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"USING NEW EXPERIMENTAL PARADIGMS AND DATA ANALYSIS FOR EVALUATING SOCIAL COGNITION AND AESTHETIC PERCEPTION ABILITIES IN INDIVIDUALS WITH AUTISM SPECTRUM DISORDER"

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Aim of the work

Autism Spectrum Disorder (henceforth ASD) is a group of neurodevelopmental conditions, which manifest itself in early childhood. It is characterized by impairments of social interaction and communication, and repetitive patterns of behaviour. Moreover, individuals with autism are characterized by an impairment of Social Cognition (henceforth SC) abilities; SC is a complex cognitive construct that allows to decode and encode the social world. It is fundamental in everyday life to improve successful social interactions. Another capacity that promotes positive social interaction is the aesthetic perception ability, a capacity closely related to the SC construct, influencing each other, in Typically Developed (TD) individuals. Impairments of these heterogeneous abilities hinder the social inclusion and lead to isolation of individuals with ASD.

Based on these knowledges, this PhD project had a double objective:

(1) Evaluating the development of SC and the role that it plays on social behaviour, implementing research lines that involve the use of different analysis models.

(2) Evaluating the aesthetic perception ability in both TD and ASD individuals in order to help the clinicians to create specific aesthetic protocols for rehabilitating the beauty perception, as well as the social functioning.

To achieve these aims we conducted the following studies that are explained in detail in this thesis:

a) we firstly demonstrated that children with ASD have a delay in the development of SC skills, rather than a total lack of these competences, compared to children with TD. To this aim we used the development trajectories analysis on three SC tests (Comic Strip tasks-CST, Eyes-tasks-ET, Social Information Processing Interview-SIPI) specific for children of a range between the ages of 5-13 years (*chapter 2*).
b) Subsequently, we demonstrated, through the mediation analysis, that in children with TD the competences of SC (measured by CST and SIPI) mediate the correct development of social behaviours appropriate to the context (*chapter 2*).
c) the early diagnosis represents a fundamental step to avoid the social isolation of individuals with autism. Currently, the Autism Diagnostic Observation Schedule-Second Edition (ADOS-2) is the only tool that allows the diagnosis of ASD and it is based on a standardized observation of the behaviour characterized by the presence

of objects/stimuli necessary for interact to the ASD individuals during the assessment. This instrument can be used from 12 months up to adult age. In our research, we applied the Formal Psychological Assessment (FPA) methodology to ADOS-2 in order to highlight strengths but also weaknesses of this diagnostic tool. The results revealed the need for a revision of the clinical tool through the implementation of an adaptive testing system, realized by FPA, which allows a more accurate evaluation and shorter execution times. A possible future perspective is to develop a software product that can assist clinicians in the path of diagnosis for ASD (*chapter 2*).

d) Finally, we evaluated the aesthetic perception ability and her relationship with SC construct, in TD and ASD individuals, using a specific aesthetic task namely Golden Beauty. On these premises our research activity focused on the study of aesthetic perception and SC in a group of adolescents with TD. The results showed that the aesthetic perception ability is related to the competences of SC. Specifically, these competences work together to improve social behaviour. Based on this, we used the same task in a group of adolescents with autism compared to adolescents with TD. Specifically, we used the Golden Beauty behavioural task adapted for eye-tracking in order to have both explicit and implicit evidences, respectively. At explicit level, our behavioural results showed an impairment in aesthetic perception ability in ASD individuals. This inability could have relevance in influencing their capability to experience pleasure during social interactions. However, at implicit level (eye-tracking results), ASD individuals conserved a good ability to feel aesthetic pleasure during the Golden Beauty task. Thus, indicating the presence of a discrepancy between the explicit and implicit evaluation of the beauty task. Finally, beauty perception appears to be linked to empathy when both these capacities are not compromised, as demonstrated in the TD group. On the contrary, this link results to be missed in ASD individuals. Overall, our results clearly showed that individuals with autism are not completely blind to the aesthetic pleasure. In fact, they conserved an implicit ability to experience the beauty. These findings could pave the way for developing new protocols to rehabilitate ASD social functioning, exploiting their conserved implicit aesthetic perception (*chapter 3*).

Chapter 1

BACKGROUND: SOCIAL COGNITION AND AESTHETIC PERCEPTION ABILITIES IN AUTISM SPECTRUM DISORDER

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1. AUTISM SPECTRUM DISORDER: A BRIEF INTRODUCTION

Autism Spectrum Disorder (ASD) are atypical neurodevelopmental disorders, which manifest in early childhood, characterized by a range of deficits in two domains: social communication and social interaction, and repetitive patterns of behaviour[1]. In the last 50 years, research in autism has constantly grown. Nevertheless, aetiology and pathogenesis of this disorder are still lacking[2] and there is no agreement about the causation of autism. Moreover, the etiopathogenetic factors of ASD are unknown. Researchers try to understand the aetiology, in terms of the epigenetic, neurobiological, genetic, neurological, and hormonal factors at the base of this complex condition[3,4].

Certainly, according to Tick and colleagues[5], the ASD has strong genetic aetiologies and the interactions between genetic and environmental factors are thought to contribute to its onset[4,6,7.]

ASD is a heterogeneous disorder that persist throughout life[8] and the severity of symptoms varies widely among affected individuals. To date, probably due to increased awareness for this disorder, 1% of the population has an autism diagnosis[8] with a male:female ratio of 3-4:1[8,9]. At the same time, it is important to emphasize that, given the dimensional nature of autistic traits, it is complex to draw a clear diagnostic line[8,10]. Specifically, based on clinical point of view, the diagnosis is carried out considering the intensity of autistic traits and level of impairment of adaptive functioning; while, based on an evolutionary point of view, an individual can be characterized by a high component of autistic traits but without the need of clinical diagnosis. In this case, the diagnosis can be necessary in presence of an inadequate environmental condition that negatively affect the individual's life, determining an impairment of adaptive operation. Indeed, according to Lai et al.,[8] the autism represents, on one hand, a "medical condition" that gives rise to disabilities, on the other, it is an example of human neurological variation, "in terms of neurodiversity, characterized by gains and cognitive challenges (duality of autism)".

Generally, the ASD alters the growth process, compromising the neurodevelopmental domains, such us cognitive, communicative-linguistic and behavioural abilities[11]. The areas mainly affected by the disorder are the ones involved in development, i.e. those related to the mutual social interaction, to the ability to communicate ideas and feelings and to the ability to establish relationships with others[12,13]. Usually, children with autism show serious impairments or complete absence of language; difficulty or incapacity in the development of emotional reciprocity, in the relationship with peers and with adults; atypical sensory behaviours, or other complex medical and psychiatric symptoms and conditions, stereotyped, repetitive behaviours and narrow interests[14,15]. Sometimes, these elements, are related to a mild, moderate or severe mental delay.. The variability in the behavioural symptoms, among the ASD individuals, can be related to the fact that the different neurodevelopmental areas can be affected unevenly.

Based on DSM-5[1] the categories of symptoms are summarized in two main domains:

1) deficit of social communication and social interactions;

2) limited and repetitive patterns of behaviour, interests and activities.

For the formal diagnosis the presence of both components of the disorder is mandatory, and it is essential to assess the severity of the symptoms of the autism spectrum based on three levels of functioning. Specifically, the three levels of gravity, based on the impairment of the social communication and on the presence of restricted and repetitive behaviour patterns, are divided in[1]:

* 3rd level, "very significant support is needed";
* 2nd level, "significant support is needed";
* 1st level, "support is needed".

The diagnostic procedure represents a fundamental step for the early identification of the autism and for the activation of a rapid and effective abi/rehabilitation intervention. Usually, during the first three years of life, some specific indicators of the possible ASD, such us joint attention deficit, atypical behaviour affiliation, delay in language and motor development, stereotypes and repetitive behaviours, imitative inability and lack of visual contact, appear[16,17]. Most of the children receive a diagnosis between 3 and 4 years of age; an early diagnosis (<3 years) is complex and sensitive to error. Indeed, during the first 2 years of life, a non-specific symptomatology associated with deficient developmental stages could represents a confounding indicator, that could bring to the wrong diagnosis. Nevertheless, so far, toddlers are frequently diagnosed because atypical development is recognised early[10]. In particular, around 2 age, specific early indicators of ASD such as the absence of a smile, motor difficulties, as well as the lack of social responsibility and linguistic difficulties, can be osserved[12].

The ASD diagnosis is usually provided by experienced clinicians according to the criteria of the DSM-5 and it is confirmed using the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2)[18]. ADOS-2 is based on a standardized observation of the behaviour characterized by the presence of objects/stimuli necessary for interact to the ASD individuals during the assessment. A comprehensive, early and accurate diagnosis allows a timely initiation of the treatments. Based on the great heterogeneity of the individuals with autism, the treatments must be individualized. Each intervention must have as final goal the enhancing adaptation and wellbeing. Evidence-based support for individuals with ASD across the lifespan is emerging[8,10]. There are many approaches used for rehabilitative interventions of individuals with autism. The behavioural approaches are used to adapt the behaviour of the ASD individuals to the daily needs (i.e Applied Behavioural Analysis, Treatment and Education of Autistic and Communication Handicaped Children, DENVER, PECS etc). Other type of interventions aims to improve the social skills (social skill training, using new technology etc…), to enhance social cognition such as emotion recognition, imitation, joint attention, pragmatic language and mentalizing; and finally, to increase work with parents (parent-mediated intervention), as well as pharmacology interventions[10.] The social impairments are the most stable and common symptoms throughout the lifespan in ASD[19]. Therefore, a specific intervention on social cognition abilities is the key step during the implementation of treatments. The evidence for effectiveness of all these interventions is still low or moderate[8,10].

2. SOCIAL COGNITION AND SOCIAL BRAIN

The neurocognitive processes that allow us to interact with others in a suitable way constitute "*social cognition*"[20.] Social Cognition (SC) is a complex cognitive construct that refers to how we perceive, process and interpret social information[21]. This includes interpreting human behaviour and drawing inferences from spoken and unspoken communication[22]. Specifically, it is a fundamental dimension of social adaptation and human intelligence and underlying the individuals' ability to "*make sense of others' behaviour*" as a crucial prerequisite of social interaction[23-25]. The term "cognition" refers to unconscious mechanisms in the mind that bring representations, i.e. a neural implementation of the experience[26,27]. On the other side, the term "social" is closely linked to the processing of a specific types of stimuli. We know that in human and non-human primates the social skills appear early during the growth, around the 14th month of life, and these abilities play a key role for the lifespan[17,25,28,29].

The pivotal role of SC in everyday life reflects the neural complexity of social processing. Indeed, the lack of the SC abilities negatively affect the daily life of individuals. This condition is typical in some pathological situations, such as autism and schizophrenia[16,25]. It is known that several different psychological processes contribute to social cognition, and they are often grouped into two broad categories: (i) the processes related to automatic processing driven more by the stimuli and (ii) those related to controlled processing driven more by the person's goals and intentions[30].

According to Arioli and co-workers[25] the cognitive processes underlying the SC can be categorized into three areas related to:

(1) social perception, i.e. perceptual processing of social information such as faces and emotional expressions;
(2) social understanding, i.e. grasping others' cognitive or affective states;
(3) social decision making, i.e. planning our own behaviours taking into the account the thinking of the other's, beyond our own.

Happè[21] suggest that the base of social cognition is constituted by an "in(ter)dependence of core socio-cognitive processes". These socio-cognitive processes include the abilities relating to affiliation and social motivation affecting the quantity of an individual's social interaction, the biological motion perception, the action recognition and imitation. In other words, the socio-cognitive processes affect all the processes underlying the capacity:

* to establish which action is being performed by an agent, and the reproduction of the same by the self;
* to determine the affective state of another (emotion recognition);
*to pay attention to social stimuli;
*to feel empathy, i.e. when recognition of another's affective state creates the share of the same state;
*to have the Theory of Mind (ToM), i.e. the ability to understand and represent one's own mental states and those of others.

As shown below, empathy and ToM are considered the two main components of social cognition. Additionally, SC is characterized by different aspects that involve a large number of different brain structures and their connectivity. The distributed nature of SC makes the latter vulnerable to trauma, but at the same time, this distribution, offers the possibility of compensation through spared components of the SC network. Finally, SC generally involves a deep level of abstraction, inference, and counterfactual thinking[31].

It is known that human beings are social creatures and currently, thanks to neuroscientific studies, we can talk about of a "*social brain*". Originally, the term social brain was proposed by Brothers[32] to explain a set of brain regions related to the SC and thus to the social interactions. The author listed amygdala, orbital frontal cortex and temporal cortex as major components of SC. Subsequently, her intuition was confirmed by studies on monkeys[27].

To date, the increasing evidences about the social brain, obtained from healthy individuals, suggest that social mechanisms in the human brain are innate and mediate the SC abilities[25,30,31]. Studies conducted with clinical populations characterized by SC impairment have confirmed the existence of a social cognition neural network[30,31].

The evidence based on neuroimaging and fMRI studies confirmed that the social brain is a complex network and the circuits and systems that contributes to this are not easily separable from the brain's interconnections and they may have multiple overlapping functions in the cortical and subcortical regions[33]. This complex network of the social brain is well described by the modularity theories[34,35].

Kennedy and Adolph[31] proposed four SC networks of the social brain in the adulthood:

*the *Mentalising network* that consists in a set of structures, such as the medial prefrontal and superior temporal regions implicated in the automatic attribution of others' internal states;

*the *Empathy network* that involves activity of the insula and amygdala, recruited when individuals empathize with other individuals and they automatically detect and respond emotionally to others' distress;

*the *Mirror network* that involves parietal and prefrontal regions containing neurons that are responsive for both observation and execution of an action;

*the *Amygdala network* that is mediated by the amygdala's activity and it function concerning emotional evaluation and emotion regulation for detecting socially salient stimuli.

These brain regions play functional roles for several aspects of SC, such as predict others' behaviour, emotion recognition, feel empathy etc... The proposal of Kennedy and Adolph[31] is in line with the evidence that social information processing is for many aspects different from non-social information processing. Thus, supporting the theory that social information processing is modular[30].

Other researchers[27,36] proposed that the key areas of the social brain include the superior temporal sulcus, anterior cingulate cortex, medial prefrontal cortex, inferior frontal gyrus, as well as the anterior insula and the amygdala. These areas mediate the most complex social abilities, i.e. the ToM ability, a dynamic process that change during adolescence and into early adulthood[23]. Indeed, neonates are born with strong tendencies that stimulate social interaction, such as eye contact, face recognition, emotional processing, attentional preference for biological motion. Subsequently, the most complex social skills (for instance perception of others, joint attention, prosociality, ToM) develop during infancy and early childhood. However, during the adolescence rapid changes in the social brain appear, affecting the social abilities such as empathy, ToM and self-awareness. These abilities correspond with specific neural activity that facilitate and accommodate the social environment simultaneously[37]. Indeed, according to Adolph[30] the social cognition is sensitive to the context, therefore the brain regions involved in this construct are modulated, in term of activation, by the social context and volitional regulation.

2.1 THEORY OF MIND

One of the main components of social cognition is the ToM. The term ToM refers to a fundamental psychological ability for social life, i.e. the ability to understand and predict behavior based on the understanding mental states (intentions, emotions, desires, beliefs) of one's own and others[35]. This definition dates back to 1978 with the pioneering work of Premack and Woodruff[38], committed to study the intentional understanding of behavior in chimpanzees. These authors used the term "theory" because mental states such as beliefs, thinking, motivations are not directly observable. Subsequently, researchers showed the existent of a more complex ToM ability in the human beings. Generally, having the ToM ability means putting in place a meta-representation of mental states. In this sense, the individual strives to infer the contents of the other's human mind, which are subjective and therefore opaque from a referential point of view[39].

During the 1980s, the publication of researches by Baron-Cohen and colleagues[39], Wimmer and Perner[40] and Perner and colleagues[41] started a rich line of studies on the development of ToM in the developmental age. Subsequently, thanks to these works, Wimmer and Perner[40] created a prototypical task, i.e, the task of false belief (*false belief task*). In this test, the experimental subject is asked to fore see how the protagonist of a story will act, taking into account the false belief of this and not the reality, known only to him and the experimenter. In the version of the "*unexpected shift"* (called experiment of Sally and Anne[39,40], the subject must predict where the protagonist of the story will look for an object. This object was initially placed in a container and then moved to another container by the other character of the story without his/her (protagonist of the story) knowledge.

The child to solve the Anna and Salle test, and the same type of tests, must momentarily suspend his "knowledge of reality", and he/she must assume the perspective of the other. Thus, he/she represents the content of his/her mind, that is a false belief with respect to reality, so as to correctly predict how the other individual will behave based on of one's false belief[39,40]. According to study of Shamay-Tsoory[42], ToM is believed to be an outgrowth of pre-existing social intelligences[43,44]. We know that it cannot be considered a unitary component, but it involves at least two dimensions: cognitive and affective sub-components[17,24,45,46]. Specifically, the cognitive component of ToM is the ability to understand what others are thinking (i.e., their mental states); whereas affective component of ToM is the ability to make inferences regarding other people's emotions[45]. These two components of ToM work togheter to promote an adeguate social life but, at the same time, they are two indipendent process. Indeed, some studies on patients with lesions that involve the right ventral medial and orbital frontal lobe, showed a dissociation between ToM abilities[45,47]. These patients exhibit impaired performance in the tasks that assess affective ToM, but not in the ones that assess cognitive ToM. The research[48,49] proposed several models to explain the ToM by introducing the closely related concepts of empathy and prosocial behavior.

2.2. EMPATHY

The ability to "*put oneself into another's shoes*", or experience emotions of another being within oneself, is know as "empathy"[50,51]. Zinn[52] described the empathy "as the process of understanding a person's subjective experience by vicariously sharing that experience while maintaining an observant stance". The construct of empathy is characterized by two type of process: bottom-up processing of affective arousal, emotion awareness; and the top-down processing in which the perceiver's motivation, intentions, and attitudes influence the extent of an empathic experience[53].

According to several authors[42,48] empathy is not an unitary concept, but it is composed by two sub-components: the cognitive empathy, i.e. the ability to adopt another psychological point of view; and the affective empathy, i.e. the ability to emotionally "resonate" with other people's feelings and understand at the same time that they are distinct from one's own.

The cognitive dimension of empathy involves complex cognitive abilities, including mentalizing ability[42,54,55], whereas emotional empathy (affective emphaty) includes experience sharing of other persons' internal states[54]. Emotional contagion is a precursor of emotional empathy, whereby embodiment entails the forming of a representation of the other person's feelings[56,57]. The ability to share others' emotional states is mediated by the activation of corresponding representations existing in the observer[56,58]. At the neural level, such ability could rely on mirror-like mechanisms similar to the mirror neurons that encode both executed and observed actions in primates[59].Indeed, mirror neurons are also involved in the understanding of the intentions that underlie action.

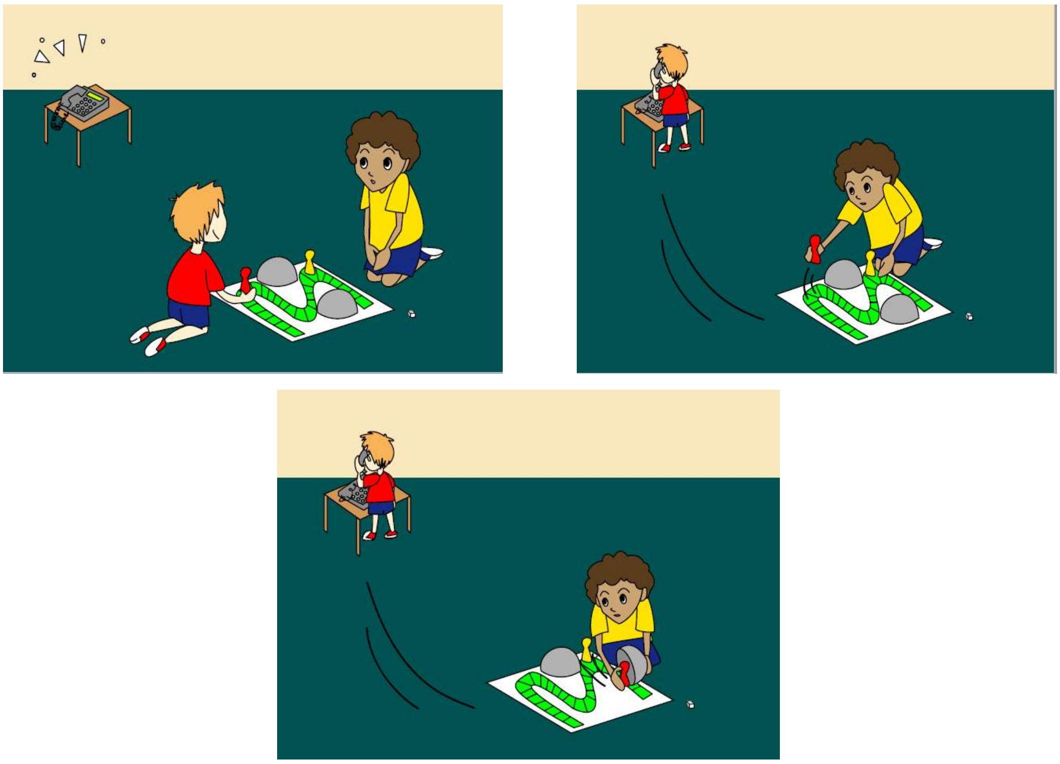
The research, for many time, focused on these two empathic processes[42,48]. Subsequently, Zaki and Ochsner[49] proposed a new three-dimensional model of empathy which specifies a pro-social concern dimension, alongside mentalizing and emotional sharing. This dimension encompasses the motivation of individuals to improve the emotional experiences of others (e.g., their suffering) and the ability to help them[49].

2.3 SOCIAL COGNITION MEASURES FOR CHILDREN

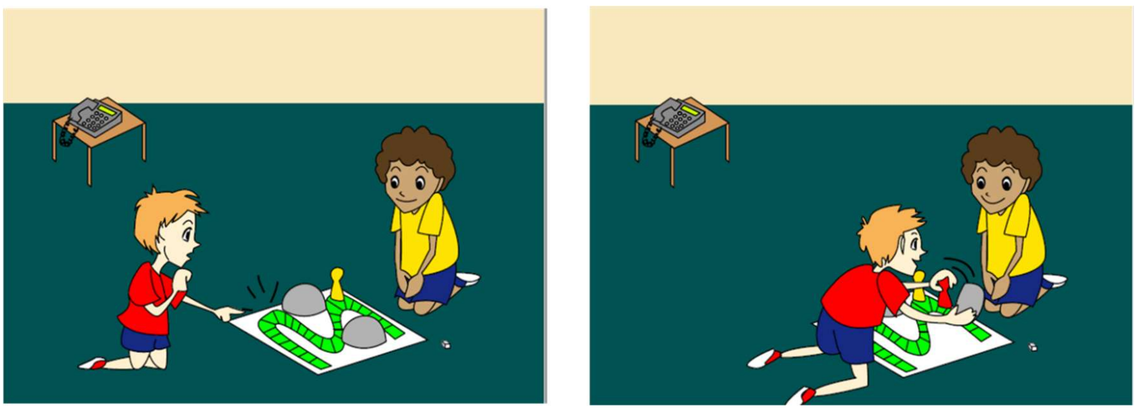
Generally, in TD children, the understanding of the intention of others appears around 4-5 years of life (pre-schooler)[60]. Among the social cognition measures that can be used with pre-schooler children we can mention:

1.Comic Strip Task (CST)[60,61]. The CST is a novel 21-item measure developed to assess three aspects of ToM; namely, the understanding of others' beliefs, intentions, and emotional states, and comprises the three sub-components testing belief-understanding (beliefs), intention-understanding (intentions), and emotion-understanding (emotions), respectively. There are 5 items in each sub-component, each comprising a 5-picture comic strip illustrating everyday social scenarios involving interpersonal interactions familiar to young children. For each item, children are shown three pictures that tell a social story, after which the children are presented with two pictures containing alternative endings to the story and asked to select the one that they think best completes the story. One option indicates a lack of understanding of others' mental states and is scored as 0; the other indicates the presence of understanding and is scored as 1. Each sub-component has a maximum score of 5, with a total test score of 15 (i.e., higher scores correspond to better ToM). Sivaratnam and collaborators[60] assessed the internal consistency reliability, as measured by Cronbach's alpha: the beliefs sub-component demonstrated low and negative internal consistency (Cronbach's $\alpha = -0.04$); the emotions and intentions sub-components demonstrated moderate internal consistency (Cronbach's $\alpha = 0.69$ and $\alpha = 0.70$, respectively). In their study, Sivaratnam et colleagues[60] found a lower internal consistency; for this reason, we calculated the internal consistency of the overall CST and each sub-component (intentions 0.56, beliefs 0.66, emotions 0.23).

***Belief - Board Game**, an example of belief story:*



Two possible finals of the story:



2. *Eyes-Task-Simplified*[62]. The task contained black and white photos of children's eye region, portraying either mental states or primary emotions. The expressions included as primary emotions were happy and surprised (positive/neutral valence), and sad and angry (negative valence), while excited and thinking (positive/neutral valence), and worried and shy (negative valence) were selected to represent mental states. Although in most cases it is unknown what the child was actually feeling at the time of taking the photographs, they were all derived from naturalistic settings (e.g., taken by parents) rather than being posed specifically for an experiment. 56 slides were prepared with each of the eight above described target emotion/mental states paired with each of the seven-remaining emotion/mental states in the series. Testing lasted approximately 15 min, based on randomised presentation of the items. Accuracy was measured on a 0–7 scale, based on the participant's selection of one of two choices in seven comparisons per target emotion/mental state (for further details, see Franco et al.[62]).

An example of eyes task-simplified:

3. Social Information Processing Interview (SIP-I)[63,64]. The SIP-I is an interview based on a storybook easel depicting a series of vignettes in which a protagonist is either rejected by two other peers or provoked by another peer. Each type of vignette is combined with each type of peer intent to generate four stories: (1) a non-hostile peer entry rejection story, (2) an ambiguous peer entry rejection story, (3) an accidental provocation story, and (4) an ambiguous provocation story. According to Ziv et al.[64], the scores correspond to four of the five mental steps of social information processing proposed by Crick and Dodge's[65] model: (1) encoding, (2) interpretation of cues, (3) response construction, and (4) response evaluation. An example of a SIP-I story is the following: Michael is watching the other children playing. Michael walks up to the other children and asks them: 'Can I play with you?'' The children say: ''Sorry. The teacher said only two can play in the block area' (for details, see Ziv et al.[64]). The encoding component evaluates the level of detail that the child recalls across the four stories. Thus, the examiner asks the child: 'Tell me what happened in the story, from the beginning to the end'. A score of 0 is given to a child who recalls no correct details for each story, and a score of 1 is given to a child who correctly recalls all the details in each story and then a sum of the scores is calculated, so scores could range from 0 (no correct coding in 4 stories) to 4 (all correct coding in 4 stories). The interpretation component evaluates the hostile attribution to others' behaviour (the question is 'Do you think the other children who didn't let Michael play are mean or not mean?'; an example of this story is reported below). The range for this score is 0–1 for each story, with higher scores representing higher levels of hostile attribution bias. The score in the interpretation component is inversely encoded compared with the other SIP-I components; that is, a higher score indicates a major tendency to consider the behaviour of other children as hostile. Regarding the response construction component, as reported by Ziv and Sorongon (2011) in their paper (page 7) the score "is derived from the child's responses to the open-ended item 'What would you say or do if this happened to you? The answers are used to create three, mutually exclusive flag variables (coded 0, 1) for each story: competent flag, aggressive flag, and avoidant flag. For example, if the child's response is coded as "competent," then he or she is given a "1" for the competent flag, a "0" for the aggressive flag, and a "0" for the avoidant flag. The final response construction score is then calculated by subtracting the aggressive and avoidant scores from the competent score. The original range of this score is minus four (only avoidant or aggressive responses) to four (only competent responses). However, to avoid negative scale scores, the scale was modified such that the presented possible range for this score is zero (only avoidant or aggressive responses) to eight (only competent responses) (Ziv & Sorongon[63] p. 7). For the response evaluation step, the scores are made from a combination of 36 Response Evaluation questions (4 stories × 3 competent/aggressive/ avoidant presented responses × 3 questions per presented response). An example of a question for the response evaluation of a SIP-I story is "Michael could kick apart the blocks and say to the other children, 'if I can't play, then you can't play either', (1) 'Is this a good thing or a bad thing for Michael to say?', (2) 'If you do that, do you think the other children would like you?', and (3) 'Do you think the other children would let you play if you do that?'. If a child evaluates as positive an aggressive behaviour the score is 0. For example, child could respond that Michael said a good thing and that other children would let Michael play with them after his aggressive behaviour, in this case the given score is 0.

"Michel would like to play", an example of SIP-I story:

Possible finals of the story:

2.4 SOCIAL COGNITION MEASURES FOR ADOLESCENTS AND ADULTS

The development of SC abilities is considered stabilized in adolescents starting from 15 years of age. Therefore, the social cognition tests that are used for adults are the same ones that are also used for adolescents. Some measures used for adolescence are reported below:

1.Basic Empathy Scale (BES)[66]. The BES is composed of two sub-scales: the Affective Empathy Sub-scale (*AES*) and the Cognitive Empathy Sub-scale (*CES*). The AES is composed of 11 items that measure the ability to share another person's emotions. Example of items on the AES are: "My friend's emotions don't affect me much" or "I often get swept up in my friend's feelings". The participants had to give their ratings on a five-point Likert-type scale ranging from 1 = Strongly Disagree to 5 = Strongly Agree. The BES-CES comprises nine items and measures the understanding of another person's emotion[67]. Examples of items in the CES are: "I can understand my friend's happiness when she/he does well at something" and "When someone is feeling down I can usually understand how they feel".

2. Interpersonal Reactivity Index (IRI)[68]. This is the most frequently used self-administered tool to assess the different components of empathy. The IRI-affective sub-scales include a total of 14 items divided into two scales: the "personal discomfort" (PD) and the "empathic concern" (EC) sub-scales. The PD sub-scale evaluates self-oriented anxiety and discomfort resulting from tense personal situations (e.g. I tend to lose control during emergencies). The EC sub-scale refers to feelings of compassion, tenderness and concern for other people (e.g. "When a friend tells me about his good fortune, I feel genuinely happy for him"). Each answer can vary from 0 (does not describe me well) to 4 (describes me very well). The scores of each sub-scale are calculated individually. The IRI does not provide a total score because each sub-scale evaluates an independent component of empathy[69]. The IRI cognitive sub-scales include 14 items divided into two scales: fantasy (FS) and perspective taking (PT). The FS sub-scale evaluates the individual's tendency to identify him/herself with fictitious personages, such as characters from books, films or video games (e.g. "When I am reading an interesting story or novel, I imagine how I would feel if the events in the story were happening to me"). The PT sub-scale evaluates the individual's tendency to spontaneously adopt the psychological point-of-view of another person (e.g. "I sometimes find it difficult to see things from the other guy's point of view").

3. Empathy Quotient (EQ)[70]. The EQ is a self-reported measure evaluating different aspects of empathy through cognitive, social skill, and emotional sub-scales. EQ-Emotional Sub-scale (EEQ) this is a self-report measure evaluating different aspects of empathy through cognitive, social skill and emotional sub-scales[69]. An example of an item is “I find it hard to understand how to behave in a social situation”. Each answer can vary from 0 (strongly agree) to 4 (strongly disagree). The cognitive dimensions of empathy are evaluated by two subscales of the EQ: cognitive empathy (CEQ) and social skills (SSQ), which measure, respectively, the capacity to take the perspective of the other person and some regulatory mechanisms that keep track of the origins of one’s own and other’s feelings.

