Fachbereich Erziehungswissenschaft und Psychologie

der Freien Universität Berlin

Social information processing in naturalistic settings:

Insights from Autism Spectrum Disorders

Dissertation

zur Erlangung des akademischen Grades

Doktorin der Philosophie (Dr. Phil.)

Doctor of Philosophy (Ph.D.)

vorgelegt von

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Dipl.-Psych.

Berlin

Vorblatt

Tag der Disputation: 15.01.2014

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Eidesstattliche Erklärung

Hiermit erkläre ich an Eides statt,

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- dass ich die zugrunde liegende Promotionsordnung vom 02.12.2008 kenne.

Berlin, den 21.10.2013 Gabriela Rosenblau

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Acknowledgements

First of all, I would like to thank my supervisor Hauke Heekeren for providing me with the opportunity to conduct my doctoral research in a highly stimulating and supportive environment, for his excellent advice and support with scientific questions in general.

I wish to express my profound gratitude to my second supervisor Isabel Dziobek for her steady scientific and nonscientific support and guidance and for teaching me how to write scientific papers.

I am grateful to all members of my dissertation committee for helping me finalize my doctoral studies.

I would also like to express my appreciation to my collaborators, colleagues, and the staff at the Cluster “Languages of Emotion” at Freie Universität Berlin. In particular, I would like to thank Henrik Walter for his valuable research advice and his help with specific research questions. I am grateful to my co-author and colleague Dorit Kliemann for her support with conducting the research of this dissertation and for her scientific and nonscientific advice. Special thanks to Claudia Preuschhof, Hannah Bruehl, Yulia Oganian, Nikos Green and Julia Rodriguez Buritica. In particular, I would like to thank Christoph Korn for the wonderful time I had while sharing an office with him. His advice and passion for science have been a great source of support and motivation for me.

Additionally, I am indebted to the student research assistants and interns that were indispensable for the stimulus production and data collection in the broader framework of the SCOTT project as well as in the empirical studies of this dissertation. I would like to especially thank Benjamin Lemme and Alexander Hatri for their help with data analysis.

I am grateful to my family and friends, in particular, to my parents, my sister, Elena and Alexa for their loving support and understanding. Finally, I would like to thank Pablo for his ceaseless support, understanding, and patience with me.

1. Summary

Real life social settings provide us with a multitude of dynamic social information (e.g. facial expressions, tone of voice, body language). Our ability to process and integrate this information to a whole is crucial for understanding others' mental states (i.e. mentalizing) and subsequently formulating an adequate social response. Individuals with Autism Spectrum Disorders (ASD) are characterized by severe social impairments, which have been linked to aberrant neural and behavioral processing of social stimuli. However, given that typical laboratory settings differ greatly from real life social interactions, it remains unclear how the experimental results obtained with mostly abstract and static stimuli can be generalized to dynamic social information processing in naturalistic settings.

Study 1 introduced two naturalistic video-based behavioral tasks for a performance based assessment of implicit (i.e. spontaneous) and explicit (i.e. controlled, more cognitively demanding) mental state inferences. The aim of this study was to characterize implicit and explicit social cognitive processes – how they are to be differentiated in typically developed individuals and individuals with ASD. Study 2 investigated the neural mechanisms of spontaneous, naturalistic mentalizing in individuals with ASD and typically developed controls. Furthermore, the study aimed at relating neural processing of mental states in naturalistic settings to accurate implicit mental state inferences as measured with the behavioral task introduced in study 1. Study 3 aimed at extending insights on dynamic social information processing to the auditory modality. Here, neural processing of emotional prosody (i.e. tone of voice) and behavioral prosody recognition performance were investigated with newly developed naturalistic tasks in individuals with ASD and typically developed controls. Similar to study 2, in a next step, the relationship between neural and behavioral prosody processing was investigated.

In typically developed individuals, implicit and explicit social cognitive processes were distinguishable to a certain degree on the behavioral and neural level. Neural activity in the amygdala correlated with accurate implicit social behavior, and activity in a network including fronto-temporal regions such as the inferior frontal gyrus (IFG) predicted explicit social behavior. Individuals with ASD performed lower on tasks addressing implicit and explicit social cognitive processes, whereby these different sets of processes were closely linked. On the neural level, the social impairments of individuals with ASD were associated with reduced activity of the amygdala and the superior temporal sulcus (STS) and a reduced relationship between neural processing of social information and accurate social behavior compared to controls.

On the basis of the current literature and the three empirical studies of this dissertation, I propose a neurocognitive model of typical and impaired social information processing in naturalistic settings. The proposed model aims at advancing the current literature by integrating behavioral and neuroscientific research on dynamic social information processing in typically developed individuals and individuals characterized by severe social impairments.

