchrony interaction between child with TD and his/her mother is less straightforward to interpret. Two are the possible explanation which might have brought such result. First mothers of children with ASD have a different concept of synchrony, which might be less linear since their child with ASD expose them with mixed and more subtle signal during the interaction (Bebko, Weiss, Demark, & Gomez, 2006; Trevarthen & Daniel, 2005). Second, recognizing the quality of a synchrony interaction between a child with TD and his/her mother means also rationalize the difficulties that still are present between a child with ASD and his/her mother, perhaps even in the synchrony interaction. The major limitation of this work is an unbalanced sample size between groups as the parents of children with ASD are considerably less than parents of children with TD. However we accounted for this limitation using non parametric statistic and considering Bonferroni correction.

The results from this study indicate that while both category easily detect deficit in the social domain in children with ASD, parents of ASD might have more difficulty in detecting problems in a child which does not show such severe symptoms as the ones they are used to. This overestimation of synchrony in absence of severe social

dysfunction might be a potential factor which could prevent the parents of children with ASD to notice possible social difficulty in children with TD or more importantly in siblings which might show an autistic phenotype but not as evident as a child with ASD. Therefore this study might have important implications for the crucial goal to promote an early diagnosis of autism. Moreover, this study would make contributions in understanding the difficulty faced by parents of children with ASD in taking an objective perspective while evaluating the social interaction with a child with TD but also in evaluating the progress of their child with ASD during therapy. One limitation of this work is that we could not directly account for the influence of the BAP in the results. Indeed because the data were not normally distributed we could not include AQ in a statistical model. However we decided to study the influence of BAP in understanding mother child interaction with a separate study.

## 4.2. Judging mother-infant interaction and Broader Autism Phenotype in non-affected population

### *4.2.1 Introduction*

As we mention in the previous chapter, the social difficulties found in ASD might not be limited to the autistic population or family member of an individual with ASD (Constantino & Todd, 2003; Piven et al., 1997; Spiker et al., 2002; Waterhouse et al., 1996), conversely less severe autistic traits might be spread in the whole population of not affected individuals. This concept defined as the Broader Autism Phenotype (BAP) might affect how social interaction are perceived by the general population. In order to address

the influence of BAP in the perception of mother child interaction we used the same paradigm of the pervious study in two group of not affected individuals. High Autism Quotient group (HAQ) and Low Autism Quotient group (LAQ). The hypothesis is that the group with higher autistic traits would show more difficulty in Judging the quality of social interaction between mother and child.

### *4.2.2 Methods*

*Participants and procedures:*

54 adult women took part in this study, 30 mothers 24 non-mothers. None of the participant had psychiatric or psychological disorders at the time of the experiment, none of the participant had an individual with ASD in their family. Because the sample included both mothers and non-mothers we performed an exploratory analysis to investigate differences between these two groups. Given the higher exposure of mother in such kind of stimulation, it could be plausible indeed that differences in judging the quality of maternal interaction exist between mothers and non-mothers. However in our sample the accuracy in judging social interaction did not vary according with the maternal status. Therefore participants were divided in two groups considering the median score of AQ: 27 female belonging to the High Autistic Traits group (HAQ) mean age 30.88 and 27 female belonging to the low autistic traits (LAQ), mean age 28.34. Stimuli and procedure were same as the one used in the previous study.

*Analysis.*

A tree way ANOVA was used to explore the influences of the autistic traits on the valuation of mother child interactions, the factors included in the ANOVA were: groups

(HAQ vs LAQ) Diagnosis (ASD vs TD) and Interaction (Synchrony vs Asynchrony). Then we proceeded with a simple main effect (SME) analysis to further investigate the ANOVA results.

### 4.2.1. Results

Three way ANOVA showed a significant effect of the "interaction" factor that is: synchrony is rated more accurately than asynchrony (p = .001). Moreover results shows an interaction between the three factors Diagnosis X Groups X Interactions (p 0.039). SME analyses was carried out in order to understand the origin of this interaction highlighting the following results:

*Groups: LAQ vs HAQ.*

No differences exist between LAQ and HAQ group.

*Interaction: synchrony vs Asynchrony.*

This comparison highlights whether there are differences in the ability to judge synchrony and asynchrony interaction: LAQ group was more accurate in judging interaction between mother and child with TD during synchrony interaction compared to asynchrony interaction (Mean: synchrony = 0.785 vs asynchrony = 0.594; p-value = .007). HAQ group were more accurate in judging interaction between mother and child with ASD during synchrony interaction compared to asynchrony interaction (mean: synchrony = 0.757, asynchrony = 0.605; p-value = .005).

*Diagnosis: ASD vs TD*

LAQ were more accurate in judging synchrony when TD child was involved in the interaction rather than ASD (TD mean = 0.787, ASD mean = 0.729; p-value =.036). On the contrary they showed no differences between ASD and TD in judging asynchrony. No differences between ASD and TD emerged in the HAQ group in judging either synchrony nor asynchrony.

### *4.2.2. Discussion*

The goal of this second study was to investigate whether BAP in not affected population might have an influence in judging a social interaction between mother and child. This has an implication for early intervention, which is crucially important in ASD treatment. A child, indeed, is not exclusively observed by his parent, it follows that the presence of autistic traits in the general population, especially in teachers and educators, might be an important factor to take into account as it might contribute to promote or hinder the detection of social difficulty in the child. Contrary to our hypothesis and in line with the previous study no differences between high and low AQ groups emerged in the results. However in this study as in the previous one, none of the participants exceeded the cut off of the AQ, therefore we might conclude that as long as concern population with not extreme manifestation of autistic phenotype, the presence of more or less autistic traits does not influence the way in which the quality of a social interaction is judged. Nonetheless within group differences emerged in both HAQ and LAQ group.

From this follow up emerged that understanding Asynchrony in social interaction, is more complex than understanding synchrony indeed both groups were more accurate in

Judging synchrony interactions. It is reasonable to think that synchronic behaviors and actions are easier to detect from external observers, however as we saw in the previous work other factors, such as defensive mechanism from parents of children with ASD, plays a role in the process affecting the way in which the interaction is perceived or consciously reported. Moreover understanding synchrony in social interaction with ASD is not straightforward because the child give often mixed signal making even for the expert eye of a clinician challenging to recognize synchrony in some kind of interaction (Bebko et al., 2006; Trevarthen & Daniel, 2005).

Said so, it is interesting to notice that in our sample, people with higher autistic traits (HAQ), even though they are accurate in recognizing synchrony in interaction with ASD, are less accurate in detecting asynchrony. Same pattern is found in people with lower autistic traits, which are more accurate in detecting synchrony than asynchrony in the interaction with TD.

This study presents several limitation as the sample include parents and non-parents female, however we accounted for this issues by controlling for preexisting differences between parents and non-parents in our task. Another limitation is that we divided the sample according with median of the AQ because none of our participants exceeded the cut-off. A more targeted sample would have helped to acquire more differences between groups and would have helped to reach more generalizable results.

Results from this study might indicate that in the general unaffected population, asynchrony might be more difficult to detect and more attention should be placed in teaching teachers and educators which constitute the signals of a successful and unsuccessful interaction. Another important factor that emerged from this study is a relationship between autistic traits of the observer and the diagnosis of the child showed

in the video, that is for the LAQ group was easier detecting synchrony in social interaction with TD while for HAQ was easier to detect synchrony in the interaction with ASD. This result suggests that there might be an attunement between people witch share the similar traits in understanding social interaction. In other words an observer which share similar autistic traits with an autistic child might actually be advantaged in understanding the quality of interaction between a child with ASD and his mother.