4. Advanced-Theory of Mind Task (A-ToM)[71]. The A-ToM is an Italian adaptation of a cognitive task that Blair and Cipolotti[72] used and was first proposed by Happè[71]. The Italian task consists of an abridged version of 13 vignettes, each accompanied by two questions: the comprehension question “Was it true, what X said?”, and the justification question “Why did X say that?”. The 12 story-types include Lie, White Lie, Joke, Pretense, Misunderstanding, Double Bluff, Contrary Emotions, Figure of Speech, Appearance/Reality, Forgetting, Irony, and Persuasion. The subject obtains a score ranging from 0 to 1 for each question. The maximum score is 13. Happè[71] used the term “advanced” to refer to a story that contains the comprehension question, where the key questions in the task concern a character’s mental states (the experimental condition).

5. *Eyes Task* (ET)[73]. The Eyes Task is a revised version of the “Reading the Mind in the Eyes Test”; this test was considered by Baron-Cohen and collaborators (2001) to be a ‘pure’ ToM test. The participants are given 36 photographs depicting the ocular area in an equal number of different actors and actresses. At the corner of every photo, four emotional descriptors (e.g., dispirited, bored, playful, or comforting) are printed, only one of which (the target word) correctly identifies the depicted person's mental state, while the others are included as foils. The overall score totals the number of items (photographs) that the participant correctly identifies. Therefore, the maximum total score is 36.

6. Multifaceted Empathy Test (MET)[48]. This test consists of a series of photographs that depict people in emotionally charged situations, taken from the International Affective Picture System (IAPS)[74]. Subjects are requested to rate their level of empathic concern for the individuals displayed in the images using a nine-point Likert scale. The MET-Emotional Empathy (EE) component is divided into implicit and explicit components. For each stimulus, the subjects are required to answer to two questions: “How aroused does this picture make you feel?” for the implicit EE; and “How strong is the emotion you feel about this person?” for the explicit EE. The scores for implicit and explicit EE range between 1 and 9, where 1 and 9 correspond to the minimum and maximum levels of arousal (implicit empathy) and empathic concern (explicit empathy), respectively (Self-Assessment

Manikin). The final score for each condition (implicit and explicit) corresponds to the mean of all responses[69]. MET-Cognitive Empathy (CE) component evaluates the capacity of the subjects to infer the emotional and mental states of the individuals shown in the image[48,69.] The stimuli present individuals feeling different emotions: positive emotions (25 pictures that include emotions like happiness and positive surprise); and negative emotions (25 pictures that include emotions like sadness, anger, disappointment). Positive and negative emotions were presented in a random order. All stimuli were displayed on a black screen. For each of the 50 stimuli presented, the subjects were required to infer the mental and emotional state of the individual/s depicted in the picture (What kind of emotion/mental state is/are the person/people feeling?). The score of cognitive empathy is the sum of correct responses (maximum score is 50)[69].

3. AESTHETIC PERCEPTION ABILITY AND EMPATHY

In recent decades, cognitive neuroscience extended its field of study on both music and figurative arts. The growing interest in this new field of study is due to the British neurobiologist Semir Zeki[75] that supported the start of a new type of neuro-scientific research, namely *Neuroaesthetic*. The term neuroaesthetic was created in order to investigate the biological and physiological mechanisms underlying the ability of aesthetic perception[76]. This new way to study the art differs from the previous ones and it is essentially characterized by two fundamental guidelines. The first investigates the ambit of vision, i.e. the conditions in which we see and the criteria that order the visual world.

The visual world was assumed as a self-sufficient phenomenon for which the picture and the panorama are first visual facts representing games for the eye between them of equal value[75,76.] On the contrary, the second guideline interprets the vision as something creative, combining the sounds with the colours, the postures with the words, showing the "metaphoricity" of the reality. Indeed, the aesthetic perception is a complex phenomenon based on many subjective variables (especially emotional reactions). The aesthetic experience, therefore, shall be understood as a complete cognitive and emotional experience that has important implications on human experience and behaviour[77]. Specifically, the ability to perceive beauty plays a key role for all living beings, driving important evolutionary behaviour of the species such as the partner selection and the reproductive capacity[78]. In higher mammals such as humans, this ability is also fundamental for guiding social interaction[79]. Aesthetic pleasure has a hedonic value in itself. Hedonism is a fundamental aspect of the motivated behaviour of highly evolved organisms such as mammals. According to Langlois and collaborators[80] the perception of beauty is the base of the socialization and the social interaction. Indeed, some research has shown that beautiful children get less punishment for the same incorrect behaviour, compared to peers deemed less attractive[78]. Just like even children prefer adults with more attractive faces[79]. Furthermore, some features of the face such as symmetry are often associated with greater moral values, health and fertility[81,82]. For example, it has been shown that more attractive women have more offspring over their lifetime than less attractive ones[81,82]. The aesthetic perception seems to play an important role in politics, too. For instance, the citizens usually express the greatest preferences for the most attractive political candidates, the judges give less heavy penalties to the most attractive defendants and finally the teachers consider the most beautiful students more capable[79]. Judgment of other people's attractiveness probably occurs subconsciously and influences us in a way we do not consciously realize. Taken together, these findings suggest that some characteristics of beauty are important social cues that can induce stereotypes or promote different behavioural expectations[83]. Ultimately, they may also affect the ability to experience pleasure, which plays an important role in SC. A fundamental capacity in order to have successful social interaction is the empathy. In addition to the cognitive and affective component of empathy, there is a third component very close to the emotional component of empathy, known as *empathic resonance.* Empathic resonance, the phenomenon by which a person unconsciously observes (mirroring) the motor actions of others, is a basic prerequisite for human interactions[57]. These shared representations function as a basis for sharing the emotional and physiological states of others, that is an important component of empathy[58].

Indeed, resonance, like emotional contagion, can be considered a base or a bottom-up input for both emotional and cognitive empathy and it is mediated by shared representation of the system of mirror neurons[35,59].

The human brain has a mirroring mechanism that maps the actions observed on the same nervous circuits that control its execution[59,77.] Using the fMRI, researchers discovered that the mirror neurons were located in the pre-motor areas 6, 44 and 45 of Brodmann, in the inferior parietal lobule and in the superior temporal sulcus. It is known that the mirroring and simulation mechanism are not only involved in the execution and observation of finalized motor actions, but also in the understanding and sharing other's emotions[59,77]. Indeed, the understanding of the other's emotional states activates neural networks normally involved in the elaboration of affective states[84].

Moreover, fMRI studies showed the activation of some neural networks of the limbic system when an individual observes or imagines another individual during an emotional experience[84]. Based on this, "seeing something" means bring into play not only the vision, but also the motor and the somatosensory systems and the circuits that drive the ability to feel emotions[77]. Freedberg and Gallese[85] evaluated the empathic and the aesthetic perception abilities. The authors believed that the vision is a multimodal process based on the activation of specific brain circuits including the sensor-motors, visceromotor and affective circuits. Their results showed that the observation of art works leads an empathic involvement of the observer, activating, through simulation mode, the motor program that corresponds to the gesture evoked by art works. The mirror neurons activation was interpreted by Freedberg and Gallese[85] as a neural expression of functional mechanism of our brain-body system, called "embodied simulation"[77,85]. Therefore, a key element of the aesthetic response to images consists in the activation of embodied simulation mechanisms of the actions, emotions and bodily sensations represented in them. As a whole, these evidences suggest a close relationship between aesthetic and empathic abilities, since beauty can influence some aspects of the empathic behaviour, as well as empathic abilities appear to partly mediate the aesthetic perception[77]. The close relationship between aesthetic perception and empathy has been demonstrated also by studies aimed to understand the neural mechanisms underlying aesthetic perception. Generally, these studies showed that at the basis of aesthetic perception, there was the same cerebral activation involved in the regulation of emotions and empathy abilities [86-88]. In this respect, Di Dio and coworkers[86] showed that the observation of classical sculptures, compared to the same sculptures with modified proportions, produced the joint activation of some lateral and medial cortical areas (lateral occipital gyrus, precuneus and prefrontal areas) responding to the physical properties of the stimuli and, importantly, of the anterior insula. Therefore, the aesthetic experience evoked by canonical art could emerge from the processing of sensorimotor input in conjunction with the emotional feeling of pleasure[89], that is crucially mediated by the activation of the insula[87]. The anterior sector of the insula is characterized by extensive connections with limbic areas and with centres involved in autonomic functions[90]. Anterior insula is thought to mediate feelings associated to emotional states through the integration of interoceptive signals in a unified meta-representation of global emotional moments[90]. Altogether, neuroimaging investigations have consistently pointed out the fundamental implication of the insula in social emotion and empathy[53] and, more recently, in aesthetic perception[86].

3.1 GOLDEN BEAUTY TASK

The Golden Beauty (GB) task consists in the evaluation of images of sculptures selected from masterpieces of Classical and Renaissance art that are commonly accepted as normative Western representations of beauty[86]. This task evaluates the sense of beauty through objective parameters (proportion) intrinsic to specific works of art and requires an objective and a subjective aesthetic judgment, as well as a proportion judgment for proportioned and modified stimuli. The main feature of this task is the use of two sets of stimuli that are identical in every respect but one: proportion. Specifically, a parameter that is considered to represent the ideal beauty specifically in the Classical representation of the human body[91,92]was modified to create an aesthetically degraded version of the same stimuli in a controlled fashion. The GB task contains 44 total images of sculptures including 22 images with modified proportions between body parts. In particular, half of the canonical stimuli were modified with a short-leg long-trunk relation, whereas the other half with the opposite modification type.

Di Dio and colleges[86] used this task in fRMI scanning. For this reason, there was four conditions:

(1) *Observation condition (O),* the volunteers were required to observe the images as if they were in a museum and, when the question mark appeared, they had to indicate whether they paid attention to the picture or not. (The question 'did you pay attention to the image?' was introduced to make sure that participants were actually looking at the stimuli during fMRI scanning.

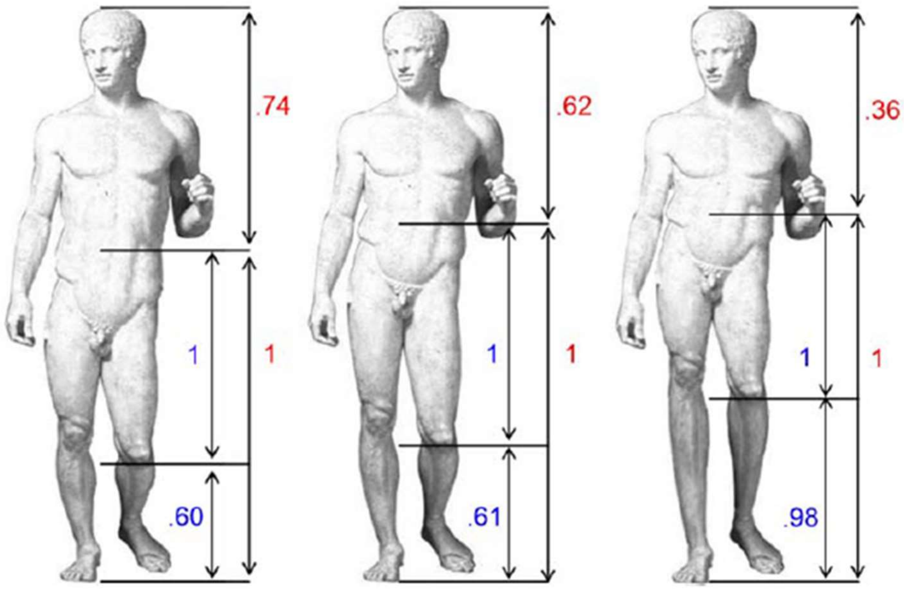
(2) *Objective Aesthetic Judgment (OAJ),* the participants were asked to observe the sculptures and to express an explicit objective judgment ("objective" aesthetic value) for each image by answering to the question: "Is the image you are seeing *beautiful*?". The participants answered on a dichotomous scale YES= it is beautiful, or NO= it is not beautiful.

(3) *Subjective Aesthetic Judgment (SAJ),* the participants were asked to observe the sculptures and to express an explicit subjective judgment ("subjective" aesthetic value) for each image by answering to the question: "Do you like the image that you are seeing?". The participants responded on a dichotomous scale YES= I like it or NO= I do not like it.

(4) Proportion Judgment (PJ), participants were asked to observe the sculptures and to express an explicit proportion judgment for each image by answering to the question: "Is the image that you are seeing proportioned?". The participants responded on a

dichotomous scale YES= It is proportional or NO= It is not proportional (an example of golden beauty task in reported below).

The aesthetic conditions (e.i. objective and subjective aesthetic judgments) was presented random while the proportion condition was always presented at the end of task. In this way, the proportion evaluation cannot affect the aesthetic judgments (for more details see Di Dio et al.[86]).



Example of canonical and modified stimuli. The original image (Doryphoros by Polykleitos) is shown at the centre of the figure. This sculpture obeys to canonical proportion (golden ratio = 1:1.618). Two modified versions of the same sculpture are presented on its left and right sides. The left image was modified by creating a short legs:long trunk relation (ratio = 1:0.74); the right image by creating the opposite relation pattern (ratio = 1:0.36). All images were used in behavioral testing. The central image (judged-as-beautiful on 100%) and left one (judged-as-ugly on 64%) were employed in the fMRI study. *Published in Di Dio et al., 2007 Plos One doi:10.1371/journal.pone.0001201.g001*

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Chapter 2

SOCIAL COGNITION AND AUTISM

Published in

Pino et al., 2017. *Simple Mindreading Abilities Predict Complex Theory of Mind: Developmental Delay in Autism Spectrum Disorders. Journal of Autism and Developmental Disorder. https://doi.org/10.1007/s10803-017-3194-1;*

Pino et al., 2018 *When do children with autism develop adequate social behaviour? Cross-sectional analysis of developmental trajectories. European Journal of Developmental Psychology. https://doi.org/10.1080/17405629.2018.1537876;*

Mazza et al., 2017.*The Role of Theory of Mind on Social Information Processing in Children with Autism Spectrum Disorders: A Mediation. Journal of Autism and Developmental Disorder. https://doi.org/10.1007/s10803-017-3069-5;*

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1. GENERAL INTRODUCTION

According to leading research in this field[1,2,3,4], the central core of autism spectrum disorder is the social cognition abilities impairment. It is known that SC is a complex cognitive construct including the cognitive mechanisms based on the ability to process the social world[4]. A main component of SC is ToM, i.e. the ability to understand another person's cognitive or affective state[3,5]. In the past, ToM ability was simply considered the ability to attribute mental states to self and others, including knowledge, beliefs and intentions. Subsequently, researchers have also included understanding feelings within the definition of ToM. In this way, ToM may be described as a construct including two dimensions: cognitive, the ability to make inferences about beliefs and intentions (cognitive ToM), and affective, the ability to infer what a person is feeling, i.e., his/her emotional states (affective ToM), sub-components[6,7]. According to Shamay-Tsoory's[8], cognitive ToM is a prerequisite for affective ToM, which also requires intact empathy processing. The recent increasing interest in ToM ability is associated with the idea that individuals with autism showed "mind-blindness"[9]. Therefore, ASD individuals have a real ToM deficit. At more general level, ASD is characterised by difficulties in two domains: (1) social communication and interaction, (2) repetitive pattern of behaviour[10,11,4]. Deficits in social skills hinder social inclusion and lead to social isolation in individuals with autism. Specifically, the ToM impairment could compromise their development of adequate social behaviour in adulthood[3,12,13,14].

We know that during the early months of their lives, individuals with ASD already display impairment of SC precursors (for example, emotion processing, sensitivity to ostensive signals, and joint attention, among others[5,15]). Indeed, the development of ToM ability follows a certain order of sequence in Typically Developing (TD) children[16,17,4]. However, children with autism displayed the same progressive order but this appeared to be delayed in age of attainment[4,14,18].

Regarding the typical development of SC's abilities, new-borns begin to develop several social competences, such as the capacity for the detection of social agents, mutual affiliation, and preference for social patterns compared to non-social stimuli[3,4,5]. By the age of 3 to 6 months, early capacities of emotion processing and sensitivity to social signals, chiefly through gaze processing, emerge[5]. Two studies on children later diagnosed with ASD suggest a reduced attention to social scenes at 6 months[19,20]. By the age of 2 years, TD children clearly show awareness of the difference between thoughts of the mind and things in the world. At this age, they also understand that a person will feel happy if he/she get what they want, and sad if he/she does not[4,21].

All these socio-cognitive abilities seem to be linked to mentalizing abilities[4]. The TD children begin to consolidate this ability at the age of 4–5 years[5,22]. Specifically, by the age of 4 or 5 years, children realize that people talk and act on the basis of what they think about the world[3,5,21]. Around the age of 6 years, this ability starts to become more elaborate, with the development of higher order ToM abilities[23,24], which are necessary to understand complex mental states[4]. For instance, prosocial behaviour is strongly evident at this age[4,5].

Thus, social behaviour seems to derive from a process of role taking (i.e., ToM ability) that produces altruistically motivated behaviour[3,25]. In this regard, Ziv et al[13]showed the existence of a link between ToM and social behaviour: a greater understanding of the mental states of other people is related to higher levels of efficiency of social information processing (SIP)[13,14]. The SIP model was proposed by Crick and Dodge[26]. According to these authors the SIP includes different steps: (1) information from the situation is perceived (encoding), so people may pay attention to social cues; (2) interpretations are made about the social cue that is perceived, such as the mental state of the other person (interpretation); (3) individuals select a desired outcome (clarification of goals); (4) possible responses to perform in the situation are generated (response access); (5) finally, the possible responses are evaluated in terms of approval, the ability to perform the behaviour, and the expectations of the outcome, and a response is selected (the response decision)[4,26,27]. During steps 1 and 2, individuals focus selectively on social cues and, based on these cues, interpret the context of the situation. In the others three steps, individuals access possible responses from previous experiences stored in their long-term memory, select their goal for the interaction, and evaluate the possible outcomes of these responses[4,13]. All these steps require a good ToM functionality[3]. Based on this, we highlight the need to know the role of ToM ability on social behaviour development and the stages of development of SC abilities in ASD compared to TD. Moreover, we suggest the need of an early and accurate diagnosis for ASD. All of this could help the clinicians and researchers in planning rehabilitation/habilitation treatments in the first years of life, avoiding the typical social isolation of ASD adults.

Based on, we conducted the studies accurately descripted below.

a) STUDY 1: SIMPLE MIND READING ABILITIES PREDICT COMPLEX THEORY OF MIND: DEVELOPMENTAL DELAY IN AUTISM SPECTRUM DISORDERS.

Aim of the work

The first purpose of this study was to evaluate ToM ability in children with ASD compared to children with TD using a simplified version of the Eyes-Test for children[28] and the Comic Strip Test[29,30], a well-known test assessing different components of ToM. In addition, children with ASD were compared to TD children by means of a *developmental trajectories approach* that allows us to study developmental effects determined by experience (chronological age) separately from effects associated with language functioning per se (verbal mental age). The aim was to evaluate the developmental delay of ToM abilities in children with autism and, in particular, to distinguish them from typical development regarding these social abilities.

Method

Participants

Demographic and clinical information of all the participants are summarized below in Table 1. Ninety-four children participated in this study: 37 individuals with ASD selected by the Reference Regional Centre for Autism Autism, Abruzzo Region Health System, L'Aquila, Italy (age range 61–157 months) and 57 TD (age range 60–147 months) recruited from local schools in the same region and matching the ASD group on chronological and verbal mental age (respectively CA and VMA henceforth).

The groups presented uneven distributions by gender (respectively, ASD 34 males and 3 females; TD 37 males and 20 females) but mean CA and VMA were not significantly different in the two groups—see Table 1. The ASD diagnosis was provided by experienced clinicians according to the new criteria of the DSM-5[10]. ASD diagnosis of patients was confirmed using the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2[31]). Verbal mental age (MA) was assessed with the TROG-2[32].

Table 1. Demographic data of the sample and clinical information concerning the ASD group.

	TD group (n=57) Mean (SD)	ASD group (n=37) Mean (SD)	F DF=1,93	p
Demographic data				
Chronological age	85.65 (26.17)	95.91 (24.9)	2.54	0.083
Verbal mental age	90.74 (28.86)	83.13 (27.40)	1.60	0.209
Gender	37 M; 20 F	34 M; 3 F	–	–
Education in years	2.47 (1.94)	2.94 (2.13)	1.22	0.271
VIQ	–	82.48 (18.24)	–	–
PIQ	–	92.19 (17.20)	–	–
TIQ	–	82.11 (17.74)	–	–
Clinical information				
ADOS—social communication and social interaction	–	9.48 (2.93)	–	–
ADOS—repetitive and stereotyped behaviours	–	1.29 (1.2)	–	–
ADOS total scores	–	10.78 (3.11)	–	–

VIQ verbal intelligence quotient, *PIQ* performance intelligence quotient, *TIQ* total intelligence quotient

Social cognition measures

Two types of ToM measures were collected from the children: (1) *Eyes-Task-Simplified*[28] and (2) *Comic Strip Task* (CST)[29,30]. For detailed description of these tests see chapter 1 (section "Social cognition measures for children").

Data Analysis

Analysis of variance was used to test participants' scores in socio-demographic, clinical and social cognition test measures. In addition, we used regression models to examine the association of ToM trajectories with developmental measures contrasting the ASD and TD groups. First, we considered functions that link performance with CA, and then consider developmental functions linking performance with VMA, assessed with a stringent test as TROG[32]. The use of trajectories in the study of developmental disorders has its origin in growth curve modelling[33,34,35] and in the wider consideration of the shape of change in development[36,37,38]. For further details of the methodology used here for estimating developmental trajectories, see Thomas et al.[38]. The Statistical Package for the Social Sciences (SPSS) software (version 22; SPSS Inc, Chicago, IL, USA) was used in all statistical analyses.

Results

Comparison of ASD to TD Groups' Performance on Social Cognition Tasks

As shown in Table 2, compared to TD children, children with ASD showed overall a significantly lower score on all eyes-test components. On the comic strip test, the two groups showed significant differences in the Belief and Emotion components, but no difference in the Intention component was found (see Table 2).

Table 2. Summary of TD and ASD groups' performance in two social cognition measures

	TD group Mean (SD)	ASD group Mean (SD)	F DF = 1,93	p	Effect size η^2_p
Eyes-test					
Positive primary emotion—PPE	6.06 (0.76)	5.50 (1.27)	7.02	0.009	0.14
Negative primary emotion—NPE	6.33 (0.63)	5.97 (1.06)	4.17	0.044	0.10
Positive mental states—PMS	5.88 (0.95)	5.11 (1.45)	9.37	0.003	0.19
Negative mental states—NMS	5.52 (0.97)	4.91 (1.14)	7.48	0.008	0.14
Comic strip test					
Beliefs	3.40 (0.66)	3.81 (0.99)	53.39	0.001	0.37
Emotions	4.49 (0.66)	3.81 (0.99)	15.49	0.001	0.20
Intentions	3.72 (1.34)	3.71 (1.36)	0	0.993	0
Total score	11.61 (1.87)	9 (2.38)	34.72	0.001	0.28

Developmental Trajectories (DT)

Linear regression was used to evaluate how CA and VMA predicted task performance between groups. The trajectory approach used here has been specifically developed as a statistical method for studying change over time, along with hierarchical linear modelling[38]. Between-groups comparison of DT allowed us to evaluate whether profiles generated from different groups differ significantly in terms of their gradients (indicating the rate of change and direction of the trajectories) or intercepts (showing the onset of the trajectories). We contrasted comparisons between the two groups for trajectories plot- ted according to CA and VMA within respectively eyes-test and CST measures. The regression results showed that CA has a significant relationship with tests used in this study, i.e. eyes-test and CST performance in TD children but not in those with ASD (Table 3). VMA showed a significant relationship with both the eyes-test and comic strip test performance in TD children; whereas for ASD group the significant relationship between VMA and mental states (both positive and negative) and between MA and intentions component were found (Table 4). No other significant relationships were found. Overall, in both ASD and TD groups, performance was significantly higher in function of CA than VMA, with the exception of comic strip/intention in TD children—see Fig. 1a, b.

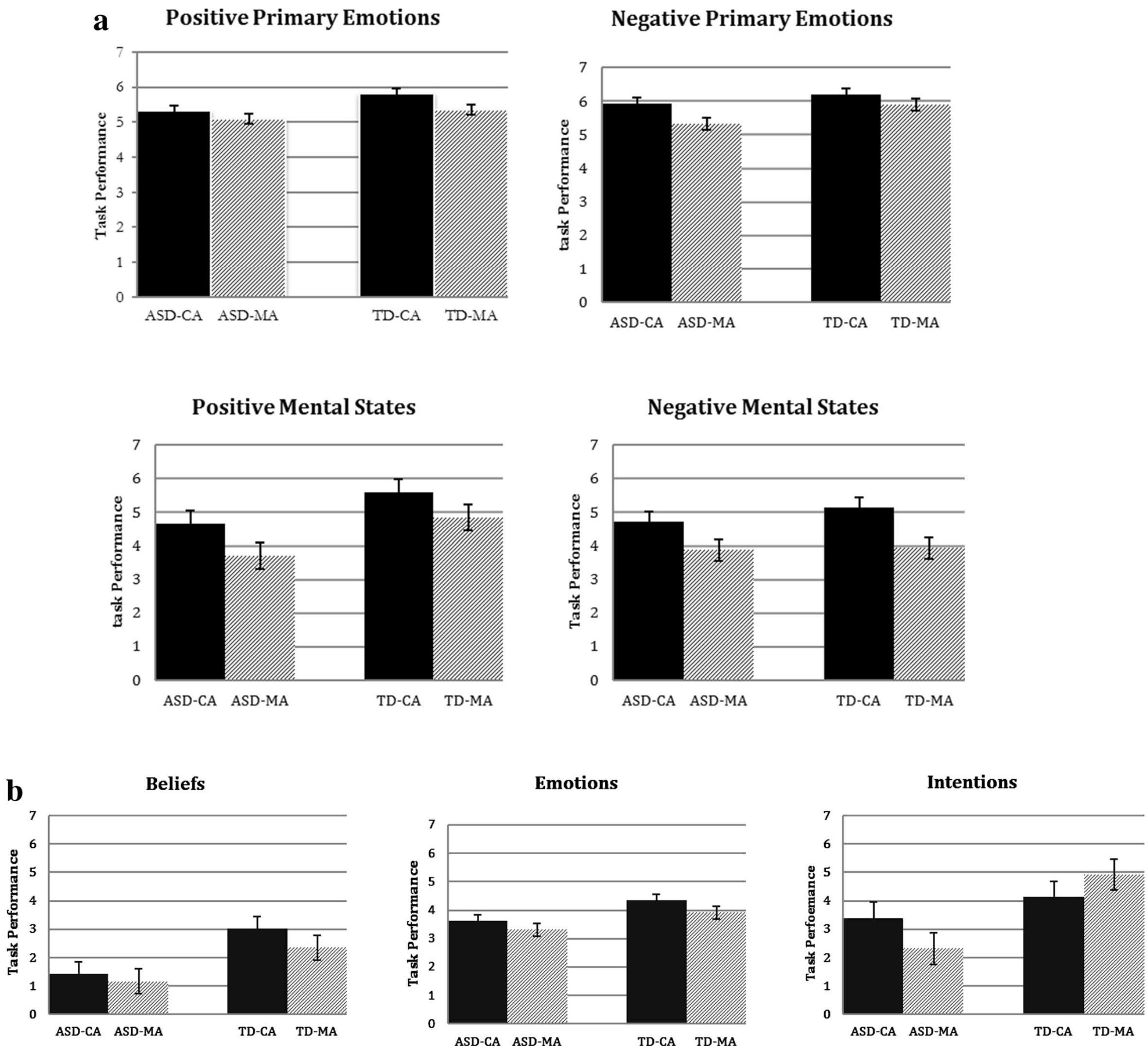


***Figure 1** Within-group comparison between CA and MA for **a** each eyes-test component evaluated, and **b** each CST component evaluated. All comparisons were significant with p ≤ 0.00.*

CA-Based Trajectories of Eyes-Test Performance Comparing ASD and TD Groups

The DT of the eyes-test scores based on CA are illustrated in Figure 2 Panel a.

Positive Primary Emotions—PPE

The regression model explained a significant proportion of variance (F1,92= 5.218; p = 0.002; ŋ2 = 0.15). The model revealed no significant effect of either Group (F1,92= 1.77; p = 0.19; ŋ2 = 0.02) or Group × CA interaction (F1,92= 0.859; p = 0.36; ŋ2 = 0.009).On the contrary, the main effect of CA was significant ($F_{1,92}$= 5.105; p = 0.02; ŋ2 = 0.05), showing a lag of 33.7 months, i.e., 2 years and 8 months in the ASD group compared to TD group, indicating impairments in developing this ability.

Negative Primary Emotions—NPE

The regression model explained a significant proportion of variance ($F_{1,92}=2.702$; $p = 0.05$; $\eta^2 = 0.10$). The model revealed very small effects, with Group ($F_{1,92}= 0.59$; $p = 0.44$; $\eta^2 = 0.0007$), CA ($F_{1,92}= 1.59$; $p = 0.221$; $\eta^2 = 0.017$) and Group × CA inter- action effect all non-significant ($F_{1,92}= 0.932$; $p = 0.337$; $\eta^2 = 0.01$). For negative primary emotion, the ASD group showed a significant delay of 27 months in comparison to the TD group.

Positive Mental States—PMS

The regression model explained a significant proportion of variance ($F_{1,92}= 7.58$; $p = 0.0001$; $\eta^2 = 0.20$). The model revealed a significant main effect of Group ($F_{1,92}= 6.14$; $p = 0.01$; $\eta^2 = 0.06$), indicating that the groups are different, as well as an effect of CA ($F_{1,92}= 10.95$; $p = 0.001$; $\eta^2 = 0.11$). No significant effect of Group × CA interaction was found ($F_{1,92}= 0.002$; $p = 0.968$; $\eta^2 = 0.0$). For positive mental states, the ASD group showed a lag of 58 months, i.e., 4 years and 8 months compared to TD group, indicating that this ability does not develop.

Negative Mental States—NMS

The regression model explained a significant proportion of variance ($F_{1,92}= 9.92$; $p = 0.001$; $\eta^2 = 0.25$). The model revealed no significant effect of either Group ($F_{1,92}= 0.96$; $p = 0.33$; $\eta^2 = 0.01$) or Group × CA interaction effect ($F_{1,92}= 3.32$; $p = 0.072$; $\eta^2 = 0.04$). On the other hand, the main effect of CA was significant ($F_{1,92}= 12.03$; $p = 0.001$; $\eta^2 = 0.12$), showing that two groups differ for CA. For negative mental states, the ASD group showed a delay of 14.6 months, i.e., 1 year and 2 months compared to TD group.

CA-Based Between-Group Comparison on Comic Strip Test Performance

The DT of the comic strip test components based on CA are illustrated in Figure 2 Panel b.

