UNIVERSITA’ DEGLI STUDI DI PALERMO
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THE INFLUENCE OF SPATIAL COGNITION IN THEORY OF MIND AND CENTRAL COHERENCE TASKS: STUDY IN AUTISM

IL DOTTORE
DOTT.SSA YINETH VALENTINA RUEDA CASTRO

IL COORDINATORE
CHIAR.MA PROF.SSA ALIDA LO COCO

IL TUTOR
CHIAR.MA PROF.SSA LISA CIPOLOTTI

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INDEX

INTRODUCTION

Autism Spectrum Disorder (ASD) is a neurodevelopment disorder characterized by deficits in social interaction and poor communication skills (Wing and Gould, 1997). Despite a growing research interest in the field, the causes of these impairments remain unknown.

This research assumes that social interaction is mediated by environmental structures and that the space representation could underlie social cognition (Krueger, 2010). Thus, the topic of spatial cognition and its neural correlates, that allow constructing neuropsychological concepts such as spatial attention and spatial frameworks, and how these in turn are linked with the body parts, objects or actions will be considered as an explicative model. (Katzky, 1998; Committeri and Galati 2004; Halligan and Fink, 2003; Lloyd 2009; Turrell et al, 2011)

The above premises offer indirect support to the importance of the ability to compare the own spatial point of view with another person point of view, which is based on aspects guided by spatial cognition. This suggest an influence in social perception and self-other recognition processes.

In this regard, two lines of research, Theory of Mind (ToM) and Central Coherence (CC), starting from experimental tasks such as visuo-spatial perspective Taking (VPT) and the local and global levels documented the importance of visuo-spatial attention and the spatial variables in the self versus other recognition, as a basis of the cognitive processes underlying the social interaction. According to spatial attention, such as observed in the Unilateral spatial neglect (USN), it may contribute to explain the differences in the spatial attention and the brain activation of autistic children in these two tasks.

Within this framework, the present research aims to investigate whether some aspects related to spatial perception could be compromised in a task of ToM and CC in a sample of adolescents with ASD and Typical Development (TD). The first three chapters of this thesis show the different neurological and conceptual underpinnings and in the fourth and final chapter the methodological and experimental part are developed.

CHAPTER 1

AUTISM

Autism literally means, "to live in terms of self". Autism is defined as a complex syndrome of development, manifested by similar clinical symptoms for multiple biological causes. This syndrome appears as a serious behavioural disorder caused by problems in neurodevelopment altering from the first years of life the ability to relate with others.

The different pathological conditions observed in autism are divided into subgroups: in the first group the conditions are defined with genetic basis and in the second group the conditions are defined by genetic mutation, caused by infections, toxins or other environmental factors. Moreover in the last prenatal period or in the postnatal period, are affected brain areas involved in the development of different cognitive functions, such as shared attention, language and reasoning (Gillberg and Coleman, 2000). Damage to postnatal Purkinje cells, often observed in the brain dysfunction of autism, involves impairments of brain functions causing dysfunctions of movement, balance, posture, symmetry and planning (Kern, 2003). The criteria for the diagnosis of autism can be summarized briefly in four areas: the first one is linked with the abnormalities associated with the social reciprocity where the early indicators show in general a priority interest in objects rather than in people. The second one is related with the abnormalities in the development of language and communication skills. The third one is associated with behaviors, interests, repetitive and restricted activities and imagination, where the early indicators are represented by the particular attraction to certain objects, sounds or movements. And the fourth one begins before age three and is related with the motor abnormalities where the early indicators are detected by the analysis of motion, and with seating and walking postures.

1.1 Impairments in social interaction

The various problems in social interaction have been represented as a macro area which, through clinical detection, can be identified an evident dysfunctionality of subject with autism in aspects like: an inadequate ability to grasp the socio-emotional cues (this is demonstrated in lack of responses to other people's emotions or absence of modulation of behavior according to social context) and poor use of social cues and a weak integration of social, emotional and communicative behaviors.

The social interactions, at an early age, are sensory-motor order, guided by the perception of the outside world and by the development of functions such as: *visual-motor coordination*, which is able to direct the action itself toward a specific target located in the space, and *the shared attention*, which is able to share the meaning of an action or a particular interest with others. These functions are essential for the development of imitation at an early age (the ability to translate the body state of someone and to observe the motor elements needed to reproduce the behavior), and for abstract game and fiction. Often, these functions are compromised in autistic subjects with difficulty to reaching development levels comparable to their peers.

One of the hypothesis that could explain the social impairment of these subjects is the hypothesis that take the action like precursor of social cognition.

1.2 Brain connectivity

The understanding of different behaviors that encompass Autism Spectrum Disorder (ASD) includes also the need to observe this disorder through brain evidence disruption in functional and structural connectivity. Several studies, with different imaging methods in ASD brain, evidenced disruptions in functional and structural connectivity. The findings of these recent studies could be classified according to three types of activations. In the first one, it was shown a reduced connectivity between anterior and posterior subnetworks in adolescents with ASD (Starck et al., 2013). Also Just et al 2012 reported a reduced long-distance connectivity of individuals with ASD. In the second one, findings have reported an increased functional connectivity of right parietal region with prefrontal regions, (Redcay et al., 2013) also in fronto-striatal circuitry in adolescents and young adults with ASD (Dimartino et al., 2011; Delmonte et al., 2013). Finally in the third one it was described both increased and decreased connectivity in autistic brain (Müller et all 2011). In addition, Maximo et al., 2013 showed local increased connectivity in posterior occipital and temporal cortices along with local decreased connectivity, in posterior cingulated and medial prefrontal regions, in adolescents with ASD. Coben et al., 2014 through these findings, suggested a theory of mixed under and over connectivity in ASD.

Regarding visuospatial task and ToM in autism and its abnormal functional connectivity, these have been associated with white matter, especially during visuospatial processing in connections between left occipital lobe and some regions in the left hemisphere (McFadden et al, 2013).

1.3 Cognitive Models

The cognitive models of mental functioning are oriented towards explanations that are related to a dysfunctional neuropsychological level and hypothesized by the interpretation of autism spectrum disorder (ASD) and its different manifestations. These models are Central Coherence and Theory of Mind.

1.3.1 Central Coherence

This model provides an explanation of some of the characteristics of autism ignored or unexplained by other models including a tendency to focus on parts of objects, extreme sensitivity to small changes in the environment and circumscribed interests (Happé, 1995). The proposal of this model is that persons with autism are deficient or have absence of normal tendency in information processing and in integrating information at a local level of organization; this means failures to draw together stimuli into coherent wholes. (Frith,1989). "*The detection of the local level is slower in the TD subjects, because there is a global interference effect, in the central coherence theory, persons with autism do not* *integrate information into higher levels of processing. Accordingly, they should display a unique local advantage as nonautistic persons typically show a faster (or better detection of global levels). Thus, with conditions designed so that persons without autism show no differences in responding to the two types of stimuli, the performance of persons with autism should be characterised by a local advantage"* (Mottron, 1999*)*. This theory has been explored with different experimental tasks such as interpretation of homographs in context (Happé, 1997; Snowling and Frith, 1986), judgments about 2D visual illusions (Happé, 1996; Ropar and Mitchell, 1999), Embedded Figures task (Shah and Frith, 1983; Brian and Bryson; 1996), block Design Task (Shah and Frith, 1993; Ozonoff et al, 1991) and hierarchization task (Mottron et al, 1999). Nevertheless the findings in these studies were contradictory.

The roots of this model were located in the old relationship between the perception of parts and wholes that has been the central topic in the study of visual perception (koffka, 1935). In this way Navon in 1997 attempted to test the local and global processing, presenting hierarchical stimuli, in order to compare the time taken to identify the local versus global letters. The findings of this experiment showed that the reaction times were faster for global than for local letters, suggesting that visual perception proceeds in a global to local direction. These findings became a link with experimental research that has been interested in the perceptual and attentional abnormalities in subjects with autism like central coherence theory.

On the other hand there are several studies that attribute the processing of Global and Local information at the brain hemispheres activity. These researches have been done with typical Development subjects (TD) and demonstrated the following results: Martin, 1979 and Sergent, 1982 showed that local stimuli presented in the right visual field were processed faster than Global stimuli and that Global targets presented in the left field were processed faster than Local targets. Robertson et al, 1993 reproduced these results. In other studies made with patients with focal brain lesions by Robertson et al, 1988 and Lamb et al, 1989, was confirmed that the left hemisphere has a processing advantage for Local targets while the right hemisphere has an advantage for processing Global stimuli. This study also proposed that a lesion in the inferior parietal lobule affects the ability to assign attention to one or the other level. This means that the temporal-parietal junction (TPJ) may have unique importance for the lateralizing aspects of performance on the Global and Local tasks. Another region in the brain important for processing the hierarchical stimuli is the Superior Temporal Gyrus (STG) that was described in a research made by Lamb et al, 1990 with twelve patients with lesions that involved this region, where seven had left-hemisphere lesion LTSG and five had right-hemisphere lesion RTSG. This study evidenced a larger Local advantage if the lesion was on the right and a Global advantage if the lesion was on the left.