### *4.2.3. Conclusion*

Although the results from the previous studies are drown from different samples they highlight some similarities. Our initial hypothesis was that sharing similar autistic traits as a child with ASD might lead to similar social difficulties which might possibly prevent parents of children with ASD or individual with high level of BAP to promptly understand and detect signals of problems in social interaction. However the results of both studies disconfirm this hypothesis as no differences were found in accuracy between parents of children with ASD and TD, and because no group differences were found as well in HAQ and LAQ groups. Conversely results from the second study highlighted a possible facilitation which might lead the LAQ group to better understand interaction with TD and HAQ group to be more accurate in judging interaction with ASD. Accordingly we also found differences between parents of ASD and TD in judging interaction with TD: in either synchrony or asynchrony parents of ASD were less accurate than parents of TD. Therefore comparing parents of children with TD and ASD we saw that mother of children with ASD have more difficulty in interpreting interaction with TD children rather than children with ASD, this might be because their daily experiences or simply because they are more attuned with such kind of interaction that a child with ASD

holds with her mother.

### *4.2.4. Future directions*

In the first chapters of these thesis we focused on how complex constructs such as interpersonal relationship might be efficiently studied in terms of brain connectivity, in particular how differences in structural and functional connectivity are associated with differences in social skills, and parenting behavior. Also differences in perceiving and evaluating mother child interaction, that we addressed with the behavioral studies described in this chapter, might be as well investigated in terms of brain networks involved in this task. In particular it would be interesting to address similarities and differences in neural processing between mother of children with TD and mother of children with ASD.

Several neuroimaging investigations studied differences in neural processing in individuals with ASD and TD, mostly focusing in face perception (Greene et al., 2011; D. Kliemann, Dziobek, Hatri, Baudewig, & Heekeren, 2012; Dorit Kliemann, Dziobek, Hatri, Steimke, & Heekeren, 2010) and biological motion perception (Castelli et al., 2002; Koldewyn, Whitney, & Rivera, 2011). Those studies reported abnormal functioning in areas including amygdala, involved in emotional process, superior temporal sulcus (STS), associated with processing biological motion, fusiform gyrus, involved in face processing, (Maximo, Cadena, & Kana, 2014; Schipul, Keller, & Just, 2011). However, one emerging consideration that come from those neural investigations is that the abnormality in ASD, and its large variety of symptoms, might be due to a dysfunction in the coordination of different set of brain regions rather than the abnormal activity of any single brain areas (Schipul et al., 2011). For example social processing deficit in ASD has

been associated with abnormal connectivity between medial frontal regions and posterior areas, including temporo-parietal junction, superior temporal sulcus, and the fusiform gyrus, a network which might be involved in mentalization, processing of biological motion and face processing (Maximo et al., 2014; Schipul et al., 2011). Other studies found underconnectivity in ASD between amygdala and temporal frontal regions associated with face processing and between insula and other regions involved in emotional and sensory processing (Ebisch et al., 2011; Monk et al., 2010).

Alongside those evidence of atypical neural functioning in ASD, there are other studies that highlight similarities between the neural functioning in ASD and their not affected family member. Kaiser et al., (2010) compared the neural activation during observation of point light biological versus scrambled motion in three population: ASD, unaffected siblings (US) and typically developing children (TD). Interestingly the authors individuate a common pattern of activation between ASD and US in which brain regions showed decreased activation in ASD and US but not in TD. The regions were the bilateral fusiform gyrus, left dorsolateral prefrontal cortex, and right inferior temporal gyrus. According with the authors those region by reflecting shared areas of dysfunction in US and children with ASD provide a robust endophenotype for ASD (Kaiser et al., 2010). One important factor to consider when aiming to study the social processing in ASD is that most of the evidence came from study addressing face perception or social interaction using low level stimulation such as point light display or geometrical shapes. While those studies have an enormous value in isolating brain regions involved in the specific domain of interest, they lack of the ecological component of an actual interpersonal interaction which is the focus of our studies; for this reason in the next follow up we plan to use our ecological experimental stimulation which would reflect as much as possible in a fMRI environment the complexity of a social interaction observed

in the real life. Doing so we will be able to address similarities and differences in the neural processing of mother child interaction in parents of children with ASD and TD as well as in populations with and without autistic phenotype. Moreover we will continue to pursue our goal to couple inter-individual differences in brain connectivity with self-reported and behavioral measure in the study of mother child relationship which we started in the first two studies presented in Chapter 2.

# 5.General discussion

In the first part of the thesis, our goal was to investigate the association between brain connectivity and mother-child relationship as well as social skills of the adult individual. Results indicate that quality in mother-child relationship during infancy and social competences in adulthood are both associated with increased structural connectivity in WM tracts which are related with emotional cognition. These findings demonstrate an association between efficiency in brain connectivity and improved social and emotional cognition. According with several studies on personality this work demonstrate the feasibility to investigate complex construct such as attachment relationship, in an fMRI environment (Buchheim, George, Kächele, Erk, & Walter, 2006; Kanai & Rees, 2011) and corroborate one of the main assumption of the attachment theory that the quality of attachment affects the social domain of the individual throughout all the life span (Ainsworth, 1989; Bowlby, 1969).

In the second part of these thesis we focused on parenting and in particular on neural response of parents to infant stimuli. We performed two studies on neural response to infant cries, in the first study we were interested in addressing automatic motor response after presentation of infant cries. Results show an automatic audio-motor association in response only to infant stimulation presented after 100ms and only for woman. The gender difference found in the results indicate a predisposition for non-parents female to prepare parenting motor response. Moreover it accords with extensive literature highlighting different set of tools that non-parents adults, male and female have in absence of experience (Seifritz et al., 2003b; Swain, 2011). However, according with several studies changes in behavioural and neural level occurs once the mother and the

father acquire more experience in their role, balancing the existing predispositions typically found in study with non-parents samples (Seifritz et al., 2003a; Swain, 2011). Similar result has been found in the second study which investigated the parenting role under a complete different view. In this study, indeed, our goal was to study the neural activation and deactivation of attentive brain networks on response to baby cries when the participant was not attending for such stimulation. The rationale for this is that a person in a natural context is not continuously waiting for the infant stimulation as it happen in an experimental setting, more probably a caregiver is either immerse in his own thoughts or doing something. This work also highlights differences between man and woman. Indeed we found a strong deactivation of DMN in woman which suggest a shift of attention from self-referential thinking to the baby cry stimuli. In men we found instead a weaker deactivation of DMN while their attention was directed toward an external task and simultaneously a sudden woman crying sound is heard in the environment. This suggests that the woman cry induce in men self-relevant processing which can contribute to mentally understand others (De Pisapia et al., 2013). Such mechanism could be evolutionary advantageous as it indicates that men are more easily distracted from an ongoing activity when a sudden potential danger such as woman cry is present, and woman's attention is more easily grasped by baby cries which can easily suspend their internal mind wandering.