Keywords: naturalistic social cognition, mentalizing, emotional prosody recognition, Autism Spectrum Disorders (ASD), dynamic social stimuli, amygdala, superior temporal sulcus (STS)

2. Zusammenfassung

Alltagssituationen beinhalten eine Vielzahl dynamischer, sozialer Informationen (z.B., Gesichtsausdrücke, Stimmklang (Prosodie), Körpersprache). Die Fähigkeit diese Informationen zu verarbeiten und zu einem Ganzen zu integrieren, ist eine wichtige Voraussetzung für die Erkennung mentaler Zustände beim Gegenüber und ermöglicht somit dass wir in sozialen Situationen angemessen reagieren. Menschen mit Autismus-Spektrum-Störungen (ASD) haben schwerwiegende soziale Beeinträchtigungen, die mit einer gestörten Verarbeitung sozialer Reize auf der Verhaltens- und der Hirnebene im Zusammenhang gebracht wurden. Da die Operationalisierung sozialer Kognition in experimentellen Untersuchungen stark von sozialer Kognition im Alltag abweicht, bleibt es unklar ob und in wie fern Ergebnisse experimenteller Studien, mit abstraktem und statischem Stimulusmaterial, auf dynamische soziale Informationsverarbeitung im Alltag generalisierbar sind.

In Studie 1 wurden zwei naturalistische video-basierte Verhaltensmaße entwickelt, um implizite (spontane) und explizite (kognitiv anspruchsvolle) mentale Attribution objektiv und direkt messbar zu machen. Ziel der Studie war es herauszufinden, ob und wie weit sich implizite und explizite soziale Kognition unterscheiden lassen in typisch entwickelten Personen und Menschen mit ASD. In Studie 2 wurden die neuronalen Mechanismen spontaner mentaler Attribution mit einer naturalistischen video-basierten Aufgabe untersucht. Des Weiteren wurde der Zusammenhang zwischen den neuronalen Mechanismen spontaner mentaler Attribution und der Performanz impliziter mentaler Attribution untersucht. Die Untersuchung der Performanz sozial kognitiver Prozesse erfolgte mit Hilfe der impliziten Verhaltensaufgabe, die in Studie 1 eingeführt wurde. In Studie 3 sollten Erkenntnisse bezüglich der sozialen Informationsverarbeitung im Hinblick auf auditorische Verarbeitung sozialer Reize generalisiert werden. Entsprechend wurde die Verarbeitung emotionaler Prosodie auf der Verhaltens- und Hirnebene mit neu entwickelten naturalistischen Aufgaben bei neurotypischen Personen und Personen mit ASD untersucht. Des Weiteren wurde auch hier der

Zusammenhang zwischen neuronaler Verarbeitung von Prosodie und Performanz untersucht.

Bei typisch entwickelten Personen konnten implizite und explizite sozial-kognitive Prozesse voneinander unterschieden werden, sowohl auf der Verhaltens- als auch auf neuronaler Ebene. Neuronale Aktivität in der Amygdala korrelierte mit impliziter sozialer Kognition auf der Verhaltensebene. Des Weiteren sagte die Aktivität eines fronto-temporalen Netzwerks, welches den inferioren frontalen Gyrus (IFG) umfasste, akkurates explizites Verhalten voraus. Menschen mit ASD wiesen niedrigere Performanzwerte in impliziter und expliziter sozialer Kognition auf und implizite und explizite sozial kognitive Performanz waren miteinander signifikant korreliert. Auf der neuronalen Ebene waren die sozialen Beeinträchtigungen von Menschen mit ASD mit verringerter Aktivität im superioren temporalen Sulcus (STS) korreliert und gingen außerdem mit einem geringerem Zusammenhang zwischen neuronaler Aktivität und sozial kognitiver Performanz einher im Vergleich zu typisch entwickelten Personen.

Auf der Grundlage der aktuellen Forschungslage und der Befunde dieser Dissertation, stelle ich ein neurokognitives Modell typischer und beeinträchtigter sozialer Informationsverarbeitung dynamisch naturalistischer Information auf. Das vorgeschlagene Modell soll die aktuelle Forschungslage erweitern, indem es Verhaltens- und neuronale Befunde zur sozialen Informationsverarbeitung dynamischer Reize bei typisch entwickelten Personen und Personen mit schwerer sozialer Beeinträchtigung integriert.