1.3.2 Theory of Mind

The theory of mind (ToM), provides one of the etiological hypotheses most convincing of cognitive disorders of autism, focusing in the analysis of the difficulties in the child's relationships.

To posses a theory of mind refers to the ability to attribute mental states (desires, emotions, intentions, thoughts and beliefs) and understand and predict the behavior of other persons on the basis of own internal states.

The concept of ToM originates in the experimental models in etiology of Premack and Woodruf in 1978. They found evidence for the attribution of mental states to humans by chimpanzees.

Baron-Cohen, Leslie and Frith (1985) have shown experimentally that autistic children have similar abilities to their typical development peers in attributing physical causality to an event, but that they would not be able to represent the state of mind of self and others. These experimental analysis were partly based on two main analyses, the first one was based in Leslie (1987), where the importance of the underlying cognitive abilities in normal children of two years old in a pretend play was presented. And the second one was based in the observations that demonstrated some difficulties in the children with autism for imagination (Wulff, 1985). These data led also to the hypothesis that there could be a specific alteration of the necessary mechanism to represent mental states or "mentalizing". Leslie (1987) suggested that this mechanism might be innate and specific, which would imply that this function was damaged in a person with a normal intelligence in other ways.

For the developmental psychology, the ToM has been an important model because from this theory the false belief paradigm has been developed (Perner and Wimmer, 1985). This paradigm has allowed the conceptual construction of social understanding in children.

The ability to assign another knowledge, conviction or emotion develops in the child around the age of four. Before that age, children are not able to attribute a false belief (recognize the difference between the actual state of things and the mental representation of self or others). Baron-Cohen et al, 1985 found that the autistic children have impairment in this ability and even children with a normal IQ (Perner et al, 1989).

Over the time and with the different researches the ToM has extended to cover theoretical fields as empathy and embodiment contributing to the development of social cognition.

In social cognition it is necessary to think about the contents of someone else's mind. But there is another mechanism for accessing to the inner world of other, this mechanism is called embodied and it mediates between the multimodal experiential knowledge of our own lived body and the way we experience others (Gallese, 2007). The embodied also could underlie the capacity of empathizing (ability to infer and share the emotional experiences of another) (Gallese, 2003).

The neural mechanisms observed in patient groups lacking ToM or empathy reveal a network of three main areas associated with the processing of ToM: the medial prefrontal cortex (mPFC), the posterior superior temporal sulcus (STS) and the temporal poles (Frith and Frith, 2003). The activation of these areas during ToM tasks also can be understood through processes such as self and other distinction (Gallagher and Frith, 2003). The areas associated with empathy were the superior and inferior frontal gyrus, the precuneus and the middle temporal gyrus (Farrow et al., 2001).

Finally Gallese, 2007 also proposed that embodied simulation could play an important role not only for the process of social cognition such as empathy but also on a more complex process like the attribution of mental states, where all these could be possible trough the mirror neuron system.

CHAPTER 2

GENERAL CONCEPTS OF SPATIAL COGNITION

2.1 Spatial Cognition and brain

The exploration of environmental structures has always been in human beings one of the main mechanisms for the collection of information. This mechanism allows the generation of a spatial representation, which is in turn the key factor for navigating in the space.

The space navigation is possible across landmarks because they help to organize the space and they are reference points in the environment (Sorrows and Hirtle, 1999). The reference points in turn constitute the spatial frame of reference, where the reference frame is a mean for representing the locations of entities in space (Klatzky, 1998). Moreover many spatial reference frames are employed to direct behaviour and parietal cortex is the key for the construction of these representations (Colby & Goldberg, 1999 for a review).

The brain uses codes for the spatial frame of reference and in this manner attributes characteristic such as *up, down, left and right* thanks to the bases generated by the different visual inputs *(*Halligan and Fink 2003). In this way the *spatial acquisition* is begun, particularly conformed by the *landmarks orienting one's self (egocentric frames).* The body plays an important role for defining the egocentric frame because the references for the spatial location are relevant body parts such as the eyes, head, trunk, and arms (Committeri and Galati 2004). The spatial position can also consider external references like objects; in this processes the coordinates are external or allocentric and have anatomical linkage between parietal and their cortical targets that furnish some insight into the spatial reference frames. Moreover parietal cortical areas are connected with areas of prefrontal cortex, premotor cortex, and the frontal and supplementary eye fields where the object locations are encoded relative to an assortment of reference frames. (Rizzolatti et al., 1981; Graziano et al., 1997)

On the other hand, the perception of the external world seems unitary but is consequence of processing information coming from different parts of the space. This is because the brain produces a set of spatial representations and each representation is connected to a different action or region of the space (Colby & Duhamel, 1996; Fogassi et al 1996; Graziano et al 1994). Therefore the neuropsychological structure of the space is defined in three fundamental regions: personal space, peripersonal space and extrapersonal space. Personal space is the space of the body surface, peripersonal space is the space within hands reach and extrapersonal space is the space beyond hands reach.

The peripersonal and extrapersonal space have neuronal correlates that prevent it from being a rigid concept due to environmental stimuli that build flexible abilities that are modified according to the different necessities. For example, the different distances that human beings keep with objects and other human beings are given by feelings as comfort, discomfort or dangerousness of a situation (Doesey and Meisels, 1969; Turrell et al 2011). This shows an inevitable connections between the actions deployed by others continuously in the ambient (Lloyd, 2009). In this way it is understood that body space and distance are defined as a dynamic concept due to social interactions.

To understand what is so special about the topic of "Space in the Brain" it is important to say that the brain uses two types of neural representation. The first type of representation is being given by the spatial frameworks linked with the body parts, object or action, and is essential for behaviours such as catching a ball or picking something. The second one is how the spatial frameworks are fixed with respect to the outside world, independent of particular actions and objects.

To make effective a representation of the space are necessary several inputs that are encoded in the brain through the primary areas like primary visual cortex and primary somatosensory cortex. The somatosensory cortex in turn integrates with the motor areas aiding to direct the movements unto a specific direction. Therefore what represents all this neuronal activity is the special relationship that exists between the information generated from the exterior and the body parts (hands, arms and trunk, etc.); thus allowing an integration of the spatial information in terms of various *egocentric* reference frames.

The support for the egocentric frames can be of single cells in the primary areas mentioned beforehand. The information gathered by the these cells needs to be translated and it seems that this translated cells are found in the front Parietal area 7a in primates. "*These neurons respond to visual stimuli at a specific retinotopic locations, but their rate of firing is also modulated by the orientation of the monkey's gaze relative to the head… area 7a is the posterior parietal area most strongly connected with the medial temporal lobe and the neurons there whose firing is modulated by the orientation…can support translation between egocentric and allocentric representations of locations*" (Andersen et al 1987 by Burges, 2008 for a review.).

On the other hand, the neurons experts for answering to stimuli available in distance are located in the medial intraparietal (MIP). These neurons show a range of response from purely somatosensory, to bimodal, to purely visual (Colby & Duhamel, 1991). For example, the somatosensory neurons have receptive fields most often in the hands, while bimodal neurons reply to visual stimulus and to passive touch too. In addition, the bimodal neurons play an important role for reaching a visual target, which means that they are important for locating the target and for the arm that is used to reach toward it. Then there are, in the purely visual regions, the neurons that receive the signal of presence when the target is moved and can be reached with the arm.

Another anatomical center for the *allocentric* frames can correspond to the "place cells" (§ 2). These cells are located in the hippocampal formation and their firing fields are anchored to the external environment and seem to be the base of the cognitive map: representation of orientation. This cognitive map in turn is being given by the representation of the environment, places and objects within it that are to some extent independent of the body posture or orientation. In this way the hippocampus establishes the connexions between the spatial components such as places, routes, resources and goals in the long-term memory (Hartley et al, 2013 for a review).

2.2 Neglect

Unilateral spatial neglect (USN) is a spatial disease characterized by the inability or failure to detect or respond to stimuli located in the contralesional side of the space. It is more frequent after a right hemisphere damage. (J. Driver, P. Vuilleumier , 2001 Heilman, Watson, & Valenstein, 1985 Vallar 2001, Parton et al. 2004).

In 1941 Russell Brain described for the first time this disorder. It can gather different clinical manifestations, sensorial level (visual, auditory or tactile), spatial reference frames (egocentric versus allocentric) and regions of space, near space (peripersonal space) and far space (extrapersonal space). These clinical manifestations in turn have contributed to the construction of the concepts referred to spatial cognition and its respective neural correlates (W.R. Brain, 1941; F.H. Previc 1998; A. E. Hillis et all, 2005; C. Grimsen, et all 2008, T. C. W. Nijboer et all, 2014).