In the third part of the thesis we tested the accuracy of parents of children with autism and parents of children with typical development in recognizing the quality in mother-child relationship. The goal was to understand whether those two parent groups vary in the ability to detect cues of social abnormalities. Our hypothesis takes the roots from the evidence that family member of individual with autism might present some autistic traits as well and therefore they might show some difficulties in understanding

social interaction. However, from the results emerge that parents of children with ASD are as accurate as parents of children with TD in recognizing quality in the interaction with ASD. Nonetheless parents of children with ASD shows more difficulty in judging the interaction with TD, in particular in judging asynchrony which they often mistaken for synchrony. This suggests that when watching a social interaction with TD, parents of children with ASD could interpret as positive, an interactions that it actually is not positive. This is a potentially critical situation because the child could still have some autistic traits or shows social difficulties which would be underestimated. Moreover in a further study we tested, with the same design, the influence of BAP in the normal population. We did so by comparing population with high autistic traits (HAQ) and population with low autistic traits (LAQ). We didn't find differences between those two groups, however it should be taken into account that even though the HAQ group had higher autistic quotients compared to the LAQ group, no participants exceeded the threshold of the AQ questionnaires. Therefore we can conclude that the presence of several autistic traits but not enough to be considered over threshold does not affect the accuracy in judging social interaction in non-affected population. Other important indication that comes from this study are that for both groups asynchrony was more difficult to understand than synchrony and that people with less autistic traits are facilitate in understanding synchrony interactions with TD while people with high autistic traits are facilitate in understanding synchrony in interaction with ASD. This is an important result which disconfirms our initial hypothesis that sharing autistic phenotype with an individual with autism might decrease the chance to detect cue of inappropriate social behaviors. Indeed LAQ group had same difficulty as HAQ group in judging asynchrony interaction, instead when judging synchrony seems that an attunement between observer and the child characteristic might help to efficiently detect cue of successful social

exchange. This results partly accords with the results drawn from the comparison between parent of TD and ASD. Taking together those two studies highlight the abilities of parents of children with ASD and individual with high autistic traits to efficiently understand the quality of the interaction with ASD however they pose question marks on their ability to correctly judge interaction with typically developed children, especially during asynchrony interaction.

# 6. Limitation and future directions

The works included in this thesis present some limitations which will be discussed in this section. Afterwards suggestions for future direction will be provided.

The results drown from the first two works (Chapter 2) came from correlational studies therefore no causal relationship can be drown from them. In other words we cannot say which factor came first, if better connectivity promotes the development of secure relationship with the mother and higher interpersonal competence and or vice versa, if people with higher social skills which experienced a secure maternal relationship developed higher WM integrity as a consequence. This which point out the need of longitudinal studies to better understand the causal relationship from mother-child relationship and brain development.

The second part of the thesis (Chapter 3) presents several limitations: in particular in both studies the small sample size is at the lower limit for between-subjects investigations of sex differences, nonetheless the results found on gender differences are in line with existent literature (De Pisapia et al., 2013; Rigo et al., n.d.; Swain & Lorberbaum, 2008). Moreover we have no information about our participant's previous experience with children caring however we ruled out the possibility that some of participants were professionally exposed to young children (kindergarten educators, teachers, professional baby-sitters). Also a cultural aspect could possibly influence the results as typically women are more involved in direct child care than men. Similarly, we have no information on other important variables such as mood, empathy, or menstrual phase which could possibly have an influence in the neural response to baby cry, future

studies are needed to address these issues. Another limitation specific for the work of Messina et al (in submission) presented in Chapter 3, regards the behavioral characterization of the reflex response. Since we recorded from only two muscles, the results cannot be generalized to a whole-body motor pattern. Although we are inclined to interpret the MEPs as generated by protective behaviors towards an infant in distress, they could actually index any other (even aggressive) behavior. Further research is needed to clarify this issue recording by recording from different muscles implicated in aggressive versus protective behavior.

Limitation from the last two behavioral studies (Chapter 4) include the limited sample size in the sample of parents of children with ASD. However as we are dealing with a clinic population such restrictions constitute often a limitation, therefore we accounted for it using appropriate non-parametric statistic. Another limitation is that the limited participation of father on the study has prevented investigations on gender difference which however could be addressed in future direction. In future words, in order to pursue the goal of coupling neuroimaging investigation with behavioral outcomes, it would be important to address differences in the neural processing of parents of children with TD and ASD during perception of social interaction between mother and child. This study would also help to understand whether there are different neutral mechanism which those two parent groups bring into act to compensate for different personal characteristic and level experiences with such interactions.

# 7. Conclusions

In conclusion this thesis constitutes an important step toward the understanding of neural processes implicated in mother-child relationship. We addressed this topic investigating key factors such as the association between quality of attachment relationship, social competences and inter-individual differences in brain structures. Doing so we supported with neuroimaging techniques the assumptions of attachment theory and we highlighted the importance of a secure relationship with the mother not only for mental health and future social skills but for neural development as well.

In addition we addressed the critical issue of parenting neural responses to baby cries finding gender differences in both neural and motor response. These results highlights the importance that both parents play in the familiar environments and the peculiarity of their different role. Moreover investigating adults' reactions to infant needs help to explicate processes that regulate the quality of the adult-infant interactions which can be used to promote positive and sensitive caregiving experiences.

Finally, we investigated the abilities to detect cues of abnormal social behaviors during observation of social interaction in population related with children with ASD or in population which present several autistic traits. The contribute of this study is crucial in order to promote early diagnosis of autism. It is extremely important, indeed, to understand which mechanisms play a role in detecting synchrony and asynchrony during observation of social interaction. Our results shows that parents of children with autism does not present difficulties in judging interaction involving children with ASD however they present difficulties in judging interaction involving children with typical

development. This difficulties could prevent parents which already have experience with a child with ASD from having an objective perspective while evaluating the social interaction with a child with TD and more importantly could prevent them from detecting social deficit in children which does not present severe impairment but could be at risk or at lower limit for a diagnosis.

In conclusion, this thesis through neural and behavioral investigation of several aspects of parenting, including detection of infant signals and quality in mother-child interactions, sets important step stones toward the understanding of dynamics involved in parenting and mother-child relationship considering its neural aspect in particular brain connectivity.

# 8.References


Abbott, J. D., Cumming, G., Fidler, F., & Lindell, A. K. (2013). The perception of positive and negative facial expressions in unilateral brain-damaged patients: A meta-analysis. *Laterality*, *18*(4), 437–59.

Adolphs, R. (2001). The neurobiology of social cognition. *Current Opinion in Neurobiology*, *11*(2), 231–9.

Ainsworth, M. D. (1982). Attachment: Retrospect and prospect. In C. M. Parkes & J. Stevenson-Hinde (TCis.) (Ed.), *place of attachment in human behavior* (pp. 3–30). New York: Basic Books.

Ainsworth, M. D. (1989). Attachments beyond infancy. *The American Psychologist*, *44*(4), 709–716.

Ameis, S. H., Fan, J., Rockel, C., Voineskos, A. N., Lobaugh, N. J., Soorya, L., … Anagnostou, E. (2011). Impaired structural connectivity of socio-emotional circuits in autism spectrum disorders: A diffusion tensor imaging study. *PLoS ONE*, *6*(11).

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders* (5th ed). Arlington, VA: American Psychiatric Publishing.

Anders, S. L., & Tucker, J. S. (2000). Adult attachment style, interpersonal communication competence, and social support. *Personal Relationships*, *7*(4), 379–389.

Andersson, J. L., Jenkinson, M., & Smith, S. (2007a). Non-linear optimisation FMRIB Technial Report TR07JA1.

Andersson, J. L., Jenkinson, M., & Smith, S. (2007b). Non-linear registration aka Spatial normalisation FMRIB Technial Report TR07JA2.

Angelini, L., Mazzucchi, A., Picciotto, F., Nardocci, N., & Broggi, G. (1981). Focal lesion of the right cingulum: a case report in a child. *Journal of Neurology, Neurosurgery, and Psychiatry*, *44*(4), 355–357.

Aoki, Y., Abe, O., Nippashi, Y., & Yamasue, H. (2013). Comparison of white matter integrity between autism spectrum disorder subjects and typically developing individuals: a meta-analysis of diffusion tensor imaging tractography studies. *Molecular Autism*, *4*(1), 25.

Bakermans-Kranenburg, M. J., van IJzendoorn, M. H., Riem, M. M. E., Tops, M., & Alink, L. R. A. (2012). Oxytocin decreases handgrip force in reaction to infant crying in females without harsh parenting experiences. *Social Cognitive and Affective Neuroscience*, *7*(8), 951–957.