3. List of Abbreviations

ADOS	Autism Diagnostic Observation Scale
ADI-R	Autism Diagnostic Interview - Revised
AS	Asperger Syndrome
ASD	Autism Spectrum Disorders
ASDI	Asperger Syndrome Diagnostic Interview
BOLD	Blood Oxygen Level Dependent
DCM	Dynamic Causal Modeling
DSM	Diagnostic and Statistical Manual of Mental Disorders
fMRI	Functional Magnetic Resonance Imaging
GLM	general linear model
HFA	High-Functioning Autism
ICD-10	International Classification of Diseases and Related Health Problems -10
IFG	inferior frontal gyrus
IQ	Intelligence Quotient
MASC	Movie of the Assessment of Social Cognition
MPFC	Medial Prefrontal Cortex
MWT	Mehrfach-Wortschatz Test
OFC	orbital frontal cortex
PC	precuneus

PDD	Pervasive Developmental Disorders
PDD-NOS	Pervasive Developmental Disorder Not Otherwise Specified
PHY	Physiological factor in a Psychophysiological Interaction analysis which contains the time-course of the seed region
PPI	Psychophysiological Interaction analysis
PSY	Psychological factor in a Psychophysiological Interaction, which represents the task versus control task related BOLD responses
RMET	Reading the Mind in The Eyes Test
STS	superior temporal sulcus
ToM	Theory of Mind
TP	temporal poles
TPJ	temporal parietal junction

4. Introduction

Social information processing in real life depends upon social skills with which we extract meaning from subtle cues such as facial expressions, the tone of voice, or body language (Zaki and Ochsner, 2009). Subsequently these pieces of information need to be integrated to a whole. The extraction and integration of multimodal information to formulate an adequate social response rely on the interplay between three levels of information processing: social brain networks, social cognition and social behavior (Kennedy and Adolphs, 2012). Individuals with pervasive developmental disorders such as ASD are characterized by severe social impairments, which have been associated with deficits on all three levels of social information processing (Baron-Cohen, 2001; Frith, 2001; Volkmar et al., 2004; Pelphrey et al., 2011). How these processing levels interact with each other and how this interplay contributes to social functioning in real life remains an open question—both for typically and atypically developed individuals. The main aim of the empirical research summarized in this thesis was to address these particular questions. To begin, I will contrast typical with impaired social functioning of individuals with ASD.

4.1. Typical and impaired social functioning

Social functioning describes the long-term ability of an individual to interact with others (Kennedy and Adolphs, 2012). Successful social interactions in real life depend on decoding and integrating multimodal dynamic information comprising visual, semantic, prosodic and contextual cues (Zaki and Ochsner, 2009). In theory, processing real life social information (various multimodal pieces of information that are related to each other) should impose high cognitive demands on our working memory capacity (Frith, 1989). Remarkably, typically developed adults generally process social information online and relatively effortlessly (Frith and Frith, 2008). Humans have an innate preference for social information and develop the necessary skills to decode and integrate social cues at very early developmental stages (Baillargeon et al., 2010; Kovacs et al., 2010). Newborns preferentially orient their attention to social signals such as facial expressions (Johnson et al., 1991; Valenza et al., 1996) and by the age of three months, infants recognize the mother's face and tone of voice (i.e. prosody) (Kurzweil, 1988). During development, children further perfect their social skills as their social networks grow. Friendships and social feedback, in particular from peers, become more and more important with age. In late adolescence and adulthood the quality and quantity of friendships are important predictors of social functioning and mental health (Gleason et al., 2009).

Individuals with ASD are a prominent example for impaired social functioning. As infants, they attend less to social cues, such as faces and voices, than typical babies (Chawarska et al., 2010; Chawarska et al., 2012, 2013). Later on, they show severe impairments in emotion recognition and mental state inferences. Impairments in the development of social skills are undoubtedly linked to a lack of friendships and social networks in childhood and adulthood (Symes and Humphrey, 2010). In particular, high functioning ASD individuals with normal to elevated intelligence levels and good language skills often report having had negative social experiences with their peers, such as social exclusion and bullying, in the school context (Humphrey and Symes, 2010). Social difficulties persist in adulthood, which makes pursuing a professional career very challenging for them (Howlin et al., 2004; Taylor and Seltzer, 2011).

In the following two sections I will outline the diagnostic criteria and diagnostic procedures for ASD.