The patient with this disorder, due to his neurological condition presents behavioural symptoms like eating only on the right side of the dish or tripping on with the left side of her body. Another example is when a stimuli is presented on both sides (bilateral), her attention is immediately directed toward the stimuli on the right side ignoring completely the stimuli on the left side (Gainotti et al 1991). In visuo-spatial testing, they omit targets on the left in search tasks, deviate rightward when bisecting lines, and do not copy the left part of drawings. All these symptoms may be resumed as impairments in visual, auditory, tactile and motor abilities (Bisiach et al., 1984).

The neurological condition of USN has helped to comprehend the brain mechanisms of attention and spatial processing such as near and far space, because different characteristics of patients with the spatial neglect have been documented. There are patients that presented neglect to near space (Berti and Frassinetti 2000), while others showed spatial neglect restricted to far space (Vuilleumier et al., 1998). And there are patients who presented spatial neglect in the absence of any distance modulation effects ((Pizzamiglio et al., 1989). USN is associated in most cases with lesions in the right posterior parietal cortex (Halligan et al., 2003) and there have been reports about the importance of parietal cortex as a component of the frontoparietal network of attention (Corbetta and Shulman, 2005). On the other hand numerous studies interrelated between spatial neglect and the egocentric and allocentric frames of reference have found a variety of results linking egocentric frame of reference with damage within the perisylvian network and damage within sub-cortical structure. In addition more posterior lesions were linked with allocentric symptoms (Chechlacz et al 2012).

Another aspect of USN is the difference between perceptual neglect and representational neglect. The first is based on viewer-centered frames of reference (Driver & Pouget, 2000) and the second involves viewer-centered and allocentric coordinates. For example mental imagery could be operating with representations preserved independent of the viewer position (Ortigue et al 2001). Other previous studies have presented strong evidence to support an initial dissociation between perceptual and representational neglect (Bartolomeo et al., 1994; Coslett, 1997; Peru & Zapparoli, 1999).

In light of the above is presented the challenge of observing this double dissociation between perceptual and representational neglect in spatial task that require the presence of another person, which enables a better observation and data collection at the behavioural level. In 2011 Becchio et al., with a spatial perspective taking task observed how patients with neglect would represent a spatial scene from the perspective of another person, finding that perspective taking significantly ameliorated neglect severity because the items were presented on the left side, and omitted when required to report from the first-person perspective (1PP), but could be reported when patients assumed a different spatial perspective as third-person perspective (3PP). This might imply that perspective taking influences the codification of space and objects in presence of another person. A similar effect was demonstrated by previous studies more associated to spatial transformation (Della Sala et al 2004; Beschin et al 2003).

2.3 Spatial orientation in subjects with Autism

Meanwhile, research on this disorder constituted a possibility through the years for understanding spatial cognition; mainly in the field oriented to the visuospatial attention or spatial orientation in non social task. The visuospatial attention is an ability that is connected with the attentive field and has been, since the beginning, interested in the visual perception of the spatial relations of objects in the external world.

Manifestations of USN opened the possibility of an explicative hypothesis about Autism based in the characteristics of the spatial attention in patients with neglect: "*we suggest that the phenomenon of spatial neglect provides a model for understanding much of what is known about autism"* (Bryson and Wainwright, 1990). This gave rise to the development of the visual spatial performance in autism with a series of studies that started with the traditional orienting task in which are described characteristics in high- functioning adults like left visual field advantage, for the process of orienting to and detecting stimulus in visual space (Wainwright and Bryson, 1996); showing that the dominant right hemisphere for this process is that of normal subjects (Heilman and Van Den Abell, 1979).

Other descriptions in visuo-spatial skills in Autism have been described through tests such as Figure Disembedding, Block Design and Navon Task, giving sustain to theories like Weak central coherence. Most of these tests have demonstrated that individuals with autism have intact and sometimes superior performance on spatial tasks that require processing capacity for the details. (Jolieffe and Baron-Cohen, 1997; Morgan, Mayberry, and Durkin 2003; Shah and Frith, 1993).

On the other hand the visuo-perceptual processing have been divided in two abilities. The first one is the ability to identify the orientation of simple, luminance- defined gratings (or first-order), and the second one is the ability for complex, texture- defined gratings (or second-order). In addition to this, in subjects with High Functional Autism (HFA) have been found data in which it is described an orientation and identification of thresholds significantly lower for the first order conditions. However, the thresholds are significantly higher for the same task using complex second-order stimuli when compared to the Typical Developmental (TD) (Bertone, Motron, et al 2005).

CHAPTER 3

SPATIAL AND SOCIAL COGNITION IN AUTISM

So far have been described various aspects and considerations of the concept spatial cognition, showing how it transversalizes many neuropsychological abilities like attention and perception. Another ability by excellence of the human being is the capacity to prosper in complex social situations (Gallese, Keysers and Rizzolatti 2004 for a review). If the social interaction is mediated by environmental structures it can be considered that the *social cognition is fundamentally an interactive form of space management"* (Krueger, 2010).

One of the disorders characterized by impairments in social interaction and communicative skills is Autism Spectrum Disorder (ADS). This disorder is a severe developmental disability. Despite a growing research interest in the field, the causes of these impairments remain unknown.

It is within this framework that new lines of research have undertaken the challenge of describing the characteristics of some concepts that are interconnected with the social abilities and the elements of spatial cognition (spatial behavior) in ADS. These studies look into the ability self versus other evaluations with the aim to explore the neural representations that involved processes in self-other distinctions (N. David et al., 2008).

In the following sections are described how the introspective ability of self versus other evaluations is investigated.

3.1 Self- other recognition

The relationship between self and other is an ability that starts to show its development during the second year of life of the child and from that date presents a rapid increase (Lewis & Brooks-Gunn, 1979). In the social cognitive framework this relation becomes established, especially in these years of development, in two categories of cognition. The first one is self-recognition ability (self-awareness) and the second one is self-consciousness, empathy and cooperation (other-awareness) (J. B. Asendorpf, V. Warketin and P. Baudonnière, 1996).

The relation self-other is a complex construct, but in the neurocognitive field this concept has been measured through an experimental task that has to do with self and other's body processing. This is because the recognition of the parts of the own body not only account for the process of constitution of the self but also for the presence of body schema that seems to be closely interrelated with the peripersonal space, because in both terms there are overlap concepts belonging to spatial and bodily representation (L. Cardinalli, C. Brozzoli, and A. Farnè, 2009). Furthermore, peripersonal space appears to be also susceptible to social interaction components (DM. Lloyd 2009).

Self and other representation in Autism has been an important theme because some differences have been found in its process with respect to subjects with typical development. These differences suggest that the nucleus of autism symptoms could be induced by a deficit in understanding the general relation between self and others (Gopnik A. and Meltzoff AN , 1994). This idea is tightly linked with the notion that impairments of higher-order mentalizing types are essential to social cognition (U. Frith, 2001).

In addition to these self body recognition in autism recently has been described by authors like Erica Gessaroli et al., in 2013, showing that ASD children demonstrated better results with self than with others' body and face parts. They proposed in this study that the children with autism were able to distinguish self and others' stimuli and to take an advantage in processing self-compared to others' stimuli. Moreover they confirmed that the body self–advantage is a process implicit in a body specific knowledge based primarily on the sensorimotor representation of one's own body-parts.

On the other hand, the process of self-other recognition has been identified with its specific brain areas for each one of the two processes. This is how Uddin et al., in 2008, described, based on a comparative study between children with high-functioning ASD and subjects with Typical Development (TD), the areas that sustain the process of self face recognition in other face recognition. In self face recognition were identified, for both groups, areas such as right lateral occipital cortex, right occipital fusiform gyrus, right temporal occipital fusiform cortex, right precentral gyrus, right inferior frontal gyrus, right insular cortex, left lateral occipital cortex, left occipital pole, and left temporal occipital fusiform cortex. However, in other self recognition the ASD Group presented activation in right occipital fusiform gyrus, right lateral occipital cortex, left occipital fusiform gyrus, right lateral occipital cortex, left occipital fusiform gyrus, and left temporal occipital fusiform cortex. In contrast the TD group demonstrated activations in right occipital fusiform gyrus, right lateral occipital cortex, right inferior frontal gyrus, right precentral gyrus, right insular cortex, right frontal operculum cortex, left occipital fusiform gyrus, and left temporal occipital fusiform cortex. Finally this studio showed significant differences for the other recognition task especially in the right prefrontal cortex for ASD, because while TD children activated the right inferior frontal gyrus (rIFG) when looking at images of others, there was no change in activity when the ASD did this same task.