Beliefs

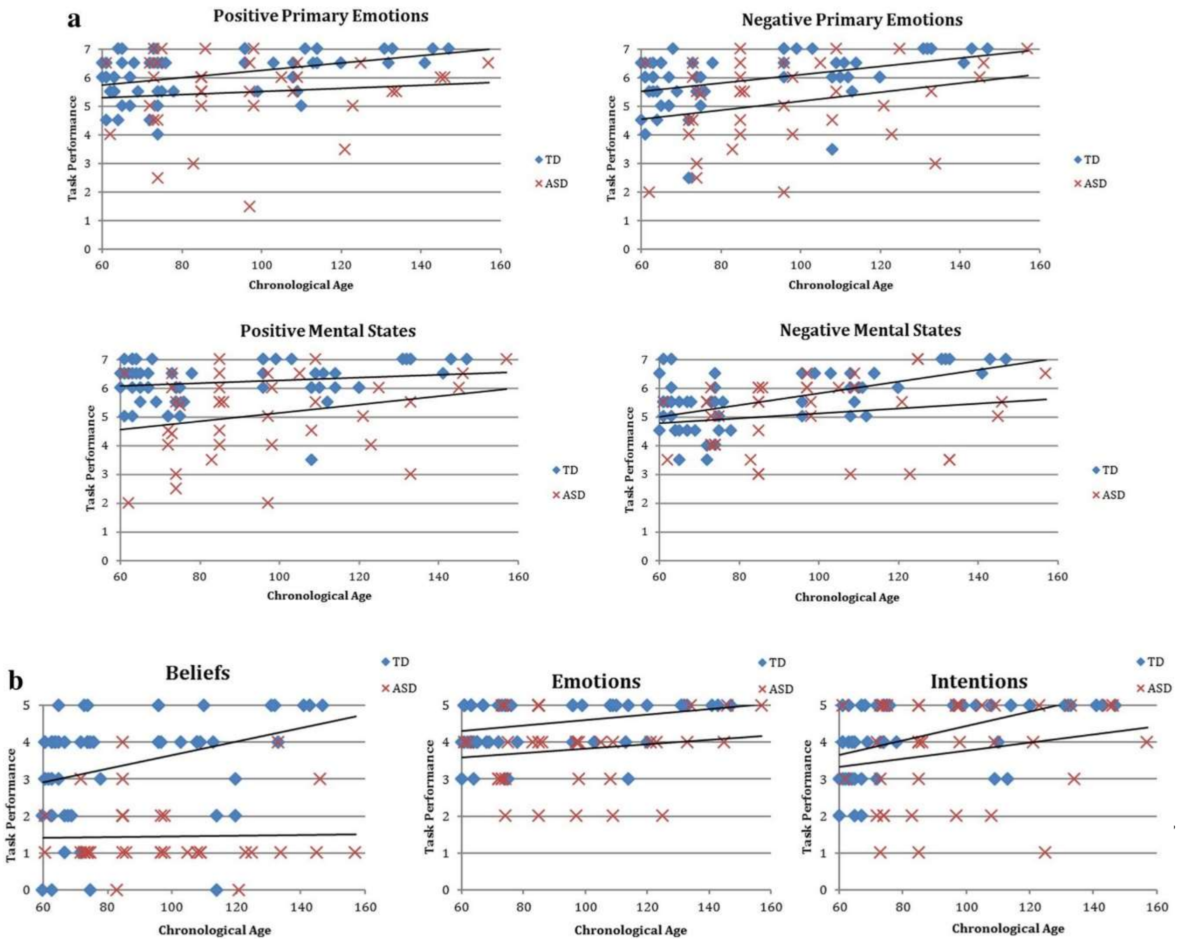
The regression model explained a significant pro- portion of variance ($F_{1,92}= 21.89$; $p = 0.001$; $\eta^2 = 0.43$) and revealed significant main effects for Group ($F_{1,92}= 13.79$; $p = 0.001$; $\eta^2 = 0.14$) showing that two groups differ and CA ($F_{1,92}= 3.54$; $p = 0.06$; $\eta^2 = 0.04$) showing that two groups have significant differences for CA, but no significant inter- action between the two factors ($F_{1,92}= 2.84$; $p = 0.096$; $\eta^2 = 0.031$). For the Beliefs dimension, the ASD group showed a significant impairment of 84.83 months, i.e., 7 years compared to the TD group.

Emotions

The regression model explained a significant proportion of variance ($F_{1,93}= 6.75$; $p = 0.0001$; $\eta^2 = 0.19$) and revealed a significant main effect of Group ($F_{1,93}= 6.58$; $p = 0.01$; $\eta^2 = 0.07$) showing that two groups are different as well as a small Group × CA interaction effect ($F_{1,93}$= 3.54; p = 0.05; ŋ2 = 0.04). On the other hand, no significant main effect of CA was found ($F_{1,93}$= 0.54; p = 0.82; ŋ2 = 0.001). For the Emotion dimension, the ASD group showed a lag of 87.5 months, i.e., 7 years and 2 months compared to the TD group, indicating an impairment on this test.

Intentions

The regression model did not explain a significant proportion of variance ($F_{1,92}$= 1.97; p = 0.12; ŋ2 = 0.06) but it revealed significant main effects of Group ($F_{1,92}$= 2.66; p = 0.01; ŋ2 = 0.003) and Group × CA interaction ($F_{1,92}$= 5.13; p = 0.02; ŋ2 = 0.05). On the other hand, no significant main effect of CA was found ($F_{1,92}$= 0.08; p = 0.77; ŋ2 = 0.001). For the Intentions dimension, the ASD group showed a lag of 52.5 months, i.e., 4 years and 3 months compared to TD group.



Between-Group Comparisons of Developmental Trajectories Based on VMA

VMA-Based Between Group Comparisons on Eyes-Test Performance (for details about DT based on VMA and eyes-test see Figure 3 Panel a).

PPE The regression model explained a significant proportion of variance ($F_{1,92}$= 3.83; p = 0.01; ŋ2 = 0.12). The model revealed no significant main effect of Group ($F_{1,92}$= 1.12;

p = 0.73; ŋ2 = 0.001) as well as the Group × VMA interaction effect ($F_{1,92}$= 0.19; p = 0.66; ŋ2 = 0.002) and VMA ($F_{1,92}$= 3.21; p = 0.077; ŋ2 = 0.03), showing a delay of 29.5 months i.e., 2 years and 5 months in the ASD group compared to TD group.

NPE The regression model explains a significant pro- portion of variance ($F_{1,92}$= 3.28; p = 0.02; ŋ2 = 0.10). The model revealed no significant main effect of Group ($F_{1,92}$= 0.88; p = 0.35; ŋ2 = 0.010) as well Group × VMA interaction effect ($F_{1,92}$= 0.151; p = 0.7; ŋ2 = 0.002). On the other hand, the effect of VMA ($F_{1,92}$= 4.98; p = 0.028; ŋ2 = 0.053) was significant showing that the groups differ for VMA. For the negative primary emotion, the ASD group showed significant delay of 38 months, i.e., 3 years and 2 months in comparison to the TD group.

PMS The regression model explains a significant pro- portion of variance ($F_{1,92}$= 8.45; p = 0.0001; ŋ2 = 0.22). The model revealed no significant main effect of Group ($F_{1,92}$= 2.14; p = 0.15; ŋ2 = 0.02) as well as Group × VMA interaction effect ($F_{1,93}$= 0.39; p = 0.53; ŋ2 = 0.004). On the other hand, the effect of VMA ($F_{1,92}$= 13.87; p = 0.0001; ŋ2 = 0.13) was significant. For positive mental states primary emotion, the ASD group showed a lag of 48 months, i.e., 4 years compared to TD group, thus indicating that this ability does not develop.

NMS The regression model explains a significant pro- portion of variance ($F_{1,92}$= 12.16; p = 0.0001; ŋ2 = 0.29). The model revealed no significant main effect of Group ($F_{1,92}$= 0.001; p = 0.97; ŋ2 = 0.0001) as well as the effect of Group × VMA interaction effect ($F_{1,92}$= 0.69; p = 0.41; ŋ2 = 0.008). On the other hand, the main effect of CA was significant ($F_{1,92}$= 21.54; p = 0.001; ŋ2 = 0.19). For negative mental states, the ASD group showing a delay of 12 months, i.e., 1 year compared to TD group.

VMA-Based Between-Group Comparisons of Comic Strip Test Performance

For details about DT based on VMA and Comin Strip Test components and total score see Figure 3 Panel b.

Beliefs The regression model explained a significant proportion of variance ($F_{1,92}$= 19.81; p = 0.001; ŋ2 = 0.43). No significant main effects for Group ($F_{1,92}$= 1.82; p = 0.18; ŋ2 = 0.02); VMA ($F_{1,92}$= 2.74; p = 0.10; ŋ2 = 0.03) and interaction between the two factors ($F_{1,92}$= 0.77; p = 0.38; ŋ2 = 0.009) were found. For the Beliefs component, the ASD group showed a lag of 98.08 months i.e., 8 years com- pared to TD group, thus indicating that this ability does not develop.

Emotions The regression model explained a significant proportion of this variance ($F_{1,92}$= 6.84; p = 0.0001; ŋ2 = 0.19). No significant main effects for Group ($F_{1,92}$= 1.14; p = 0.28; ŋ2 = 0.01) and the effect of Group × VMA interaction effect ($F_{1,92}$= 0.004; p =

0.94; ŋ2 = 0.0001). On the other hand, a significant effect for VMA (F1,92= 4.28; p = 0.04; ŋ2 = 0.05) was found. For the Emotions component, the ASD group showed a lag of 99.5 months i.e., 8 years and 2 months compared to TD group, thus indicating that this ability does not develop.

Intentions The regression model explained a significant proportion of variance (F1,92= 2.79; p = 0.04; ŋ2 = 0.09). Significant main effect of Group (F1,92= 7.58; p = 0.007; ŋ2 = 0.08) and Group × VMA interaction (F1,92= 8.37; p = 0.005; ŋ2 = 0.09) were found. On the other hand, no significant main effect of VMA was found (F1,92= 0.42; p = 0.51; ŋ2 = 0.005). For the Intentions component, the ASD group showed an atypical delay of 53.2 months i.e., 4 years and 4 months compared to TD group.

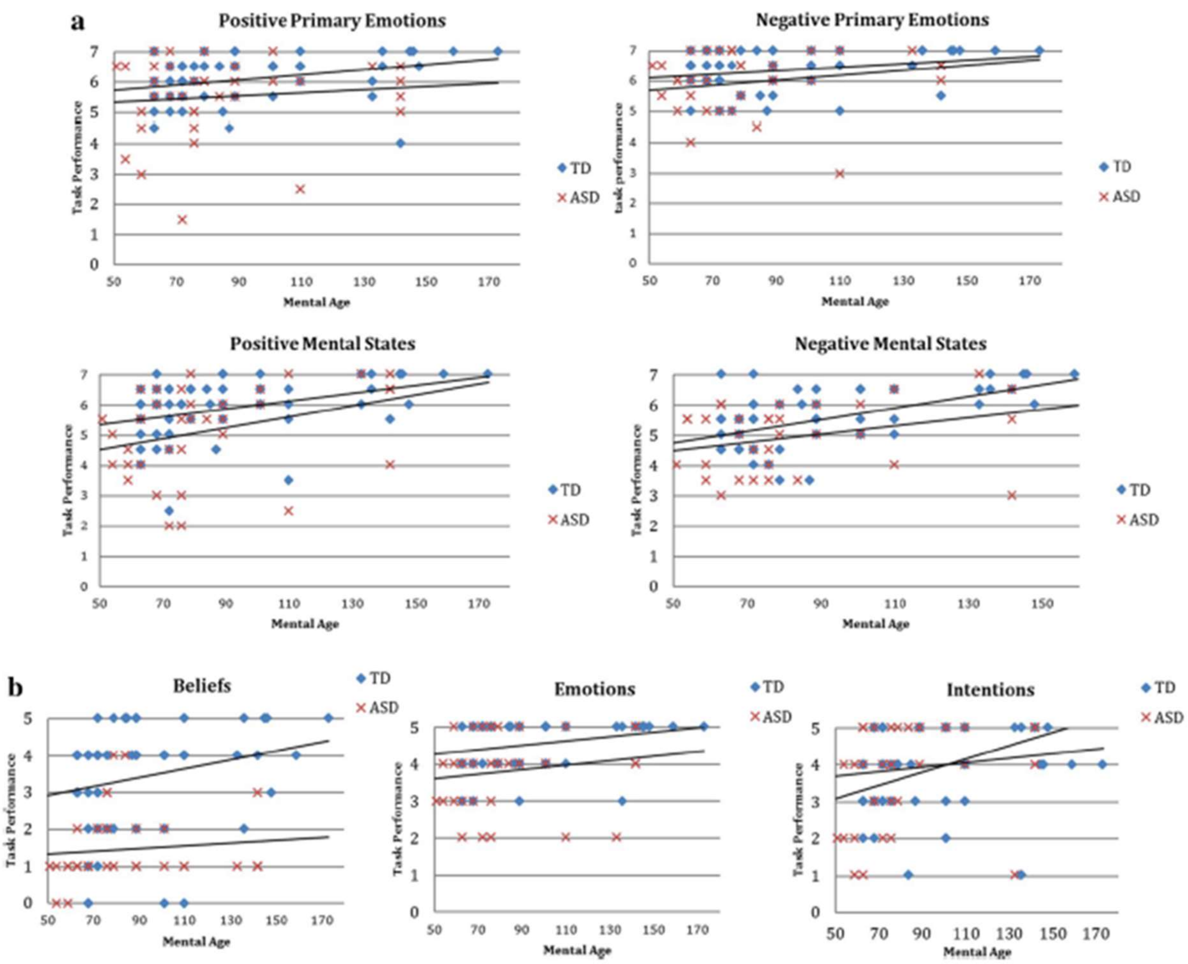


Figure 3 *Between-groups comparison of developmental trajectories based on MA: a on the eyes-test and b on the comic strip task.*

Discussion

Primary, this study showed that ASD and TD groups perform significant different in all eyes-test components, i.e. both primary emotions (positive and negative) and mental states (positive and negative). ASD showed lower scores in the task requiring them to understand emotional and mental states when observing photos of other children's eyes[4,28]. Moreover, the ASD group also displayed lower scores in the beliefs and emotions components of CST compared to the TD group, but no significant difference between groups for the CST intentions component, was found. This is in line with the suggestion that the ability to understand others' beliefs and emotions is more complex with respect to the ability to understand the intentions of other people[4,5]. Our study supports the hypothesis that the ability to recognize the intentions of other people represents implicit ToM and develops relatively early; it is already present at the age of 3 to 4 months and an important prerequisite for the appropriate development of explicit ToM[5]. Moreover, the capacity to understand and recognize the beliefs and emotions of other people is an explicit ability of ToM that develops at 3 to 4 years of age. Thus, this complex competence is based on mentalizing tasks, for example, as assessed by the false beliefs test[5,39].

Secondly, the linear regression analyses, carried out to evaluate the relationship between CA/VMA and ToM measures within each group (TD and ASD), our results showed that CA has a significant relationship with tests used in this study, i.e. eyes-test and CST performance in TD children but not in those with ASD. Therefore, when controlling for CA, all abilities to understand the mental and emotional states of other people are compromised in children with ASD. On the other side, VMA appears to be a good predictor of ToM abilities[4,39]. Indeed, scores on the VMA in the ASD group showed a significant relationship between this variable and mental states (both positive and negative), and intentions component (CST).

Finally, regarding the developmental trajectories approach conducted on the simplified eyes-test our results showed a developmental difference between the ASD/TD groups of 2;08 and 2;05 years for positive primary emotions on CA and VMA respectively. At the same way, the difference between the two groups was 2;02 and 3;02 years for negative primary emotions respectively on CA and VMA. The developmental delay grew when considering mental states: for positive mental states, compared to the TD-group, the ASD-group showed a delay of 4;08 years for CA and 4;00 years for VMA. When considering negative mental states, the ASD delay with respect to the TD group was smaller: 1;02 months for CA and 1 year for VMA, respectively. We thus suggest that the understanding of negative mental state is also a complex ability for children with TD.

The DT analysis for CST showed that the delay in the ASD compared to the TD-group was larger than in the eyes-test, which is consistent with the higher level of difficulty and complexity of this test. Indeed, this test requires good expressive and receptive language ability, that is abilities specifically impaired in ASD[40]. The DT analysis on CST/belief performance showed that the difference between the two groups was 7 and 8 years, for CA and VMA respectively, whereas the ASD-group's performance was impaired on the CST/emotion component with 7;02 on CA and 8;02 on VMA. However, for the CST/intention component the ASD/TD group difference in the development of this ability was less prominent, with 4;03 for CA and 4;04 for VMA, respectively. Interestingly, this suggests that, similarly to the eyes-test, development in CST/intention is delayed in the ASD group, rather than lacking as in the CST/belief and emotion component. As already mentioned, the groups were not statistically different in CST/intentions; however the DT approach allowed us to elucidate that the ASD-group has a delay in the development of the ability to recognize other people's intentions; on the contrary the abilities to recognize beliefs and emotions of others is severely compromised in ASD.

Conclusion

The DT results highlighted that the ASD profile is best described in terms of delay in the development of mentalizing abilities rather than by a total lack of ToM. More specifically, the results showed that the development of the CST/intention component is delayed in children with ASD compared to TD children. Moreover, the delay of basic components of ToM does not allow ASD children to develop complex ToM abilities such as the recognition of beliefs and emotions of other people. Thus, early habilitation programs of these abilities could improve social competences, attenuate the social deficit in children with autism and reduce their isolation.

Specifically, habilitation programmes ought to be developed using ToM concepts and divided in several steps in agreement with results of DT analysis: (1) knowledge of the primary emotions with different valences; (2) knowledge of the mental states with different valences; (3) observe the gaze of people or other social cues to learn to interpret someone's intentions/emotions through the interpretation of these cues; (4) awareness that other people can have intentions different by own intentions; (5) ability to discern others' emotions/beliefs based on the knowledge about social context; (6) ability to use the vocabulary of emotions and expression terms in adequate way with own culture; (7) capacity for emotional self-efficacy[41].

b) STUDY 2: WHEN DO CHILDREN WITH AUTISM DEVELOP ADEQUATE SOCIAL BEHAVIOUR? CROSS-SECTIONAL ANALYSIS OF DEVELOPMENTAL TRAJECTORIES.

Aim of the work

The ability to process social information is part of the social cognition construct and it includes the ability to select the appropriate social responses. Children with ASD show difficulties in these competences that could compromise the development of an adequate social behaviour. The aim of the study was to examine the development of the ability to process social cues across the Social Information Processing Interview (SIP-I)[13,42] conducted with ASD children compared with TD children using developmental trajectory analysis (the same approach used in study 1).

Method

Participants

Thirty-eight children with ASD were selected by the Reference Regional Centre for Autism <anonymised> (age range 5–13 years) along with thirty- nine TD children (age range 5–12 years) recruited from local schools in the same < anonymised> region and matching the ASD group on chronological and verbal mental age (respectively CA and VMA henceforth). The groups presented uneven distributions by gender, because autism affects more male than female individuals (respectively, ASD 34 males and 4 females; TD 35 males and 4 females), but the CA and VMA were not significantly different in the two groups (Table 1). The ASD diagnosis was provided by experienced clinicians according to the new criteria of the DSM-5[10]. The ASD diagnosis of patients was confirmed using the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2[31]). The VMA was assessed with the Test for Reception of Grammar – Version 2 (TROG-2)[32]. Informed consent was obtained from all parents of children before the study. Ethical approval was obtained from the hospital's Ethics Committee. The Ethics Committee approved the experimental protocol number 186061/17 prior to the recruitment of the participants.

Table 1. Between-group differences for chronological age, verbal mental age and SIP-I measure. The clinical information for ASD group is also reported in the table.

	ASD (N=38) Mean (SD)	TD (N=39) Mean (SD)	F (df =1, 102)	P	Effect Size η^2_p
Chronological age (in years)	7.84 (2.06)	7.74 (2.24)	0.04	.838	0
Verbal Mental age (in years)	7.17 (2.15)	7.79 (2.34)	1.48	.228	.03
Gender	34 M; 4 F	35 M; 4 F			
Clinical information					
ADOS-social communication and social interaction	9.48 (2.93)				
ADOS-Repetitive and Stereotyped Behaviours	1.29 (1.2)				
ADOS Total scores	10.78 (3.11)				
Social Information Processing-Interview					
Encoding	3.15(1.03)	3.92 (0.48)	16.48	.0001	.18
Interpretation*	1.30(0.89)	0.64 (0.62)	12.47	.001	.15
Responce construction	1.93(1.34)	4.43 (0.75)	144.59	.0001	.67
Responce evaluation	6.56(1.98)	10.76 (1.28)	281.86	.0001	.81

**higher scores represent higher levels of hostile attribution.*

Social cognition measures

In this study we used as SC measure the Social Information Processing Interview-SIP-I[13,42]. For detailed description of this test see chapter 1 (section "Social cognition measures for children").

Data Analysis

ANOVA analysis was used to test participants' scores in CA, VMA, and all the components of the SIP-I (encoding, interpretation, response construction, and response evaluation). In addition, we used regression models to examine the association of SIP trajectories with developmental measures contrasting the ASD and TD groups. Firstly, we considered functions that link performance with CA and then considered developmental functions linking performance with VMA, assessed with a stringent test such as the TROG. The use of trajectories in the study of developmental disorders has its origin in growth curve modelling[4,34] and in the wider consideration of the shape of change in development[38].

The first step in the trajectory analysis was to establish whether there is a reliable relationship between performance on the experimental task (SIP-I) and CA in the typically developing group. In other words, it was necessary to demonstrate that we had chosen an experimental measure that is sensitive to developmental change. Subsequently, we also calculated this relationship in the ASD group. In addition, we evaluated whether there is a reliable relationship between performance on the experimental task and VMA for each group. According to the methodology proposed by Thomas et al.[38], the trajectory approach used in the present study is a cross-sectional design, and it has been specifically developed as a statistical method for studying change over time, along with hierarchical linear modelling. A between-group comparison of developmental trajectories allowed us to evaluate whether the profiles generated from different groups differed significantly in terms of their gradients (indicating the rate of change and direction of the trajectories) or intercepts (showing the onset of the trajectories; for details, see Thomas et al.[38]). The overall statistical significance of the analyses was set at the 0.05 level. The Statistical Package for the Social Sciences (SPSS) software (version 22; SPSS Inc, Chicago, IL, USA) was used in all the statistical analyses.

Results

Differences in the SIP-I score between ASD and TD children

The results of the ANOVA analysis of the SIP-I components showed that the ASD children had lower scores than the TD children regarding their social information processing competencies. Specifically, children with ASD showed difficulties in all the components of the SIP-I compared with the TD children (for details, see Table 1).

Trajectory analysis

The regression results showed that CA has a significant relationship with the test used in this study, namely SIP-I performance, in TD children but not in those with ASD (see Table 2). Regarding the relationship between VMA and SIP-I, our results showed that VMA has significant effects with the SIP-I on TD performance. For ASD, a significant relationship between VMA and the response construction component was found (see Table 3). No other significant relationship in ASD was found.

Table 2. Summary of linear regression analyses evaluating the relationship between chronological age and ToM measures within each group (TD and ASD).

	B	**R^2**	**F**	**P**
TD				
Encoding	0.554	0.121	2.08	0.04
Interpretation	0.310	0.1	2.37	0.02
Response construction	0.282	0.08	2.14	0.03
Response evaluation	0.477	0.23	3.29	0.002
ASD				
Encoding	0.06	0.003	0.35	0.72
Interpretation	0.007	0	0.04	0.97
Response construction	0.071	0.005	0.39	0.69
Response evaluation	0.175	0.031	0.97	0.34

Table 3. Summary of linear regression analyses evaluating the relationship between verbal mental age and ToM measures within each group (TD and ASD).

	B	**R^2**	**F**	**P**
TD				
Encoding	0.554	0.121	2.08	0.04
Interpretation	0.344	0.118	2.66	0.01
Response construction	0.264	0.07	1.99	0.05
Response evaluation	0.465	0.21	3.191	0.003
ASD				
Encoding	0.19	0.036	0.19	0.25
Interpretation	0.017	0	0.091	0.92
Response construction	0.367	0.135	2.161	0.03
Response evaluation	0.156	0.02	0.86	0.39

CA-based trajectory analysis

The developmental trajectories of the SIP-I scores based on CA are illustrated in Figure 1.

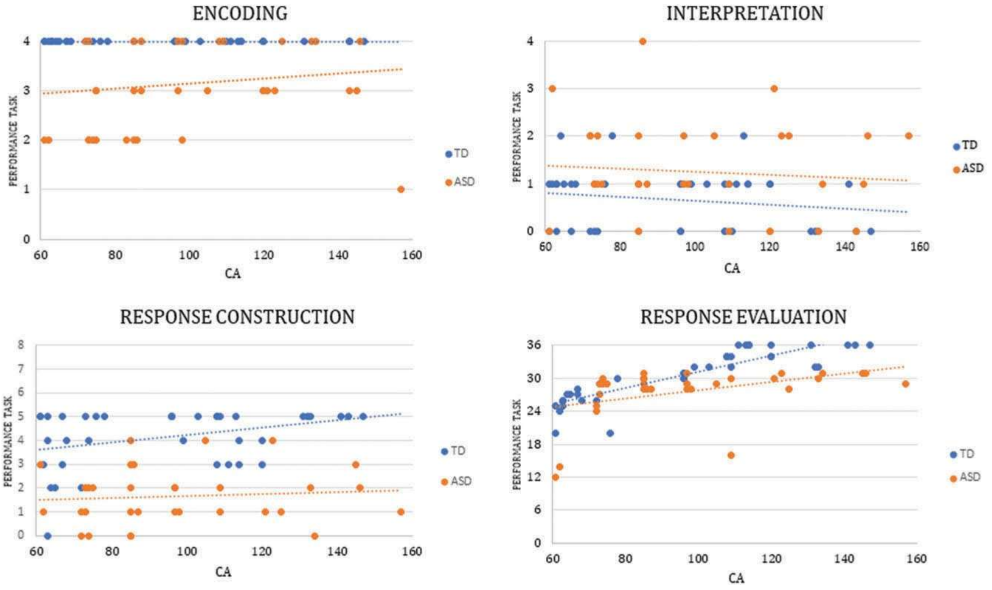


Figure 1*. The developmental trajectories of the SIP-I scores based on CA.*

Encoding. The regression model explained a significant proportion of the variance [F(1,76) = 5.575; p = 0.002; ŋ2= 0.19]. The model revealed a significant main effect of the group [F(1,76) = 4.828; p = 0.03; ŋ2 = 0.06]. In addition, the model did not show significant effects of CA [F(1,76) = 0.539; p = 0.465; ŋ2 = 0.007] and group × CA interaction effect [F(1,76) = 0.046; p = 0.832; ŋ2 = 0.001]. For the encoding component, the ASD group showed an age difference of 2 years and 5 months (2;05) compared with the TD group (see Figure 1, panel A).

Interpretation. The regression model explained a significant proportion of the variance [F(1,76) = 4,633; p = 0.005; ŋ2 = 0.17]. No significant effects of the group [F(1,76) = 1.913; p = 0.171; ŋ2 = 0.02], CA [F(1,76) = 0.534; p = 0.468;2 = 0.008], and group × CA interaction [F(1,76) = 0.777; p = 0.381; 2= 0.01] were found. This result demonstrated that the two groups did not showed significant difference in this component; indeed, the age difference is very small (1 year; Figure 1, panel B).

Response construction. The regression model explained a significant proportion of the variance [F(1,76) = 47.869; p = 0.0001; ŋ2 = 0.68]. The model revealed a significant main effect of the group [F(1,76) = 49.269; p = 0.0001; ŋ2= 0.42]. However, there were no significant effects for CA [F(1,76) = 0.995; p = 0.322; ŋ2= 0.01] and group × CA interaction [F(1,76) = 0.004; p = 0.953; ŋ2 = 0.001]. For the response construction, the ASD group showed a CA difference of 9 years and 2 months (9;02) compared with the TD group (Figure 1, panel C).

Response evaluation. The regression model explained a significant proportion of the variance [F(1,76) = 12.96; p = 0.0001; ŋ2 = 0.32]. The model revealed a significant main effect of the group [F(1,76) = 17.28; p = 0.0001; ŋ2p = 0.17]. On the other hand, the model revealed no significant effect for CA [F(1,76) = 1.84; p = 0.2; ŋ2 (1,76) = 0.72; p = 0.4; ŋ2= 0.02] and for the group × CA interaction [F= 0.009]. For the response evaluation, the ASD group showed a CA difference of 3 year and 9 months (3;9) compared with the TD group (Figure 1, panel D).

VMA-based trajectory analysis

The developmental trajectories of the SIP-I scores based on VMA are illustrated in Figure 2.

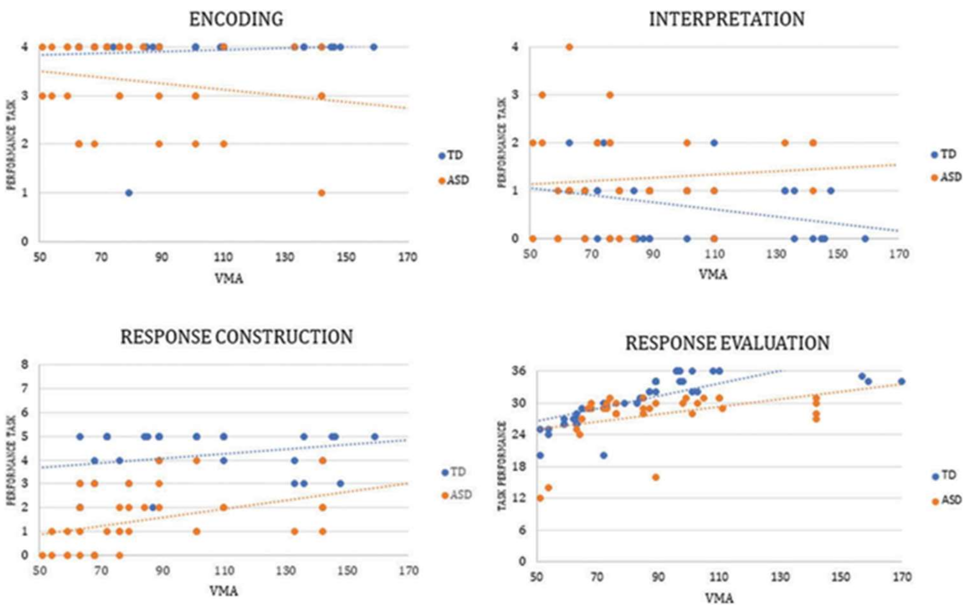


Figure2. *The developmental trajectories of the SIP-I scores based on VMA.*

Encoding. The regression model explained a significant proportion of the variance [F(1,76) = 6.065; p = 0.0001; ŋ2 = 0.20]. No significant main effects of the group [F(1,76) = 2.079; p = 0.154; ŋ2= 0.02] and VMA [F(1,76) = 0.440;p = 0.509; ŋ2= 0.006], as well as group × VMA interaction [F(1,76) = 1.530; p = 0.220; ŋ2= 0.02], were found. For the encoding component, the ASD group showed a very small, not significant, VMA difference of 5 months compared with the TD group (Figure 2, panel A).

Interpretation. The regression model explained a significant proportion of the variance [F(1,76) = 5.152; p = 0.003; ŋ2 = 0.18]. No significant effects of the group [F(1,76) = 2.028; p = 0.159; ŋ2p = 0.02], VMA [F(1,76) = 2.121; p = 0.150;2= 0.03], or group × VMA interaction [F(1,76) = 0.268; p = 0.606;2 = 0.004] were found. This result demonstrated that the two groups did not showed significant different in this component; indeed, the age difference is about of 1 year (Figure 2, panel B).

Response construction. The regression model explained a significant proportion of the variance [F(1,76) = 95.099; p = 0.0001; ŋ2 = 0.81]. The model revealed significant main effects of the group [F(1,76) = 94.709; p = 0.0001; ŋ2= 0.58]. However, the model revealed no significant effect for VMA [F(1,76) = 2.280; p = 0.136; ŋ2= 0.03] and for group × VMA interaction [F(1,76) = 0.130; p = 0.720; ŋ2p = 0.002]. For the response construction, the ASD group showed a VMA difference of 6 years and 4 months (6;04) compared with the TD group (Figure 2, panel C).

Response evaluation. The regression model explained a significant proportion of the variance [F(1,76) = 12.878; p = 0.0001; ŋ2 = 0.32]. The model revealed a significant main effect of the group [F(1,76) = 17.62; p = 0.0001; ŋ2= 0.18]. However, the model revealed no significant effect for VMA [F(1,76) = 1.854; p = 0.17; ŋ2= 0.02] and for group × VMA interaction [F(1,76) = 0.17; p = 0.68; ŋ2p = 0.002]. For the response evaluation, the ASD group showed a VMA difference of 1 years and 2 months (1;02) compared with the TD group (Figure 2, panel D).