4.1.1. Introducing ASD: Diagnosis and levels of functioning

Autism is a disorder of development with biological, mainly genetic, causes (Frith, 1989; Levy et al., 2009). Ever since the first case reports of low- and high-functioning autistic children by Kanner (1943, 1944) and Asperger (1944) respectively, the prevalence of ASD (i.e. the proportion of the total population diagnosed with ASD) has greatly increased. The present prevalence rates for ASD are estimated to be about 1% (Bolte, 2009). Changes in prevalence over the years are most likely due to policy and practice changes (e.g. new autism specific screening instruments for infants; for a discussion of increased prevalence rates please refer to Levy et al. (2009) and Bolte (2009)). Furthermore, the prevalence of ASD differs significantly for males and females. The sex ratio has been consistently reported to be approximately 4 (boys) to 1 (girls) (Bolte, 2009). Furthermore, autistic characteristics can considerably differ between males and females. A growing body of evidence suggests significant gender differences in cognitive abilities (Bolte et al., 2011; Lai et al., 2011) including social cognition (Sucksmith et al., 2013) between boys and girls with an ASD diagnosis. For instance, females with ASD are more likely to have lower intelligence quotient (IQ) scores than males diagnosed with ASD (Lord et al., 1982; Volkmar et al., 1993). With regards to social cognitive impairments the findings remain inconclusive. Some studies found that females are more impaired than males (Carter et al., 2007; Golan et al., 2007), other studies report the opposite pattern (Golan et al., 2006; Sucksmith et al., 2013).

In the empirical studies of this dissertation, autism has been diagnosed based on the Diagnostic and Statistical Manual of Mental Disorders (4th ed., DSM-IV (American Psychiatric Association, 2000)) and the International Classification of Diseases and Related Health Problems (10th ed. World Health Organisation (1992); ICD-10). The term used in the DSM-IV and ICD-10 to describe ASD is pervasive developmental disorders (PDD). A triad of symptoms characterizes PDD, including impaired social interactions, stereotypical behavior, and impairments in communication (Levy et al., 2009). The subcategories autistic disorders, childhood disintegrative disorder, Rett’s disorder, Asperger Syndrome (AS), and pervasive developmental disorder not otherwise specified (PDD-NOS) differ in the constellation and severity of symptoms.

The unofficial but commonly accepted term *autism spectrum disorders* (ASD) emphasizes that the severity of autistic symptoms can greatly differ between the subcategories of PDD. To date, there is only one accepted and widely used clinical classification of ASD individuals into low-functioning and high-functioning individuals (Bolte, 2009). Low- and high-functioning individuals differ with respect to the intellectual level. High-functioning individuals with ASD, diagnosed with high-functioning autism (HFA) or with AS, have normal to elevated intelligence levels and good language skills. Thus, their impairments in social cognition seem more evident and dissociable from general cognitive abilities. This is the main reason why, in particular, high-functioning individuals with ASD provide a model for impaired social cognition and have been the target population for the majority of research on impairments in social information processing (Frith and Happe, 1999).

In the empirical studies of this dissertation my co-authors and I investigated social information processing in high-functioning individuals with ASD (i.e. individuals diagnosed with AS or HFA in accordance with the DSM-IV criteria). Given that in the current manual DSM-V all previous sub-categories of ASD have been merged together (Huerta et al., 2012; Huerta and Lord, 2012), we referred to individuals with AS and HFA as high-functioning ASD individuals, without further differentiating between these diagnoses.

4.1.2. Diagnostic Instruments

Structured interviews and behavioral observation measures based on the DSM criteria are nowadays the standard means to diagnose ASD. Two instruments are particularly common in the diagnostic practice: the Autism Diagnostic Observation Schedule (ADOS, (Lord et al., 2002)) and the revised Autism Diagnostic Interview (ADI-R, (Lord et al., 1994)). The ADOS is a semi-structured standardized observational instrument, which covers a variety of tasks and interview elements. The ADI-R is a semi-structured interview conducted with the individual’s parent or caregiver. Both the ADOS and ADI-R assess the previously mentioned triad of symptoms: impaired social interactions, stereotypical behavior, and impairments in communication. Studies investigating large samples of individuals with ASD (ranging from children to adults diagnosed with PDD with low- and high intelligence levels) found that both the ADOS and ADI-R have good psychometric properties such as reliability (ADOS: 0.78-0.89; ADI-R: 0.91), sensitivity (ADOS: 90.4%) and validity (concurrent validity or agreement between ADOS and ADI-R: 79%; concurrent validity between ADOS and clinical diagnosis: 77%; concurrent validity between ADI-R and clinical diagnosis: 74%) (Rutter et al., 2003; Bolte and Poustka, 2004), and are thus referred to as the gold-standard assessment methods (Levy et al., 2009). Furthermore, the Asperger Syndrome Diagnostic Interview (ASDI, (Gillberg et al., 2001)) is a short standardized interview which has proved to be sensitive and reliable in the diagnosis of higher-functioning individuals, including AS and HFA. In the empirical studies of this dissertation, ASD participants were diagnosed based on all three instruments: ADOS, ADI-R and ASDI.