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., & Clubley, E. (2001). The autism-spectrum quotient (AQ): evidence from Asperger syndrome/high-functioning autism, males and females, scientists and mathematicians. *Journal of Autism and Developmental Disorders*, *31*(1), 5–17.

Bartels-Tobin, L. R., & Hinckley, J. J. (2005). Cognition and discourse production in right hemisphere disorder. *Journal of Neurolinguistics*, *18*(6), 461–477.

Beaulieu, C. (2002). The basis of anisotropic water diffusion in the nervous system - a technical review. *NMR in Biomedicine*, *15*(7-8), 435–455.

Bebko, J. M., Weiss, J. a., Demark, J. L., & Gomez, P. (2006). Discrimination of temporal synchrony in intermodal events by children with autism and children with developmental disabilities without autism. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *47*(1), 88–98.

Benedetti, F., Bollettini, I., Radaelli, D., Poletti, S., Locatelli, C., Falini, A., … Colombo, C. (2014). Adverse childhood experiences influence white matter microstructure in patients with bipolar disorder. *Psychological Medicine*, 1–14.

Benetti, S., McCrory, E., Arulanantham, S., De Sanctis, T., McGuire, P., & Mechelli, A. (2010). Attachment style, affective loss and gray matter volume: A voxel-based morphometry study. *Human Brain Mapping*, *31*(10), 1482–1489.

Bolton, P., Macdonald, H., Pickles, A., Rios, P., Goode, S., Crowson, M., … Rutter, M. (1994). A case-control family history study of autism. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *35*(5), 877–900.

Boorman, E. D., O'Shea, J., Sebastian, C., Rushworth, M. F. S., & Johansen-Berg, H. (2007). Individual Differences in White-Matter Microstructure Reflect Variation in Functional Connectivity during Choice. *Current Biology*, *17*(16), 1426–1431.

Bornstein, M. H. (2013). Mother-infant attunement: A multilevel approach via body, brain, and behavior. (A. Ackermann Adamson, Ainsworth, Ainsworth, Alarlo, Alvergne, Anderson, Archer, Arsalidou, Bakeman, Bales, Barnard, Barrett, Bartels, Bartels, Beebe, Beeghly, Bigelow, Birch, Biringen, Booth, Bornstein, Ed.)*The Infant Mind: Origins of the Social Brain.* Guilford Press.

Bornstein, M. H. (2014). Human Infancy ... and the Rest of the Lifespan. In S. Fiske (Ed.), *annual review of psychology, vol 65* (Vol. 65, pp. 121–158). ANNUAL REVIEWS.

Boukydis, C. F., & Burgess, R. L. (1982). Adult physiological response to infant cries: effects of temperament of infant, parental status, and gender. *Child Development*, *53*(5), 1291–1298.

Bowlby, J. (1969). *Attachment and Loss.* New York: Basic Book.

Brackett, M. A., Rivers, S. E., Shiffman, S., Lerner, N., & Salovey, P. (2006). Relating emotional abilities to social functioning: a comparison of self-report and performance measures of emotional intelligence. *Journal of Personality and Social Psychology*, *91*(4), 780–95.

Breitenstein, C., Daum, I., & Ackermann, H. (1998). Emotional processing following cortical and subcortical brain damage: contribution of the fronto-striatal circuitry. *Behavioural Neurology*, *11*(1), 29–42.

Bretherton, I., & A Munholland, K. (1999). *Internal working models in attachment relationships: A construct revisited.* (J. A. Cassidy & P. R. Shaver, Ed.)*Handbook of attachment Theory research and clinical applications*. New York: Guilford Press.

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

Brüne, M., Nadolny, N., Güntürkün, O., & Wolf, O. T. (2012). Stress induces a functional asymmetry in an emotional attention task. *Cognition & Emotion*.

Buchheim, A., George, C., Kächele, H., Erk, S., & Walter, H. (2006). Measuring adult attachment representation in an fMRI environment: Concepts and assessment. *Psychopathology*, *39*(3), 136–143.

Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2007). The brain's default network: Anatomy,function, and relevance to disease. *Annals Of The New York Academy Of Sciences*, *1124*(section III), 1–42.

Buhrmester, D. (1990). Intimacy of friendship, interpersonal competence, and adjustment during preadolescence and adolescence. *Child Development*, *61*(4), 1101–11.

Burgess, N., Maguire, E. A., Spiers, H. J., & O'Keefe, J. (2001). A temporoparietal and prefrontal network for retrieving the spatial context of lifelike events. *NeuroImage*, *14*(2), 439–453.

Castelli, F., Frith, C., Happé, F., & Frith, U. (2002). Autism, Asperger syndrome and brain mechanisms for the attribution of mental states to animated shapes. *Brain : A Journal of Neurology*, *125*(Pt 8), 1839–1849.

Catani, M., Howard, R. J., Pajevic, S., & Jones, D. K. (2002). Virtual in Vivo Interactive Dissection of White Matter Fasciculi in the Human Brain. *NeuroImage*, *17*(1), 77–94.

Cattaneo, L., & Rizzolatti, G. (2009). The mirror neuron system. *Archives of Neurology*.

Chapple, E. D. (1970). Experimental production of transients in human interaction. *Nature*, *228*(5272), 630–633.

Charlton, R. a, Barrick, T. R., McIntyre, D. J., Shen, Y., O'Sullivan, M., Howe, F. a, … Markus, H. S. (2006). White matter damage on diffusion tensor imaging correlates with age-related cognitive decline. *Neurology*, *66*(2), 217–22.

Cheung, C., Chua, S. E., Cheung, V., Khong, P. L., Tai, K. S., Wong, T. K. W., … McAlonan, G. M. (2009). White matter fractional anisotrophy differences and correlates of diagnostic symptoms in autism. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *50*, 1102–1112.

Chow, C. M., Ruhl, H., & Buhrmester, D. (2013). The mediating role of interpersonal competence between adolescents' empathy and friendship quality: A dyadic approach. *Journal of Adolescence*, *36*(1), 191–200.

Collignon, O., Dormal, G., Albouy, G., Vandewalle, G., Voss, P., Phillips, C., & Lepore, F. (2013). Impact of blindness onset on the functional organization and the connectivity of the occipital cortex. *Brain*, *136*(9), 2769–2783.

Collins, W. A., & van Dulmen, M. (n.d.). "The Course of True Love(s)...": Origins and Pathways in the Development of Romantic Relationships.

Constantino, J. N., & Todd, R. D. (2003). Autistic traits in the general population: a twin study. *Archives of General Psychiatry*, *60*(5), 524–530.

Daley, S. E., & Hammen, C. (2002). Depressive symptoms and close relationships during the transition to adulthood: perspectives from dysphoric women, their best friends, and their romantic partners. *Journal of Consulting and Clinical Psychology*, *70*(1), 129–141.

Dawson, G., Webb, S., Schellenberg, G. D., Dager, S., Friedman, S., Aylward, E., & Richards, T. (2002). Defining the broader phenotype of autism: genetic, brain, and behavioral perspectives. *Development and Psychopathology*, *14*(3), 581–611.

De Pisapia, N., Bornstein, M. H., Rigo, P., Esposito, G., De Falco, S., & Venuti, P. (2013). Sex differences in directional brain responses to infant hunger cries. *Neuroreport*, *24*(3), 142–6. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3618419&tool=pmcentrez&rendertype=abstract

De Pisapia, N., Serra, M., Rigo, P., Jager, J., Papinutto, N., Esposito, G., … Bornstein, M. H. (2014). Interpersonal competence in young adulthood and right laterality in white matter. *Journal of Cognitive Neuroscience*, *26*(6), 1257–65.

de Wied, M., Branje, S. J. T., & Meeus, W. H. J. (2007). Empathy and Conflict Resolution in Friendship Relations Among Adolescents. *Aggressive Behavior*, *33*(2007), 48–55.