Discussion

Regarding the ANOVA results, this study showed that the ASD and TD groups performed significantly differently in all the SIP-I components. Specifically, the children with ASD showed difficulties in understanding the story (encoding); in the capacity to evaluate the tendency to attribute hostile intentions to other people in positive social situations (interpretation); in addition, ASD children respond to peer rejection or provocation either with aggression or with avoidance (response construction), and they evaluate positively an aggressive and avoidant behaviour (or they evaluate competence response negatively; response evaluation[3]). The ANOVA results could confirm that ASD children have a severe deficit in social information processing.

Moreover, the developmental trajectory analysis carried out to evaluate the relationship between CA/VMA and SIP-I showed an age difference in the development of the abilities evaluated between the ASD/TD groups. Indeed, the ASD group showed both CA and VMA differences during the development of SIP abilities compared with TD children. Specifically, the difference between the two groups was larger for the response construction component of the SIP-I. This competence seems to be closely linked with ToM, because the child is asked: 'What would you do?'; thus, to answer, the child has to put himself/herself in the shoes of the main character of the story and try to explain how he/she would act in the same situation. However, although ToM is associated with the capacity of perspective taking implied in the SIP-I, this ability is not directly evaluated in this study. In addition, in accordance with Ziv et al.[13], higher levels of competent response construction were related to lower levels of externalizing behaviours, and the positive evaluation of an aggressive response was related to lower levels of prosocial behaviour. Thus, if an ASD child has a delay in the development of this competence compared with a TD child, these data could explain the difficulty that ASD individuals face in interacting with their peers, building/maintaining social relations, and making adequate behavioural responses to the social context. In our study, we used CA and VMA as predictors of developmental trends. In some studies, CA has been found to be the most sensitive predictor of developmental trends[4,28]. In addition, the use of VMA is theory-dependent; indeed, it is based on a theory-driven view in which standardized tests adequately measure developmental progression in the domain that the experimental task is thought to evaluate[4,38]. However, the age difference is smaller in ASD children than in TD children when the predictor is VMA rather than CA. This result could mean that the social abilities of ASD individuals depend on their verbal abilities. What has just been said supports the hypothesis of the existence of a strong correlation between social abilities and language. The clinical implication of this result is that, when we assess a child with autism, we also have to consider VMA and not only CA to select appropriate age neuropsychological or social measures.

Thus, the results obtained by developmental trajectory analysis highlighted that the ASD profile is best described in terms of slower development of social abilities rather than by a total lack of these competences[4]. We support the hypothesis of Thomas et al. (2009) about the concept of 'delay'. According to Thomas et al.[38], the concept of delay is considered as slower development; thus, delay can amount to little more than a redescription of behavioural data indicating that the disorder group has produced scores and error patterns similar to those of younger TD children.

Conclusion

Considering the slower development of SIP competences of the ASD children compared with the TD group, early habilitation programmes should plan treatment specific to social abilities aimed to attenuate the social deficit in children with autism, reduce their isolation, and promote the interaction of ASD children within their social context. In light of the results obtained in this study, the future perspectives in the developmental approach studies in individuals with ASD should be: (1) evaluate the development of social precursors in infants and toddlers (2) identify the severity of symptoms on the development of social abilities in children with ASD (3) creation of rehabilitation treatments consistent with a delay hypothesis of social abilities, and not to a general deficit of these social competences. The creation of evidence-based habilitation treatments should be the main objective of the clinicians and researchers who work in this field.

c) **STUDY 3: THE ROLE OF THEORY OF MIND ON SOCIAL INFORMATION PROCESSING IN CHILDREN WITH AUTISM SPECTRUM DISORDERS: A MEDIATION ANALYSIS**

Aim of the work

(1) The first goal of this study was to evaluate the ToM ability using the CST[29,30] and the social information processing abilities through the SIP-I[13,42] in children with ASD and to compare them to TD children. Based on previous evidences[21,29,40,43,44] there is evidence about a delay in the development of language in children with ASD. However, a consistent relationship between language development and ToM has been shown. For this reason, our sample of children (both TD and with ASD) covered an age range from 5 to 13 years, because both tasks (CST and SIP-I) require well-developed expressive and receptive language skills. (2) The second goal of the present study was to examine the role and effect of ToM on the social information processing patterns using a *mediation analysis.* Our hypothesis was that a deficit of ToM could adversely affect the ability of social information processing and subsequently compromise the development of adequate social behaviour. Therefore, we used the mediation analysis to examine the impact of different components of ToM (intentions, beliefs and emotions) on the development of social behaviour, first in TD children and then in children with ASD.

Method

Participants

One-hundred and seven children participated in our study: 52 children (42 male, 10 female) with ASD ranging in age from 5 to 13 years and 55 TD, age-matched children (37 male; 18 female) ranging in age from 5 to 12.25 years. No differences between groups (ASD and TD) emerged for chronologic age ($F_{1,102} = 3.03$; $p = 0.095$; Ƞ2 p = 0.09) and mental age ($F_{1,102} = 1.85$; $p = 0.177$; Ƞ2 p = 0.01). The TD children were selected from a nursery (for children of 5 years), a primary school (for children from 6

to 10 years), and a lower secondary school (for children from 11 to 13 years) located in Frosinone, central Italy. Participants with ASD were inpatients of the Reference Regional Centre for Autism of L'Aquila, central Italy. According to the principles established by the Declaration of Helsinki, ethical approval was obtained by the Ethical Committee of the NHS Local Health Unit (Azienda Sanitaria Locale 1). The children's parents provided informed consent to participate in the study. Diagnosis of ASD was established by experienced clinicians using the Autism Diagnostic Observation Schedule, Second Edition (ADOS- 2[31]) according to criteria of the DSM-5[10]. VMA was assessed with the Test for Reception of Grammar, Version 2 (TROG-2[32]).
Demographic and clinical information of all the participants are summarized in Table 1.

Table 1. Between-group differences for demographic data, clinical information and social cognition measures.

	ASD (N = 52) Mean (SD)	TD (N = 55) Mean (SD)	F (df=1, 102)	P	Effect Size p
Demographic data					
Chronological age (in years)	8.17(2.17)	7.42(2.81)	2.41	0.12	0.23
Verbal Mental age (in years)	6.97(2.30)	7.33(2.42)	0.64	0.43	0.12
ADOS-social communication and social interaction	9.48 (2.93)	–	–	–	–
ADOS- Repetitive and Stereotyped Behaviours	1.29 (1.2)	–	–	–	–
ADOS Total scores	10.78 (3.11)	–	–	–	–
Social cognition measures					
Social Information Processing Interview					
Encoding	3.15(1.03)	3.92(0.41)	26.96	**0.0001**	0.26
Interpretation	1.30(0.89)	0.71(0.64)	14.85	**0.0001**	0.15
Responce evaluation	6.56(1.98)	9.64(1.54)	78.80	**0.0001**	0.46
Responce construction	1.93(1.34)	4.15(1.08)	86.80	**0.0001**	0.47
Comic Strip Task					
Emotions	3.90(0.99)	4.49 (0.66)	13.02	**0.0001**	0.17
Beliefs	1.67(1.23)	3.40(1.42)	44.84	**0.0001**	0.27
Intentions	3.84(1.31)	3.72(1.33)	0.214	0.645	0.009

Social cognition measures

Two types of ToM measures were collected from the children: (1) SIPI[13,42] and (2) CST[29,30]. For detailed description of these tests see chapter 1 (section "Social cognition measures for children").

Data Analysis

One-way ANOVA was used to test differences between groups (ASD, TD) regarding demographic parameters and in the component measures of the SIPI (encoding, interpretation, response construction, and response evaluation) and the CST (emotions, beliefs, and intentions).

Correlations Analysis

Exploratory Pearson's correlations were computed to assess the relationships between the components of the SIPI (encoding, interpretation, response construction, and response evaluation) and CST (emotions, beliefs, and intentions), both in the ASD and TD group. On the basis of the correlation results, the mediation models were performed.

Regression Analysis

A linear regression analysis was performed in order to evaluate the relations between the dependent variable and one (simple linear regression) or more explanatory variables (multiple linear regression). In this study, the variables for the regression analysis were the components of the SIPI (encoding, interpretation, response construction, and response evaluation) and the sub-components of CST (beliefs, emotions, and intentions).

Mediation Analysis

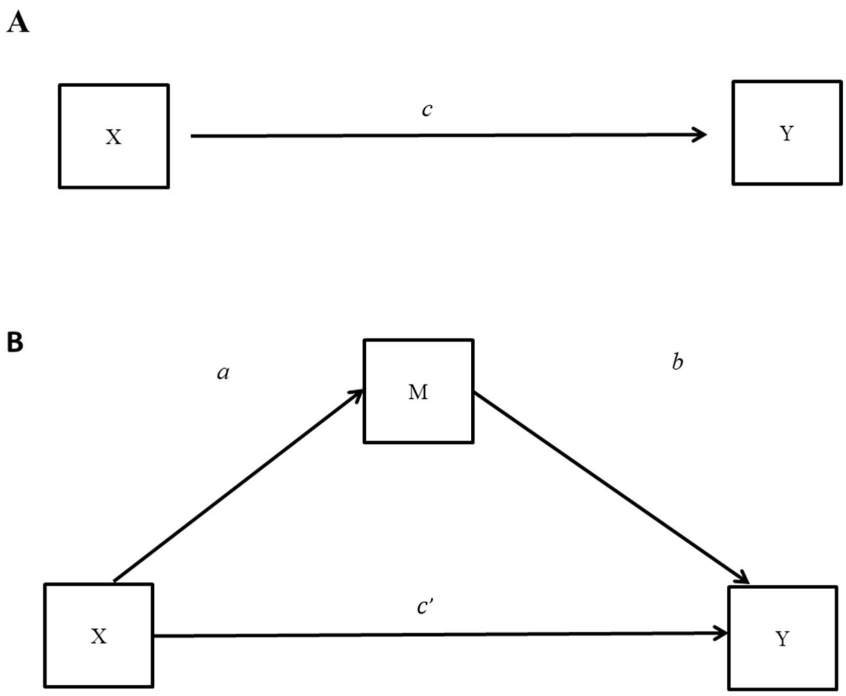
Mediation analysis has stimulated interest among researchers due to its potential to provide answers to a series of important research questions and due to the dissatisfaction with the methods and approaches that have tended to dominate clinical research[45]. The aim of using this analysis is to develop an increasingly sophisticated hypothesis of the systemic relationships and processes that generate empirical regularities[46,47]. In this vein, mediation analysis can inform intervention strategies. The mediation model is important for understanding the mechanism through which the causal variable affects the outcome (Kenny et al. 2003; Preacher and Hayes 2008).

In the mediation process, the relationship between the independent variable (X) and the dependent variable (Y) is hypothesized to be an indirect effect that exists due to the influence of a third variable (M, the mediator). According to Baron and Kenny's[48] suggestion, we followed a four-step approach, in which several linear regression analyses are conducted, and the significance of the coefficients is examined at each step:

Step 1: Show that the causal variable is correlated with the outcome. Conduct a linear regression analysis with X predicting Y to test for path *c* (see Figure 1, Panel a and b). This step establishes that there is an effect that may be mediated.

Step 2: Show that the causal variable is correlated with the mediator. Conduct a linear regression analysis with X predicting M to test for path *a* (see Figure 1, Panel a and b). This step essentially involves treating the mediator as if it were an outcome variable.

Step 3: Show that the mediator affects the outcome variable. Conduct a linear regression analysis with M predicting Y to test the significance of path *b* (see Figure 1, Panel a and b). It is not sufficient to just correlate the mediator with the outcome; in fact, the mediator and the outcome may be correlated because they are both caused by the causal variable X. Therefore, the causal variable must be con- trolled when establishing the effect of the mediator on the outcome.



Step 4: Establish that M completely mediates the X-Y relationship, the effect of X on Y controlling for M (path *c'*) should be zero (see Figure 1, Panel a and b). The effects in both Steps 3 and 4 are estimated in the same equation.

Figure 1 (A) Illustration of a direct effect. X affects Y. (B) Illustration of a mediation design. X is hypothesized to exert an indirect effect on Y through M[49].

If the criteria for all four of these steps are met, then the data are consistent with the hypothesis that variable M completely mediates the X-Y relationship, which supports *full mediation*; on the other hand, if the first three steps are met but Step 4 is not, then *partial mediation* is indicated[47,50]. In this study, we found full mediation for each mediation model. Finally, we used the Sobel test[51,52] to explore the significance of a mediation effect. Particularly, in our study, the Sobel test was performed to evaluate whether the social information processing ability, measured by the SIPI[13,42], was mediated by the ToM abilities measured by the CTS[29,30] in both the ASD and TD group. The indirect effect of X on Y through M can then be quantified as the product of a and b (i.e., ab). The total effect of X on Y is quantified with the unstandardized regression weight c (Figure 1, Panel a)[49].

The Sobel test involves computing the ratio of ab to its estimated standard error (SE). The overall statistical significance of the model was set at the 0.01 level. The Statistical Package for the Social Sciences (SPSS) software (version 22; SPSS Inc., Chicago, IL, USA) was used.

Results

The ANOVA of the SIPI components showed that the ASD group had lower scores compared to the TD group with regard to social information processing competences. Specifically, children with ASD showed difficulties in all components of the SIPI: encoding ($F1,102 = 26.96$; $p = 0.0001$; $\eta 2\ p = 0.26$), interpretation ($F1,102 = 14.85$; $p = 0.0001$; $\eta 2\ p = 0.15$), response evaluation ($F1,102 = 78.80$; $p = 0.0001$; $\eta 2\ p = 0.46$), and response construction ($F1,102 = 86.80$; $p = 0.0001$; $\eta 2\ p = 0.47$), compared to the TD children (see Table 1). Furthermore, the ASD group had lower scores in beliefs ($F1,102 = 44.84$; $p = 0.0001$; $\eta 2\ p = 0.27$) and emotions ($F1,102 = 13.02$; $p = 0.0001$; $\eta 2\ p = 0.17$), but there were no significant differences in the intentions ($F1,102 = 0.214$; $p = 0.645$; $\eta 2\ p = 0.009$) sub-component of the CST compared to the TD group.

Correlational Analysis

TD Group

Significant correlations were found in the TD group between the emotions CST sub-component (affective ToM) and three components of the SIPI (interpretation, response construction, and response evaluation). Specifically, we found a significant negative correlation between the emotions sub-component of the CST and the interpretation component of the SIPI ($r = -0.388$; $p = 0.002$). A significant positive correlation was also found between the CST emotions sub-component and both the response construction ($r = 0.378$; $p = 0.002$) and response evaluation ($r = 0.251$; $p = 0.032$) components of the SIPI. Furthermore, the three SIPI components (interpretation, response construction, and response evaluation) showed significant correlations with the beliefs sub-component of the CST (cognitive ToM). The beliefs sub-component of the CST was negatively correlated with the SIPI interpretation component ($r = -0.368$; $p = 0.003$). Finally, the beliefs sub-component of the CST was positively correlated with the response construction ($r = 0.514$; $p = 0.001$) and response evaluation ($r = 0.202$; $p = 0.70$) components of the SIPI.

ASD Group

A significant positive correlation was found in the ASD group between the emotions sub-component of the CST (affective ToM) and the response construction component of the SIPI

($r = 0.270$; $p = 0.035$). Significant correlations were also found between the intentions sub-component of the CST (cognitive ToM) and the three SIPI components (interpretation, response construction, and response evaluation). Specifically, the CST intentions sub-component was negatively correlated with the SIPI interpretation component ($r = -0.223$; $p = 0.68$). Finally, we found a significant positive correlation between the CST intentions sub-component and both the response construction ($r = 0.532$; $p = 0.001$) and response evaluation ($r = 0.253$; $p = 0.45$) components of the SIPI.

Regression Analysis

According to the results obtained by the correlation analysis and in order to create the mediation models, a linear regression analysis was performed. The corresponding results allowed us to conduct the Sobel test[51,52] to explore the significance of the mediation effects between the different variables.

TD Group

Firstly, we conducted a first regression analysis using the emotions sub-component of the CST as the dependent variable and the interpretation component of the SIPI as predictor ($R2 = -0.39$, $SE = 0.13$, $p = 0.003$). This was followed by a second regression analysis where the emotions sub-component of the CST became the predictor together with the interpretation component of the SIPI, while the SIPI response construction component was the dependent variable ($R2 = 0.63$, $SE = 0.22$, $p = 0.007$).

Secondly, we conducted a first regression analysis using the beliefs sub-component of the CST as the dependent variable and the interpretation component of the SIPI as predictor ($R2 = -0.79$, $SE = 0.28$, $p = 0.006$). This was followed by a second regression analysis where the beliefs sub-component of the CST became the predictor together with the interpretation component of the SIPI, while the SIPI response construction component was the dependent variable ($R2 = 0.41$, $SE = 0.09$, $p = 0.001$). Thirdly, we conducted a first regression analysis using the emotions sub-component of the CST as the dependent variable and the interpretation component of the SIPI as predictor ($R2 = -0.39$, $SE = 0.13$, $p = 0.003$). This was followed by a second regression analysis where the emotions sub-component of the CST became the predictor together with the interpretation component of the SIPI, while the SIPI response evaluation component was the dependent variable ($R2 = 0.64$, $SE = 0.32$, $p = 0.05$). Finally, we conducted a first regression analysis using the beliefs sub-component of the CST as the dependent variable and the interpretation component of the SIPI as predictor ($R2 = -0.79$, $SE = 0.28$, $p = 0.006$). This was followed by a second regression analysis where the beliefs sub-component of the CST became the predictor together with the interpretation component of the SIPI, while the SIPI response evaluation component was the dependent variable (R2 = 0.23, SE = 0.15, p = 0.13).

ASD Group

Firstly, we conducted a first regression analysis using the intentions sub-component of the CST as the dependent variable and the interpretation component of the SIPI as predictor (*R2* = −0.33, *SE* = 0.22, *p* = 0.13). This was followed by a second regression analysis where the intentions sub-component of the CST became the predictor together with the interpretation component of the SIPI, while the SIPI response construction component was the dependent variable (*R2* = 0.52, *SE* = 0.13, *p* = 0.001). Secondly, we conducted a first regression analysis using the intentions sub-component of the CST as the dependent variable and the interpretation component of the SIPI as predictor (*R2* = −0.33, *SE* = 0.22, *p* = 0.13). This was followed by a second regression analysis where the intentions sub-component of the CST became the predictor together with the interpretation component of the SIPI, while the SIPI response evaluation component was the dependent variable (*R2* = 0.32, *SE* = 0.22, *p* = 0.16).

Mediation Analysis

Mediation models were performed on the basis of the correlation and regression analyses. In order to elucidate whether the interpretation of other people's social behaviour is mediated by the ability to understand intentions, beliefs, and emotions of others, four separate models for the TD group and two for the ASD group were conducted.

TD Group

Firstly, the relationship between the interpretation (X) and response construction (Y) components of the SIPI, using the emotions sub-component of the CST (affective ToM) as a mediator, was explored. The Sobel test showed that this model was significant (*Z* = −2.07; *SE* = 0.11; *p* = 0.03; see Figure 2).

Secondly, the relationship between the interpretation (X) and response construction (Y) components of the SIPI, using the CST beliefs sub-component (cognitive ToM) as a mediator, was examined. The Sobel test showed that this model was significant (*Z* = −2.39; *SE* = 0.13; *p* = 0.01; see Figure 3).

Thirdly, we explored the relationship between the interpretation (X) and response evaluation (Y) components of the SIPI, using the CST emotions sub-component (affective ToM) as a mediator; however, this model did not show any significant indirect effect of mediation.

Finally, we explored the relationship between the interpretation (X) and response evaluation (Y) components of the SIPI, using the CST beliefs sub-component (cognitive ToM) as a mediator; however, this model did not show any significant indirect effect of mediation.

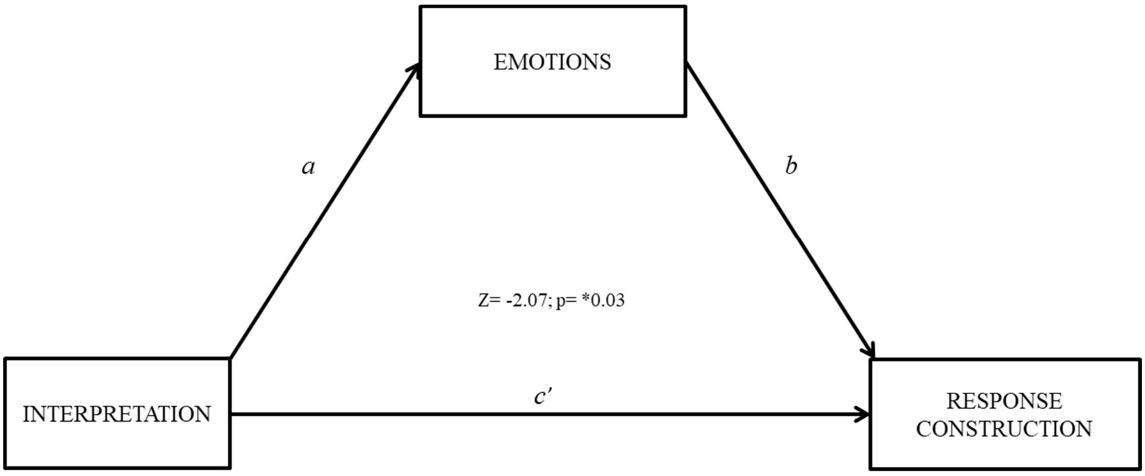


Figure 2. *The Sobel test significance levels, for the relationship between interpretation and response construction sub-components of SIP-I as mediated by emotions sub- component (affective TOM) of CST. *p<0.001.*

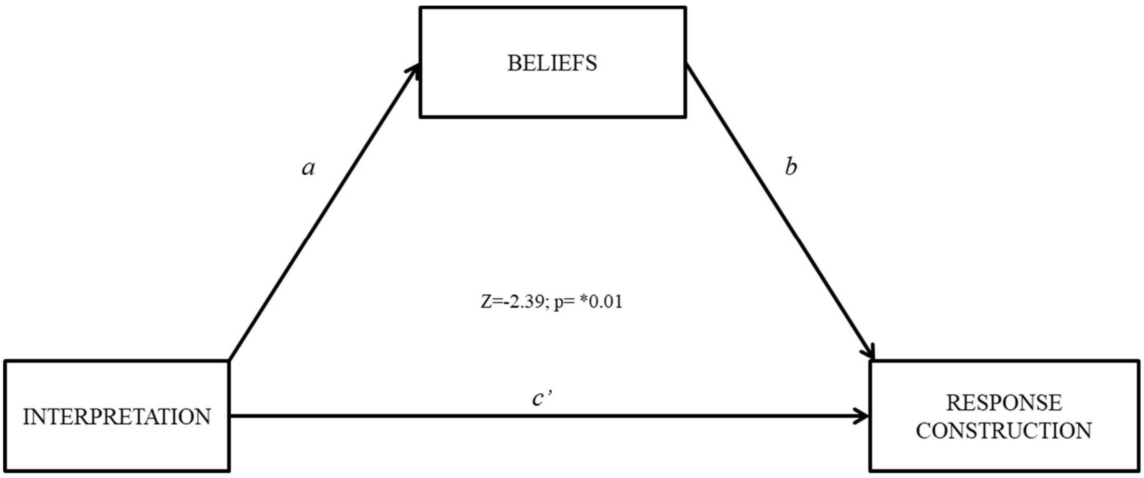


Figure 3. *The Sobel test significance levels, for the relationship between interpretation and response construction sub- components of SIP-I as mediated by beliefs sub- component (cognitive TOM) of CST. *p<0.001.*

ASD Group

Firstly, we explored the relationship between the interpretation (X) and response construction (Y) components of the SIPI, using the CST intentions sub-component (cognitive ToM) as a mediator. Secondly, we explored the relationship between the interpretation (X) and response evaluation (Y) components of the SIPI, using the CST intentions subcomponent (cognitive ToM) as a mediator. The Sobel test for both models did not show any significant indirect effect of mediation.

Discussion

The main aim of the present study were to evaluate the differences between the two groups (TD and ASD) in the used tests and to examine the role of ToM abilities in the development of social information processing capacities through mediation analysis, which is a methodology to evaluate the impact of ToM components on social skills. The ANOVA analysis showed that the ASD group had difficulties in all the components of SIP-I that measures the social information processes (as described in study 2), compared to TD group. This incorrect interpretation of other people's behaviour can lead children to exhibit an incorrect social response and compromise the relationship with their peers. These SIP-I results are in line with the literature[5,13], which confirmed the impairment in social information processing abilities in children with autism. On the contrary, regarding the ToM abilities (measured by CST) the ASD group showed an impairment of ToM competences compared to the TD group. Particularly, children with autism scored lower in the beliefs and emotions sub-components of ToM, but there was no significant difference in the ToM intentions sub-component between the two groups (as described in study 1).

Regarding the second aim, two mediation models for the ASD group and four mediation models for the TD group were performed. For children with ASD, the mediation analysis results showed that the two models using the intentions sub-component of ToM as a mediator were not significant. We used the intentions sub-component of ToM as a sole mediator because it was the only ability that correlated with the SIP-I components. In the ASD group, there was no evidence of mediation. Thus, in children with ASD, the ability to recognize the intentions of other people does not reduce their difficulty in social information processing[53]. A non-significant mediation model indicates that the association between the IV and DV (i.e., for the first model, the SIP-I interpretation and response construction components, respectively; for the second model, the SIP-I interpretation and evaluation response components, respectively) was not reduced significantly by the inclusion of the mediator (i.e., CST intentions sub-component) in the model. Regarding TD children, the results of the mediation analysis revealed two significant models out of four models, using the beliefs and emotions sub-components as mediators. Specifically, the two significant models showed that the correct interpretation of social cues (interpretation component of the SIP-I, IV) and the response construction component of the SIP-I (DV) were mediated by both the emotions and beliefs sub-components of the CST (see Figs. 2, 3). It would seem that the ability to recognize emotions (Fig. 2) and beliefs (Fig. 3) of other people improves the relationship between the interpretation of social cues and the generation of an adequate behavioural response in TD children. On the contrary, both ToM components had no mediator role in the relationship between the interpretation and response evaluation components of the SIP-I. We hypothesize that the capacity to evaluate other people's social behaviour as right or wrong requires a higher level of ToM abilities, such as the knowledge of moral and conventional rules[54]. If a child does not know the moral or conventional rules, he/she cannot judge the social behaviour of his/her peers. According to Blair[54], moral rules comprise the respect for other people, whereas conventional rules comprise the respect of behavioural rules in specific social contexts such as school, home, and so on. Thus, the response evaluation component does not need ToM abilities, but the knowledge of these rules is laid down by society. In the present study, the knowledge of moral and conventional rules was not examined but may represent a future study.

Conclusion

In conclusion, using the mediation analysis, we determined that the ability to understand emotions and beliefs is necessary to implement an adequate social behaviour. Taken together, the results of the present study show that the capabilities to infer other people's emotions (affective ToM) and to understand their beliefs (cognitive ToM) play a key role in determining the appropriate acquisition of social competences[6] in TD children. On the contrary, the lack of these ToM abilities compromises the appropriate development of social behaviour in children with autism.

d) STUDY 4: FORMAL PSYCHOLOGICAL ASSESSMENT FOR AUTISM SPECTRUM DISORDER DIAGNOSIS: A NEW METHODOLOGY TO BUILD AN ADAPTIVE TESTING SYSTEM

Aim of the work

The early diagnosis represents a fundamental step to avoid the social isolation of individuals with autism. Currently, the Autism Diagnostic Observation Schedule-Second Edition (ADOS-2[31]), is the only tool that allows the diagnosis of ASD and it is based on a standardized observation of the behaviour characterized by the presence of objects/stimuli necessary for interact to the ASD individuals during the assessment. Based on this, we applied a novel approach to the ADOS-2[31] known as the Formal Psychological Assessment (FPA). Our aim was to use a practical application of the FPA on the ADOS-2, the clinical test defined as the gold standard for ASD diagnosis, to reduce the time required for the test and to allow an adaptive assessment of an individual with ASD. Its introduction in psychological assessment will allow a deeper understanding of the evaluation process for an adaptive assessment procedure[55] and a clear connection between the item asked and the clinical elements collected. In addition, we aimed at validating the clinical structures obtained for both the T module and module 1 of the tool. This process involves estimating the parameters and testing the fit of the model to the available data. This operation allows for the calibration of an adaptive version of the ADOS-2 able to provide detailed information about the symptoms displayed by each patient according to the FPA methodology. The innovation of the FPA methodology comes from the construction of a matrix that allows (1) the identification of the existing relations among items in terms of clinical symptoms and (2) an adaptive assessment of an individual. Particularly, this research raises some important considerations regarding the evaluation of this population and the authors propose future work to improve the quality of clinical assessment.

The following descriptions is faithful to the reference article[56] in order to give to the reader a clear explanation of the complex FPA methodology.

The Formal Psychological Assessment

When assessing an individual, a clinician is more interested in the symptoms the individual presents rather than in the score he/she obtains on an instrument. The FPA produces an attempt to provide the clinician with exhaustive information about a patient's specific set of clinical issues, to identify the situation in a both quantitatively and qualitatively rigorous way. What allows the FPA to carry out this critical task are its mathematical and theoretical foundations. In fact, the FPA is a conjoint application into the clinical framework of two theories from mathematical psychology: The Knowledge Space Theory[57,58], and formal concept analysis[59]. A very trivial intuition behind the FPA's conceptualization is the possibility of describing each item of an instrument in terms of the clinical- diagnostic issues it explores[60,61]. In this way, it is possible to identify which clinical issues are investigated by any item of an assessment tool for some specific disorder. In the FPA, each item is named a *clinical object*, while each clinical-diagnostic issue (*e.g.*, DSM diagnostic criteria) is named a *clinical attribute*. Starting from these basic definitions it is possible to build a matrix where each row is an object and each column is an attribute. Each cell *ij* of such a matrix, named *clinical context*, contains either a 1, whenever the item *i* investigates the attribute *j*, or a 0 otherwise. The clinical context displays and represents the object-attribute assignment. Notice that, once the set of attributes is specified, any item can be analysed with respect to the presence/absence of each attribute; this means that the same matrix could even contain items from different tools. Furthermore, this representation allows the clinician to discriminate between response patterns having the same numerical score. This aspect is particularly relevant because a patient could reach a given score by satisfying different sets of symptoms: each item is therefore important not for the score it provides, but for the attributes it investigates. This possibility is completely lost in traditional tools, and it represents one of the most relevant improvements provided by the FPA that differentiates patients not based on their score, but on the clinical symptoms they present. Starting from the clinical context, through some formal passages[61] a clinical structure can be built. This structure uses the information included in the context to derive the prerequisite relations among the items of the context. This passage is crucial in the construction of an adaptive algorithm for psychological assessment[55]. In fact, the structure defines the admissible response patterns (also named the *clinical states*) that are defined by the item-attribute assignment of the context. For instance, if an item i_1 investigates attributes $\{a_1, a_2\}$ and a second item i_2 investigates attributes $\{a_1, a_2, a_3\}$, any pattern including item i_2 but not i_1 will be excluded from the structure given the item-attribute assignment. So far, the deterministic skeleton of the FPA has been described. In the deterministic case no error is assumed during the assessment phase; in other words, the answer to a specific item is assumed not to be affected by any kind of error, and therefore the collected information is treated as certain. It is clear how such an assumption does not adequately describe reality for two main reasons. On the one hand, two main errors could occur in the assessment phase; for instance, in the case of the ADOS-2, the clinician could report a certain behaviour even if it did not occur, or could miss a behaviour that did occur. These two kinds of errors are respectively a "false positive" and a "false negative"[58,60]. On the other hand, the clinical states (*i.e.*, the different clinical conditions in which a patient could be) could present different prevalence rates in the population. For these reasons, the introduction of a probabilistic model is needed. In the FPA, a model that accounts for both error rates and probability of the states is the Basic Local Independence Model (BLIM)[57]. Within the BLIM, all the responses to the items are locally independent given the state of the individual; moreover, a probability value is associated with each state. Formally, the clinical structure becomes a probabilistic clinical structure (*Q, p*) where (*Q,*) is the clinical structure and *p* is a probability distribution of the states of. Given (*Q, p*), each response pattern has a probability value: This last one is defined by means of a response function which assigns each response pattern its conditional probability given a state K (for all states

$$p(R) = \sum_{K \in \mathcal{K}} \rho(R, K)\pi(K)$$

K in[58,61]:

The conditional probability *p* (*R, K*) is determined by the two error parameters *β* and *η*, respectively the false negative and false positive errors related to each item, as

$$\rho(R, K) = \prod_{q \in K \setminus R} \beta_q \prod_{q \in K \cap R} (1 - \beta_q) \prod_{q \in R \setminus K} \eta_q \prod_{q \in K \cap R} (1 - \eta_q)$$

expressed by the following equation:

The model parameters are the two error rates *ηq* and *βq* for each item, and a probability value *πK* for each state. In this way, it is possible to estimate the probability of observing the real clinical state of a patient.