4.2. Social cognition in typically developed individuals and ASD

A common characteristic of individuals with ASD, whether high- or low-functioning, is a pervasive impairment in social cognition. The term social cognition describes the sum of processes that allow individuals of the same species to interact with one another (Frith and Frith, 2007). One of the most important social cognitive skill for successful social interactions is the ability to infer others’ mental states and intentions based on social cues such as facial expressions, language, emotional prosody, and body language (Zaki and Ochsner, 2011). In real life, all these sources of social information show temporal dynamics (i.e. they change over time). Thus, our ability to perceive others’ goals and intentions crucially depends on the ability to integrate dynamic social information over time.

In the last two decades, most research on social cognition has been devoted to investigating differences between typically developed individuals and individuals with ASD (Baron-Cohen et al., 1985; Happe, 1993, 1994; Frith, 2001; Dziobek and Bolte, 2011). Investigating social cognition in individuals with ASD has proved fruitful in two ways. First, it has led to an advanced understanding of social impairments in ASD. Second, it has deepened the understanding of the mechanisms underlying social cognition in typically developed individuals. In the three empirical studies summarized in this dissertation we aimed at extending previous literature on social cognition by approximating social cognitive processes in real life social settings. To identify social cognitive processes that are necessary for typical social functioning, we investigated typically and atypically developed individuals with ASD, the latter representing a model for impaired social cognition.

4.2.1. Implicit and explicit social cognition

Social cognitive skills, such as recognizing someone else’s emotional state or intention, are the most important tools for successful social interactions (Premack and Woodruff, 1978). Interestingly, hardly anyone could claim to remember how he or she acquired such skills. The reason is that we did not acquire them explicitly (i.e., consciously and effortfully), but rather implicitly (i.e., automatically and without conscious awareness) by watching other people (Frith and Frith, 2007). During the first year of life, children acquire much implicit knowledge about their social environment from simply observing the behavior of others (Frith and Frith, 2012). Over the course of development, implicit processes that need less conscious effort and are less controlled precede explicit processes that require higher cognitive load (Low and Perner, 2012). Implicitly imitating facial expressions and engaging in joint attention are important precursors to explicit emotion recognition and mental state inferences, respectively (Carpenter et al., 1998). It has been proposed that both types of social cognitive processes, implicit and explicit, coexist in adulthood, mediating distinct aspects of social behavior (Frith and Frith, 2008; Apperly and Butterfill, 2009; Low and Perner, 2012; Kliemann et al., 2013). The questions of whether implicit and explicit social cognitive processes are distinguishable and how they interact, however, have not yet been conclusively answered.

Given that social cognition in real life occurs most often implicitly (Frith and Frith, 2007), indirect tasks, which assess implicit processes, might represent more ecologically valid measures of social cognition – and the social impairments of individuals with ASD – than explicit tasks (Senju, 2013). In line with this notion, individuals with ASD have been shown to have greater impairments in processing social cues implicitly than explicitly (Senju et al., 2009). It is, however, not possible to categorize all social cognitive processes into automatic and unaware implicit processes versus controlled and effortful explicit processes (Adolphs, 2009). This differentiation rather represents the two extremes of a continuum. To take an example from a different domain, racial prejudices are rather implicitly revealed (e.g. causing a particular bias on an indirect task) than explicitly reported (Fazio and Olson, 2003). That does not mean, however, that prejudiced people lack conscious awareness for their prejudices. This example illustrates that unawareness of the tested psychological construct is not always guaranteed and also not necessarily a criterion for an implicit process (Fazio and Olson, 2003; Nosek et al., 2011).

In the following two sections of this chapter I will introduce two core social cognitive skills that require the integration of dynamic social information: mental state inferences (i.e. mentalizing) and emotion recognition from the tone of voice (i.e. prosody).

4.2.1. Mentalizing

Mentalizing, or Theory of Mind (ToM), has been defined as the ability to predict the relationships between external states of affairs and internal states of mind (Frith, 1989). In other words, we infer the mental states (emotions, thoughts, intentions) of others on the basis of how they behave. Mentalizing thus represents a key component of human interaction (Premack and Woodruff, 1978). Our ability to mentalize not only allows us to make sense of others' behavior, but crucially enables us to predict what they will do next (Frith, 1989). As such it constitutes an important basis for understanding our friends' emotional states (Walter, 2012) or someone else's strategic behavior, for instance in an economic context (Behrens et al., 2008). In the following two paragraphs, I will first introduce the standard direct tasks for the assessment of explicit mentalizing performance, and subsequently introduce newer indirect measures that aim at capturing implicit mental state processing.