Deary, I. J., Bastin, M. E., Pattie, A., Clayden, J. D., Whalley, L. J., Starr, J. M., & Wardlaw, J. M. (2006). White matter integrity and cognition in childhood and old age. *Neurology*, *66*(4), 505–512.

Decety, J., & Lamm, C. (2007). The role of the right temporoparietal junction in social interaction: how low-level computational processes contribute to meta-cognition. *The Neuroscientist : A Review Journal Bringing Neurobiology, Neurology and Psychiatry*, *13*(6), 580–93.

Delahunty, K. M., McKay, D. W., Noseworthy, D. E., & Storey, A. E. (2007). Prolactin responses to infant cues in men and women: Effects of parental experience and recent infant contact. *Hormones and Behavior*, *51*(2), 213–220.

Devinsky, O. (2000). Right Cerebral Hemisphere Dominance for a Sense of Corporeal and Emotional Self. *Epilepsy & Behavior*, *1*(1), 60–73.

Di, X., & Biswal, B. B. (2014). Modulatory interactions between the default mode network and task positive networks in resting-state. *PeerJ*, *2*, e367.

Ebisch, S. J. H., Gallese, V., Willems, R. M., Mantini, D., Groen, W. B., Romani, G. L., … Bekkering, H. (2011). Altered intrinsic functional connectivity of anterior and posterior insula regions in high-functioning participants with autism spectrum disorder. *Human Brain Mapping*, *32*(7), 1013–1028.

Esposito, G., Valenzi, S., Islam, T., & Bornstein, M. H. (2015). Three physiological responses in fathers and non-fathers' to vocalizations of typically developing infants and infants with Autism Spectrum Disorder. *Research in Developmental Disabilities*, *43-44*, 43–50.

Esposito, G., Venuti, P., De Falco, S., & Bornstein, M. H. (2009). "Maternal emotional availability and infant smiling and crying at 5 months of age." In T. M. D. P. H. Krause (Ed.), *Handbook of parenting: styles, stresses, and strategies* (pp. 30–46). New York: Nova Science.

Fitzgerald, S. T., Brown, K. M., Sonnega, J. R., & Ewart, C. K. (2005). Early antecedents of adult work stress: Social-emotional competence and anger in adolescence. *Journal of Behavioral Medicine*, *28*(3), 223–230.

Fleming, A. S., Corter, C., Stallings, J., & Steiner, M. (2002). *Testosterone and prolactin are associated with emotional responses to infant cries in new fathers. Hormones and behavior* (Vol. 42).

Fournier, N. M., Calverley, K. L., Wagner, J. P., Poock, J. L., & Crossley, M. (2008). Impaired social cognition 30 years after hemispherectomy for intractable epilepsy: the importance of the right hemisphere in complex social functioning. *Epilepsy & Behavior : E&B*, *12*(3), 460–71.

Fox, M. D., & Raichle, M. E. (2007). Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. *Nature Reviews. Neuroscience*, *8*(9), 700–711.

Frith, C. D., & Frith, U. (2012). Mechanisms of Social Cognition. *Annual Review of Psychology*, *63*(1), 287–313.

Frodi, A. M., & et al. (1978). Fathers' and mothers' responses to the faces and cries of normal and premature infants. *Developmental Psychology*.

Frodi, A. M., Lamb, M. E., & Wille, D. (1981). Mothers' responses to the cries of normal and premature infants as a function of the birth status of their own child. *Journal of Research in Personality*.

Gilboa, A., Winocur, G., Grady, C. L., Hevenor, S. J., & Moscovitch, M. (2004). Remembering our past: Functional neuroanatomy of recollection of recent and very remote personal events. *Cerebral Cortex*, *14*(11), 1214–1225.

Govindan, R. M., Behen, M. E., Helder, E., Makki, M. I., & Chugani, H. T. (2010). Altered Water Diffusivity in Cortical Association Tracts in Children with Early Deprivation Identified with Tract-Based Spatial Statistics (TBSS). *Cerebral Cortex*, (20), 561–569.

Govindan, R. M., Behen, M. E., Helder, E., Makki, M. I., & Chugani, H. T. (2010). Altered water diffusivity in cortical association tracts in children with early deprivation identified with tract-based spatial statistics (TBSS). *Cerebral Cortex*, *20*(3), 561–569.

Greene, D. J., Colich, N., Iacoboni, M., Zaidel, E., Bookheimer, S. Y., & Dapretto, M. (2011). Atypical neural networks for social orienting in autism spectrum disorders. *NeuroImage*, *56*(1), 354–362.

Gunter, H. L., Ghaziuddin, M., & Ellis, H. D. (2002). Asperger Syndrome: Tests of Right Hemisphere Functioning and Interhemispheric Communication. *Journal of Autism and Developmental Disorders*, *32*(4), 263–281.

Gustafson, G. E., & Harris, K. L. (1990). Women's responses to young infants' cries. *Developmental Psychology*.

Hagemann, D., Hewig, J., Naumann, E., Seifert, J., & Bartussek, D. (2005). Resting Brain Asymmetry and Affective Reactivity. *Journal of Individual Differences*.

Happé, F., Brownell, H., & Winner, E. (1999). Acquired "theory of mind" impairments following stroke. *Cognition*, *70*(3), 211–40.

Harter, S. (1982). The Perceived Competence Scale for Children. *Child Development*, *53*(1), 87–97.

Hasan, K. M., Iftikhar, A., Kamali, A., Kramer, L. A., Ashtari, M., Cirino, P. T., … Ewing-Cobbs, L. (2009). Development and aging of the healthy human brain uncinate fasciculus across the lifespan using diffusion tensor tractography. *Brain Research*, *1276*, 67–76.

Heberlein, A. S., Adolphs, R., Pennebaker, J. W., & Tranel, D. (2003). Effects of Damage to Right-Hemisphere Brain Structures on Spontaneous Emotional and Social Judgments. *Political Psychology*, *24*(4), 705–726.

Helmeke, C., Ovtscharoff, W., Poeggel, G., & Braun, K. (2001). Juvenile emotional experience alters synaptic inputs on pyramidal neurons in the anterior cingulate cortex. *Cerebral Cortex (New York, N.Y. : 1991)*, *11*(8), 717–27.

Hua, K., Zhang, J., Wakana, S., Jiang, H., Li, X., Reich, D. S., … Mori, S. (2008). Tract probability maps in stereotaxic spaces: Analyses of white matter anatomy and tract-specific quantification. *NeuroImage*, *39*(1), 336–347.

Iacoboni, M., & Dapretto, M. (2006). The mirror neuron system and the consequences of its dysfunction. *Nat Rev Neurosci*, *7*, 942–951.

Jackson, P. L., Brunet, E., Meltzoff, A. N., & Decety, J. (2006). Empathy examined through the neural mechanisms involved in imagining how I feel versus how you feel pain. *Neuropsychologia*, *44*(5), 752–761.

Jones, D. K. (2004). The effect of gradient sampling schemes on measures derived from diffusion tensor MRI: a Monte Carlo study. *Magnetic Resonance in Medicine : Official Journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine*, *51*(4), 807–815.

Jones, D. K., Horsfield, M. A., & Simmons, A. (1999). Optimal strategies for measuring diffusion in anisotropic systems by magnetic resonance imaging. *Magnetic Resonance in Medicine : Official Journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine*, *42*(3), 515–525.

Kaiser, M. D., Hudac, C. M., Shultz, S., Lee, S. M., Cheung, C., Berken, A. M., … Pelphrey, K. A. (2010). Neural signatures of autism. *Proceedings of the National Academy of Sciences of the United States of America*, *107*(49), 21223–21228.