METHODS

Context Construction and Validation

The first step in applying the FPA is the construction of the clinical context that depicts the item/attribute assignment. This operation first requires the specification of the attributes that must be included in the context. Recalling that the clinical attributes can be symptoms, diagnostic criteria or theoretical considerations related to the disorder at hand, this operation has been conducted by referring to the DSM-5[10] and other information from the literature[11,31]. Table 1 lists the main attributes considered when assessing ASD symptoms.

Table 1. List of attributes of the clinical context for the ASD diagnosis.

A1	Visual exploration of objects
A2	Vocal signals
A3	Used gestures to indicate requests
A4	Stereotyped and repetitive use of objects
A5	Symbolic play
A6	Involvement of other people
A7	Eye contact
A8	Face expression
A9	Use of gaze to understand the action of the examinator
A10	Responce to name
A11	joint attention
A12	Expression of affections
A13	Enjoyment sharing
A14	Integration of facial expressions and vocal signals and gestures
A15	Unusual body movements and unusual sensory interests
A16	Functional play
A17	Social smile
A18	The child's response to a lack of social input
A19	Interactive behavior
A20	Verbal request
A21	Creative and immaginative abilities
A22	Verbal communication
A23	Roles of conversation
A24	Gestures associated with verbal language
A25	Irony
A26	Flexibility and social adaptation
A27	Emotions description
A28	Vocal intonation
A29	Awareness of social relationship
A30	Responsibility for own action
A31	Isolation
A32	Imitation of facial expression, sounds and gestures
A33	Emotional reaction to the change of routine
A34	Perception of cues of danger
A35	Understanding of request
A36	Understanding of nonverbal communication

The second operation conducted to build the context was the selection of the items. In the current application, all items of the ADOS-2 were included in the context. To have a clearer picture of the instrument, the five main parts of the tool were analysed separately. Therefore, the items of the ADOS-2 were subdivided into five different contexts (one for each part). Finally, six experts (four psychologists and two child psychiatrists) in the field of ASD and in the administration of the ADOS-2 independently performed the item/attribute assignment. Disagreements among raters were solved through direct discussion about the specific criticisms. Whenever a clinical context is built, five important and informative configurations may occur due to the item- attribute assignment. First, some empty rows may occur (*i.e.*, rows of the matrix that contain only 0s), meaning that the specific item does not investigate any of the selected attributes. Second, some empty columns may occur, indicating that none of the items of the tool investigate that specific attribute. This is crucial because it indicates that the assessment tool at hand does not investigate some of the selected (and thus necessary) attributes. Third, equal columns may occur (*i.e.*, columns having 1s in the same positions) indicating that it is impossible to distinguish between the presence/absence of either of the equivalent attributes in the assessment. Fourth, equivalent rows may occur, which indicate equivalent items (*i.e.*, items that convey, from a clinical perspective, the same information). These items are redundant and thus, in terms of efficiency, could be collapsed. Fifth, some rows are present that are included in other rows (*i.e.*, the 1s in one row are all present in the other row that also has some other 1s). This last case is important because the included items represent so-called prerequisites of the included ones. In other words, in this case there is one item that investigates some attributes and another item that investigates all the attributes of the first item, plus some other attributes. Therefore, from a clinical perspective, an affirmative answer to this last item implies an affirmative answer to the first one as well. The last step of the application of the FPA is the statistical testing of the robustness of the model in describing the collected data. To this aim, the BLIM parameters have been estimated starting from a dataset of patients evaluated by means of the ADOS-2. Parameter estimation has been iteratively carried out based on the Expectation-Maximization (EM) algorithm[61,62,63]. Through this procedure, we were able to obtain an estimate of the two error parameters for each item (false negative and false positive) and the probability of each clinical state in the structure. The procedure computes a fit statistic based on Pearson's Chi-square; this statistic, due to the sparseness of this kind of data matrix, is not reliable.

Therefore, the obtained value has been tested by means of a parametric bootstrap (with 5000 replications) to check for the reliability of the obtained value. Of course, the estimate of the error rates for each item can be viewed as fit indices. It has been observed[62] that, in general, such values must be as low as possible. More precisely, the following condition must hold true for every item: $\eta_q < 1- \beta_q$. In other words, a positive answer to an item is more likely to occur if the patient has its attributes, rather than as the result of a false positive on the item. In the next section, the results obtained from the construction and analysis of the contexts are displayed. The BLIM was defined and tested on the collected data

Results

Clinical Contexts

T MODULE

For this module, 18 attributes were identified as relevant for the assessment of ASD, namely attributes A2, A7, A3, A5, A8, A12, A13, A16, A4, A6, A11, A15, A1, A9, A10, A14, A17 and A18 in Table 1. For the T module, there are no empty rows. This means that there are no useless items with respect to the selected attributes. Moreover, even if no empty columns were found, then all the selected attributes are investigated by at least one item of this module. In this module, equal columns are not present, but there are equivalent rows. In fact, two items (free play and free play-ball) of the T module evaluate the same set of attributes. These items are repetitive and thus, in terms of efficiency, one of them could be deleted to reduce the duration of the test and stress on the child (Table 2). The analysis showed that each item evaluates at least one selected attribute. This information shows that the T module assesses the main abilities to make ASD diagnosis in the age range of 12–30 months. However, two items (free play and free play-ball) perfectly evaluate the same attributes. Thus, these items should be considered repetitive.

Table 2. The Toddler module containing the 14 items and the 18 attributes. The items named free play and free play-Ball have been combined into a single item because they are equivalent.

-	A2	A7	A3	A5	A8	A12	A13	A16	A4	A6	A11	A15	A1	A9	A10	A14	A17	A18	TOT
1. Bubbles-play	1	1	1	0	1	1	1	0	1	0	1	1	0	0	0	0	0	0	**9**
2a. Free play *2b. Free play-Ball*	1 1	0	1 1	1 1	0	1 1	0	1 1	1 1	1 1	0	0	1 1	0	0	0	0	0	**8**
3. Blocking toy play	1	1	1	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	**5**
4. Bubbles-play (teasing toy play)	1	1	0	0	1	0	0	0	0	0	0	1	0	1	0	0	0	0	**5**
5. Response to joint attention	1	1	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0	0	**5**
6. Snack	1	1	1	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	**5**
7. Unable toy play	1	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	**4**
8. Anticipation of a routine with objects	0	0	0	0	0	1	1	0	0	0	1	1	0	0	0	0	0	0	**4**
9. Bath time- ignore	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	**4**
10. Response to name	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	**3**
11. Anticipation of a social routine	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	1	0	0	**3**
12. Functional and symbolic imitation	0	0	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0	**3**
13. Bath time	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	**2**
14. Responsive social smile	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	**1**
TOTAL	**10**	**8**	**7**	**5**	**5**	**5**	**5**	**4**	**3**	**3**	**3**	**3**	**2**	**2**	**1**	**1**	**1**	**1**	-

MODULE 1

For this module, the following 17 attributes were selected: A13, A2, A5, A7, A9, A12, A3, A11, A16, A4, A6, A8, A15, A1, A10, A14 and A17 (Table 1). For module 1, there are no empty rows, so each item investigated at least one selected attribute. In this module, equal columns are not present, but there are equivalent rows. This result means that two items (symbolic and functional imitation and birthday party) of module 1 evaluate the exact same set of attributes (*e.g.*, A13, A5 and A16). For this module we found two equivalent rows for module 1 (symbolic and functional imitation and birthday party). These items evaluate the same attributes and can be considered repetitive.

Table 3. The module 1 containing the 9 items and the 16 attributes. The items named functional and symbolic imitation and birthday party have been combined into a single item because they are equivalent. The A9 has been not inserted in the table because not examined by any items of this module.

-	A13	A2	A5	A7	A12	A3	A11	A16	A4	A6	A8	A15	A1	A10	A14	A17	TOTAL
1. Bubbles-play	1	1	0	1	1	1	1	0	1	0	1	1	0	0	0	0	**9**
2. Free play	0	1	1	0	1	1	0	1	1	1	0	0	1	0	0	0	**8**
3. Response to joint attention	1	1	1	1	0	0	1	0	0	0	0	0	0	0	0	0	**5**
4. Snack	0	1	0	1	0	1	0	0	0	1	1	0	0	0	0	0	**5**

-	A13	A2	A5	A7	A12	A3	A11	A16	A4	A6	A8	A15	A1	A10	A14	A17	TOTAL
5. Anticipation of a routine with objects	1	0	0	0	1	0	1	0	0	0	0	1	0	0	0	0	**4**
6. Response to name	0	1	0	1	0	0	0	0	0	0	0	0	0	1	0	0	**3**
7. Anticipation of a social routine	1	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	**3**
8a. Functional and symbolic imitation *8b. Birthday Party*	1 1	0	1 1	0	0	0	0	1 1	0	0	0	0	0	0	0	0	**3** **3**
9. Responsive social smile	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	**1**
TOTAL	**6**	**5**	**4**	**4**	**4**	**3**	**3**	**3**	**2**	**2**	**2**	**2**	**1**	**1**	**1**	**1**	**-**

MODULE 2

For this module, the following 24 attributes were selected: A2, A3, A6, A7, A13, A8, A4, A5, A11, A12, A16, A22, A15 A1, A10, A19, A20, A21, A23, A24, A9, A14, A17 and A18 (see Table **1**). Nevertheless, only 20 out of 24 attributes were investigated because, in this module, the A9, A14, A17 and A18 are not examined (see Table 4). In this module, there are no equivalent rows, but there are equal columns. This result means that two attributes (A19 and A20) of module 2 are identical and are assessed in only one item (construction task).

Table 4. The module 2 containing the 14 items and the 20 attributes. The A9, A14, A17 and A18 have been not inserted in the table because not examined by any items of this module.

-	A2	A3	A6	A7	A13	A8	A4	A5	A11	A12	A16	A22	A15	A1	A10	A19*	A20*	A21	A23	A24	TOTAL
1. Bubbles-play	1	1	0	1	1	1	1	0	1	1	0	0	1	0	0	0	0	0	0	0	**9**
2. Anticipation of a routine with objects	0	0	0	0	1	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	**4**
3. Free play	1	1	1	0	0	0	1	1	0	1	1	0	0	1	0	0	0	0	0	0	**8**
4. Imagination Play	0	1	1	0	0	1	1	0	0	0	0	1	0	0	0	0	0	1	0	0	**6**
5. Response to joint attention	1	0	0	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	**5**
6. Snack	1	1	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**5**
7. Construction task	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	**4**
8. Response to name	1	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	**3**
9. Telling a story from a book	0	0	1	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	**3**
10. Description of a picture	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	**1**
11. Birthday party	0	0	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	**3**
12. Joint interactive play	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**2**
13. Demonstration task	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	**2**
14. Conversation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	**1**
TOTAL	**5**	**5**	**5**	**5**	**5**	**4**	**3**	**3**	**3**	**3**	**3**	**3**	**2**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**-**

*Equal columns

MODULE 3

For this module, the following 30 attributes were selected: A22, A3, A8, A27, A29, A6, A21, A23, A30, A4, A13, A14, A25 A26, A18, A7, A19, A20, A28, A16, A24, A1, A2, A5, A9, A10, A11, A12, A15 and A17 (Table 1).

However, only 21 out of 30 attributes were investigated because, in this module, A1, A2, A5, A9, A10, A11, A12, A15 and A17 are not examined. Particularly, A9 (use of gaze to understand the action of the examiner) and A15 (unusual body movements and unusual sensory interests) are important attributes in ASD diagnosis that were evaluated in this module. Equivalent rows and equal columns are present in this module (Table **5**). Regarding equivalent rows, this result means that two items (social relationship difficulties and friendships, relationships and marriage) of module 3 perfectly evaluate the same attributes (A29 and A30). As to the equal columns, this result means that three attributes (A14, A25 and A26) are indicated in the same item (cartoons). In addition, three attributes (A7, A19 and A20) are indicated in the same item (construction task). Finally, both A16 and A24 are indicated in the same item (joint interactive play).

Table 5. The module 3 containing the 13 items and the 21 attributes. The items named Social difficulties and annoyance and friends, relationship and marriage have been combined a single item because they are equivalent. The A1, A2, A5, A9, A10, A11, A12, A15 and A17 have been not inserted in the table because not examined by any items of this module.

-	**A22**	**A3**	**A8**	**A27**	**A29**	**A6**	**A21**	**A23**	**A30**	**A4**	**A13**	**A14***	**A25***	**A26***	**A18**	**A7 ****	**A19 ****	**A20 ****	**A28**	**A16 *****	**A24 *****	**TOTAL**
1. Imagination Play	1	1	1	0	0	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	**6**
2. Creating a story	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**1**

-	A22	A3	A8	A27	A29	A6	A21	A23	A30	A4	A13	A14*	A25*	A26*	A18	A7 **	A19 **	A20 **	A28	A16 ***	A24 ***	TOTAL
3. Description of a picture	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**1**
4. Telling a story from a book	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**3**
5. Cartoons	1	1	0	1	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	**6**
6. Conversation and reporting	1	1	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	**6**
7. Construction task	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	**4**
8. Emotions	1	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**4**
9. Loneliness	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**2**
10. Joint interactive play	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	**2**
11. Demonstration task	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	**2**
12a. Social difficulties and annoyance. *12b. Friends, relationship and marriage*	0	0	0	0	1 1	0	0	‘0	1 1	0	0	0	0	0	0	0	0	0	0	0	0	**2** **2**
13. Break	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	**2**
TOTAL	**6**	**4**	**4**	**4**	**4**	**3**	**2**	**2**	**2**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	-

*equal columns **equal columns ***equal columns.

MODULE 4

For this module, the following 30 attributes were selected: A22, A29, A30, A27, A3, A8, A6, A23, A13, A18, A7, A19, A20, A21, A14, A25, A26, A28, A1, A2, A4, A5, A9, A10, A11, A12, A15, A16, A17 and A24 (see Table 1).

Nevertheless, the following 12 attributes were not considered in this module: A1, A2, A4, A5, A9, A10, A11, A12, A15, A16, A17 and A24. Some of the attributes not considered in module 4 that are important for making an ASD diagnosis in this age range include the following: A9 (use of the gaze to understand the action of examiner), A15 (unusual body movements and unusual sensory interest) and A24 (gestures associated with verbal language). Equivalent rows and equal columns are present in this module (Table 6). Regarding equivalent rows, this result means that two items (current work or school; friends, relationship and marriage) in module 4 perfectly evaluate the same attributes (A29 and A30). In addition, another two items (daily living; plans and hopes) examined only one attribute (A30). For the equal columns, three attributes (A7, A19 and A20) are examined by the same item (construction task). In addition, three attributes (A14, A25 and A26) are examined by the same item (cartoons).

Table 6. The module 4 containing the 13 items and the 18 attributes. The items named daily living and plans and hopes have been combined a single item because they are equivalent. The A1, A2, A4, A5, A9, A10, A11, A12, A15, A16, A17 and A24 have been not inserted in the table because not examined by the items of this module.

-	**A22**	**A29**	**A30**	**A27**	**A3**	**A8**	**A6**	**A23**	**A13**	**A18**	**A7***	**A19***	**A20***	**A21**	**A14****	**A25****	**A26****	**A28**	**TOTAL**
1. Conversation and reporting	1	0	0	1	1	1	0	1	0	0	0	0	0	0	0	0	0	1	**6**
2. Cartoons	1	0	0	1	1	0	0	0	0	0	0	0	0	0	1	1	1	0	**6**
3. Emotions	1	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	**4**
4. Telling a story from a book	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	**3**
5. Description of a picture	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**1**
6. Construction task	0	0	0	0	1	0	0	0	0	0	1	1	1	0	0	0	0	0	**4**
7a. Current work or school *7b. Friends, relationship and marriage*	0	1 1	1 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**2** **2**
8a. Daily living 8b. Plans and hopes	0	0	1 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**1** **1**
9. Social difficulties and annoyance	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	**2**
10. Dimostraction task	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**2**
11. Break	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	**2**
12. Loneleness	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**2**
13. Creating a story	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	**1**
TOTAL	**5**	**5**	**5**	**4**	**3**	**3**	**2**	**2**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	-

*equal columns **equal columns.

Clinical Structures

The clinical structure is the formal and graphical representation of the relations among the items of the context and, furthermore, it can display the relations between sets of items and sets of attributes. It is usually represented by a graph in which every node is a collection of items (*i.e.*, the clinical state) and the corresponding set of attributes (*i.e.*, the set of criteria satisfied by a patient having that clinical state). The structure is built according to both the relations among items and the attributes depicted in the clinical context and the prerequisite relations depicted by the same context. Some of the crucial configurations regarding the rows and columns of the context have precise counterparts in the structure. For instance, an empty row (*i.e.*, an item that does not investigate any of the selected attributes) will result in the absence of that item in the structure. The same happens to empty columns. When two rows are equivalent, the corresponding items will be included systematically in the same states. Finally, the prerequisite relation occurring whenever the attributes investigated by an item *i* are a subset of those investigated by *j* in terms of states in the structure means that there will not be any state including *j* that does not also include *i*.

T MODULE

There are 14 items in the T module. The obtained structure has 1156 states. Remembering that if no relations among items were present, the total theoretical response patterns would be 2^{14} = 16384 (*i.e.* the cardinality of the power set of the domain). The obtained structure contains only 7% of the potential patterns, indicating how an adaptive version of the instrument could be much more efficient in evaluating patients. The application of this analysis demonstrates the existence of prerequisite relations between several items of the T module. In particular, item 1 is a prerequisite of items 7 and 8; item 2 is a prerequisite of item 13; items 3 and 6 are prerequisites of item 7; and item 12 is a prerequisite of item 13 (Table 2).

This implies that if the child does not pass item 1, and item 1 is a prerequisite of other items, it is not necessary to administer those items.

MODULE 1

There are 9 items in module 1. The obtained structure has 224 states, 43% of the potential patterns. The application of this analysis demonstrates the existence of a prerequisite relation between two items of module 1. In particular, item 1 is a prerequisite of item 5 (Table 3). This implies that if the child does not pass item 1, it is not necessary to administer item 5.

MODULE 2

There are 14 items in module 2. The obtained structure has 1384 states, 8% of the potential patterns. The application of this analysis demonstrates the existence of prerequisite relations between several items of the T module. In particular, item 1 is a prerequisite of item 2; in addition, item 4 is a prerequisite of items 9 and 10; and item 9 is a prerequisite of item 10 (Table 4). This analysis demonstrates that it is not necessary to administer item 2 (free play) if the child does not pass item 1 (bubbles-play), because item 1 is a prerequisite of item 2. Besides this, item 10 no longer needs to be administered if the child does not pass items 4 and 9.

MODULE 3

There are 13 items in module 3. The obtained structure has 1136 states, which is 13% of the potential patterns. The application of this analysis demonstrates the existence of prerequisite relations between several items of module 3. In particular, item 1 is a prerequisite of items 2, 3 and 4. In addition, items 4, 5 and 6 are prerequisites of item 3;

and item 8 is a prerequisite of items 3 and 9 (Table **5**). This suggests that the order of appearance of items in the module should be reviewed.

MODULE 4

There are 13 items in module 4. The obtained structure has 592 states, 7% of the potential patterns, indicating how an adaptive process could be much more efficient in evaluating patients. The application of this analysis demonstrates the existence of prerequisite relations between several items of module 4. In particular, items 1, 2, 3 and 4 are prerequisites of item 5; item 3 is a prerequisite of item 12; item 7 is a prerequisite of items 8 and 10; finally, item 10 is a prerequisite of item 8 (Table 6). This result means that the clinician can select the items based on the item the child passed previously. In this way, it is possible to reduce the time it takes to administer the test.

Clinical structures validation: application to t module and module 1

The clinical structure of both the T module and module 1 were tested using the BLIM. The fit of the model parameters was estimated by means of the EM procedure[62,63]. To test the reliability of the observed Chi-square, a parametric bootstrap with 5000 replications was conducted for each of the two modules[61]. Concerning the T module, the results showed that the model adequately fit the data ($x^2(260,952) = 757.04$; $p > .05$; number of states = 1,156). The reliability of this result was confirmed by the parametric bootstrap (bootstrap $p > .05$). Moreover, the estimates of the error rates for the T module, reported in Table **7**, satisfy the condition of acceptability (*i.e.*, $\beta_q + \eta_q < 1$) for every item.

Table 7. Estimated parameters η and β for each item of T Module.

-	**Item**																-	-
-	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
η	.00	.00	.00	.00	.00	.00	.00	.00	.09	.50	.00	.50	.38	.00	.50	.03	.00	.50
β	.50	.50	.50	.00	.00	.33	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00

On the other hand, for module 1, the model fit the data quite well ($x^2(65, 280) = 17, 585$; $p > .05$; number of states =224) even though the reliability of the observed results is not supported by the bootstrap (bootstrap $p > .05$). Nonetheless, as can be seen in Table 8, even for this module the error rate estimates are acceptable for every item. In general, it can be concluded that the two models accurately explain the observed data. The estimates can then be implemented into an algorithm constituting an adaptive tool for the assessment of the diagnostic issues for ASD. Such a tool is derived from the ADOS-2 by removing its redundancies and focusing on the specific issues useful for diagnosis.

Table 8. Estimated parameters η and β for each item of Module 1.

-	Item															
-	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
η	.11	.05	.00	.02	.00	.00	.00	.00	.19	.13	.15	.39	.39	.00	.00	.00
β	.58	.63	.00	.72	.24	.00	.00	.00	.10	.53	.40	.22	.10	.00	.13	.00

Discussion

The aim of the present study was to analyse the single modules of ADOS-2 using the FPA methodology. Diagnosis is a fundamental process that determines which disorder or condition explains the symptoms of a person. Clinical assessment can be described as an intelligent procedure the clinician carries out with the aim of collecting information about a patient to formulate the diagnosis and propose therapeutic treatment. The investigation proceeds through a sequence of hypothesis formulations and validations[55]. This process is more difficult in neurodevelopmental disorders where it is not possible to ask patients to describe their symptoms (such as in the T module or module 1) or to measure the general capacity of the patient's social and relational abilities (for example in modules 2, 3 and 4). In addition, the information provided by caregivers through diagnostic interviews is not always related to the hypothesis of a clinician. For this reason, it is important to maximize and optimize the collected information, reduce the errors, focus on the critical areas of an individual (*e.g.*, deficit in social interaction), and reduce the number of items and time of evaluation, while trying to preserve its accuracy. We hypothesized that the reduction of the number of items considered redundant by the FPA would correlate with the improvement of the quality and quantity of information collected[55]. Notice that such reduction has no effect on the amount of information collected and, in general, it does not necessarily mean the removal of the item from the tool. In fact, the adaptive assessment procedure could store the redundant items into a buffer and use them if needed. For example, the answers may not be coherent and, therefore, it would be necessary to administer the same item twice. In this case, having the redundant items available in the buffer would allow the clinician to investigate the same attributes twice, without repeating the same item twice. This is a strong advantage of such an approach. This methodology could be applied to all clinical tests used in the autism field (such as the Autism Diagnostic Interview – Revised, Vineland), to reduce the weight of items without diagnostic or repetitive significance based on evidence from an FPA analysis and the validation of its clinical structure. Our goal is to improve the diagnostic process for ASD by making it adaptive. This adaptive system can perform logically correct inferences based on all the information collected during the testing process[55]. The system is adaptive in the sense that the question posed by the system at a given moment depends on the previously collected answers of the patient or behaviours observed. The adaptivity of this system lets it dynamically choose the best sequence of items or stimulus situations to be posed to maximize the informational content of each answer[55,64]. In this way, the system can often avoid posing the entire set of questions by inferring the answers to logically connected questions, thus saving time. A previous study found that the application of an adaptive version of a questionnaire allowed people to reach the end of the assessment without using 25-50% of the items[55]. Once an adaptive algorithm is defined that can take into account the ADOS-2 assessment modality, a similar time savings is expected.

Conclusion

In conclusion, we highlight that an important limit of the ADOS-2, like all tests based on observation, is that diagnostic characteristics seem to change among clinicians and the results for the same individual can be different if the evaluation is subsequently repeated. Unfortunately, the FPA method cannot enhance the reliability of the ADOS-2, but the main aim is to create an adaptive testing system for ASD diagnosis. We suppose that the reduction of the number of items considered repetitive by the FPA could to be correlated with an improvement of the quality and quantity of information collected. This issue represents a future goal of our research on autism. Nonetheless, some work is being carried out to provide new methodological tools for an accurate assessment of the inter-rater agreement for tasks like those involved in the administration of the ADOS-2,[65]. In addition, another limitation of this study is that the items of the ADOS-2 are then assigned to the attributes by six experts (four psychologists and two child psychiatrists) in the field of ASD and in the administration of the ADOS-2, thus these assignments are subjective. Nevertheless, we believe our study is important and addresses a critical issue in the literature on autism. This study represents the first step toward creating an adaptive testing system for ASD based on an existing clinical test that would improve the diagnosis of ASD and assist clinicians in their diagnosis formulation. For example, if a clinician assigns the score 2 to an item that evaluates "used gestures to indicate requests", the system, using the updating rule, increases the likelihood of the states containing the same attributes; on the contrary, if the clinician assigns the score 0 to this item, the system decreases the other attributes[55,64].

3. CONCLUSION

In conclusion, the above-described studies highlight that:

(1) children with ASD have a deficit in the social cognition abilities compared to TD children;

(2) however, the individuals with autism showed a delay in development of these capacities (developmental trajectories approach) rather than a total lack of ToM and social abilities. Indeed, in our clinical experience we observe children with autism with preserved social cognition abilities (measured by CST, Eyes Task- children version and SIPI tasks) even if minimal;

(3) Subsequently, we demonstrated, through the mediation analysis, that in children with TD the competences of SC (measured by CST and SIP-I) mediate the correct development of social behaviors appropriate to the context. On the contrary the deficit of ToM competencies in children with autism impairs their social interaction;

(4) therefore, an early specific rehabilitative treatment of social cognition abilities could improve the social deficit in children with autism and it could reduce social isolation of ASD adults;

(5) in this regard, the early diagnosis represents a fundamental step. In our research, we applied the FPA methodology to ADOS-2 in order to highlight strengths but also weaknesses of this diagnostic tool. The results revealed the need for a revision of the clinical tool through the implementation of an adaptive testing system, realized by FPA, which allows a more accurate evaluation and shorter execution times. A possible future perspective is to develop a software product that can assist clinicians in the path of diagnosis for ASD.

All together our results showed that the ASD individuals are not "mind-blindness" but rather they showed a delay in the development of SC abilities, compared to TD individuals. This delay increases with increasing of the complexity of SC task. In ASD individuals, the delay of develop of ToM ability affects the correct develop of social behaviour, as showed by mediation analysis.

Finally, we can conclude that the new knowledge on the autism could promoting the creation of specific treatment protocol with consequently reduction of the costs and time in clinical practice and at the same time improve the ASD’s quality of life.

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Chapter 3

AESTHETIC PERCEPTION ABILITY AND AUTISM

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1. GENERAL INTRODUCTION

Neuroaesthetic is a field of scientific research emerging at the intersection of psychological aesthetics, neuroscience and human evolution. The term neuroaesthetic was created by Semir Zeki[1] in order to investigate the biological and physiological mechanisms underlying the ability of aesthetic perception[2]. The main aim of neuroaesthetic is to explain the neurobiological foundations and evolutionary history of the cognitive and emotional processes involved in aesthetic experiences and artistic or other creative activities[3]. The aesthetic experience, therefore, shall be understood as a complete cognitive and emotional experience that has important implications on human experience and behaviour[4]. Specifically, the ability to perceive beauty plays a key role for all living beings, driving important evolutionary behaviour of the species such as the partner selection and the reproductive capacity[5]. In higher mammals such as humans, this ability is also fundamental for guiding social interaction[3]. Across different cultures exist features of beauty that determine an 'objective beauty'. At the same time, beauty can induce a 'subjective pleasure' in each person[5,6]. In fact, human aesthetic judgment is a complex mix of genetic, cultural, objective and subjective factors[7]. For instance, it was shown that more attractive women have more offspring over a lifetime compared to less attractive women. In addition, some features of faces, like symmetry, are generally associated with fertility and even higher moral values[3,8]. In bargaining, attractive people receive higher offers[9] and tend to be considered as more reliable, even by children[10] supporting a strongly rooted proclivity to aesthetics. Judgment of other people's attractiveness probably occurs subconsciously and influences us in a way we do not consciously realize[3]. Taken together, these findings suggest that some characteristics of beauty are important social cues that can induce stereotypes or promote different behavioural expectations[11]. Ultimately, they may also affect the ability to experience pleasure, which plays an important role in social interactions[12,13]. A fundamental capacity for successful social interactions is Social Cognition (SC), a complex cognitive construct that allows one to encode and decode the social world[14,15]. A main component of SC is empathy. Empathy can be defined as the ability to share the emotional state of another person[16]. According to Dziobek and collegues[17], empathy should be considered a multidimensional process that includes two dimensions: the cognitive component, also known as "Theory of Mind", consisting of the ability to understand the mental states of others (i.e. thinking, feeling)[17,18,19]; and the emotional component, that is the ability to emotionally "resonate" with other people's feelings while understanding that they are distinct from one's own[17]. The emotional empathy includes experience sharing of other persons' internal states[20]. Emotional contagion is a precursor of emotional empathy, whereby embodiment entails the forming of a representation of the other person's feelings[21]. Therefore, empathic ability is crucial in human interactions allowing one to automatically understand and share the actions and internal states of others. Researchers have suggested that, in typically developing (TD) individuals, empathic abilities are related to aesthetic perception, enabling people to anticipate, promote or avoid interaction with others[11]. Additionally, it has also been suggested that empathic abilities may represent a prerequisite for aesthetic perception capacity[22]. Along these lines, the aesthetic experience of artworks has been proposed to consist of the activation of the embodied simulation of actions, as well as of corporeal and emotional sensations. In this respect, mirror systems have been understood as a substantial part of the basic functional mechanism in SC in terms of embodied simulation[23,24], thus supporting the central role of empathy in aesthetic experiences[23,25]. Moreover, neuroimaging studies[24,26,27,28,29] have shown that the perception of beauty is mediated by the activity of cerebral areas also involved in empathic ability. Di Dio et al.[24] showed that the observation of classical sculptures, compared to the same sculptures with modified proportion between body parts, induced the joint activation of lateral and medial cortical areas (lateral occipital gyrus, precuneus and prefrontal areas), responding to the physical properties of the stimuli, and the anterior insula. In particular, the aesthetic experience induced by canonical art could emerge from the processing of sensorimotor input in conjunction with the emotional feeling of pleasure that is mediated by the activation of the insula[6]. In this respect, it is worth noting that the anterior portion of the insular cortex has been most often associated with tasks involving empathic engage with others' feelings or sensations[19,30,31,32]. In addition, it was shown that tasks requiring an aesthetic judgment often activate the same reward network in the brain that responds to the sensory pleasures associated with love, food and drugs via dopaminergic pathways[33,34]. It is also known that the reward system is active in general empathic behaviour and especially prosocial behaviour, such as cooperation[34,35]. Taken together, these data suggest the presence of relationship between aesthetic and empathic abilities, in fact beauty can affect different aspects of the empathic behaviour, just like empathic abilities could partly mediate aesthetic perception[15.]