For having a description closer to the different hemispheric functions in the brain in the self and other's body processing in children F. Frassinetti et al., in 2012, tested 74 children (57 healthy controls and 17 brain damaged) with stimuli that represented body parts and face parts of other people or of body parts of the children that did the experiment. The results of this research were interesting because they proposed three contributions: the first one is that the right hemisphere is specialized in processing self information of body parts and the left hemisphere is specialized in processing other information in children. Suggesting with this that the processing of self and others' body parts is independent and could correspond to an anatomical independence. The second one proposed that self-body and self-face parts seem separate as well as others' body and others' face parts processing. Finally this study found that in healthy children the self advantage is a normal process in the brain just like in the adults.

The studies described above help to understand the process in autism. However, if these process are not clear and classified at the level of the brain, it is necessary to make the comparison with the specific damages in comparable subjects to try to understand how this process develop in autism and how it affects its complexity.

3.2 Sense of agency

The sense of agency is a crucial aspect to successfully navigate in the shared representation between self and other and in the ability to differentiate the personal perspective with that of the third person perspective (Decety and Sommerville, 2003; Decety, 2005). Another characteristic of the sense of agency is the ability to recognize one self as causally involved in action (Gallagher, 2000; Gallagher & Frith, 2003); this is fundamental to social interaction.

At the same time, the sense of agency involves efferent copies of motor signals, and is expressed only for voluntary movements. The self-produced movements are constantly monitored, through the sensory feedback and efferent copies allowing to continually remodelling it. This system of control of movement is also able to establish 'who' has generated the observed movement. According to Jeannerod (2001), if the copies of motor and sensory feedback are triggered at the same time, the action is experienced as generated by itself. When subjects are aware of causing an action, compared to the situation when they believe that it is performed by another, it is observed bilateral activation of the anterior insula, supplementary motor area (SMA), the lateral premotor cortex, and the cortex primary somatosensory (Farrer & Frith, 2002). For the perception of the acts of others, studies show a preference lateralized to the right (Ruby & Decety, 2001, 2003; Leube, 2003), at the level of the inferior parietal cortex (Ruby & Decety, 2001, 2003). Its activation seems to express the sense of the discrepancy between the own action and those performed by others (Farrer et al., 2003). In addition in the parietal cortex some neurons expressing bimodal property, reflect efferent copies and visual feedback. Moreover, the parietal cortex arises as a place where perception and action share a common code and neural architecture.

Leube et al. (2003) made participants to observe a video illustrating their actions, where there was a short delay in time between the action performed and that shown on the monitor. The authors observed a positive correlation of activation in the superior temporal sulcus (STS) with the increase of the delay time. The dyssynchrony time between the observed action and the performed one, made the action to seem as not belonging to the self. These regions are also involved in the Theory of Mind (ToM) (Apperly et al., 2004; Saxe & Wexler, 2005).

The inferior parietal cortex and premotor cortex represent a frontoparietal connection. This connection is able to make consistent the external stimuli with our own body image, and in some cases transforms the body sensory experience just to make it consistent with the information collected (Ehrsson et al., 2004). Observations of psychiatric patients emphasize the role of parietal cortex in supporting the sense of the agent. Damage to the parietal cortex, in fact, expresses the inability to recognize oneself as an agent of the action, and the feeling that it is controlled by someone outside the self (Murata & Ishida, 2007).

Regarding the problematic with the sense of agency in ASD it could be identified as a process that underlie difficulties such as imitation, motor performance, visual processing of dynamic motion and executive function (David et al., 2008).

The studies developed in persons with ASD that have investigated sense of agency have linked the ability to distinguish between animate and inanimate objects (Celani, 2002; David et al., 2008). They found that individuals with ASD tested did not demonstrated impairments in the sense of agency or an intact system matching observed actions onto representations of one's own actions (Sebanz et al, 2005) or a typical "self-reference effect" recalling their own actions better than those of the experimenter (Williams & Happé, 2008).

Several studies that inquire the attribution of action in autism are mixed with the attribution of mental states or imitation since they conform the nucleus of social cognition. For demonstration of the results found, Splengler et al (2010) with eighteen participants with autism tested with imitation-inhibition task, theory of mind task and functional magnetic resonance imaging showed that the brain areas that presented decreased activity during mentalizing with increased interference effect in the imitation-inhibition task were mPFC, the TPJ and posterior superior temporal sulcus, confirmed that the activation in the mPFC is the key area in Theory of Mind (ToM) processing. As for the imitation-inhibition task the participants with autism showed increased imitation of hand actions compared with control participants demonstrating in turn more deficits to inhibit automatic imitation. These results were associated to a reduced mentalizing.

On the other hand Jan Zwickel et al., throw a study in 2011 with nineteen participants with high functioning autism and eighteen neurotypical participants, observing the eye movements when watching animate triangles in short movies that normally evoke mentalizing, demonstrating that there were not differences in both groups because they showed the same increase in mean fixation duration, an indicator of information integration. This indicates that the operation involved in detecting a social agent is intact.

3.3 Visual-spatial Perspective Taking

In the present epoch researchers have been interested in how the impairments in social cognition and abilities that require the use of spatial and social abilities are interrelated (A. Pearson 2013 for review). One way to assess this relation is the visual perspective taking (VPT). VPT is defined as the capacity to appreciate the world from another person's perspective and have two levels defined by Flavell in 1977. The level one (VPT1) is the ability to know what another person can and cannot see and the level two (VPT2) is the ability to comprehend that when two persons see the same scene or object simultaneously, may nevertheless appear different to each person. In both levels the people should utilize the spatial and social information (reference frames of the viewer, position of target and the position of the object in the space in relation to self and others), because, “by interpreting the spatial relationships between objects in a social framework it becomes possible to form a rich representation of differing viewpoints which are useful in a variety of social tasks” (A. Pearson 2013 for review).

VPT has been a topic of importance for autism, because it has provided value to the research of Theory of Mind (ToM) (despite of others points of view). VPT and ToM seem to share cognitive processes (Hamilton, 2009). In different studies VPT in children with ASD and TD was compared, finding contradictory results in respect to the two levels of VPT. In respect to VPT1 some of them report no differences between typical and autistic participants. On the contrary, in VPT2 some of them found differences. Therefore the differences between VPT1 and VPT2 are not quite significant since the methodology between them is not clear either.

The following table describes some of the studies related to VPT1 and VPT2.

Authors	Paradigms	Results
Hobson (1984) Reed (2002)	Task with question about item visibility (the child has to respond to whether the adult can see the item) (“hide and seek game” paradigm) (VPT1)	The findings suggest that children with ASD are able to understand the concept of “hiding” and what other people can see.
Leslie and Frith (1988) Baron-Cohen (1989)	Line of sight paradigm (VPT1)	Results showed no significance difference between TD and ASD groups. They suggest that the autistic children had a basic understanding of what the other could and could not see.
Leekman et al (1997) Warreyn et al (2005)	Line of sight paradigm (VPT1)	The authors suggested that VPT may develop later in children with autism and that they may be delayed compared to TD children.

Mizuno et al (2011)	Item appearance paradigm (VPT1)	Showed that participants with autism were slower in the "what" condition than in the "who" condition.
Reed and Peterson (1990)	ToM and item appearance paradigm (VPT2)	Found that the children with autism performed similarly to the typical children in the VPT task, but worse in the cognitive perspective taking task.
Tan and Harris (1991)	Item location paradigm and ToM (VPT2)	The autistic children performed similarly to the typical children on both VPT and desired understanding.
Yimiya et al (1994)	Object rotation paradigm (VPT1)	Found that children with ASD showed a higher number of errors than the typical children.

Hamilton et al (2009)	Object rotation paradigm and ToM	Results showed that the children with ASD were significantly worse on the VPT trials compared to the typical children, but performed better on the mental rotation task.
Dawson and Fernald (1987)	VPT and ToM	In ToM task results showed that the ASD participants were significantly slower and less accurate at identifying the correct answer when mentalizing for other. They were also trending toward slower mentalizing for self. There were no differences found between groups for speed accuracy in the VPT task, for self or other.

Zwickel et al (2011)	VPT and ToM	Typical and autistic participants showed a congruency effect, demonstrating that they could spontaneously consider the left/right orientation of an animated shape. However, the autistic participants were less good at judging the mental states of the triangles in the same animations.

VPT is an ability that each day more researchers have linked to spatial terms. Proofs of this are the VPT studies that have been involved recently in the spatial transformations. Spatial transformations are the process we use to align different three dimensional representations with each other across variations in position and orientation. By transforming ourselves to a different point in space it becomes possible to judge what is on another person's left or right, or to make predictions about how things may appear from a different visual perspective. (Pearson et al., 2014).

The spatial transformations are divided in two types, egocentric transformations and mental rotations. The first one, is self based and is used when the person transforms her body as a whole aligned with a new position in space (Zacks et al, 1999). This contributes to VPT, because they allow a person to place herself in another person location, and then to imagine what another person can see from a different viewpoint (Steggeman et al 2011; Surtees et al 2013; Yu and Zacks 2010). The second one is the process by which the persons can manipulate the orientation of objects in their minds (Shepard and Metzler 1971; Wraga et al., 2003) and could be used to take another person's perspective (A. Pearson et al., 2014).