Kanai, R., & Rees, G. (2011). The structural basis of inter-individual differences in human behaviour and cognition. *Nature Reviews. Neuroscience*, *12*(4), 231–242.

Kerns, K. a., Klepac, L., & Cole, A. (1996). Peer relationships and preadolescents' perceptions of security in the child-mother relationship. *Developmental Psychology*, *32*(3), 457–466.

Kliemann, D., Dziobek, I., Hatri, A., Baudewig, J., & Heekeren, H. R. (2012). The Role of the Amygdala in Atypical Gaze on Emotional Faces in Autism Spectrum Disorders. *Journal of Neuroscience*.

Kliemann, D., Dziobek, I., Hatri, A., Steimke, R., & Heekeren, H. R. (2010). Atypical reflexive gaze patterns on emotional faces in autism spectrum disorders. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *30*(37), 12281–12287.

Kline, R. B. (2011). *Principles and practice of structural equation modeling*. (T. D. Little & D. A. Kenny, Eds.)*Structural Equation Modeling* (Vol. 156). Guilford Press.

Koldewyn, K., Whitney, D., & Rivera, S. M. (2011). Neural correlates of coherent and biological motion perception in autism. *Developmental Science*, *14*(5), 1075–1088.

Kully-Martens, K., Denys, K., Treit, S., Tamana, S., & Rasmussen, C. (2012). A Review of Social Skills Deficits in Individuals with Fetal Alcohol Spectrum Disorders and Prenatal Alcohol Exposure: Profiles, Mechanisms, and Interventions. *Alcoholism: Clinical and Experimental Research*, *36*(4), 568–576.

Ladd, G. W. (1999). Peer relationships and social competence during early and middle childhood. *Annual Review of Psychology*, *50*, 333–359.

Lebel, C., & Beaulieu, C. (2011). Longitudinal development of human brain wiring continues from childhood into adulthood. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *31*(30), 10937–10947.

Lebel, C., Walker, L., Leemans, A., Phillips, L., & Beaulieu, C. (2008). Microstructural maturation of the human brain from childhood to adulthood. *NeuroImage*, *40*(3), 1044–1055.

Likert, R. (1932). A technique for the measurement of attitudes. *Archives of Psychology*, *22*(140), 1–55.

Lombardo, M. V, Chakrabarti, B., Bullmore, E. T., & Baron-Cohen, S. (2011). Specialization of right temporo-parietal junction for mentalizing and its relation to social impairments in autism. *NeuroImage*, *56*(3), 1832–8.

Lopes, P. N., Brackett, M. a, Nezlek, J. B., Schütz, A., Sellin, I., & Salovey, P. (2004). Emotional intelligence and social interaction. *Personality and Social Psychology Bulletin*, *30*(8), 1018–1034.

Lorenz, K. (1952). *King Solomon's Ring*. New York: Crowell.

Loui, P., Li, H. C. C., Hohmann, A., & Schlaug, G. (2011). Enhanced Cortical Connectivity in Absolute Pitch Musicians: A Model for Local Hyperconnectivity. *Journal of Cognitive Neuroscience*, *23*(4), 1015–1026.

Maggs, J. L., Jager, J., Patrick, M. E., & Schulenberg, J. (2012). Social role patterning in early adulthood in the USA: adolescent predictors and concurrent wellbeing across four distinct configurations. *Longitudinal and Life Course Studies*, *3*(2), 190–210.

Maguire, E. A. (2001). Neuroimaging studies of autobiographical event memory. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *356*(1413), 1441–1451.

Mahoney, J. L., Cairns, B. D., & Farmer, T. W. (2003). Promoting interpersonal competence and educational success through extracurricular activity participation. *Journal of Educational Psychology*, *95*(2), 409–418.

Main, M., Kaplan, N., & Cassidy, J. (1985). Security in infancy; childhood, and adulthood: A move to the level of representation. Monographs of the Society for Research in Child Development, *50*(1-2), 66–104.

Maximo, J. O., Cadena, E. J., & Kana, R. K. (2014). The implications of brain connectivity in the neuropsychology of autism. *Neuropsychology Review*, *24*(1), 16–31.

McKelvey, J. R., Lambert, R., Mottron, L., & Shevell, M. I. (1995). Right-hemisphere dysfunction in Asperger's syndrome. *Journal of Child Neurology*, *10*(4), 310–314.

McKelvie, S. J. (1987). Sex Differences, Lateral Reversal, and Pose as Factors in Recognition Memory for Photographs of Faces. *The Journal of General Psychology*, *114*(1), 13–37.

Messina, I., Cattaneo, L., De Pisapia, N., Serra, M., Farneti, A., Rigo, P., … Bornstein, H, M. (n.d.). specific automatic responses to infant cries: TMS reveals greater excitability in females than males in motor evoked potentials. *Frontiers in Psychology*.

Metzler-Baddeley, C., Jones, D., Steventon, J., Westacott, L., Aggleton, J. P., & O'Sullivan, M. J. (2012). Cingulum microstructure predicts cognitive control in older age and mild cognitive impairment. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *32*(49), 17612–9.

Molesworth, T., Sheu, L., Cohen, S., Gianaros, P., & Verstynen, T. (2014). Social network diversity predicts white matter microstructural integrity in humans. *Psychosomatic Medicine*, *76*(3), A–9.

Monk, C. S., Weng, S.-J., Wiggins, J. L., Kurapati, N., Louro, H. M. C., Carrasco, M., … Lord, C. (2010). Neural circuitry of emotional face processing in autism spectrum disorders. *Journal of Psychiatry & Neuroscience : JPN*, *35*(2), 105–114.

Montoya, J. L., Landi, N., Kober, H., Worhunsky, P. D., Rutherford, H. V, Mencl, W. E. i, … Potenza, M. N. (2012). Regional brain responses in nulliparous women to emotional infant stimuli. *PLoS ONE*, *7*(5).

Mori, S., Oishi, K., Jiang, H., Jiang, L., Li, X., Akhter, K., … Mazziotta, J. (2008). Stereotaxic white matter atlas based on diffusion tensor imaging in an ICBM template. *NeuroImage*, *40*(2), 570–582.

Muthén, L., & Muthén, B. (2009). *Mplus user's guide (version 7.0)*. *Los Angeles: Author*. Muthén and Muthén.

Papinutto, N., & Jovicich J. (2008). Optimization of brain tissue contrast in structural images at 4T: a computer simulation and validation study. In *Procdgs ESMRMB, 25th Annual Mtg 17.*

Park, H.-J., Kim, J. J., Lee, S.-K., Seok, J. H., Chun, J., Kim, D. I., & Lee, J. D. (2008). Corpus callosal connection mapping using cortical gray matter parcellation and DT-MRI. *Human Brain Mapping*, *29*(5), 503–16.

Parker, J. D. a, Summerfeldt, L. J., Hogan, M. J., & Majeski, S. a. (2004). Emotional intelligence and academic success: Examining the transition from high school to university. *Personality and Individual Differences*, *36*(1), 163–172.

Parkinson, C., & Wheatley, T. (2014). Relating anatomical and social connectivity: White matter microstructure predicts emotional empathy. *Cerebral Cortex*, *24*(3), 614–625.

Parsons, C. E., Young, K. S., Parsons, E., Stein, A., & Kringelbach, M. L. (2012). Listening to infant distress vocalizations enhances effortful motor performance. *Acta Paediatrica, International Journal of Paediatrics*, *101*(4).

Pascual-Leone, a, Walsh, V., & Rothwell, J. (2000). Transcranial magnetic stimulation in cognitive neuroscience--virtual lesion, chronometry, and functional connectivity. *Current Opinion in Neurobiology*, *10*(2), 232–7.

Pascual-Leone, A., Amedi, A., Fregni, F., & Merabet, L. B. (2005). The plastic human brain cortex. *Annual Review of Neuroscience*, *28*, 377–401.