However, we known that individuals with ASD show an impairment of SC abilities[14]. Specifically, they have difficulties with the ability to experience empathy. In this regard, we support the idea that individuals with ASD could have a diminished aesthetic perception ability compared to typically developing individuals, which may be possibly associated with a potential impaired of empathic abilities[17]. On this basis, we *(1)* firstly evaluated the role of the sleep in mediating the aesthetic perception ability and empathy and their relationship, in TD individuals, using how aesthetic task the Golden Beauty task. In this study, we evaluated the role of sleep in mediating the aesthetic perception ability and empathy based on the fact that it has a critical role in emotional brain functioning.

Subsequently *(2)*, we used the same aesthetic task in a group of individuals with autism. In this second study we evaluated the aesthetic perception ability in ASD individuals compared to TD individuals, using the Golden Beauty behavioural task adapted for eye-tracking. The eye-tracking technique was used to gather additional information about sensory-driven coding of the stimuli by assessing eye movement behaviour. Finally, the relationship between empathic and aesthetic perception abilities was evaluated, as well by this study.

a) STUDY 1: THE ROLE OF SLEEP IN AESTHETIC PERCEPTION AND EMPATHY: A MEDIATION ANALYSIS

Aim of the work

The main purpose of this study was to evaluate if empathy and aesthetic perception are mediated by sleep in TD individuals. Our hypothesis was that duration and quality of sleep could be related to empathy and aesthetic perception abilities. More specifically, we expected that a longer sleep duration and an overall better sleep quality could positively affect emphatic and aesthetic competencies (i.e. improves them). We also evaluated the relationship between empathy and aesthetic perception capacities. We performed a mediation analysis to examine the role of sleep on cognitive and emotional empathy and aesthetic perception abilities in a group of healthy subjects with different sleep characteristics. Subsequently, the same approach was replicated in a sleep-deprived group, to evaluate the effects of the absence of sleep.

Method

Participants

One-hundred and twenty-six subjects met the criteria for the study after the screening phase (for more details see Peretti et al.[15]). They were then randomized to either a sleep or a sleep-deprived group. One-hundred and one subject slept at home (Sleep Group, SG; mean age

standard deviation: 21.65 ± 2.84 years; age range: 19–- 31 years). Twenty-five subjects (mean age ± standard deviation:
21.4 ± 1.91 years; age range: 19–27 years) were included in the Sleep-Deprived Group (SD group) and tested after 1 night of sleep deprivation, to assess the effects of lack of sleep on aesthetic perception
and empathy. Each participant was asked to maintain a regular sleep–wake cycle in the 3 days before each experimental session; each morning, all the participants completed a sleep diary to assess their subjective report of sleep duration and sleep quality. Moreover, to obtain an objective assessment of sleep, all participants wore an actigraph on the non-dominant wrist (AMI MicroMini Motionlogger; Ambulatory Monitoring, Ardsley, NY, USA) for the 3 days prior to testing. Actigraphs were initialized by ACT Millennium software (Ambulatory Monitoring, Ardsley, NY, USA) for "zero crossing mode"
to collect data in 1-min epochs. Between-group differences for demographic data, clinical and sleep quality measures, actigraphic data (the mean of 3 nights prior to the experiment) of all the participants
(SG and SD groups) are summarized in Table 1.
The investigation was approved by the local research ethics board and was conducted at the Laboratory of Sleep Psychophysiology and Cognitive Neurosciences of the University of L'Aquila, according to the principles established by the Declaration of Helsinki. Informed consent was obtained from all the participants before the study.

Table 1. Means (SD) and between-group differences for demographic data, clinical and sleep quality measures, actigraphic data (the mean of 3 nights prior to the experiment) for each of the two groups (SG and SD).

	SG (N=101) Mean (SD)	**SD (N=25) Mean (SD)**	**U**	**P**
Age (in years)	21.65 (2.84)	21.40 (1.91)	1.246.50	.80
Level of education (in years)	13.80 (1.93)	13.43 (0.84)	836.00	.38
Clinical and sleep quality measures				
Beck Depression Inventory *(BDI)*	9.98 (6.24)	7.52 (4.08)	980.50	.06
Toronto Alexithymia Scale *(TAS)*	44.03 (9.62)	43 (8.12)	1.201.50	.60
Pittsburgh Sleep Quality Index *(PSQI)*	4.83 (1.30)	4.64 (0.99)	1.028.50	.11
Insomnia Severity Index *(ISI)*	4.66 (1.98)	4.08 (2.19)	1.003.50	.20
Subjective sleep variables (diary)				
Subjective Total Sleep Time *(S-TST)*	7.05 (1.37)	7.42 (0.63)	1.186.00	.54
Subjective Wake After Sleep Onset *(S-WASO)*	9.03 (14.49)	7.8 (18.63)	1.188.00	.76
Subjective Awakenings *(SA)*	1.21 (1.42)	1.4 (1.63)	1.210.50	.62
Objective sleep variables (actigraphy)				
Total Sleep Time *(TST)*	449.05(67,56)	457.16 (71,20)	1.087.00	.22
Time in Bed *(TIB)*	483.69(64.89)	502.16 (61.57)	1.093.00	.24
Mean Activity *(ACT)*	12.74 (6.84)	13.78 (5.35)	1.149.50	.40
Sleep Efficency *(EFF)*	92.77 (6.12)	90.61 (7.54)	1.188.00	.55
Wake After Sleep Onset *(WASO)*	23.39 (23.38)	33.64 (23.58)	1.202.00	.60

The results of the Mann Whitney-U tests comparing SG and SD groups are also reported.

Procedure

The sleep group (SG; n = 101) performed the test session after 1 night of sleep at home; the sleep deprivation group (SD; n = 25) performed the test session after 1 night of sleep deprivation in the laboratory. During the night of sleep deprivation, the participants stayed awake in the laboratory under the direct supervision of two experimenters. They were allowed to briefly walk around, listen to music,

read, play cards, watch the television and use the computer. Lying down, sleeping and vigorous physical activity were not permitted. Light snacks were permitted, while caffeinated beverages, chocolate,

alcohol, and medications that can induce or counteract sleepiness were not allowed during the deprivation protocol. Time information was available to subjects. The laboratory was constantly illuminated by neon lamps. All participants performed the same test battery (Basic Empathy

Scale (BES), Empathy Quotient (EQ), Interpersonal Reactivity Index (IRI), Multifaceted Empathy Test (MET), Golden Beauty task (GB), but the order of the tasks was randomized for each participant. The cognitive and emotional empathy measures (BES, EQ, IRI, MET)

were comprised of different components, as described below. Regarding the GB task, the two blocks of objective and subjective
aesthetic judgements (OAJ and SAJ, respectively) were administered in a random order, while the block of proportion quality judgements (PJ) was always presented at the end of the task for all participants so as not to influence the subjects' aesthetic evaluation with a prior exposure to the proportion assessment.

Detailed instructions were provided before the experimental session during a task practice session. The instructions were again presented on the screen at the beginning of each test block. Specifically, for cognitive and emotional empathy measures (BES, EQ, IRI, MET) the stimuli were presented with an interstimulus interval of 1,000 ms. Each item remained on screen until the participant's response on a computer keyboard. Regarding the GB task, for all conditions (OAJ, SAJ, PJ) the stimuli were visually presented for 2,000 ms each, with an interstimulus interval of 250 ms, which was followed by instructions to respond. The test battery, lasting _60 min, was administered on a 21-inch computer monitor placed at _50 cm from the subject. The stimuli were delivered using a custom software (programmed in SuperLab, version 4.5 for Mac) also recording the participants' responses and reaction times.

Sleep measures

Five variables were obtained by actigraphic data: time in bed (TIB); mean activity (ACT); total sleep time (TST); sleep efficiency (EFF); wake after sleep onset (WASO). The SG and SD groups did not differ on mean TST, TIB, ACT, EFF and WASO in the 3 days preceding the sleep and sleep deprivation conditions (Table 1).

Empathy measures

All empathy tests used in this study evaluated empathy as a stable feature of personality.

We used to assess emotional empathy: BES-Affective Empathy Sub-scale (BES-AES)[36,37]; IRI-Affective Sub-scales[38]; EQ-Emotional Sub-scale (EEQ)[39]; MET-Emotional Empathy (EE) component[17]. For detailed description of this test see chapter 1 (section "Social cognition measures for adolescents and adults").

We used to assess cognitive empathy: BES-Cognitive Empathy Sub-scale (BES-CES)[36,37]; IRI cognitive sub-scales, divided into two scales: fantasy (FS) and perspective taking (PT)[38]; EQ scale cognitive sub-scale, divided into two sub- scales cognitive empathy (CEQ) and social skills (SSQ)[39]; MET-Cognitive Empathy (CE)[17]. For detailed description of this test see chapter 1 (section "Social cognition measures for adolescents and adults").

Aesthetic perception task: Golden Beauty

Aesthetic perception was evaluated by a modified version of the GB task[24]. This task consists of the evaluation of images of sculptures selected from masterpieces of Classical and Renaissance art that are commonly accepted as normative Western representations of beauty[24]. An important feature of this task is the use of two sets of stimuli

that are identical in every respect but one: proportion. Specifically, a parameter that is considered to represent the ideal beauty, and namely the golden ratio (1:0.618)[40,41], was modified to create an aesthetically degraded version of the same stimuli in a controlled fashion. The GB task contains 44 total images of sculptures, including 22 with modified proportions between body parts. Specifically, half of the canonical stimuli were modified with a short-leg long-trunk relation (whereas the other half with the opposite modification type). All stimuli (canonical and modified sculptures) were presented in three experimental conditions: (1) OAJ for proportioned stimuli (OAJP) and modified stimuli (OAJM); (2) Non pensavo di essere così voglio tutto originale come te avvia colmare SAJ for proportioned stimuli (SAJP) and modified stimuli (SAJM); and (3) PJ for proportioned stimuli (PJP) and modified stimuli (PJM). In the first condition, OAJ, participants were asked to observe the sculptures and express an explicit objective judgement ("objective" aesthetic value) for each image by answering the question: "How beautiful is the image that you see?". The participants responded on a seven-point Likert-type scale from 1 = It's not at all beautiful to 7 = It's very beautiful. In the second condition, SAJ, participants were asked to observe the sculptures and express an explicit subjective judgement ("subjective" aesthetic value) for each image by answering the question: "How much do you like the image that you see?". The participants responded on a seven-point Likert-type scale from 1 = I don't like it at all to 7 = I like it very much. In the third condition, PJ, participants were asked to observe the sculptures and express an explicit judgement of proportion (proportion quality) for each image by answering the question: "How proportioned is the image that you see?". The participants responded on a seven-point Likert-type scale from 1 = not at all proportionate to 7 = very proportionate. The original version of the task is described in chapter 1 (section "Golden Beauty Task").

Data Analysis

Between-group comparisons

Due to the largely different sample size of the two groups, a nonparametric approach (Mann–Whitney U-test) was used to test differences between SG and SD groups on demographic, clinical and sleep quality measures, actigraphic data, and empathy and aesthetic perception variables.

Exploratory factor analysis

We used Exploratory factor analysis (EFA) with varimax rotation to identify complex interrelationships among items that are part of unified concepts (Factors). Instead of selecting an "a priori" criterion for
the choice of the number of components, we opted for a solution that accounts for at least 60% of the total variance[42]. The EFA on emotional and cognitive empathy measures, aesthetic perception and sleep variables in the SG group yielded seven factors that explain the 64.91% of the total variance. The factors are listed as follows.

• FACTOR 1 called "Emotional Empathy" is composed of implicit and explicit emotional empathy components of MET, EC subscale of IRI, AES sub-scale of BES, EEQ sub-scale of EQ. Factor 1 explains 16.95% of the total variance.

• FACTOR 2 called "Objective Sleep Quality" is composed of SE, WASO, ACT. Factor 2 explains 9.57% of the total variance.

• FACTOR 3 called "Aesthetic Perception" is composed of all components of the GB task (OAJ, SAJ, PJ). Factor 3 explains 8.93% of the total variance.

• FACTOR 4 called "Cognitive Empathy" is composed of the cognitive empathy component of MET. Factor 4 explains 8.72% of the total variance.

• FACTOR 5 called "Sleep Duration" is composed of TST, subjective (S)-TST, TIB. Factor 5 explains 7.49% of the total variance.

• FACTOR 6 called "Subjective Sleep Quality" is composed of PSQI, ISI, subjective (S)-WASO, subjective awakenings (SA). Factor 6 explains 6.89% of the total variance.

• FACTOR 7 called "Theory of Mind" is composed of PT sub-scale of IRI, FS sub-scale of IRI, CES sub-scale of BES, CEQ sub-scale of EQ, SSQ sub-scale of EQ. Factor 7 explains 6.36% of the total
variance.

Correlations

Pearson's correlations were performed to explore the relationship among the sleep factors (Factors 2, 5 and 6), the emotional and cognitive empathy factors (Factors 1, 4 and 7) and the aesthetic perception
factor (Factor 3) obtained by EFA, and the single variables of emotional and cognitive empathy and aesthetic perception abilities in both SG and SD groups. The mediation models were performed according to the correlation results (see below).

Regression analysis

A linear regression analysis was performed to evaluate the relations between a dependent variable and one (simple linear regression) or more (multiple linear regression) explanatory variables. In this study,
the variables for the regression analysis were the emotional and cognitive empathy measured by different tests (EQ, BES, MET, IRI), the aesthetic perception ability measured by the GB task and the sleep variables.

*Mediation Analysis (*For detailed description of this analysis see chapter 2 (section c "Study 3: the role of theory of mind on social information processing in children with autism spectrum disorders: a mediation analysis").

Results

Between-group comparisons

Regarding clinical and sleep measures the Mann–Whitney U-test showed no significant differences
between groups (SG and SD) regarding all sleep (sleep quality, subjective sleep variables and actigraphic data) and clinical measures (Table 1).

Regarding empathy measures the Mann–Whitney U-test of the BES test showed that the SD group had lower scores compared with the SG group in both affective (AES of BES: $U = 952.50$; $p = .04$) and cognitive (CES of BES: $U = 863.00$; $p = .01$) sub-scales of BES. No significant differences between SG and SD groups regarding all sub-scales of IRI (cognitive sub-scale: FS, PT; emotional sub-scale: PD, EC), EQ (cognitive subscales: CEQ, SSQ; emotional sub-scale: EEQ) and MET (cognitive sub-scale: CE; emotional sub-scales: implicit EE and explicit EE) were found (Table 2).

Regarding the aesthetic perception task, the Mann–Whitney U-test showed no significant between-groups differences in performance on all components (OAJP–OAJM, PJP–PJM, SAJP-SAJM) of the GB task (Table 2).

Table 2. Means (SD) and between-group differences for empathy and aesthetic perception variables obtained by the two groups (SG and SD).

	SG (N=101) Mean (SD)	SD (N=25) Mean (SD)	U	P
Empathy measures				
Emotional Empathy				
AES of BES	44.28(5.79)	40.97(8.09)	952.50	**.04***
EEQ of EQ	14.00(4.63)	13.26(4.30)	1.082.50	.21
EC of IRI	28.48(4.61)	27.53(4.24)	1.028.50	.11
PD of IRI	19.35(5.65)	19.20(4.27)	1.280.50	.96
Implicit EE of MET	4.28(1.17)	4.14(1.28)	1.201.50	.60
Explicit EE of MET	4.44(1.18)	4.30(1.36)	1.221.50	.69
Cognitive Empathy				
CES of BES	38.32(3.23)	36.01(5.03)	863.00	**.01****
CEQ of EQ	13.48(3.99)	12,72(4.11)	1.203.50	.61
SSQ of EQ	6.32(1.88)	6.09(2.05)	1.201.50	.61
FS of IRI	24.53(5.22)	23.84(5.61)	1.195.50	.57
PT of IRI	26.88(4.02)	26.35(4.51)	1.153.50	.41
CE of MET	10.46(1.04)	10.38(1.28)	1.285.00	.98
Golden Beauty task				
OAJP	3.69(1.09)	3.68(1.27)	1.280.50	.96
OAJM	3.60(1.09)	3.55(1.22)	1.232.00	.73
PJP	4.80(0.84)	4.70(1.12)	1.278.00	.85
PJM	4.06(1.10)	3.76 (1.18)	1.211.00	.64
SAJP	3.67(1.06)	3.66(1.15)	1.275.00	.94
SAJM	3.59(1.07)	3.57(1.11)	1.286.50	.99

The results of the Mann–Whitney U-tests comparing SG and SD groups are also reported. Significant correlations are highlighted in bold, with asterisks representing significance levels: *p < .05; **p < .01.

Legend: *AES*, Affective Sub-scale; *BES*, Basic Empathy Scale; *CE*, Cognitive Empathy; *CEQ*, Cognitive Empathy; *CES*, Cognitive Sub-scale; *EC*, Empathic Concern; *EE*, Emotional Empathy explicit and implicit; *EEQ*, Emotional Empathy; *EQ,* Empathy Quotient; *FS*, Fantasy Scale; *GB*, Golden Beauty task; *IRI*, Interpersonal Reactivity Index; *MET*, Multifaced Empathy Test; *OAJM*, objective aesthetic judgement for modified stimuli; *OAJP,* objective aesthetic judgement for proportion stimuli; *PD*, Personal Discomfort; *PJM*, proportion judgement for modified stimuli; *PJP*, proportion judgement for proportion stimuli; *PT*, Perspective Taking; *SAJM,* subjective aesthetic judgement for modified stimuli; *SAJP*, subjective aesthetic judgement for proportion stimuli; *SD*, Sleep-Deprived Group; *SG,* Sleep Group; *SSQ*, Social Skills.

Correlation analysis

The significant correlations among cognitive and emotional empathy and aesthetic perception abilities on the one hand and the sleep variables on the other hand are described below.

Moreover, below are also reported the significant correlations between cognitive and emotional empathy and aesthetic perception as well as the significant correlations between aesthetic perception

ability and the factors of cognitive and emotional empathy. The significant correlations among single measures of empathy, aesthetic perception and sleep with the factors that gather together the same measures (such as the significant correlations between single sleep measures and the sleep factors) are not described in the text (Tables 3 and 4).

Regarding SG significant correlations were found between the "Sleep Duration" factor (Factor 5), single emotional and cognitive empathy measures and the PJM component of the GB task. Specifically, we found a significant negative correlation between the "Sleep Duration" factor and the PJM component of the GB task (r = _.327; p = .0005). A significant positive correlation was also found between the

"Sleep Duration" factor and emotional empathy measured by the AES sub-scale of BES (r = .304; p = .004), the EEC sub-scale of EQ (r = .371; p = .0005), the EC (r = .294; p = .004) and PD (r = .269;

p = .01) sub-scales of IRI. Furthermore, the "Sleep Duration" factor showed a significant negative correlation with the cognitive empathy measured by the SSQ sub-scale of EQ (r = _.242; p = .01) and a

positive correlation with cognitive empathy measure by the FS subscale of IRI (r = .346; p = .0005).

We found significant positive correlations between the "Subjective Sleep Quality" factor (Factor 6) and emotional empathy measured by PD sub-scale of IRI (r = .389; p = .0005). In addition, significant positive correlations were found between the "Emotional Empathy" factor (Factor 1) and components of the GB task: SAJP (r = .245; p = .01). The "Emotional Empathy" factor also positively correlated with cognitive empathy measured by the FS (r = .442; p = .0005) sub-scale of IRI. Finally, we found significant correlations between the "Theory of Mind" factor (Factor 7) and emotional empathy measures. Specifically, significant positive correlations were found between the

"Theory of Mind" factor and the AES sub-scale of BES (r = .407; p = .0005), the EEQ sub-scale of EQ (r = .566; p = .0005) and the EC sub-scale of IRI (r = .335; p = .0005). Moreover, a negative correlation

between "Theory of Mind" factor and emotional empathy measured by PD sub-scale of IRI (r = _.295; p = .004) was found.

Regarding SD group no significant correlations among sleep, cognitive and emotional empathy and aesthetic perception variables were found.

Table 3. Pearson's correlation coefficients for sleep variables (Factors 2, 5 and 6), emotional and cognitive empathy abilities (Factors 1, 4 and 7) and aesthetic perception ability (Factor 3) obtained by EFA, and single variables of emotional and cognitive empathy measured by different tests (EQ, BES, IRI, MET) and aesthetic perception ability measured by the GB task, in the SG.

	FACTOR 1 *Emotional empathy*	FACTOR 2 *Objective sleep quality*	FACTOR 3 *Aesthetic perception*	FACTOR 4 *Cognitive empathy*	FACTOR 5 *Sleep duration*	FACTOR 6 *Subjective sleep quality*	FACTOR 7 *Theory of Mind*
SLEEP GROUP							
			Golden Beauty task				
OAJP	.169	-.017	**.918***	.020	.064	-.088	.039
OAJM	.162	-.005	**.930***	-.007	.069	-.090	.027
PJP	.223	-.009	**.470***	.067	-.148	.230	.126
PJM	-.230	.009	**.400***	.185	**-.327****	.078	-.030
SAJP	**.245***	-.025	**.892***	.005	-.008	-.120	.045
SAJM	.222	-.019	**.904***	-.008	.020	-.099	.047
EMPATHY MEASURES							
			Emotional Empathy				
AES of BES	**.433***	-.079	-.012	.087	**.304****	.128	**.407****
EEQ of EQ	**.422***	-.072	.045	-.039	**.371****	.093	**.566****
EC of IRI	**.400***	-.051	-.102	.150	**.294****	.117	**.335****
PD of IRI	.266	.040	-.157	.048	**.269****	**.389****	**-.295****
Implicit EE of MET	**.948***	.001	.092	-.017	.020	.057	.044
Explicit EE of MET	**.950***	-.039	.111	-.016	-.037	.002	.063
			Cognitive Empathy				
CES of BES	.090	-.049	.052	.055	.067	.056	**.745***
CEQ of EQ	.029	-.047	.078	.061	-.018	-.006	**.723***
SSQ of EQ	-.027	-.021	.111	.029	-.242	-.201	**.666***
FS of IRI	**.442****	-.104	.105	-.195	**.346****	.124	.103
PT of IRI	.170	.005	.003	-.070	.048	.150	**.764***
CE of MET	-.004	.098	.068	**.934***	-.192	-.018	.062

Significant correlations that are not described in the text are highlighted in bold with the symbol * representing significance level: *p ≤ .013, adjusted after FDR correction.
Significant correlations that are described in the text are highlighted in bold, with the symbol ** representing significance level: **p ≤ .013, adjusted after FDR correction.

Table 4. Pearson's correlation coefficients for sleep variables (Factors 2, 5 and 6), emotional and cognitive empathy abilities (Factors 1, 4 and 7), and aesthetic perception ability (Factor 3) obtained by EFA, and single variables of emotional and cognitive empathy measured by different tests (EQ, BES, IRI, MET) and aesthetic perception ability measured by the GB task, in the SD group.

	FACTOR 1 *Emotional empathy*	FACTOR 2 *Objective sleep quality*	FACTOR 3 *Aesthetic perception*	FACTOR 4 *Cognitive empathy*	FACTOR 5 *Sleep duration*	FACTOR 6 *Subjective sleep quality*	FACTOR 7 *Theory of Mind*
SLEEP DEPRIVATION GROUP							
Golden Beauty task							
OAJP	.263	-.002	.409	-.061	.205	.010	.057
OAJM	.318	-.029	.385	-.108	.195	-.001	.006
PJP	-.011	.384	.313	-.084	.225	.167	.239
PJM	.166	.403	.339	-.143	-.030	.156	.093
SAJP	.320	-.096	.433	.094	.183	.158	.048
SAJM	.378	.043	.457	.063	.233	.171	.015
EMPATHY MEASURES							
Emotional Empathy							
AES of BES	-.034	-.235	-.036	.227	-.246	-.150	.439
EEQ of EQ	-.172	-.218	-.081	.012	-.258	-.060	.255
EC of IRI	.066	.047	.153	.227	-.140	-.251	.135
PD of IRI	.122	-.220	.154	.522	-.016	-.140	.187
Implicit EE of MET	.141	-.134	.202	.127	.345	.182	.544
Explicit EE of MET	.005	.021	.235	.145	.282	.135	.589
Cognitive Empathy							
CES of BES	-.573	.052	-.053	.163	-.115	.178	-.167
CEQ of EQ	-.589	-.205	.026	-.040	.013	.237	-.309
SSQ of EQ	-.312	.399	.162	-.199	.077	-.119	-.201
FS of IRI	.133	-.009	-.117	-.047	-.330	-.105	-.003
PT of IRI	-.163	.097	.053	.076	-.315	-.072	-.049
CE of MET	.041	-.477	.092	.378	.081	.060	-.067

No correlation is significant after p adjustment with FDR correction ($p \leq .001$).

Legend: *AES*, Affective Sub-scale; *BES*, Basic Empathy Scale; *CE*, Cognitive Empathy; *CEQ*, Cognitive Empathy; *CES*, Cognitive Sub-scale; *EC*, Empathic Concern; *EE*, Emotional Empathy explicit and implicit; *EEQ*, Emotional Empathy; *EQ,* Empathy

Quotient; *FS*, Fantasy Scale; *GB*, Golden Beauty task; *IRI*, Interpersonal Reactivity Index; *MET*, Multifaced Empathy Test; *OAJM*, objective aesthetic judgement for modified stimuli; *OAJP,* objective aesthetic judgement for proportion stimuli; *PD*, Personal Discomfort; *PJM*, proportion judgement for modified stimuli; *PJP*, proportion judgement for proportion stimuli; *PT*, Perspective Taking; *SAJM,* subjective aesthetic judgement for modified stimuli; *SAJP*, subjective aesthetic judgement for proportion stimuli; *SD*, Sleep-Deprived Group; *SG,* Sleep Group; *SSQ*, Social Skills.

Regression analysis

Based on the results obtained from the correlation analysis, the following linear regression analyses were performed. These were further used to create the mediation model.

SG

- We conducted a first regression analysis using Factor 5 "Sleep Duration" as the dependent variable and the EEQ sub-scale of EQ (emotional empathy) as the predictor (R2 = .37, SE = 0.09, p = .001). This was followed by a second regression analysis where "Sleep Duration" became a predictor together the EEQ sub-scale of EQ, while the PJM component of the GB task was the dependent variable (R2 = .36, SE = 0.10, p = .001).
- We then carried out a regression analysis using "Sleep Duration" as the dependent variable and the EC sub-scale of IRI (emotional empathy) as the predictor (R2 = -.30, SE = 0.09, p = .003). This was followed by a second regression analysis where "Sleep Duration" became a predictor together with the EC sub-scale of IRI, while the PJM component of the GB task was the dependent variable (R2 = .35, SE = 0.09, p = .001).
- Subsequently, a regression analysis was carried out using "Sleep Duration" as the dependent variable and the FS sub-scale of IRI (cognitive empathy) as the predictor (R2 = -.34, SE = 0.09, p = .001). This was followed by a second regression analysis where "Sleep Duration" became a predictor together with the FS sub-scale of IRI, and the PJM component of the GB task was the dependent variable (R2 = .34, SE = 0.10, p = .001).
- We then conducted a regression analysis using "Sleep Duration" as the dependent variable and the PD sub-scale of IRI (emotional empathy) as the predictor (R2 = -.27, SE = 0.09, p = .006). This was followed by a second regression analysis where "Sleep Duration" became the predictor together with the PD sub-scale of IRI, and the PJM component of the GB task was the dependent variable (R2 = .34, SE = 0.09, p = .001).

- A regression analysis was carried out using "Sleep Duration" as the dependent variable and the AES sub-scale of BES (emotional empathy) as the predictor (R2 = -.30, SE = 0.09, p = .002). This was followed by a second regression analysis where "Sleep Duration" became a predictor together with the AES sub-scale of BES, while the PJM component of the GB task became the dependent variable (R2 = .33, SE = 0.10, p = .001).
- We performed a regression analysis with "Sleep Duration" as the dependent variable and the SSQ sub-scale of EQ (cognitive empathy) as the predictor (R2 = -.24, SE = 0.09, p = .01). This was followed by a second regression analysis where "Sleep Duration" became the predictor together with the SSQ sub-scale of EQ, and the PJM component of the GB task was the dependent variable (R2 = .33, SE = 0.09, p = .001).

SD group

Based on the lack of significant correlations among empathy, aesthetic perception and sleep variables, the regression and mediation analyses were not performed.

Mediation Analysis

Mediation models were performed according to the correlation and regression analyses. To clarify whether emotional and cognitive empathy and aesthetic perception are mediated by "Sleep Duration"
(Factor 5), six separate mediation models for the SG group were conducted. The results of the regression analysis allowed us to carry out the Sobel test[43] to explore the significance of mediation effects among variables.

SG

With these analyses, we assessed the relationship between specific emotional (EEQ sub-scale of EQ and EC sub-scale of IRI) and cognitive (FS sub-scale of IRI) measures (X) and proportion judgement of modified stimuli (PJM component of the GB task – Y), using "Sleep Duration" as the mediator (M).

Significant results (Sobel test) are summarized as follows.

- EEQ sub-scale of EQ (X) and PJM (Y), and "Sleep Duration" as the mediator (Z = 2.67; SE = 0.04; p = .007; Figure 2a).
- EC sub-scale of IRI (X) and PJM (Y), and "Sleep Duration" as the mediator (Z = _2.53; SE = 0.04; p = .01; Figure 2b).

- FS sub-scale of IRI (X) and PJM (Y), and "Sleep Duration" as the mediator (Z = _2.52; SE = 0.04; p = .01; Figure 2c).