Wimmer and Perner (1983) introduced the now classic Sally-Anne experiment to assess mentalizing skills in young children. In this test, children see two dolls (Sally and Anne). Sally has a marble and puts it into her basket. Then she leaves the room. Anne takes the marble out of Sally's basket and puts it into her box while Sally is away. Now Sally comes back into the room. The critical question is where would Sally look for her marble? If children are able to take Sally’s belief into account, that is, if they understand that she has a false belief about the location of the marble, which differs from their own true belief, they would answer that Sally would look for her marble in the basket where she put it. Using this test or related versions, researchers in developmental psychology suggested that around the age of four years children reach an important developmental milestone: they explicitly understand another person’s false belief (Perner et al., 2011). After the age of about three to four, typically developed children show a ceiling effect in simple false belief tasks (Perner and Wimmer, 1985). The next step in mentalizing development is to understand so called nested beliefs or second-order beliefs (e.g., Anne thinks that Sally thinks something). Typical children pass second-order false belief tasks at an age of about six or seven years (Perner and Wimmer, 1985).

Children with ASD failed to recognize Sally’s false belief, despite the fact that they were around five years older than the previously tested typically developed children (Baron-Cohen et al., 1985). Concluding from this and various other studies that compared mentalizing skills of typically and atypically developed children (Baron-Cohen, 1989; Perner et al., 1989), researchers in the field established that the lack of false-belief recognition constitutes the core deficit in ASD (Baron-Cohen et al., 1985; Leslie and Thaiss, 1992; Baron-Cohen et al., 1997; Baron-Cohen et al., 2001). However, ASD individuals with normal intelligence levels learn to solve false-belief tests in later development, which is why simple false-belief tests have been reported to cause ceiling effects in adults with ASD (Baron-Cohen et al., 1997). As a consequence, more advanced ToM tests have been introduced. These tests assessed the understanding of complex emotional states that require mental state inferences from either short stories (e.g. “Strange Stories” task by (Happe, 1993, 1994)) or photographs of persons’ eye regions (i.e. the Reading the Mind in the Eyes test (RMET) by (Baron-Cohen et al., 2001)). Although these tests proved sensitive in picking up subtler mentalizing deficits of adults with ASD, they consist of static and simple stimuli that differ substantially from the dynamic, multimodal information we are confronted with in real life (Zaki and Ochsner, 2009). Paralleling the observation that individuals with ASD show greater impairments in unstructured real life than in constrained experimental settings (Volkmar et al., 2004), Dziobek and colleagues (2006) reported that a naturalistic video based mentalizing task (the Movie of the Assessment of Social Cognition, MASC) was more sensitive in picking up mentalizing difficulties of individuals with ASD than static tasks such as the “Strange Stories” task or the RMET.

In summary, mentalizing has traditionally been investigated using direct, verbal tasks that ask participants to make explicit, verbal mental state inferences. Using such tasks, developmental psychologists have defined stages in the typical development of mentalizing and have established the most influential neuropsychological model of ASD (Dziobek and Bolte, 2011), which proposes a lack of mentalizing skills or ‘mindblindness’ in individuals with ASD.

Recently, there has been a significant shift away from direct performance-based measures of mentalizing, especially in the field of social neuroscience. Researchers have become more interested in investigating implicit mentalizing processes with indirect tasks (i.e. tasks in which the construct of interest is inferred indirectly from behavior (De Houwer and Moors, 2010). The most frequently used indirect measure is gaze tracking. Participants’ gazes are tracked while watching false belief scenarios (Senju et al., 2009) or complex social scenes (Klin et al., 2002). A different approach to assessing implicit mentalizing is the use of tasks derived from game theory that measure how much participants take another person’s perspective into account while making strategic decisions (Behrens et al., 2008; Hampton et al., 2008; Coricelli and Nagel, 2009; Yoshida et al., 2010). Assessing implicit mentalizing with indirect tasks has led to significant advances in the field. First, developmental psychologists have found that children younger than four years show some understanding of false belief without being able to explicitly report it (Low and Perner, 2012). Second, indirect tasks have been able to detect mentalizing difficulties of individuals with ASD with a high degree of sensitivity. For example, (Yoshida et al., 2010) found that the strategic behavior of individuals with ASD in a social cooperative game was less guided by implicit belief inference than in typically developed individuals. Moreover, individuals with ASD seem to be more impaired in implicit as compared to explicit mentalizing (Senju et al., 2009; Senju, 2013). Senju and colleagues (2009) found that high-functioning adults with ASD did not show impairments in explicit mentalizing, including the previously mentioned Sally-Anne task, but anticipated false belief significantly less with their gaze than typically developed adults.