The spatial transformations are an important factor in the social interaction because they allow to imagining our own body in the place of another person's body (Michelon and Zacks 2006). This can imply that spatial transformations underlie VPT and for this reason plays an important role in trying to understand the mechanisms that lie behind the social impairments in autism.

Regarding autism and mental transformations recent studies have searched the definition of these characteristics in subject with ASD with different methods and doing comparison with proves in TD. David et al. (2010) published results that showed no significant differences in regards to response time or accuracy between the ASD and TD groups, suggesting no differences in egocentric transformation abilities. In regard to response time or accuracy between the ASD and TD groups they suggested no differences in egocentric transformation abilities. On the contrary, Kessler and Wang (2012), Brunye (2012) and Pearson et al. (2014), in three separate studies but using a similar method, found that participants with higher levels of autistic traits displayed difficulty with performing egocentric transformations and were more likely to rely on an object focused rotation strategy.

As for mental rotation in autism several studies have shown that people with ASD appear to have an intact mental rotation ability (Falter et al., 2008; Hamilton et al., 2009; Soulieres et al. 2011; Pearson et al., 2014).

Another important aspect to review are the brain regions recruited in VPT tasks. As have seen before different methods have been designed to investigate not only the behavioural aspect but also the brain zones involved in the process of VPT. In these studies it is evident how the concept “self” has been adopting different approaches as for example the skill to assume a first-person perspective (1PP) is a way to make reference to the self- referring; namely, the 1PP can be treated as an elemental component of a “minimal self” (Gallagher, 2000). Based on this the aim have been to provide an understanding to the differentiation of self-other investigating the neural correlates of first-person perspective (1PP) and third-person perspective (3PP).

In the same line Volgeley et al., (2004) with a functional magnetic resonance imaging (fMRI), revealed both common and differential neural correlates for perspective taking in a simple visuo-spatial task to be performed from either someone else viewpoint (3PP) or one’s own viewpoint (1PP). The findings demonstrated differential brain activations, meanwhile in 3PP the activations were located in precuneus, the right superior parietal and right premotor cortex; in the 1PP was observed an increase of activation in mesial cortical regions.

In the following table a detailed description of the other brain activations found in the study described previously is presented.

Brain activations		
1PP-3PP common activations	**3PP relative to1PP**	**1PP relative to 3PP**
Right medial occipital gyri	Precuneus	Right insula
Left precuneus	Right inferior frontal gyrus	Left inferior temporal gyrus
Left inferior occipital gyri	Left cerebellum	Superior frontal gyrus
Right inferior frontal gyrus	Left inferior occipital gyri	Posterior cingulate gyrus
Left cerebellum	Right cerebellum	Left medial temporal gyrus
Left inferior parietal lobule	Left inferior frontal gyrus	Left posterior cigulate gyrus
Left superior frontal gyrus	Left inferior parietal lobule	Anterior cingulate gyrus
Left precentral gyrus	Left medial frontal gyrus	Left medial frontal gyrus
Left superior frontal gyrus	Left occipital gyrus	Right postcentral gyrus
		Right posterior cingulated gyrus

On the other hand in 2006 N. David et al., with an experiment where the participants play a virtual ball-tossing game, searched the neural representations of first-person (1PP) vs. third-person perspective (3PP). In this studio the increased neural activity during 1PP was observed in cortical middle structures such as the left medial prefrontal cortex (MPFC) (extending to the superior frontal and right anterior cingulated cortex) and bilateral posterior cingulate cortices and in temporal regions including bilateral middle temporal gyrus, left superior temporal gyrus, and left amygdala. In addition in this perspective were elicited activations in the angular gyrus within the left inferior parietal lobe (IPL), in the right buscentral gyrus, bilateral posterior insula, left visual cortical areas such as the calcarine sulcus and cuneus, and left posterior orbital gyrus. On the other hand, neural activity in 3PP was showed in the right superior parietal lobe and the right cuneus, in the left inferior frontal cortex, in the right middle frontal-premotor cortex, right brainstem, bilateral thalamus, bilateral anterior insula, right anterior cingulated cortex, and right cerebellum.

In 2007 D'argembeaud et al., remarks the distinct regions of the Medial Prefrontal Cortex (MPFC) associated with self referential processing and perspective Taking while the participants made judgments on a series of adjectives describing personality traits. In the results these authors described in the self-referential processing the principal effect of judgment target that yielded a large activation cluster in the MPFC, which encompassed the dorsal (BA 9) and ventral (BA 10) portions of the anterior MPFC and the anterior cingulated cortex (BA 32). Respect to the self targets and other targets they showed one difference in the MPFC. This difference demonstrated an increase in neural activity in self targets and lesser decrease in neural activity in other targets in this region. Regarding to the results of the ability of perspective taking in this same research the authors described the main effect of judgment perspective that showed activation in the left dorsal MPFC (BA 6), posterior to the medial prefrontal regions. The changes in this area were increased for the third-person perspectives as compared to the first-person perspectives. Moreover the principal effect of judgment perspective also produced activation in the lingual gyrus (BA 18), in the left inferior parietal lobe (BA 40), in the precuneus (BA 7), in the left temporal pole (BA 20) and in the left lateral orbitofrontal cortex (BA 10).

Finally in 2013 Mazzarella and colleges registered the activation in brain areas while the participants did egocentric and alterecentric tasks. The brain areas described for alterecentric were bilateral inferior occipital gyrus extending into fusiform gyrus and lateral occipitotemporal cortex, intraparietal sulcus (IPS) and dorsal premotor cortex (PMd). In addition the brain areas corresponding to the egocentric task were bilateral inferior occipital gyrus extending into fusiform gyrus and lateral occipitotemporal cortex, right IPS.

These studies mention the outstanding areas in the different task that comprehend the ability of perspective taking with a prevalence of three areas together but with different parts such as premotor cortex, parietal lobe and medial prefrontal cortex. Finally with all the studies described previously it can be observed how it has been investigated in Autism the process of recognition and differentiation of self-other in different tasks. Although there is a great diversity of this disturb, these studies have shown different impairments in this process, shedding light in general on the descriptions made by Kanner in 1943 where he noted self-deficits linked with difficulties in maintaining a constant self-concept and problems for adapt its "self" to the rapidly changing environment, that are better defined in depth both as at the behavioural level and its neural correlates. Therefore concluding in general that there exist specific disruptions in self-information and its neural systems involved. These neural systems comprehend two main areas where some failures of individuals with autism have been found. The first one is the middle cingulate cortex that in autism responds better to other than self-tasks especially in the mentalizing judgements tasks (Lombardo et al., 2010). Meanwhile the second one is the lack of responsiveness to self information in the ventromedial prefrontal cortex. Thus demonstrating that the centrality of an impaired relation of self-other in ASD has been the focus because it might be essential for understanding the deficits in social interaction. Furthermore, with all the research "*there is substantial evidence that early deficits in self-development including impaired relations with others result in a fragmented and atypical sense of self in ASD*" (Lyons & Fitzgerald, 2013).

3.4 Social interaction and spatial cognition

Self-other body recognition, sense of agency and Visuospatial Perspective Taking are abilities that in their description demonstrated how the body, the appreciation of different perspectives and the understanding of actions interact with spatial cognition. Therefore becoming themselves variables that contributed to the understanding and research of the problems of autism; in specific the problem that has to do with social interaction and communication.

In this line of reasoning, Iachini et al., in a research made in 2013, revealed the existence of a strong relationship between body space and social interactions. In this study eighteen participants made four experimental conditions related to the judgment of distance in Immersive Virtual Reality (IVR). The main results showed that peripersonal reaching and interpersonal comfort spaces (given by the distance between self and the virtual stimulus that makes one feel uncomfortable) share a common motor nature and are sensitive, at different degrees, to social modulation. In this way, the findings reported a close relationship between basic visuomotor-spatial processing and complex social processing. Furthermore, in a framework where sensory information is processing by the body (embodiment), this study suggested too that social distance is influenced by the experience of the body acting in space.

On the other hand, the body represents an important agent in ASD, especially in body self-other recognition tasks. About this, Zamagni et al., 2011 tested the influence of emotional body posture on bodily self-processing in typical development (TD) and subject with autism (ASD), founding that the bodily self advantage was presented in both TD group and ASD group suggesting with this, that the low level of self awareness could be intact in autism. Finally, the second result showed that self-advantage is modulated by emotional body posture. This advantage was found also in both TD and ASD groups with expressions such as happy and neutral but not with fear, because in this last one there was a selective advantage for other stimuli as a sign of the importance of safety in evolution.