Figure 2 (A)

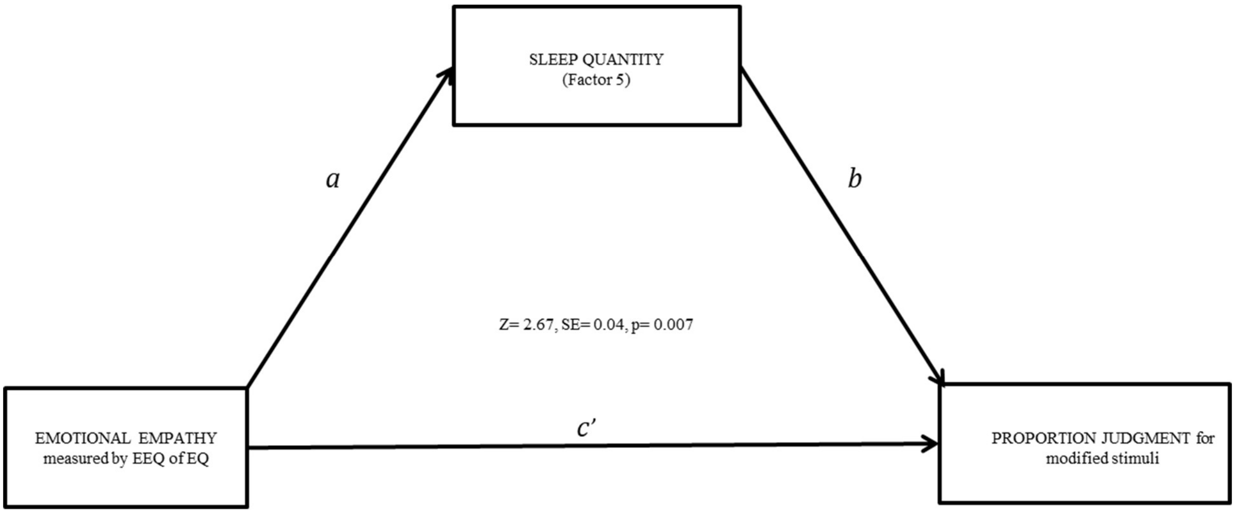


Figure 2 (B)

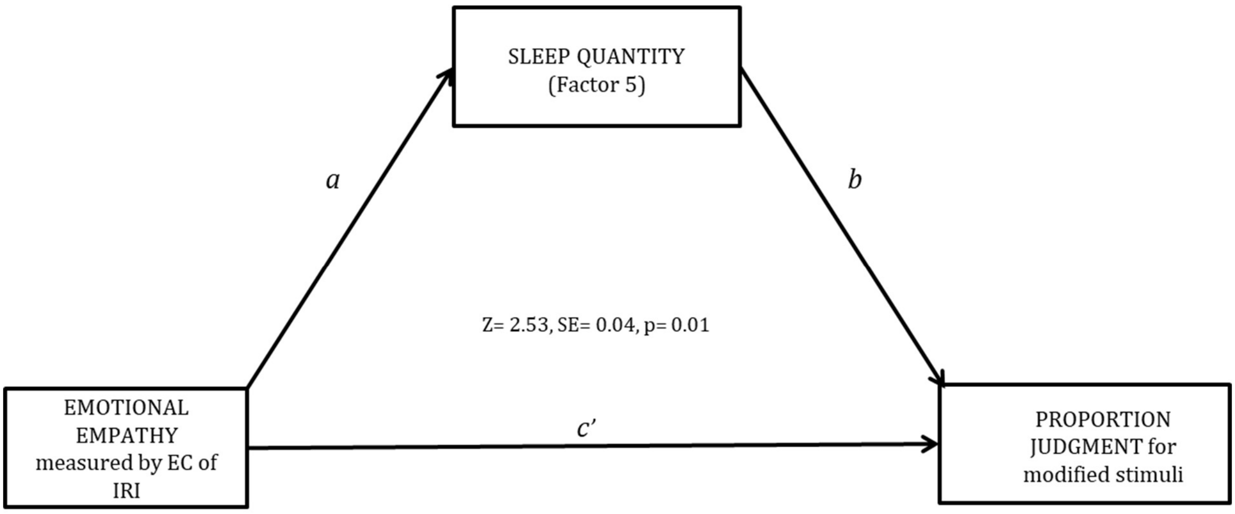


Figure 2 (C)

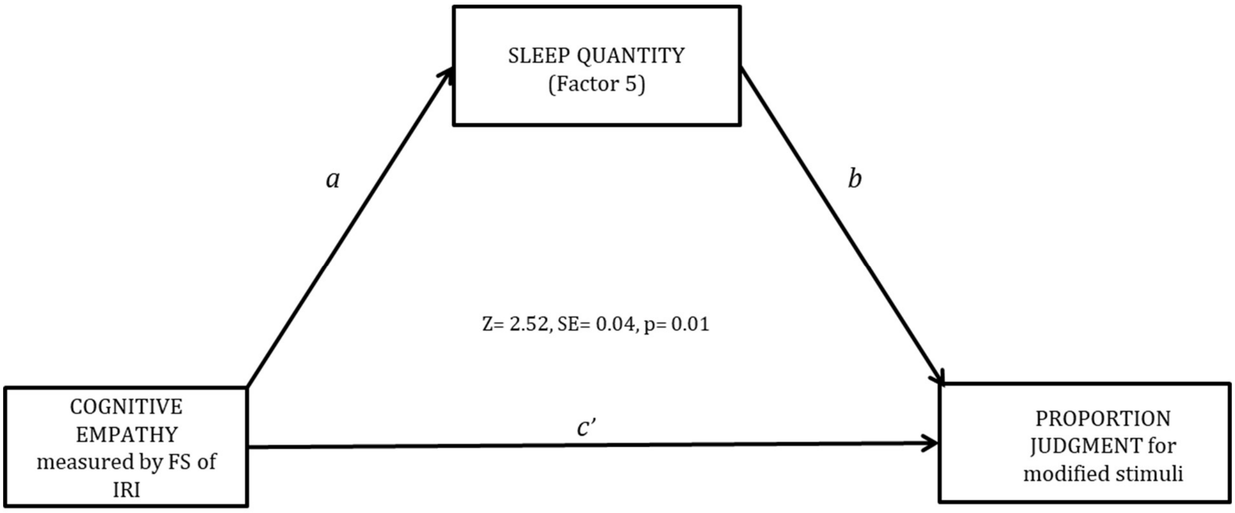


Figure 2. The Sobel test significance levels for the Sleep Group (SG). (a) The Sobel test significance levels, for the relationship between emotional empathy measured by Emotional sub-scale (EEC) of Empathy Questionnaire (EQ) and proportion quality judgements for modified stimuli (PJM) component of Golden Beauty (GB) as mediated by Sleep Quantity (Factor 5). (b) The Sobel test significance levels, for the relationship between emotional empathy measured by Empathic Concern (EQ) sub-scale of Interpersonal Reactivity Index (IRI) and PJM component of GB as mediated by Sleep Quantity (Factor 5). (c) The Sobel test significance levels, for the relationship between cognitive empathy measured by Fantasy Scale (FS) sub-scale of IRI and PJM component of GB as mediated by Sleep Quantity (Factor 5).

Moreover, we also obtained three not significant models. In this case, we assessed the relationship between other specific emotional (PD sub-scale of IRI and AES sub-scale of BES) and cognitive (SSQ
sub-scale of EQ) measures (X) and PJM stimuli (PJM component of the GB task – Y), using "Sleep Duration" as the mediator (M). Results that were not significant are summarized as follows.

- PD sub-scale of IRI (X) and PJM (Y), and "Sleep Duration" as the mediator (Z = _2.34; SE = 0.03; p = .02).
- AES sub-scale of BES (X) and PJM (Y), and "Sleep Duration" as the mediator (Z = _2.34; SE = 0.04; p = .02).
- SSQ sub-scale of EQ (X) and PJM (Y), and "Sleep Duration" as the mediator (Z = _2.15; SE = 0.03; p = .03).

Discussion

In this study we evaluated, for the first time, the role of sleep on aesthetic perception and empathy abilities in healthy subjects, using mediation analysis. We analysed both aesthetic and empathy skills because recently the interest for aesthetic perception has increased, considering its important role in promoting or obstructing social interactions[13]. Indeed, as was already known, empathy ability is fundamental to have positive social interactions. Moreover, accumulating evidence has suggested a critical role of sleep in the emotional brain functioning. Neuroimaging studies showed that sleep deprivation negatively influences the functionality of brain areas associated with emotional regulation[44,45]. After sleep loss, an amplified hyper-limbic activation in response to negative emotional stimuli has been observed[45]. Sleep loss and poor sleep quality can also lead to functional alterations of the insula[44,46], suggesting that this structure, involved in empathy and aesthetic perception, could be specifically vulnerable to alterations in sleep duration and sleep quality. Accordingly, at the behavioural level, studies evaluating the relationship between sleep and empathic abilities showed that sleep may significantly modulate complex, higher order emotional processes, such as those involved in empathy[47,48,49,50]. Specifically, sleep curtailment[48] and poor sleep quality[49] impair the ability to understand the other's feelings and to be empathic with them. Notably, a recent functional magnetic resonance imaging investigation[49] showed that, in subjects with better subjective sleep quality, the completion of an emotional empathy task is associated to increased blood oxygen level-dependent signal in a selective region of the left anterior insula, as well as to an increased functional segregation within the anterior insular cortex. These results suggest a significant role of the anterior insula in the processing of emotional empathy, mediated by the individuals' quality of sleep[49]. Nevertheless, to date, there was a surprising lack of studies aimed at assessing the role of sleep on aesthetic perception ability and its relations with empathy. For this reason, the present study focused on the evaluation of the role of sleep on emotional and cognitive empathy abilities measured by a comprehensive battery of tests (BES, EQ, MET, IRI), and on the aesthetic perception ability measured by the GB task. This task aims at evaluating the sense of beauty through objective parameters intrinsic to works of art (proportion), and requires objective and subjective aesthetic judgement, as well as a proportion judgement for proportionate and modified stimuli[24]. Proportion judgement can be regarded as the perceptual-cognitive component of the task. In this study, all the evaluations were performed in healthy subjects after a normal sleep night and after a night of sleep deprivation, used to control for the effects of the absence of sleep. The explorative between group comparisons did not show any significant difference between SG and SD in the GB task and in all the empathy measures, apart from the notable exception of the BES.

Hence, the SD group obtained lower scores compared with the SG group, indicating lower empathy, in both the affective and cognitive sub-scales of the BES test. In order to address the main aim of our study, i.e. to examine the impact of sleep variables on empathy and aesthetic perception skills, we used a mediation analysis approach (within-group analysis). Specifically, six mediation models for the sleep group were performed. Only the "Sleep Duration" factor was used as mediator, because it was the only factor that correlated with the emphatic measures (cognitive and emotional) and with the components of the GB task. The results revealed three significant models. Two models showed that the relation between emotional empathy ability measured by two tests (EEC sub-scale of EQ and EC sub-scale of IRI as independent variables, IVs) and the proportion judgement for modified stimuli of the GB task (as dependent variables, DVs) is mediated by the "Sleep Duration" factor. In addition, one model showed that also the relation between cognitive empathy ability, measured by FS sub-scale of IRI and the proportion judgement for modified stimuli of the GB task (DV) is mediated by the "Sleep Duration"

factor. Therefore, the duration of sleep (Figure 2) subtends the relationship between the ability to emotionally "resonate" with other people's feelings (emotional empathy) and to understand the

mental states of others (cognitive empathy), and the generation of a correct judgement of body proportions. The mediation effect of sleep was more evident on emotional empathy measures. This

result is in line with previous studies showing that the individuals' duration and quality of sleep especially affect emotional empathy, rather than cognitive empathy[48,49].

In the SG, we obtained significant correlations and, consequently, significant models only with self-report measures of empathy and not with the more objective MET test. This result is not surprising considering that emphatic ability represents a stable disposition of personality. Indeed, an impairment of empathic abilities could characterize several psychiatric disorders, such as autism[51]. Therefore, an objective measurement of empathy is unlikely to be affected only by minor decreases of sleep duration in otherwise healthy subjects. Coherently, it has been recently shown that the ability to correctly perform

a task of categorization of the other's emotions is not associated with sleep duration, sleep quality and acute sleep deprivation[52]. Therefore, the significant correlations between sleep

duration and self-report measures of empathy suggest a specific sensitivity of these measures also to slight and temporary variations of sleep duration. The fact that sleep duration, but not sleep quality, correlated with the emphatic and aesthetic measures was unexpected. We can hypothesize that sleep duration may be a crucial common factor shared by both good and poor sleepers. In other words, on the one hand we can assume that an adequate sleep duration characterizes good sleepers; on the other hand, this variable would also be crucial for poor sleepers, by possibly helping them to compensate for their poor sleep quality. A longer sleep, although of low quality, could even be helpful in sustaining empathic and aesthetic abilities. The sleep deprivation condition was introduced here as a control for the effects of the lack of sleep on the relation between empathy and aesthetic perception. In the SD group, based on the lack of correlations among empathy, aesthetic perception and sleep variables, the mediation models were not performed. This suggests that if sleep is set to zero, it is no longer able to mediate the relations with empathy and aesthetic abilities. However, we cannot exclude that the lack of effects in the SD group could be due to the small sample size. Accordingly, further evidences are needed with larger samples of sleep-deprived individuals to strengthen the robustness of this finding. Against this interpretation, a correlation analysis (data not shown) in a subgroup of 25 subjects randomly selected from the sleep group revealed no differences in the general pattern of correlations between variables compared with those reported in the whole sample. This suggests that the relationship between sleep, empathy and aesthetic perception is robust, and that, in principle, the small sample size in the sleep-deprived group could have hardly affected the results obtained. Our data do not directly support the influence of sleep duration on aesthetic judgement, but only on its more perceptual-cognitive component. However, in consideration of the positive association observed between aesthetic and proportion judgements, as well as between aesthetic judgement and empathic abilities, we may regard
"objective" aesthetic perception and empathy as strictly related. This is strongly supported by neuroimaging evidence showing activation of the insula in response to aesthetic judgements, when this is mediated by visual physical properties of the stimuli (i.e. canonical proportions)[24], as well as by emotional empathic tasks[19]. Thus, we hypothesize that sleep, by influencing the empathy ability, could indirectly affect also the aesthetic experience. This could have a significant impact on social interactions and on the capacity to experience pleasure that is strongly linked with the ability to perceive beauty. The perception of beauty has a hedonic value. For instance, schizophrenic patients can show anhedonia, that is a decreased capacity to experience pleasure for things that generally induce pleasure (such us

love relationships, attractive individuals)[13]. This determines the incapacity to experience interpersonal and social pleasure (for more detailed discussion see Peretti et al.[15]).

Conclusions

We showed by mediation analysis that sleep duration sustains the relation between empathy and aesthetic perception elicited by objective parameters (i.e. proportion) of the observed stimuli, an ability

that is strictly involved in mediating our sense of beauty. Taken together, the results of this study suggest that adequate sleep (in terms of duration) may play a key role in improving the capability to infer other people's emotions (emotional empathy), to understand their mental state (cognitive empathy), and to give accurate aesthetic judgements.

b) STUDY 2: DISCREPANCIES BETWEEN EXPLICIT AND IMPLICIT EVALUATION OF AESTHETIC PERCEPTION ABILITY IN INDIVIDUALS WITH AUTISM: A POTENTIAL WAY TO IMPROVE SOCIAL FUNCTIONING.

Aim of the work

The aim of the present study was to evaluate the aesthetic perception ability in individuals with ASD compared to TD control subjects using the Golden Beauty behavioural task adapted for eye-tracking. Importantly, the relationship between empathic and aesthetic perception abilities was also evaluated. Furthermore, the eye-tracking technique was used to gather additional information about sensory-driven coding of the stimuli by assessing eye movement behaviour.

Method

Participants

The study included 20 participants: 10 subjects with ASD selected by the Reference Regional Centre for Autism of L'Aquila, Abruzzo Region (ASD group, mean age±SD:20.7±4.64), according to the principles established by the Declaration of Helsinki, ethical approval was obtained by the Ethical Committee of the NHS Local Health Unit (Azienda Sanitaria Locale 1), and 10 TD subjects (TD group, mean age±SD:20.17±0.98). The TD subjects were recruited from the University of L'Aquila.

The ASD group presented uneven distribution by gender (ASD 9 males and 1 female), thus we matched the TD group by gender (TD 9 males; 1 female). No differences between groups (ASD and TD) emerged for chronologic age ($t_{1.19}$= 0.27; p= 0.78). On the basis of chronological age, individuals with ASD, were tested with the Wechsler Adult Intelligence Scale (WAIS-IV)[53]. The ASD diagnosis was provided by experienced clinicians according to the new criteria of the DSM-5[54]. ASD diagnosis was confirmed using the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2)[55]. Socio-demographic and clinical information of the two groups of participants are summarized in Table 1.

Table 1. Between-groups differences for demographic data, clinical information and empathy measures.

	ASD (N=10) Mean (SD)	**TD** (N=10) Mean (SD)	t (df =1, 19)	*p*
Chronological age (in years)	20.70(4.64)	20.17(0.98)	0.27	0.78
Clinical information				
ADOS-social communication and social interaction	10.00 (4.25)	-	-	-
ADOS- Repetitive and Stereotyped Behaviours	1.20 (1.13)	-	-	-
ADOS Total scores	11.90 (3.81)	-	-	-
QIV	98.00(23.27)	103.40(19.72)	-0.549	0.590
QIP	95.00(13.50)	95.60(12.34)	-0.104	0.919
QIT	96.40(15.23)	97.40(13.03)	-0.158	0.876
Empathy measures				
Advanced Theory of Mind task	7.60(3.37)	12.67(0.51)	-3.60	**0.003**
Eyes-task	17.90(3.84)	28.50(3.01)	-5.75	**0.0001**
Basic Empathy Scale				
Affective Empathy sub-scale	33.30(6.76)	42.00(3.68)	-2.87	**0.012**
Cognitive Empathy sub-scale	28.40(5.40)	40.67(3.44)	-4.45	**0.0001**
Empathy Quotient				
Cognitive empathy sub-scale	8.30(1.88)	16.33(3.20)	-6.37	**0.0001**
Social skill sub-scale	4.00(0.81)	10.83(1.32)	-12.85	**0.0001**
Emotional empathy sub-scale	9.40(3.59)	16.66(3.26)	-4.04	**0.001**

Significant comparisons are highlighted in bold.

Procedure

Both ASD and TD groups performed the same test sessions. The participants were evaluated in two sessions. During the first session, the participants completed the empathy-related tests (Eyes Task, Basic Empathy Scale, Empathy Quotient, Advanced Theory of Mind task) using paper and pencil measures. This session lasted approximately 50 min. During the second session, the participants performed the aesthetic perception task called *Golden Beauty* (see below for more details) using Tobii-T120- Eye Tracker and E-Prime® Extensions for Tobii Pro™ for simultaneous behavioural data acquisition. The eye-tracking session lasted 20 minutes. All the subjects were mother tongue Italian and a normal or correct to normal vision. Moreover, all participants were untrained in the arts. The participants were tested individually in a quiet room according to the principles established by the Declaration of Helsinki. The investigation was approved by the Ethical Committee of the NHS Local Health Unit (Azienda Sanitaria Locale 1) that approved the experimental protocol prior to the recruitment of participants, according to the principles established by the Declaration of Helsinki. Informed consent in written form was obtained from all the participants before the study.

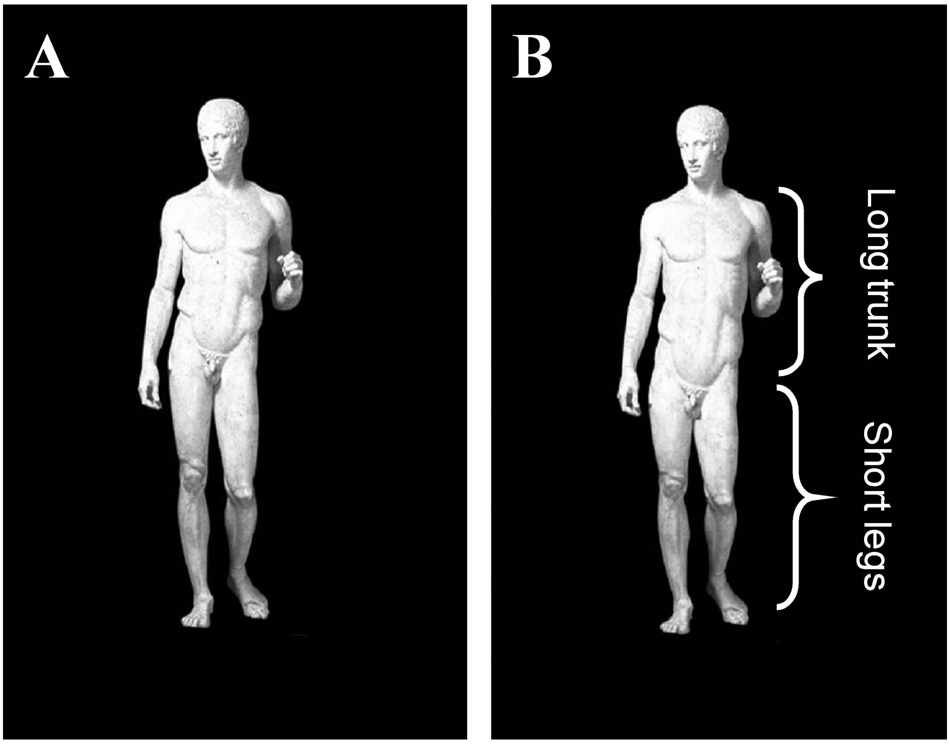
Empathy measures

The empathy capacities were assessed by the BES that is composed of two sub-scales: the Affective Empathy Sub-scale (AES) and the Cognitive Empathy Sub-scale (CES)[36,37]; the EQ that is composed of three sub-scales: cognitive empathy (CEQ) and social skills (SSQ), which measure the cognitive empathy and the emotional sub-scale (EEQ) for emotional dimension evaluation[39]; the A-ToM[56] and the Eyes-task[57]. For detailed description of this test see chapter 1 (section "Social cognition measures for adolescents and adults").

Golden Beauty task

To evaluate aesthetic perception, we used a modified version of the *Golden Beauty* (GB) task[24] The GB task consists in the evaluation of images of sculptures selected from masterpieces of Classical and Renaissance art that are commonly accepted as normative Western representations of beauty[24]. This task evaluates the sense of beauty through objective parameters (proportion) intrinsic to specific works of art and requires an objective and a subjective aesthetic judgment, as well as a proportion judgment for proportioned and modified stimuli. The main feature of this task is the use of two sets of stimuli that are identical in every respect but one: proportion. Specifically, a parameter that is considered to represent the ideal beauty specifically in the Classical representation of the human body[40,41] was modified to create an aesthetically degraded version of the same stimuli in a controlled fashion. The GB task contains 44 total images of sculptures including 22 images with modified proportions between body parts. In particular, half of the canonical stimuli were modified with a short-leg long-trunk relation, whereas the other half with the opposite modification type. All stimuli (canonical and modified sculptures) were presented in three experimental conditions: 1) Objective Aesthetic Judgment (OAJ) for Proportioned stimuli (OAJP) and Modified stimuli (OAJM); 2) Subjective Aesthetic Judgment (SAJ) for Proportioned stimuli (SAJP) and Modified stimuli (SAJM); 3) Proportion Judgment (PJ) for Proportioned stimuli (PJP) and Modified stimuli (PJM). In the first condition- OAJ, participants were asked to observe the sculptures and to express an explicit objective judgment ("objective" aesthetic value) for each image by answering to the question: "Is the image you see *beautiful*?". The participants responded on a dichotomous scale YES= it is beautiful, or NO= it is not beautiful. In the second condition- SAJ, participants were asked to observe the sculptures and to express an explicit subjective judgment ("subjective" aesthetic value) for each image by answering to the question: "Do you *like* the image that you see?". The participants responded on a dichotomous scale YES= I like it or NO= I don't like it. In the third condition - PJ, participants were asked to observe the sculptures and to express an explicit proportion judgment for each image by answering to the question: "Is the image that you see *proportioned*?". The participants responded on a dichotomous scale YES= It is proportional or NO= It is not proportional (an example of golden beauty task in reported below).

Example of Golden Beauty task.



A: represents a sculpture with canonical proportions between body parts

B: represents a sculpture with modified proportions between body parts

Eye-tracker stimuli and Settings

The experiment with GB task was performed using E-Prime® Extensions for Tobii Pro™ and Tobii T120- Eye Tracker equipment consisting of a GL-2760-LED backlight monitor with resolution of 1920 × 1080 pixels, on which the stimuli were presented and from which gaze behavior was recorded simultaneously. The eye-tracking system is non-invasive with little indication that eye movements are being tracked, and artificially constrain head movements are not required. The system tracks both eyes to a rated accuracy of 0.5 degrees with a sampling rate of 60 Hz. The Tobii equipment was connected to a Lenovo-laptop computer (Windows 7 Professional) that was used to run the tasks. The two blocks of GB task, i.e. objective and subjective aesthetic judgments (OAJ and SAJ, respectively) were administered in a random order, while the block of proportion judgment (PJ) was always presented at the end of the task for all participants to not influence the subjects' aesthetic evaluation with a prior exposure to the proportion assessment. All participants were seated facing the eye-tracker monitor at a distance of roughly 70 cm with the experimenter sitting next to the subject to control the pc screen without interfering with the observation of the images. Detailed instructions were provided just before the experimental session; the instructions were again presented on the screen at the beginning of each test block. The participants looked at a total of 132 stimuli (sculptures) divided in 44 stimuli (22 proportionate and 22 modified) for each block (OAJ, SAJ, PJ). The presentation of the stimulus lasted 4 seconds. The subjects were asked to look at the stimuli (sculptures) as they were presented on the screen, and then, a task-related question about the stimulus appeared, which was associated with one of the three blocks (OAJ- Is the image that you see *beautiful*?; SAJ- Do you *like* the image that you see?; PJ- Is the image that you see *proportioned*?). The duration of the question slide was 5 seconds. A calibration test consisting of 5 registration points was performed before GB task. The calibration was repeated if one of the 5 points was not valid. During the calibration phase, the participants were asked to visually follow a small red ball presented on the screen. Calibration procedures, stimulus creation, data acquisition and visualization were performed using the Tobii Studio™ Analysis Software. The behavioral data were acquired using E-Prime® Extensions for Tobii Pro™.

Eye-tracker data acquisition and model analysis

Data were collected using the Tobii Studio™. For each of the stimuli of GB task, Areas Of Interest (AOI) were drawn to investigate fixations to specific regions of the human body. A total of four AOI (face, arms, trunk and legs) were created to have fixations of all parts of body. Two gaze parameters were analyzed: *Time to first fixation*- the time from when the stimulus was shown until the start of the first fixation within an AOI, and *Total fixation duration*- the addition of all fixations durations recorded within an AOI. A fixation event was defined as such by the Tobii fixation filter (I-IV-filter) when the point of gaze remained within 0.5 degree of visual angle for at least 100 milliseconds. Data for each AOI were normalized with respect to the total area of the image.

Data analysis

All of the continuous variables were normally distributed with skewness between -1 and 1. The homogeneity of variance was checked for all parametric tests and eventual corrections are reported. For the factorial analyses, the Greenhouse-Geisser correction was used for violations of Mauchy's Test of Sphericity (p=.05). All multiple comparisons were Bonferroni adjusted (p=.05).

Results

Between-group comparisons on empathy measures

We used independent t-test analyses to compare ASD and TD groups on empathy scores. The results showed that the ASD group was impaired in all empathy measures (Eyes-task, BES, EQ, and A-ToM task) compared to the TD group. Specifically, regarding the Eyes- task, the ASD group obtained a lower score ($t_{1,19}$= -5.75; p= 0.0001) compared to the TD group; similarly, individuals whit autism showed difficulties in both AES ($t_{1,19}$= -2.87; p= 0.01) and CES ($t_{1,19}$= -4.95; p= 0.0001) sub-scales of BES compared to the TD group. Additionally, the ASD group received lower scores compared to the TD group in EEQ ($t_{1,19}$= -4.04; p= 0.001), CEQ ($t_{1,19}$= -6.37; p= 0.0001), and SSQ ($t_{1,19}$= -12.85; p= 0.0001) sub-scales of EQ. Finally, ASD individuals showed impaired performance in A-ToM task ($t_{1,19}$= -3.60; p= 0.003) compared to the TD group. The results of these analyses are reported in Table 1.

Correlation between empathy measures and conditions of Golden Beauty task

Pearson's correlations were computed to assess the relationships between the conditions of GB task (OAJP-OAJM, SAJP-SAJM, PJP-PJM) and the empathy measures (Eyes-task, BES, EQ and A-ToM task).

ASD group

No significant correlations were found between any of the empathy measures and the conditions in the GB task for the ASD group.

TD Group

For the TD group, significant correlations were found between OAJP, SAJP and PJM task of GB and Eyes-task, CEQ sub-scale of EQ, and both sub-scales (AES, CES) of BES. Specifically, a significant positive correlation was found between the OAJP condition of GB task and Eyes-task ($r = .711$; $p = .022$). The SAJP of GB task positively correlated with both the AES ($r = .251$; $p = .032$) and CES ($r = .707$; $p = .034$) sub-scales of BES. Finally, we found significant negative correlations between PJM of GB task and CES ($r =- .849$; $p = .033$) sub-scale of BES, the CEQ ($r = -.889$; $p = .020$) sub-scale of EQ, as well as the Eyes-task ($r =- .888$; $p = .018$).

Behavioral results on Golden Beauty task

Aesthetic judgments

To assess differences in the participants' attributions of aesthetic preference in the two aesthetic tasks (objective and subjective) for the canonical and modified stimuli, we carried out a repeated measures general linear model (GLM), with 2 levels of type of task (OAJ and SAJ) and 2 levels of stimulus type (canonical and modified) as the within-subject factors, and group (ASD and TD) as the between-subject factor. The results showed a main effect of stimulus type (Canonical>Modified; $F_{1,18}=21.07$, $p=.0001$, partial-$\eta^2=.53$, $\delta=.99$), as well as significant interactions between stimulus type and group ($F_{1,18}=10.09$, $p=.005$, partial-$\eta^2=.36$, $\delta=.85$). Additionally, the results showed a significant difference in performance between the two groups, which was independent of the other factors (TD>ASD; $F_{1,18}=30.71$, $p=.0001$, partial-$\eta^2=.63$, $\delta=.99$). A post-hoc analysis (Bonferroni corrected) showed that the interaction between stimulus type and group stemmed from the lack of significance between canonical and modified stimuli in the ASD group (Mdiff=.80, SE= .80, p=.33), whereas this difference was significant for the TD group (CANONICAL>MODIFIED; Mdiff=4.40, SE= .80, p=.0001; see Table 2).

Proportion judgment

To assess differences in the participants' evaluation of proportion in the two stimulus types (canonical and modified) between the ASD and TD groups, we carried out a repeated measures general linear model (GLM). The results showed a main effect of stimulus type (Canonical>Modified; $F_{1,18}$=83.35, p=.0001, partial-η^2=.82, δ=.1), as well as significant interactions between stimulus type and group ($F_{1,18}$=46.62, p=.0001, partial-η^2=.72, δ=1). Assessing the interaction effect, it revealed that there was no difference in proportion evaluation between canonical and modified stimuli in the ASD group (Mdiff=1.50, SE= .92, p=.12), whereas this difference was significant for the TD group (CANONICAL>MODIFIED Mdiff=10.40, SE= .92, p=.0001; see Table 2).

Table 2. Mean differences between canonical and modified stimuli in aesthetic and proportion judgments task for both groups (ASD and TD), separately.

Golden Beauty task	Group	(I)Canonical stimuli type Mean (SE)	(J)Modified stimuli type Mean (SE)	$Mean_{diff}$ (I-J) (SE)	*p*
Aesthetic Judgment task	ASD group	10.300 (.715)	9.500 (.431)	.800 (.801)	.331
	TD group	15.500 (.715)	11.100 (.431)	4.400 (.801)	**.0001**
Proportion judgment task	ASD group	14.500 (.962)	13.000 (1.301)	1.500 (.922)	.121
	TD group	19.300 (.962)	8.900 (1.301)	10.400 (.922)	**.0001**

Significant comparisons are highlighted in bold.