One important limitation of indirect tasks to date is the lack of a direct and objective performance measure of implicit mentalizing (Zaki and Ochsner, 2011). Instead, mental state inferences are indirectly inferred from behavior, for instance from the participants' gaze patterns. In consequence, it is not possible to determine the accuracy of mental state inferences. Whether or not mental state inferences are accurate is however of crucial importance, as they determine the quality of social interactions and consequently a person's level of social functioning.

The observed differences between implicit and explicit mentalizing have led to the notion that there are two systems of belief inferences. The implicit system is postulated to be efficient but inflexible, while the explicit system is considered more flexible but also demanding in terms of general cognitive resources (Apperly and Butterfill, 2009). However, direct tasks assess the accuracy of explicit mentalizing processes, whereas in indirect tasks mentalizing performance is indirectly inferred from behavior. Due to these substantial differences in methodology, the questions of how implicit and explicit mentalizing processes can be distinguished and how they interact with each other remain unclear (Nosek et al., 2011; Frith and Frith, 2012). In conclusion, to investigate the relationship and differentiation of explicit and implicit mentalizing, there is a need to develop performance-based tasks to objectively compare direct and indirect task performances, respectively.

4.2.2. Emotional prosody recognition

Social interactions and communication depend upon the understanding of subtle social cues such as emotional prosody (i.e., i.e. tone of voice or speech melody). Prosody (is a highly dynamic feature of speech, which is determined by the speaker’s pitch (fundamental frequency), intensity (amplitude), and speech duration (Eigsti et al., 2012). Prosody represents suprasegmental information, which is not bound to the speaker’s specific word choice or sentence structure and may convey linguistic, semantic, or emotional information.

Emotional prosody signals the speaker’s emotional state and reflects the communicative intention of the speaker. Emotions have been classified as either universal or culturally dependent. Basic emotions (e.g. fear, anger, sadness, joy, disgust, and surprise) have been claimed to involve universal, highly stereotypical physiological reactions (Ekman and Friesen, 1971; Ekman et al., 1987; Ekman, 1992; Zinck and Newen, 2008), whereas social emotions (e.g. gratitude or jealousy) require the interpretation of social relations and intentions, which depend upon certain cultural norms (Zinck and Newen, 2008). As a consequence, the recognition of social emotions requires a higher degree of mentalizing skills than the recognition of basic emotions (Burnett et al., 2009; Chevallier et al., 2011). In real life communication, social emotions occur more frequently than some basic emotions (Scherer et al., 2004; Hepach et al., 2011).

To date, most research on emotion recognition has focused on the visual modality, i.e. recognizing emotions from faces (Ekman, 1992), whereas relatively few studies have investigated emotional prosody recognition (Scherer, 2003). Compared to facial emotional expressions, emotional prosodic cues are more subtle and more difficult to recognize. Scherer (2003) reported that the recognition accuracy of emotions from voices lies between 55% and 65%, whereas accuracy rates for facial emotion recognition lie at around 75%. Given the dynamic nature of prosodic cues and the fact that they represent more subtle social information than facial expressions, emotional prosody recognition tasks might represent more naturalistic and sensitive measures of the subtle social impairments of high-functioning individuals with ASD.

While deficits in facial emotion recognition in individuals with ASD have been firmly established (see e.g., Baron-Cohen et al. (2001); Ashwin et al. (2006); Kliemann et al. (2013)), studies on emotional prosody recognition in ASD have produced mixed results. Some studies have reported aberrant prosody recognition of individuals with ASD (Hobson, 1986; Hobson et al., 1988; Baron-Cohen et al., 1993; Loveland et al., 1995; Golan et al., 2007). Other studies, however, have not found group differences in emotional prosody recognition between individuals with ASD and typically developed controls (Loveland et al., 1997; Boucher et al., 2000; Chevallier et al., 2011). These inconsistencies are likely due to substantial differences in methodology between studies (see McCann and Peppe (2003)).

One important difference between studies is whether or not the stimulus material includes social emotions. The majority of studies have only investigated prosody recognition of very few basic emotions (Boucher et al., 2000; Paul et al., 2005). Social emotions have been reported to be more difficult to recognize (Scherer, 2003) and also more sensitive in differentiating between typically developed individuals and individuals with ASD (Baron-Cohen, 2001). In the ASD population, deficits in recognizing social emotions might be tightly linked to their pervasive impairments in understanding others' mental states (e.g., Baron-Cohen, 1992, 2001). For instance, individuals with ASD have shown significantly lower performance than typically developed controls on a naturalistic task, which comprised real life vocal dialogues conveying a variety of social emotions (Rutherford et al., 2002; Golan et al., 2007). However, one limitation of this particular task was that the effect of the emotional prosody could not be differentiated from the emotional semantics of the speech segments.