One recent research that linked the corporeal distance during the social interaction in ASD was developed by Gessaroli et al., 2013, by studying how concepts as body space and personal space are closely related to the self-other process. They used an adapted version of the stop distance paradigm for comparing the interpersonal distance before and after the interaction with the adult confederate in TD and ASD groups of children. The findings of this experiment evidenced that personal space regulation is impaired in the ASD group because the ASD children were less tolerant to close proximity to a strange adult and prefer more interpersonal distance than TD children. However the interpersonal distance increased when the ASD children moved away than when they approximated toward the target feeling more uncomfortable and react. The authors suggested that personal space in ASD is damaged in two characteristics, permeability and flexibility, reflecting in turn impairments in their social interaction.

CHAPTER 4

THE INFLUENCE OF SPATIAL COGNITION IN THEORY OF MIND AND CENTRAL COHERENCE TASKS: STUDY IN AUTISM

4.1 Experiment 1.

Local and global processing in the spatial attention

The weak central coherence hypothesis of Frith is one of the main cognitive models interested in the perceptual and attentional abnormalities in Autism Spectrum Disorder (ASD). Under this hypothesis, experimental research has been interested in describing the performance of individuals with autism on tasks that involve local and global processing. In general, it has been found that there are impairments in the global processing in autism. One of the most important considerations in this experiment was that the left hemisphere has a processing advantage for local targets while the right hemisphere has an advantage for processing global stimuli (Robertson et al., 1988; Lamb et al., 1989). For this reason, in this experiment the spatial perception was an important element because the question in general was: if the spatial elements (right and left) could influence the response in the global and local task.

4.1.1 Objective of the experiment

The aim of the experiment was to investigate the attentional local and global processing, modulating the stimuli presentation in the spatial horizontal plan (left vs. central vs. right)

4.1.2 Material and Methods

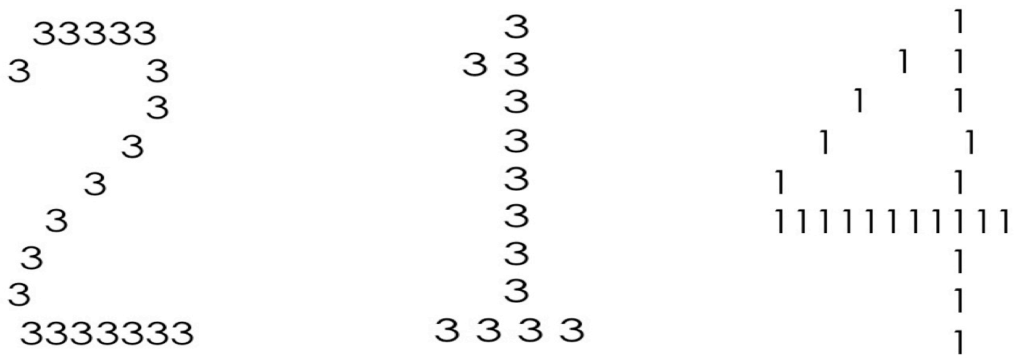
4.1.2.1 *Participants*

20 adolescents: 10 adolescents with autism spectrum disorder (ASD) and 10 adolescents with typical development (TD) were selected for this study. The Autistic adolescents (mean age= 13,5 ±2 years) were recruited from the 'Laboratorio dei Talenti' project. They have been diagnosed by clinicians according to current diagnosis of Autism that requires scores above the ASD cutoffs on the Autism Diagnostic Observation schedule (ADOS) and *the DSM-IV criteria for autism.* The TD adolescents (mean age 14,2 ±2 years) were recruited at a local school and were free of current or past psychiatric or neurological illness, as determined by clinical history. ASD and TD participants had an IQ ≥ 70 on the Wechsler Intelligence Scale for children (WISC). Parents gave written informed consent.

4.1.2.2 *Stimuli*

A set of hierarchically formed numbers with global and local levels was constructed. The larger global numbers were composed of the appropriate placement of the smaller local numbers within a 3 (horizontal) x 5 (vertical) cm matrix. Global stimuli were 25x45mm and subtended approximately 2.6° visual angle horizontally and 4.7° vertically. Local stimuli were 2x3mm and subtended approximately a visual angle of 0.21° horizontally and 0.31° vertically. The numbers 1 and 2 served as targets, while 3 and 4 served as distractors. Each task contained one target and one distractor crossed with the global and local levels (see figure 1). There was another stimulus call neutral that consisted in a simple number target 1or 2 with the same measures of global level but without distractors. The stimulus neutral was presented randomly like the local and global stimuli. All stimuli were black and presented on a white background.

Figure.2



Target: global 2   Target: global 1   Target: local 1

Figure 1. Example of stimuli constructed in three different tasks. The first image represents the task that contains the target global 2 and distractor 3, the second one represents the task that contains the target global 1 and distractor 3 and the last one represents the task that contains the target local 1 and distractor 4.

4.1.2.3 *Procedure*

Stimuli were presented in a Macbook Air 13'. Each task contained one target and one distractor crossed with the global, local and neutral levels. The stimuli were presented one at a time to the left, center or right of the screen randomly, there was a 1000msec inter trial interval always with the central fixation point. The participant was sat directly in front of the computer at standard distance of approximately 54 cm from the screen. His hand rested over the x mark that was positioned at 30 cm of the keyboard where were placed the buttons with the numbers 1 and 2 for answering in the left, center and right.

Eighteen practice trials were administered and in the instruction was specified that the response should be as rapid and accurate as possible, always returning the hand over the x mark after each response. The participant mark 1 when there was a one in the trial or 2 when there were a two in the trial, respectively in the space where it was found (left, center or right). Reaction times were recorded with Psyscope X B77.

4.1.3 Experimental design

The experiment includes 3x3 factorial design with the factors: Level (Local vs. Global vs. Neutral) and Space (Left vs. Right vs. Central). The within factor was the subject variable, the between factor was the Group (ASD vs TD). This paradigm has one session of 144 trials.

4.1.4 Results

The reaction times were analyzed using ANOVA repetitive measure. On the basis of the results, ANOVA showed significant main effect for the factor Group [(f (1,18) = 17.45 p = 0.0006], this evidence that the ASD group was slower than the TD group. The Level factor was also significant [f (2,36) = 26.11 p = 0.0001] showing a decrease in reaction times in the condition Neutral.

The interaction of Group x Level was significant [f (2,36) =5,27 p = 0.009]. Also the third interaction between the factors Group x Level x Space was significant [F (4,72) = 3.16; p = 0.01] (see figure 2), this evidence suggests that the ASD group was slower to respond to the left in the global level. Also the double interaction was significant like the third interaction.

The Duncan test for post-hoc analysis evidenced that the ASD group takes longer in the global level to the left space compared with the local level to the left space (p = 0.0008). Also to the left the ASD Group was slower in both global and local level compared with the neutral level (p = 0.0001). The neutral Level in the central Space compared with the local (p = 0.0001) and global level (p = 0.0002) in the same central space showed to be faster. Also, to the right neutral Level, it was faster than global (p = 0.0001) and local level (p = 0.0002) to the right.

In all conditions the ASD group had the worst performance or a number of reaction time longer than TD group. The TD group in the neutral vs. right, neutral vs. left and neutral vs. central had a greater performance than in the local vs. left (p = 0.006), local vs. central (p = 0.005) and local vs. right (p = 0.02).

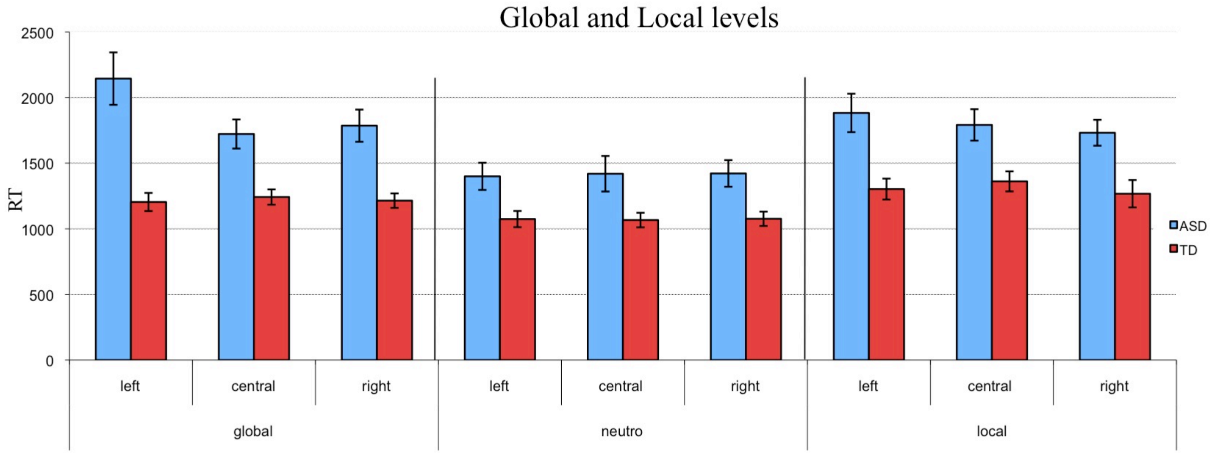


Figure 2. Mean RTs of correct responses in the different experimental conditions (Global, Neutro and Local levels; Left, Right and Central space in ASD and TD subjects). In general it is possible to observe that the longer times in Global x Left in ASD subject. Error bars indicate standard error of mean.