Phelps, L. a., & Hanley-Maxwell, C. (1997). School-to-Work Transitions for Youth With Disabilities: A Review of Outcomes and Practices. *Review of Educational Research*, *67*(2), 197–226.

Philippi, C. L., Mehta, S., Grabowski, T., Adolphs, R., & Rudrauf, D. (2009). Damage to association fiber tracts impairs recognition of the facial expression of emotion. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *29*(48), 15089–99.

Pierpaoli, C., & Basser, P. J. (1996). Toward a quantitative assessment of diffusion anisotropy. *Magn Reson Med*, *36*(6), 893–906.

Piven, J., Palmer, P., Jacobi, D., Childress, D., & Arndt, S. (1997). Broader autism phenotype: evidence from a family history study of multiple-incidence autism families. *The American Journal of Psychiatry*, *154*(2), 185–190.

Porges, S. W., & Furman, S. A. (2011). The early development of the autonomic nervous system provides a neural platform for social behaviour: A polyvagal perspective. *Infant and Child Development*, *20*(1), 106–118.

Querleu, D., Lefebvre, C., Titran, M., Renard, X., Morillion, M., & Crepin, G. (1984). Reaction of the newborn infant less than 2 hours after birth to the maternal voice. *Journal de Gynécologie, Obstétrique et Biologie de La Reproduction*, *13*(2), 125–134.

Raichle, M. E., & Snyder, A. Z. (2007). A default mode of brain function: A brief history of an evolving idea. *NeuroImage*, *37*(4), 1083–1090.

Rankin, K. P., Gorno-Tempini, M. L., Allison, S. C., Stanley, C. M., Glenn, S., Weiner, M. W., & Miller, B. L. (2006). Structural anatomy of empathy in neurodegenerative disease. *Brain : A Journal of Neurology*, *129*(Pt 11), 2945–56.

Reese, T. G., Heid, O., Weisskoff, R. M., & Wedeen, V. J. (2003). Reduction of eddy-current-induced distortion in diffusion MRI using a twice-refocused spin echo. *Magnetic Resonance in Medicine : Official Journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine*, *49*(1), 177–182.

Rigo, P., De Pisapia, N., Bornstein, M. H., Putnick, D. L., Serra, M., Esposito, G., & Venuti, P. (n.d.). Neurocognitive processes in women and men to emotive sounds. *Social Neuroscience*.

Rigon, A., Duff, M. C., & Voss, M. W. (2015). Structural and functional neural correlates of self-reported attachment in healthy adults: evidence for an amygdalar involvement. *Brain Imaging and Behavior*.

Robson, M. D., & Porter, D. A. (2005). Reconstruction as a source of artifact in non-gated single-shot diffusion-weighted EPI. *Magnetic Resonance Imaging*, *23*(9), 899–905.

Schipul, S. E., Keller, T. A., & Just, M. A. (2011). Inter-regional brain communication and its disturbance in autism. *Frontiers in Systems Neuroscience*, *5*, 10.

Schmithorst, V. J., Wilke, M., Dardzinski, B. J., & Holland, S. K. (2002). Correlation of white matter diffusivity and anisotropy with age during childhood and adolescence: a cross-sectional diffusion-tensor MR imaging study. *Radiology*, *222*(1), 212—8.

Schneewind, K. A., & Gerhard, A.-K. (2002). Relationship Personality, Conflict Resolution, and Marital Satisfaction in the First 5 Years of Marriage. *Family Relations*, *51*(1), 63–71.

Schneider, W., Eschman, A., & Zuccolotto, A. (2007). E-Prime 2. New Features Guide.

Scholz, J., Klein, M. C., Behrens, T. E. J., & Johansen-Berg, H. (2009). Training induces changes in white-matter architecture. *Nature Neuroscience*, *12*(11), 1370–1.

Schore, A. N. (1994). *Affect Regulation and the Origin of the Self: The Neurobiology of Emotional Development*. Lawrence Erlbaum Associates.

Schore, A. N. (1997). Early organization of the nonlinear right brain and development of a predisposition to psychiatric disorders. *Development and Psychopathology*, *9*(4), 595–631.

Schore, A. N. (2000). Attachment and the regulation of the right brain. *Attachment & Human Development*, *2*(1), 23–47.

Schore, A. N. (2001). Effect of a Secure Attachment Relationship on Right Brain Development, Affect Regulation, and Infant Menta Health. *Infant Mental Health Journal*, *22*(818), 7–66.

Schore, A. N. (2009). The Paradigm Shift: The Right Brain and the Relational Unconscious. In *American Psychological Association 2009 Convention*. Toronto, Canada.

Seifritz, E., Esposito, F., Neuhoff, J. G., Lüthi, A., Mustovic, H., Dammann, G., … Di Salle, F. (2003a). Differential sex-independent amygdala response to infant crying and laughing in parents versus nonparents. *Biological Psychiatry*, *54*(12), 1367–1375.

Seifritz, E., Esposito, F., Neuhoff, J. G., Lüthi, A., Mustovic, H., Dammann, G., … Di Salle, F. (2003b). Differential sex-independent amygdala response to infant crying and laughing in parents versus nonparents. *Biological Psychiatry*, *54*(12), 1367–75.

Semrud-Clikeman, M., Goldenring Fine, J., & Zhu, D. C. (2011). The role of the right hemisphere for processing of social interactions in normal adults using functional magnetic resonance imaging. *Neuropsychobiology*, *64*(1), 47–51.

Shamay-Tsoory, S. G., Tomer, R., & Aharon-Peretz, J. (2005). The neuroanatomical basis of understanding sarcasm and its relationship to social cognition. *Neuropsychology*, *19*(3), 288–300.

Shanahan, M. J. (2000). Pathways to Adulthood in Changing Societies: Variability and Mechanisms in Life Course Perspective. *Annual Review of Sociology*, *26*(1), 667–692.

Shobe, E. R. (2014). Independent and collaborative contributions of the cerebral hemispheres to emotional processing. *Frontiers in Human Neuroscience*, *8*, 230.

Smith, S. M. (2002). Fast robust automated brain extraction. *Human Brain Mapping*, *17*(3), 143–155.

Smith, S. M., Jenkinson, M., Johansen-Berg, H., Rueckert, D., Nichols, T. E., Mackay, C. E., … Behrens, T. E. J. (2006). Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. *NeuroImage*, *31*(4), 1487–1505.

Song, S. K., W, S. S., Ramsbottom, M. J., Chang, C., Russell, J., & Cross, A. H. (2002). Dysmyelination revealed through MRI as increased radial (but unchanged axial) diffusion of water. *NeuroImage*, *17*(3), 1429–1436.

Song, S. K., Yoshino, J., Le, T. Q., Lin, S. J., Sun, S. W., Cross, A. H., & Armstrong, R. C. (2005). Demyelination increases radial diffusivity in corpus callosum of mouse brain. *NeuroImage*, *26*(1), 132–140.

Spence, S., Shapiro, D., & Zaidel, E. (1996). The role of the right hemisphere in the physiological and cognitive components of emotional processing. *Psychophysiology*, *33*(2), 112–122.

Spiers, H. J., Burgess, N., Maguire, E. A., Baxendale, S. A., Hartley, T., Thompson, P. J., & O'Keefe, J. (2001). Unilateral temporal lobectomy patients show lateralized topographical and episodic memory deficits in a virtual town. *Brain : A Journal of Neurology*, *124*(Pt 12), 2476–2489.

Spiker, D., Lotspeich, L. J., Dimiceli, S., Myers, R. M., & Risch, N. (2002). Behavioral phenotypic variation in autism multiplex families: Evidence for a continuous severity gradient. *American Journal of Medical Genetics - Neuropsychiatric Genetics*, *114*(2), 129–136.