Summary of behavioural results

The behavioural findings associated with the empathic measures used in the study (Eyes-task, BES, EQ and A-ToM) showed that individuals with autism are impaired in all measures of empathy (and their subscales). Moreover, in the TD group, but not in the ASD group, we found that GB objective, subjective and proportion tasks correlated with three empathy measures, i.e. BES (AES and CES subscales), EQ (CEQ subscale), and Eyes-task. Specifically, in the TD group, cognitive empathic ability as measured by Eyes-task correlated with a good ability to give an objective judgment of beauty for the proportioned sculptures (OAJP). In addition, the capacity to evaluate their subjective pleasure for proportioned sculptures (SAJP) correlated with affective and cognitive empathic ability, measured through the AES and CES subscales of BES. Finally, the ability to evaluate as less proportioned the sculptures with modified proportion between body parts correlated with cognitive empathic ability (measured by Eyes-task, CES subscale of BES and CEQ subscale of EQ). This is in line with the idea that proportion evaluation can be regarded as the perceptual-cognitive component of the task[24]. On the whole, these results suggest that beauty perception appears to be linked with empathy when these capacities are not compromised. Additionally, our results indicated that people with ASD also showed impairment in aesthetic perception ability. In fact, the ASD group had lower ability to judge as objectively beautiful and subjectively pleasing (aesthetic judgments) both canonical and modified sculptures, compared to TD people. At the same time, in the ASD group there were no differences in the evaluation of proportion for the canonical and modified sculptures (proportion judgment). On the contrary, the TD group evaluated the canonical sculptures as more proportional, compared to modified stimuli. In addition, the TD group evaluated the sculptures with canonical proportions as more pleasant and beautiful (subjective and objective judgments, respectively) and more proportional (proportion judgment) compared to the sculptures with modified proportion.

Eye-tracking data

To assess differences in the participants' observation pattern during GB tasks (objective aesthetic task, subjective aesthetic task, and proportion evaluation task) for each eye-tracking parameter (*time to first fixation* and *total fixation duration*), repeated measures GLM analyses were carried out with four levels of AOI (body parts: face, arms, trunk and legs) and two levels of stimulus type (canonical and modified sculptures) as the within-subject factors, and group (ASD and TD) as the between-subject factor.

Eye-tracking results of Golden Beauty task

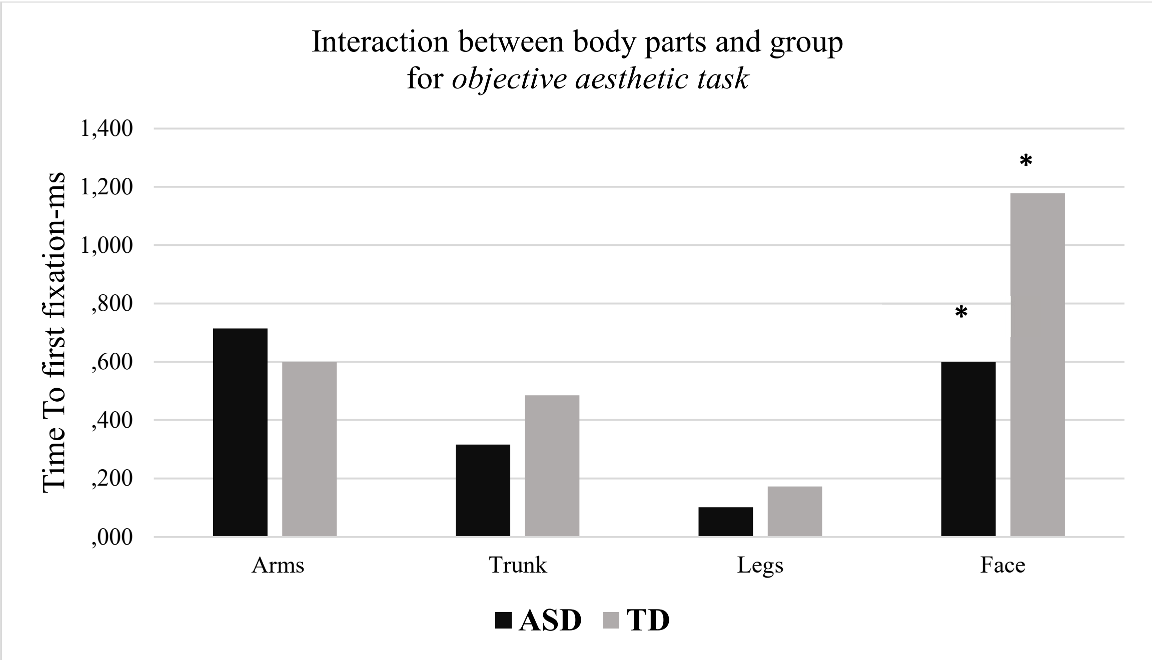
Objective Aesthetic task

With respect to time to first fixation, the results showed a main effect of body parts (LEGS>OTHER BODY PARTS; $F_{1,18}$=17.88, p=.0001, partial-η^2=.49, δ=.1), as well as significant interactions between body parts and group ($F_{1,18=}$3.63, p=.01, partial-η^2=.16, δ=76). Assessing the interaction effect, we found that the interaction between body parts and group was significant for the face area (p=.05; see table 3 and figure 1) in ASD group. With respect to total fixation duration, the results showed a main effect of body parts (FACE>OTHER BODY PARTS; $F_{1,18}$=22.54, p=.0001, partial-η^2=.55, δ=.1), as well as a significant interaction between body parts and group ($F_{1,18=}$3.96, p=.01, partial-η^2=.18, δ=80). The interaction stemmed from significantly longer total fixation duration on the face area in the TD group, but not in the ASD group, compared to the other body parts (p=.05; see table 3 and figure 2).

Table 3. Descriptive statistics and mean differences between groups (ASD and TD) of eye-tracking parameters (time to first fixation and total fixation duration in milliseconds) in objective aesthetic task for all body parts (arms, trunk, legs, face).

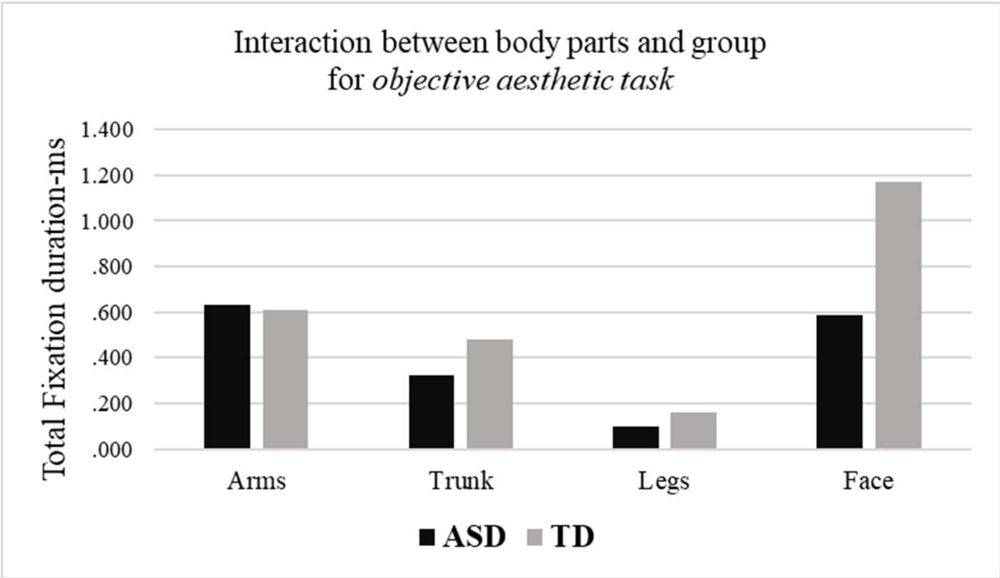
ET-parameters	**Task**	**Body Parts**	**(I)ASD group Mean (SE)**	**(J)TD group Mean (SE)**	**Mean$_{diff\ (J-)}$ (SE)**	***p***
Time to First Fixation	Objective Aesthetic task	Arms	.714 (.151)	.599 (.151)	.115 (.214)	.598
		Trunk	.316 (.90)	.485 (.090)	-.169 (.127)	.202
		Legs	.101 (.059)	.172 (.054)	-.071 (.076)	.359
		Face	.600 (.188)	1.178 (.188)	-.578 (.266)	**.044**
Total Fixation Duration	Objective Aesthetic task	Arms	.629 (.103)	.612 (.103)	.018 (.145)	.905
		Trunk	.326 (.088)	.478 (.088)	-.153 (.125)	.238
		Legs	.099 (.052)	.158 (.052)	-.058 (.073)	.437
		Face	.590 (.189)	1.173 (.189)	-.583 (.268)	**.043**

Significant comparisons are highlighted in bold



*= p<.05

Figure 1. Significant interaction between body parts (arms, trunk, legs, face) and group (ASD and TD) for *objective aesthetic task* in relation to the time to first fixation (in milliseconds).



*= *p*<.05

Figure 2. Significant interaction between body parts (arms, trunk, legs, face) and group (ASD and TD) for *objective aesthetic task* in relation to the total fixation duration (in milliseconds).

Subjective Aesthetic task

The results for time to first fixation (TFF) and total fixation duration (TFD) showed a main effect of body parts (LEGS>OTHER BODY PARTS; TFF: $F_{1,18}$=26.89, p=.0001, partial-η^2=.59, δ=1; ARMS>OTHER BODY PARTS TFD: $F_{1,18}$=27.79, p=.0001, partial-η^2=.60, δ=1), indicating that both groups looked first at the legs and longer at the arms compared to other body parts (p= .05; see table 4). No differences were found between groups with respect to time to first fixation and total fixation duration.

Table 4. Mean differences in eye-tracking parameters (time to first fixation and total fixation duration in milliseconds) between body parts (arms, trunk, legs, face) during the subjective aesthetic task, in both groups (ASD and TD).

ET-parameters	**Task**	**(I)Body parts**	**(J)Body parts**	**M_{diff} (I-J) (SE)**	***p***
Time to First Fixation	Subjective Aesthetic task	Arms	Trunk	.325 (.055)	**.0001**
			Legs	.574(.075)	**.0001**
			Face	.122 (.067)	.525
		Trunk	Arms	-.325 (.055)	**.0001**
			Legs	.250 (.040)	**.0001**
			Face	-.203 (.069)	.054
		Legs	Arms	-.574 (.075)	**.0001**
			Trunk	-.250 (.040)	**.0001**
			Face	-.453 (.093)	**.001**
		Face	Arms	-.122 (.067)	.525
			Trunk	.203 (.069)	.054
			Legs	.453 (.093)	**.001**
Total Fixation Duration	Subjective Aesthetic task	Arms	Trunk	.269 (.049)	**.0001**
			Legs	.525 (.0.62)	**.0001**
			Face	.066 (.075)	1.00
		Trunk	Arms	-.269 (.049)	**.0001**
			Legs	.256 (.042)	**.0001**
			Face	-.203 (.058)	**.015**
		Legs	Arms	-.525 (.062)	**.0001**
			Trunk	-.256 (.042)	**.0001**
			Face	-.459 (.085)	**.0001**
		Face	Arms	-.066 (.075)	1.00
			Trunk	.203 (.058)	**.015**
			Legs	.459 (.085)	**.0001**

Significant comparisons are highlighted in bold

Proportion evaluation task

The results for time to first fixation showed a main effect of body parts (LEGS>OTHER BODY PARTS; $F_{1,18}$=21.33, p=.0001, partial-η^2=.54, δ=1). Indeed, both groups look first at the legs compared to other body parts (p=05; see table 5). No differences were found between groups with respect to time to first fixation.

Regarding total fixation duration, the results showed a main effect of stimulus type (Canonical>Modified; $F_{1,18}$=7.94, p=.01, partial-η^2=.30, δ=.76), a main effect of body parts (FACE>OTHER BODY PARTS; $F_{1,18}$=25.27, p=.0001, partial-η^2=.58, δ=1), as well as a significant interaction between stimulus type and body parts ($F_{1,18}$=3.66, p=.01, partial-η^2=.16, δ=.77). Additionally, the results showed a significant difference in performance between the two groups (TD-mean=.434; SE=.057)>ASD-mean=.257; SE=.057) $F_{1,18}$=4.77, p=.04, partial-η^2=.21, δ=.54), suggesting that TD group generally fixated longer than the ASD group. A post-hoc analysis showed that the interaction between stimulus type and body parts stemmed from the lack of significance between canonical and modified stimuli in terms of total fixation duration on the arms (M_{diff}=.14, SE=.07, p=.07), trunk (M_{diff}=.01, SE=.04, p=.81) and legs (M_{diff}=.03, SE=.01, p=.11); whereas this difference was significant for the face area (M_{diff}=.20, SE=.07, p=.01) in both groups. That is, participants generally fixated longer the face area of canonical with respect to the modified stimuli (p=.05; see table 6 and figure 3).

Table 5. Mean differences in time to first fixation (in milliseconds) between body parts (arms, trunk, legs, face) during the subjective aesthetic task, in both groups (ASD and TD).

ET-parameters	**Task**	**(I)Body parts**	**(J)Body parts**	**M_{diff} (I-J) (SE)**	***p***
Time to First Fixation	Proportion evaluation task	Arms	Trunk	.343 (.072)	**.001**
			Legs	.567 (.069)	**.0001**
			Face	-.077 (.126)	1.00
		Trunk	Arms	-.343 (.072)	**.001**
			Legs	.224 (.036)	**.0001**
			Face	-.420 (.094)	**.002**
		Legs	Arms	-.567 (.069)	**.0001**
			Trunk	-.224 (.036)	**.0001**
			Face	-.644 (.122)	**.0001**
		Face	Arms	.077 (.126)	1.00
			Trunk	.420 (.094)	**.002**
			Legs	.644 (.122)	**.0001**

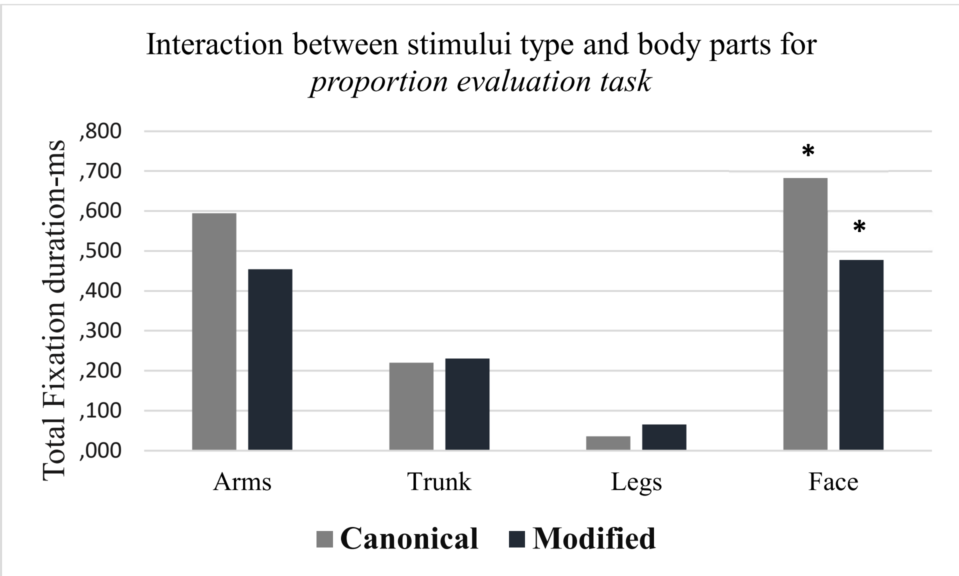
Significant comparisons are highlighted in bold

Table 6. Descriptive statistics and mean differences in total fixation duration (milliseconds) between stimuli type (canonical and modified) for all body parts (arms, trunk, legs, face), during the proportion evaluation task in both groups (ASD and TD).

Significant comparisons are highlighted in bold.

ET-parameters	**Task**	**Body Parts**	**(I)Canonical stimuli type Mean (SE)**	**(J)Modified stimuli type group Mean (SE)**	**Mean$_{diff}$ (I-J) (SE)**	***p***
Total Fixation Duration	Proportion evaluation task	Arms	.594 (.078)	.454 (.052)	.140 (.075)	.078
		Trunk	.220 (.053)	.230 (.037)	-.010 (.042)	.811
		Legs	.036 (.015)	.066 (.018)	-.030 (.018)	.116
		Face	.683 (.117)	.477 (.088)	.206 (.078)	**.016**

Figure 3. Significant interaction between body parts (arms, trunk, legs, face) and stimuli type (canonical and modified) for *proportion evaluation task* in relation to the total fixation duration (in milliseconds)



*= p<.05

Summary of the eye-tracking results

The eye-tracking results showed no differences between groups in the observation pattern for the subjective aesthetic judgment task. On the other hand, in the objective aesthetic judgment task, the TD group, but not the ASD group, fixated significantly longer the face, compared to the other body parts, of both canonical and modified sculptures. Additionally, we found that the ASD group produced lower score (total fixation duration) for the face of all sculptures, compared to the TD group. According to research in this field[25,58,59] during their visual exploratory behavior, observers concentrate their gaze on specific areas of an image. The parts of an image with longer fixation durations were interpreted as indicating the observer's interest in informative elements of the image[25,60]. Additionally, it is known that eye movements are the expression of the relation between what is looked at and its importance to the observer's interest[61]. Longer fixation time for the TD individuals indicates that faces were of much interest to them compared to the ADS group. Faces are complex visual stimuli that have a special role in social perception and SC because they convey important information for effective interpersonal interactions and non-verbal communication[62]. It is well known that face perception is atypical in people with ASD[62,63,64]. This also supported by longer total fixation duration found for the TD group. As shown in Massaro et al.[25] and Savazzi et al.[65] when a human subject is depicted in an image, regardless of other contextual cues possibly present in the representation, the viewer's attention is automatically driven towards exploration of the face area. The pre-rational visual search within the image towards this element, the face, determines longer time to first fixation to the face compared to representations in which this element is lacking and for which any point of the image can be a potential area of attraction. Faces represent a rather complex feature for ASD individuals to process and, taken together, our results suggest that the ASD group produced lower scores in all gaze parameters associated with faces because of their atypical processing of faces.

However, in the proportion evaluation task both groups (ASD and TD) produced longer total fixation durations on face of canonical sculptures, compared to both the modified stimuli and the other body parts. This was plausibly due to the fact that, when proportion was preserved, the face area represented the most interesting area of scrutiny. Opposite, when proportion was altered, as in the modified sculptures, attention was oriented towards the parts of the body that underwent modification, and namely legs and trunk. Comparable exploration patterns found for the objective aesthetic and proportion evaluation tasks support the idea that the objective appreciation of artworks travels alongside the perceptual recognition of the physical properties of the stimuli (i.e., proportion)[24,28].

In sum, our results support the idea that, when people with autism give a judgment of objective beauty or subjective pleasantness, they do not rely on the face to evaluate beauty, as it appears to be for TD individuals. On the contrary, when ASD individuals evaluate the proportions (more perceptual-cognitive condition), they explore the whole body and also the face if the sculpture has canonical proportions between body parts, although, at the level of behavioral performance, the ASD group was less skilled at assessing proportions compared to TD group (see behavioral results above).

Finally, a significant difference between groups was found in proportion evaluation task with TD group producing greater scores on both gaze parameters (time to first fixation and total fixation duration), compared to ASD group. This result suggests that ASD individuals' attention to the stimuli was lower during proportion evaluation task compared to TD group, possibly affecting ASD disproportion identification as shown by the behavioral results (PJP task).

Discussion

This study shows, for the first time, that individuals with ASD are impaired in their aesthetic perception ability. We used the Golden Beauty task, which aims at evaluating the sense of beauty through use of objective parameters intrinsic to Classical works of art, i.e. proportion, and that requires objective and subjective aesthetic judgments of proportioned and proportion-modified stimuli, as well as a proportion evaluation of the same stimuli[24]. Our behavioural results on different measures of empathy (Eyes-task, BES, EQ, A-ToM) confirmed the findings of previous studies[14,18,66] and showed that people with ASD have difficulties in both cognitive and affective empathy, compared to the TD group. As known, these deficiencies affect ASD individuals' ability to understand and share others' emotions and mental states, resulting in the inability to engage in adequate social behaviour with other people[14,15]. With respect to the GB task, our behavioural result showed that individuals with autism have a lower capacity to evaluate objectively-defined beauty (at least in the Western culture), compared to the TD group. We have previously suggested that "beauty" can be defined as an important social factor creating positive or negative expectations about others' relations promoting or avoiding interactions with other people[7,14,66.] Therefore, impairment in aesthetic perception ability, as well as in empathic abilities, observed in individuals with autism could negatively strengthen their inability to be socially adequate. Moreover, our results regarding the subjective aesthetic judgment condition (subjective pleasantness) showed that the ASD group always had lower subjective pleasure evaluations compared to the evaluation of objective beauty and proportion of sculptures with both canonical and modified proportion, also compared to TD group. Beauty has a hedonic value, and, for this reason, it is strongly linked to the capacity to experience pleasure[67]. The opposite of hedonic, i.e. anhedonia, is a symptom of some psychiatric conditions (such as schizophrenia). Anhedonia consists of a decreased capacity to experience pleasure for those things that usually induce pleasure (such as attractive individuals or pleasant relationships). This affects negatively the ability to experience interpersonal and social pleasure[13]. Based on that, our results may suggest that ASD individuals' functional impairment in specific processing abilities, as outlined above, may affect their capacity to perceive aesthetics, which may ultimately compromise their ability to experience subjective pleasure with consequent impact on social interactions.

Additionally, in this study, we gathered information about sensory-driven coding of the stimuli exploring eye movement behaviour during the Golden Beauty task. The eye-tracking results showed that individuals with autism obtained lower scores (lower total fixation duration) for face area of both modified and canonical sculptures in the *objective aesthetic judgment task*, compared to TD group. The ASD group showed that faces were not a salient visual aspect of the artwork during objective aesthetic judgment task, as opposed to the TD group that, on the other hand, paid great attention to the face area when judging the objective aesthetic of the stimuli. It is known that beauty perception is linked to the ability to appreciate or neglect faces based on their level of attractiveness, as suggested by studies showing that beauty perception shares the same neural network deputed to face processing[3,67], which involve areas such as the fusiform gyrus[68-71]. Notably, individuals with autism have difficulties processing faces. According to Pavlova et al.[62], for example, atypical face processing in individuals with autism could be due to their difficulties in visual integration, i.e. global perceptual ability. Additionally, poor attendance to faces in the ASD group may also possibly depend on the fact that faces are stimuli carrying information about emotions, non-verbal communication and personality[62]. On the contrary, no differences between groups in terms of observation pattern for the *subjective aesthetic judgment task* were found. The latter point is worth noting also in consideration of the eye-tracking results associated with the *proportion evaluation task* in the present study. Indeed, with respect to the *proportion evaluation task*, we found in both groups longer total fixation duration on face of canonical sculptures compared to other body parts and modified stimuli. Crucially, no differences were found between groups in the exploration pattern of the face region. Proportion evaluation is the perceptual-cognitive component of GB task, whereas both aesthetic judgment tasks involve an emotional component. The fact that ASD individuals did attend to the face area when judging proportion, and namely, when there was no emotional involvement, suggests that avoidance to look the face region is strongly related to ASD individuals' impairment in processing emotions[14,62]. This difficulty in ASD has relevance, not only for beauty processing as our data suggest, but also for empathic abilities, both fundamental components during social interaction. This idea is further supported by the correlations between both cognitive and affective empathy measures and all conditions of the Golden Beauty task. Our results, in fact, showed significant correlations in the TD group, but not in the ASD one, in agreement with previous research investigating empathic and aesthetic abilities, and showing that empathic and aesthetic perception abilities influence each other[4,15]. At the same time, we highlight that the ASD and TD individuals showed the same pattern of observation during the *subjective aesthetic judgment task* that involve an emotional evaluation. This result is fundamental because suggest that at implicit level (eye-tracking results), ASD individuals conserved a good ability to feel aesthetic pleasure during the Golden Beauty task thus, indicating the presence of a discrepancy between the explicit (behavioural results) and implicit evaluation (eye-tracking results) of the beauty.

Conclusion

Our findings showed that beauty perception appears to be linked to empathy when both these capacities are not compromised, as demonstrated in the TD group. On the contrary, this link results to be missed in ASD individuals. Moreover, at explicit level, our behavioural results suggest that individuals with autism are impaired in the ability to evaluate beauty, at least when beauty is associated with objective parameters intrinsic to works of art (proportion in the case of Classical representations). Their incapacity to process aesthetic features may have relevance in influencing the capacity to experience and recognize interpersonal and social pleasure, with a significant negative impact on their already compromised social interaction capacities.

However, at implicit level (eye-tracking results both *subjective and proportion conditions*), ASD individuals conserved a good ability to evaluate and feel aesthetic pleasure during the Golden Beauty task. Thus, indicating the presence of a discrepancy between the explicit and implicit evaluation of the beauty task.

Overall, our results clearly showed that individuals with autism are not completely blind to the aesthetic pleasure. In fact, they conserved an implicit ability to experience the beauty. Importantly, these findings could pave the way for developing new protocols to rehabilitate ASD social functioning, exploiting their conserved implicit aesthetic perception. Specifically, this new concept could be useful in the design of individualized intervention goals on beauty and empathy abilities, in order to improve the quality of life and social behaviour of ASD young adults.

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Chapter 4

GENERAL CONCLUSIONS

General conclusions

Autism spectrum disorder are atypical neurodevelopmental disorders characterized by a range of deficits in two domains: social communication and social interaction, and repetitive patterns of behaviour[1].

ASD individuals are characterized by an impairment of SC abilities and its main components such as ToM and empathy[2,3,4,5]. SC is a crucial cognitive construct that lead to positive social behaviours and successful social interactions. Indeed, on the one hand a good functioning of social cognition abilities represents an evolutionary advantage and on the other it allows stable and positive social and interpersonal relationships[6]. Moreover, ToM and empathy enable individuals to understand other's mental and emotional states and to share these states[7]; without empathy and ToM, the individuals would not be able to explore the social world. Thus, these skills are fundamental because they allow individuals to live in society and to be comfortable with others.

To date, it is believed that individuals with autism showed “mind-blindness”[8]. Therefore, they would be totally incapable of having social cognition, determining their typical social isolation.

However, based on our clinical experience, we hypothesized that in the ASD individuals some SC skills are preserved.

Indeed, **(1)** the first aim of this PhD project was to evaluate the *development* of SC and its role in social behaviour, implementing research lines that involve the use of different analysis models. In this regard, as descripted in chapter 2, we demonstrated, firstly, that children with ASD have a delay in the development of SC skills, rather than a total lack of these competences, compared to children with TD. To this aim we used the development trajectories analysis on three SC tests (Comic Strip tasks-CST, Eyes-tasks-ET, Social Information Processing Interview-SIPI) specific for children of a range between the ages of 5-13 years. Our finding showed that this delay of SC competencies increases with increasing of the complexity of SC task. Specifically, the delay of basic components of SC, such as intention component of ToM, does not allow ASD children to develop complex abilities such as the recognition of beliefs and emotions of other people. Subsequently, we demonstrated, through the mediation analysis, that in children with TD the competences of SC (measured by CST and SIP-I) mediate the correct development of social behaviours appropriate to the context. On the contrary, the deficit of SC competencies in children with autism impairs their social interactions. Therefore, we suggest that early habilitation programs of these abilities could improve social competences, attenuate the social deficit in children with autism and reduce their social isolation. In this regard, we support the idea that the early diagnosis represents a fundamental step. Thus, we applied the FPA methodology to ADOS-2 in order to highlight strengths but also weaknesses of this diagnostic tool. The results revealed the need for a revision of the clinical tool through the implementation of an adaptive testing system, realized by FPA, which allows a more accurate evaluation and shorter execution times. A possible future perspective is to develop a software product that can assist clinicians in the path of diagnosis for ASD.

Overall, our results showed that the ASD individuals are not "mind-blindness" but rather they showed a delay in the development of SC abilities, compared to TD individuals. This delay increases with increasing of the complexity of SC task. In ASD individuals, the delay of develop of SC ability affects the correct develop of social behaviour. In this regard, an early and accurate diagnosis represents a pivotal tool for early habilitation intervention on social skills.

Based on these observations (reported in chapter 2), we have opened our activity to new line of neuro-scientific research, closely related to SC abilities, namely *neuroaesthetic*. Indeed, **(2)** the second objective of this PhD project (described in chapter 3) was to evaluate the aesthetic perception ability in both TD and ASD individuals in order to find a new potential way to improve the ASD social functioning. In recent years, the neurosciences have expanded their own field of inquiry to aesthetic perception, mainly because it is closely linked to empathy; indeed, according to Gallese[9] we can introduce the term "*aesthetic emotion*" because of the close relationship that it has with empathy. Freedberg and Gallese[10] evaluated the empathic and the aesthetic perception abilities. The authors believed that the vision is a multimodal process based on the activation of specific brain circuits including the sensor-motors, visceromotor and affective circuits. Their results showed that the observation of art works leads an empathic involvement of the observer, activating, through simulation mode, the motor program that corresponds to the gesture evoked by art works.

At the same time, Dio and coworkers[11] showed that the observation of classical sculptures, compared to the same sculptures with modified proportions, produced the joint activation of some lateral and medial cortical areas responding to the physical properties of the stimuli and, importantly, of the anterior insula. The aesthetic experience evoked by canonical art could emerge from the processing of sensorimotor input in conjunction with the emotional feeling of pleasure[12], that is crucially mediated by the activation of the insula[13].

Therefore, the aesthetic experience shall be understood as a complete cognitive and emotional experience that has important implications on human experience and behaviour[14]. Specifically, the ability to perceive beauty plays a key role for all living beings, driving important evolutionary behaviour of the species such as the partner selection and the reproductive capacity[15]. In higher mammals such as humans, this ability is also fundamental for guiding social interaction[16].

On these premises, as descripted in chapter 3, we firstly focused on the evaluation of the role of the sleep in mediating the aesthetic perception ability and empathy and their relationship in TD individuals. This because we know that the sleep has a critical role in emotional brain functioning. To achieve our objective, we measured the empathy by a comprehensive battery of tests (BES, EQ, MET, IRI), and the aesthetic perception ability by the Golden Beauty task. The Golden Beauty task aims at evaluating the sense of beauty through objective parameters intrinsic to works of art (proportion), and requires objective and subjective aesthetic judgement, as well as a proportion judgement for proportionate and modified stimuli[11]. Our results showed that sleep duration sustains the relation between empathy and aesthetic perception elicited by objective parameters (i.e. proportion) of the observed stimuli, an ability that is strictly involved in mediating our sense of beauty. Moreover, the results showed that the aesthetic perception ability is related to the empathic competences.

Subsequently, we used the same task in a group of adolescents with autism compared to adolescents with TD. Specifically, we used the Golden Beauty behavioural task adapted for eye-tracking in order to have both explicit and implicit evidences, respectively. In both groups the relationship between empathic and aesthetic perception abilities was also evaluated. At explicit level, our behavioural results showed an impairment in aesthetic perception ability in ASD individuals. This inability could have relevance in influencing their capability to experience pleasure during social interactions. However, at implicit level (eye-tracking results), ASD individuals conserved a good ability to feel and evaluate the aesthetic pleasure during the Golden Beauty task (both subjective and proportion conditions). Thus, indicating the presence of a discrepancy between the explicit and implicit evaluation of the beauty task. Finally, beauty perception appears to be linked to empathy when both these capacities are not compromised, as demonstrated in the TD group. On the contrary, this link results to be missed in ASD individuals.

Taken together our results clearly showed that individuals with autism are not completely "blind" to the aesthetic pleasure. In fact, they conserved an implicit ability to experience the beauty. Importantly, these findings could pave the way for developing new protocols to rehabilitate ASD social functioning, exploiting their conserved implicit aesthetic perception.

In conclusion, the work done during my PhD allowed us to better understand the typical profile of ASD individuals. We demonstrated (in chapter 2) on the one hand that individuals with autism not showed "mind-blindness" (total lack of social cognition abilities) and on the other hand (in chapter 3) that they have a preserved implicit ability to try pleasure from aesthetic experience (aesthetic perception ability).

Overall, these findings have important implications for rehabilitation intervention. Firstly, it is necessary implement early habilitation programs of social cognition abilities, this could improve social competences, reducing the development gap of more complex social skills. Secondly, it is necessary consider new pathways, for instance based on their preserved ability to aesthetic perception, to improve social functioning. Specifically, these new concepts could be useful in the design of individualized intervention goals on beauty and SC abilities, in order to improve the quality of life and social life of ASD individuals.

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