4.1.5 Discussion

The aim of the experiment was to investigate the attentional Local and Global processing, modulating the stimuli presentation in the spatial horizontal plan (left vs. central vs. right). The main results showed an evidence for the presence of dysfunction of right hemispheric spatial attention mechanism in ASD group. In general the ASD group have more times longer than the TD group. But when the task in Global level was positioned in the left space the ASD group took longer times respect to local and neutral levels in the left, right and central space. This phenomenon could be associated with several studies that attribute the processing of global and local information at the brain hemispheres activity. These researches have demonstrated that Local stimuli presented in the right visual field were processed faster than Global stimuli and that Global stimuli presented in the left field were processed faster than Local stimuli. (Martin, 1979; Sergent, 1982; Robertson et al., 1993). This phenomenon refers to the fact that the left hemisphere has a processing advantage for Local targets while the right hemisphere has a processing advantage for processing Global targets (Robertson et al, 1988; Lamb et al., 1989). Starting from this, we hypothesize impairments in ASD subjects in the right hemisphere not only to process the global stimuli but also in the spatial attention in general because in the computing of hierarchical stimuli also play an important role areas such as inferior parietal lobe. A lesion in this area affects the ability to assign attention to Global or Local level (Robertson et al., 1988), to respond to relevant stimuli when these appear in unexpected locations in the visual field (Posner et al., 1984) and the performance on spatial relations tasks. These abilities most often present some difficulties in ASD subjects. According with this interpretation, it is well known that the right parietal damage could result in hemispatial neglect, so it is for this reason that we modulate the stimuli in the spatial horizontal plan (left vs. central vs. right). This is because, according to spatial attention such as observed in the Unilateral Spatial Neglect (USN), we hypothesize that explaining the differences in the spatial attention could contribute for understanding autism spectrum disorder.

4.2 Experiment 2.

Perspective Taking from the space

Visual perspective taking (VPT) is defined as the capacity to appreciate the world from another person's perspective contributing not only to research how the impairments in social cognition and abilities that require the use of spatial and social abilities are interrelated (Pearson, 2013 for a review), but also to provide value to the research of Theory of Mind (ToM). VPT and ToM seem to share cognitive processes (Hamilton, 2009), and bring the possibility to explain of complex symptoms of Austim Spectrum Disorder. For this reason this experiment took a methodology where it was possible to investigate how children with autism would represent a spatial differentiation in a task where the self-other differentiation also was possible. In this way, the general findings showed important differences in left and right space in the first and third person perspectives that could be explained through the different clinical manifestations in Unilateral Spatial Neglect (USN).

4.2.1 Objective of the experiment

The aim of this study was to investigate how children with autism would represent a spatial differentiation (left-right) in a task of perspective taking with a first person perspective (1PP) and a third person perspective (3PP) modulated in two dimensions.

4.2.3 Material and Methods

4.2.3.1 *Participants*

20 adolescents: 10 adolescents with autism spectrum disorder (ASD) and 10 adolescents with typical development (TD) were selected for this study. The Autistic adolescents (mean age= 13,5 ±2 years) were recruited from the 'Laboratorio dei Talenti' project. They have been diagnosed by clinicians according to current diagnosis of Autism that requires scores above the ASD cutoffs on the Autism Diagnostic Observation schedule (ADOS) and *the DSM-IV criteria for autism.* The TD adolescents (mean age 14,2 ±2 years) were recruited from a local school and were free of current or past psychiatric or neurological illness, as determined by clinical history. ASD and TD participants had an IQ ≥ 70 on the Wechsler Intelligence Scale for children (WISC). All participants had normal visual-perspective taking, ability necessary for the task. Parents gave written informed consent.

4.2.3.2 *Stimuli*

Stimuli consisted in a real Display case of 51cm x 51cm with sets 3x3 shelves with measures of 17cm x 17cm. Each shelf was identified by its position in the Display case. In each shelf was placed one object. Three pairs of objects were used. Each pair consisted in the same object differing by the color.

In addition two experimental conditions were compared. Common Ground (CG), and Privileged Ground (PG). In the CG condition the experimenter's question included a target object that had a contrasting object that differed in color (red apple and green apple) (see figure 1.) In this condition, the objects were visible to the participant and to the experimenter who ask the question.

The second condition PG, also included the target and the contrasting object, but crucially here the contrasting object was obscured from the 3PP experimenter's view (see figure 2.).

The Display case and the keyboard were placed on a table. The participant was seated in front of the display case and the keyboard. There were 2 experimenters, 1PP (first personal perspective) and 3PP (third personal perspective). The 1PP experimenter stood in front of the display and next to the participant. The participant and the 1PP experimenter had the same visual perspective and could see all the objects, while the 3PP experimenter stood behind of the display and could not see the objects placed in the obscured shelves.

Reaction times were recorded with Psyscope X B77.

4.2.3.3.Procedure

The participant was seated across the table at standard distance of approximately 58 cm from the display. Before starting the task the participant was shown both sides of the display and was asked how many objects could see 1PP and 3PP experimenters and if the 3PP experimenter could see something that was placed in the obscured compartment.

In each trial 1PP and 3PP experimenters (randomly) made the questions "*where is*" referring, to a particular pair of objects that could be in PG or CG condition. The participant responded by pressing the key that corresponded at the object in the display. The keyboard had a drawing of display and the number of keys corresponded to the numbers and positions of shelves.

Figure 1. Example of Common Ground (CG) condition.

Figure 2. Example of Privileged Ground (PG) condition.

4.2.3.4 *Experimental design*

The experiment includes 2x2x2 factorial design with the factors: Perspective (1PP vs. 3PP) Dimension (Privileged Ground-PG vs. Common Ground-CG) and Space (Left vs. Right). The within factor was the subject variable and between factor was the Group (ASD vs TD). This paradigm has 4 sessions, each of 14 trials for a total of 56 trials.

4.2.4 Results

The reaction times were analyzed using ANOVA repetitive measure. On the basis of the results, ANOVA showed significant main effect for the factor Group [f (1,19) = 13,35; p = 0.001], this evidence that the ASD group was slower than the TD group. The space factor was also significant [F (1,19) = 5.89; P = 0.02] showing an increase in reaction times to the right space.

The interaction of Space x Perspective was significant [f(1,19) = 7.34; p = 0.01] with reaction times of the 3PP factor that increase in the right space and decrease to the left space. The fourth interaction between the factors Group x Perspective x Dimension x Space was significant [F(1,19) = 4.51; p = 0.04].

It was effected the Duncan test for post-hoc analysis evidencing a difference between 1PP and 3PP in the ASD group to the left space in CG, the ASD group was faster for response in 3PP rather than 1PP (p = 0.01). Likewise, to the left space the 3PP was faster than to the right space also in 3PP (p = 0.03). Also the ASD group in the CG to the left space in 3PP showed to be faster compared with right space in PG (p = 0.01) and in 1PP (p = 0.01).

In the comparison between ASD and TD Groups, in the interaction 1PP in CG to the left space, the ASD Group was slower than TD group (p = 0.001) (see figure 3). In this same comparison between groups, in PG to the left space in 3PP the ASD group was slower than TD group (p = 0.02), while in 1PP the ASD group was slower to the right space compared to TD group (p = 0.007) always in PG (see figure 4.).