Sridharan, D., Levitin, D. J., & Menon, V. (2008). A critical role for the right fronto-insular cortex in switching between central-executive and default-mode networks. *Proceedings of the National Academy of Sciences of the United States of America*, *105*(34), 12569–12574.

Storey, A. E., Delahunty, K. M., McKay, D. W., Walsh, C. J., & Wilhelm, S. I. (2006). Social and hormonal bases of individual differences in the parental behaviour of birds and mammals. *Canadian Journal of Experimental Psychology = Revue Canadienne de Psychologie Experimentale*, *60*(3), 237–245.

Swain, J. E. (2011). The human parental brain: in vivo neuroimaging. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *35*(5), 1242–1254.

Swain, J. E., & Lorberbaum, J. P. (2008). *Imaging the Human Parental Brain*. *Neurobiology of the Parental Mind*. Academic Press.

Swain, J., Kim, P., & Ho, S. (2011). Neuroendocrinology of parental response to baby-cry. *Journal of Neuroendocrinology*, *23*(11), 1036–1041.

Takahashi, M., Ono, J., Harada, K., Maeda, M., & Hackney, D. B. (2000). Diffusional anisotropy in cranial nerves with maturation: quantitative evaluation with diffusion MR imaging in rats. *Radiology*, *216*(3), 881–885.

Tkaczyszyn, M., Olbrycht, T., Makowska, A., Soboń, K., Paleczny, B., Rydlewska, A., & Jankowska, E. a. (2013). The influence of the sounds of crying baby and the sounds of violence on haemodynamic parameters and autonomic status in young, healthy adults. *International Journal of Psychophysiology : Official Journal of the International Organization of Psychophysiology*, *87*(1), 52–9.

Tranel, D., Bechara, A., & Denburg, N. L. (2002). Asymmetric functional roles of right and left ventromedial prefrontal cortices in social conduct, decision-making, and emotional processing. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior*, *38*, 589–612.

Trevarthen, C., & Daniel, S. (2005). Disorganized rhythm and synchrony: early signs of autism and Rett syndrome. *Brain & Development*, *27 Suppl 1*, S25–S34.

Uddin, L. Q., Iacoboni, M., Lange, C., & Keenan, J. P. (2007). The self and social cognition: the role of cortical midline structures and mirror neurons. *Trends in Cognitive Sciences*, *11*(4), 153–157.

Vallortigara, G. (1992). Right hemisphere advantage for social recognition in the chick. *Neuropsychologia*, *30*(9), 761–768.

Venuti, P., Caria, A., Esposito, G., De Pisapia, N., Bornstein, M. H., & de Falco, S. (2012). Differential brain responses to cries of infants with autistic disorder and typical development: An fMRI study. *Research in Developmental Disabilities*, *33*(6), 2255–2264.

Wakana, S., Caprihan, A., Panzenboeck, M. M., Fallon, J. H., Perry, M., Gollub, R. L., … Mori, S. (2007). Reproducibility of quantitative tractography methods applied to cerebral white matter. *NeuroImage*, *36*(3), 630–644.

Waterhouse, L., Morris, R., Allen, D., Dunn, M., Fein, D., Feinstein, C., … Wing, L. (1996). Diagnosis and classification in autism. *Journal of Autism and Developmental Disorders*, *26*(1), 59–86.

Weed, E., McGregor, W., Feldbaek Nielsen, J., Roepstorff, A., & Frith, U. (2010). Theory of Mind in adults with right hemisphere damage: What's the story? *Brain and Language*, *113*(2), 65–72.

Whittle, S., Yap, M. B. H., Yucel, M., Sheeber, L., Simmons, J. G., Pantelis, C., & Allen, N. B. (2009). Maternal responses to adolescent positive affect are associated with adolescents' reward neuroanatomy. *Social Cognitive and Affective Neuroscience*, *4*(3), 247–256.

Wicker, B., Perrett, D. I., Baron-Cohen, S., & Decety, J. (2003). Being the target of another's emotion: A PET study. *Neuropsychologia*, *41*(2), 139–146.

Winner, E., Brownell, H., Happé, F., Blum, A., & Pincus, D. (1998). Distinguishing lies from jokes: theory of mind deficits and discourse interpretation in right hemisphere brain-damaged patients. *Brain and Language*, *62*(1), 89–106.

Woolley, S. C., Zhang, Y., Schuff, N., Weiner, M. W., & Katz, J. S. (2011). Neuroanatomical correlates of apathy in ALS using 4 Tesla diffusion tensor MRI. *Amyotrophic Lateral Sclerosis : Official Publication of the World Federation of Neurology Research Group on Motor Neuron Diseases*, *12*(1), 52–58.

# 9. Acknowledgments

Ringrazio innanzi tutto la mia tutor Prof.ssa Paola Venuti per aver creduto in me e per avermi dato la possibilità di continuare l'ottima collaborazione iniziata durante gli anni del master. Inoltre la ringrazio per la disponibilità sempre dimostrata e per il supporto nella ricerca ma anche morale durante i momenti difficili.

Ringrazio ovviamente i miei genitori per aver creato una condizione di tranquillità necessaria allo svolgimento di ogni mia attività e per avermi sempre appoggiato e supportato nelle mie scelte come ad esempio quella di andare prima ai confini dell' Italia e poi del mondo per studiare/lavorare. Immagino che per dei genitori non sia assolutamente facile da accettare, nonostante questo non ho sentito alcun peso e ho sempre potuto decidere liberamente quello che ritenevo giusto per me.

Ringrazio i miei amici, in primis Yagmur con la quale ho condiviso cinque anni bellissimi, la ringrazio per essere stata una splendida compagna e una splendida amica ma la ringrazio anche per tutto l'aiuto incondizionato che mi ha dato in questi anni.

Ringrazio Nadia che è la persona che mi conosce meglio di tutte e che è sempre un punto di riferimento importante per me. Ringrazio tutti i colleghi di Melbourne che mi hanno fatto sentire parte importante del gruppo ed in particolare la mia supervisor Sarah Whittle. Ringrazio tutti gli amici di Melbourne perché le esperienze che ho fatto con loro mi hanno cambiato e li avrò sempre nel cuore. In particolare ringrazio Elena anche ma non solo per i suoi preziosi consigli pre-presentazioni.

Ringrazio i miei compagni di "corsetta salutare" che sono stati un salvagente indispensabile dopo il mio ritorno dall'Australia. Ringrazio Andrea col quale ho

condiviso l’avventura di questa tesi e tutto il travaglio della decisione di chiedere o non chiedere l’anno. Lo ringrazio perché è stato un compagno unico durante i momenti di crisi e per avermi insegnato a prenderla alla leggera e godersi la vita anche durante i momenti stressanti. Ringrazio Valeria per averci sopportato durante i nostri scleri e per saper essere sempre li quando ti serve una parola di conforto o quando ti serve di ridere a squarcia gola per cavolate. Poi ringrazio Marco che si farebbe in quattro per aiutare un amico e lo ringrazio per essere stato un ottimo compagno durante questa pazza estate trentina. Ringrazio Francesco che purtroppo non è stato sempre presente durante i nostri deliri di fine dottorato ma quando c’era si sentiva eccome. Ringrazio la bomber Isabel con la quale ho condiviso gli ultimi pazzi giorni della stesura di questa tesi e tanti altri bei momenti.

Ultimi per apparizione ma non certo per importanza ringrazio tutti gli amici della Vallarsa che mi hanno accolto nella loro famiglia facendomi sentire parte integrante della loro comunità ed in particolare ringrazio i tesori della Vallarsa: Veronica, Gioia e Cristina per i bei momenti passati insieme nelle pause di svago che sono fondamentali tanto quanto le ore di lavoro.