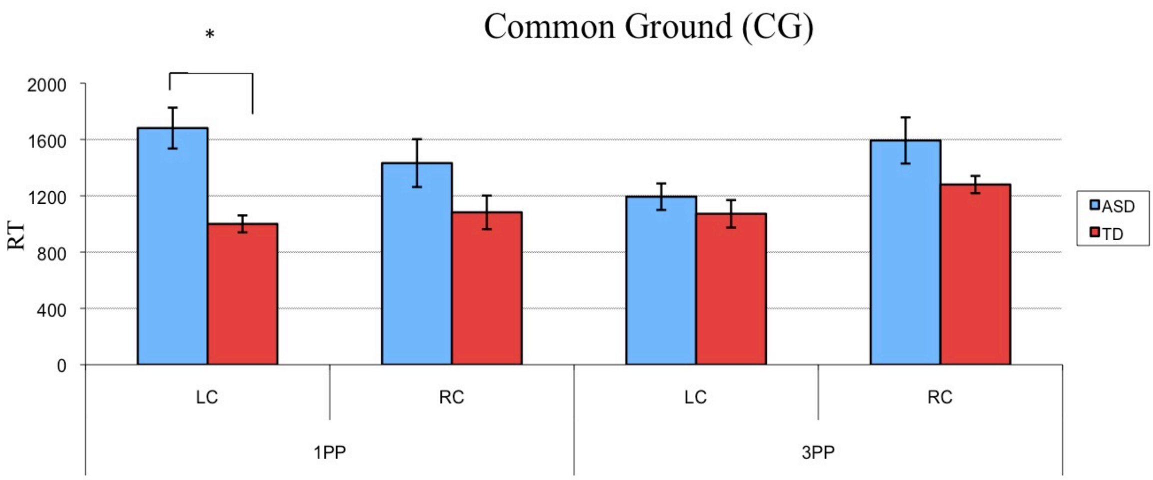


Figure 3. Mean RTs of correct responses in the dimension CG with the different experimental conditions (1PP and 3PP perspective in Left and right space). It is possible to observe that ASD subjects showed longer times in the left space when the perspective was in 1PP respect to the TD subjects. Asterisk indicates significant comparison ($p = 0.001$). Error bars indicate standard error of mean.

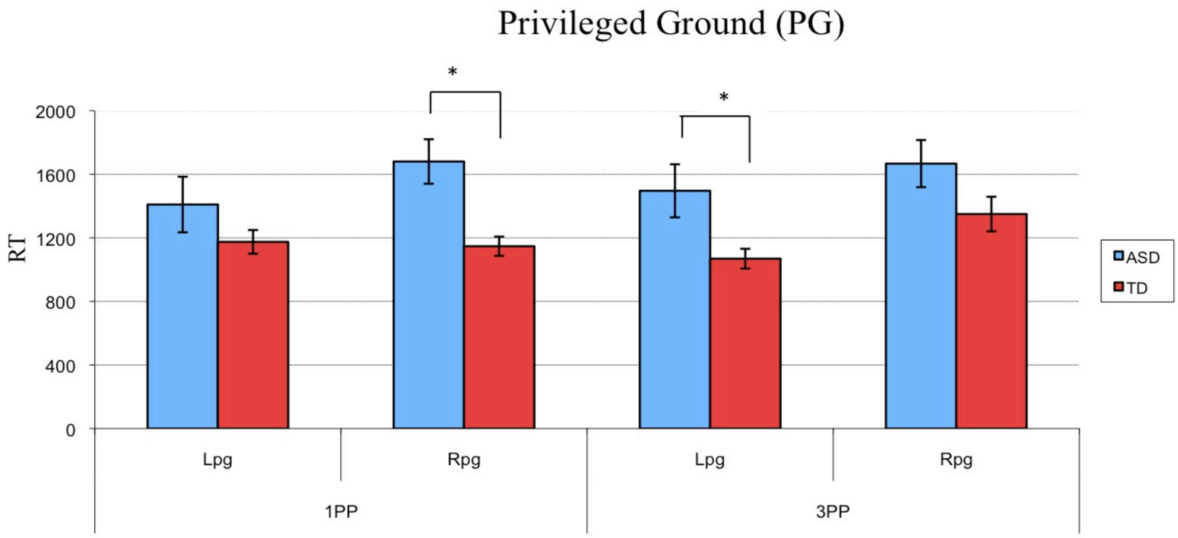


Figure 4. Mean RTs of correct responses in the dimension PG with the different experimental conditions (1PP and 3PP perspective in left and right space). It is possible to observe that ASD subjects showed longer times to left space when the perspective was 3PP ($p = 0.002$) and longer times to right space when the perspective was 1PP respect to TD subjects. Asterisk indicates significant comparison. Error bars indicate standard error of mean.

4.2.5 Discussion

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social communication and restricted interests (Wing and Gould 1997). Here we consider that the social interaction is mediated by environmental structures and that the space representation could underlie the social cognition (Krueger, 2010).

In this line of reasoning, the aim of this study was to investigate how children with autism would represent a spatial differentiation in a task of perspective taking with a first person perspective (1PP) and a third person perspective (3PP) in two dimensions. The first one being a perceptual dimension (CG) linked to the spatial orientation and the second one being a representative dimension (PG) of the social type. The result of this experiment showed significant differences in perspective factor (1PP and 3PP) related with the factor space (left and right) in both dimensions highlighting, in the perceptual dimension (CG), the comparison between ASD subjects, and in the representational dimension (PG), the comparison between ASD and TD group.

We suggest that Unilateral spatial neglect (USN) has different clinical manifestations that contribute to explain the differences in the perceptual dimension (CG) of autistic children in a task of Visuo-spatial perspective taking (VPT).

For these reasons, in the perceptual dimension CG the results showed that the autistic group in the 1PP was slower in the left space in respect to TD children for whom in this condition there were no significant differences in the factor space (left and right). Meanwhile in the 3PP, the ASD group was faster in the left space and the TD group did not obtain significant differences. These findings suggest that the ASD children have a similar behavior in VPT task as the patients with neglect, because there is an ease in children with ASD for answering in the right space and take longer times toward the left space in the 1PP.

On the other hand, in the 3PP the results demonstrated how the difficulties disappear in the left space just like patients with neglect have demonstrated (C. Becchio et al., 2011). This is because it seems that perspective taking significantly ameliorated the responses (RT) in the left space when the ASD children assumed a different spatial perspective (3PP-self). In addition it is known that lesion in the right parietal is the main cause of neglect. For this reason, we suggest impairments in right parietal in children with ASD because this area along with the right premotor cortex are involved in spatial tasks (Colby and Golberg, 1999), including tasks related to spatial transformation of objects (Lamm et al., 2001). These findings could explain the shorter times in ASD in answering to the stimuli that were in the left space. Furthermore these regions are also activated in egocentric tasks, in which subjects make judgments on the midsagittal position of objects in relation to themselves (Misaki et al., 2002). This could offer a possibility to explain how these regions are interrelated in the 1PP task in this experiment. Finally, it is likely that the activations in these brain areas are common for 1PP and 3PP and for this reason the parietal regions are involved in general processes of perspective taking in autism.

On the other hand, the social representative dimension (PG) exhibited that the autistic children in 1PP were significantly slower to the right space in respect to TD for whom there were no differences at the spatial level respect to 1PP in the factor space. This confirms the findings of different studies that account for impairments in different tasks that are related to the self perspective in autism (Lee and Hobson, 1998; Loveland and Landry 1986; Lee et al., 1994; O´keefe, 2008; Baron- Cohen, 1998; Leslie and Thaiss, 1992; Kasari et al., 1993; Heerey et al., 2003; Hobson et al., 2006; Lombardo et al., 2007; Silani et al., 2008 and Henderson et al., 2009). Therefore, demonstrating that there exist difficulties in the self in a visual perspective task in children with ASD.

Moreover the ASD group showed in PG Dimension, unlike in 1PP, that in 3PP was slower to the left space in comparison with the TD group.

These results could suggest that the subjects with autism have some impairments in the left hemisphere to perform social tasks associated with the 1PP and also some impairments in the right hemisphere to perform tasks related with the 3PP, because the neural correlates mostly linked with 1PP were observed in the left hemisphere and the right hemisphere regions in task related with 3PP (Rubi and Decety, 2001; Volgeley et al., 2004).

CONCLUSION

This research could increase the knowledge about some aspects related to how spatial perception could be compromised in Autism Spectrum Disorder (ASD) and how this in turn affect the social interaction.

The findings of the first experiment could be an evidence for the presence of dysfunction in right hemispheric spatial attention mechanism in ASD children, using a procedure from cognitive neuropsychology known as the global/local task. This could be the beginning of an evidence of certain spatial perception symptoms that could yield neural characteristics in ASD.

On the other hand, the findings of the second experiment suggest that the ASD children have a similar behaviour in VPT task as the patients with neglect because there is an ease in children with ASD for answering in the right-side and longer times toward the left-side in a base condition as the 1PP in a predominantly perceptual task. Meanwhile in this same task, in the 3PP the results demonstrated how the difficulties disappear in the left space just like patients with neglect have demonstrated (Becchio et al., 2011). This is because it seems that perspective taking significantly ameliorated the responses (RTs) in the left space when the ASD children assumed a different spatial perspective (3PP).

Finally, in a representational task the autistic children in 1PP were significantly slower to the right in respect to TD, this findings suggest that there is dissociation between perceptual and representational tasks just like patients with neglect show (Ortigue et al., 2001). Moreover this could demonstrate the findings of different studies that account for impairments in different tasks that are related to the self-perspective difficulties in the 1PP in a visual perspective task in children with ASD. For this reason we might hypothesize a predominant less activation on the left structures of the brain for doing tasks related with the self but reinforced when there is a social representative dimension.

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