In general, emotional prosody tasks have comprised a restricted set of emotional expressions recorded by very few speakers, often exclusively males or females. Investigating emotional prosody recognition with naturalistic stimuli involving a broad range of male and female speakers and social emotions could considerably help to elucidate the role of emotional prosody recognition in typical and impaired real life social communication.

4.3. The social brain in typically developed individuals and ASD

The term ‘social brain’ was first used by Leslie Brothers (1990) to define brain regions implicated in social cognition. Brothers and colleagues (1990) defined social cognition very broadly as information processing that supports the accurate perception of others’ dispositions and intentions. The social brain mainly implicated the superior temporal sulcus (STS), the amygdala, the orbital frontal cortex (OFC) and the fusiform gyrus. These regions were found to have reciprocal connections within the monkey brain and to be sensitive and selective to social stimuli in monkeys and humans (Brothers, 1989; Brothers and Ring, 1993; Brothers, 1996). Today, the term social brain refers to a much broader network of regions. For instance the temporal parietal junction (TPJ) and medial prefrontal cortex (MPFC) have been repeatedly discussed to play prominent roles in the conscious evaluation of another person’s belief (Amodio and Frith, 2006; Saxe, 2006; Saxe and Powell, 2006).

Neuroimaging studies investigating high-functioning individuals with ASD have established that their selective impairments in social cognition correspond to abnormal activity of the social brain (Adolphs, 2002, 2009, 2010b). The social cognitive deficits of individuals with ASD have been repeatedly linked to reduced activation of social brain regions, such as the STS, TPJ, and MPFC (Happe et al., 1996; Castelli et al., 2002; Lombardo et al., 2011) as well as to a reduced connectivity between them (Lombardo et al., 2011). The most extensively implicated brain regions in the social cognitive deficits of individuals with ASD have been the amygdala and the STS (see Adolphs (2009) and Pelphrey et al. (2011) for a review).

To date, however, most research in the field investigated the neural mechanisms of mentalizing whether or not they support accurate mental state inferences (Zaki and Ochsner, 2011). In consequence, the relationship between the social brain, social cognition and social behavior remains unclear. For instance, identifying social brain regions that support accurate social cognition and behavior could significantly advance our understanding of typical social information processing as well as of disorders characterized by impaired social functioning, such as ASD (Kennedy and Adolphs, 2012).

In the following sections I will outline two well established networks for social information processing: the mentalizing network and the emotional prosody network. Finally, I will focus on two core regions of the social brain, the STS and amygdala, that play an important role in mentalizing and in emotional prosody processing, and have been repeatedly implicated in the social cognitive impairments of individuals with ASD.

4.3.1. Neural processing of mental states

The neural mechanisms of mentalizing have been investigated with a variety of direct and indirect tasks including static as well as dynamic stimuli (e.g. (Vogeley et al., 2001; Castelli et al., 2002; Saxe and Kanwisher, 2003; Walter et al., 2004; Wolf et al., 2010). The network of regions most consistently implicated in mentalizing comprises the MPFC, TPJ, STS, the temporal poles (TP), the posterior cingulate cortex / precuneus (PCC / PC), as well as the IFG (Amodio and Frith, 2006; Bahnemann et al., 2010; Mar, 2011). Amygdala involvement has also been consistently reported in studies using certain static and dynamic tasks (Mar, 2011).

The mentalizing network comprises regions that support higher-level, explicit social cognition and regions that have been strongly implicated in lower-level implicit social cognition (Olson and Fazio, 2003). The MPFC and the TPJ have been consistently implicated in higher-level cognitive processes such as the conscious attribution of mental states. In particular, the TPJ has been repeatedly associated with explicitly taking a third person perspective (Saxe and Kanwisher, 2003; Saxe, 2006). In contrast, the STS and amygdala have been most strongly implicated in implicitly coding biological movements that signalize intentions (i.e., processing and integrating information from facial expressions or body movements) (Allison et al., 2000; Adolphs et al., 2005). The amygdala, in particular, is not thought to be involved in mental state inference per se, but rather in mediating arousal or biological salience associated with the respective stimuli (Olsson and Ochsner, 2008; Adolphs, 2010b).

Real life social information processing relies on both implicit and explicit processes (Cunningham and Zelazo, 2007; Adolphs, 2010a). However, in real life social interactions implicit mentalizing processes occur more frequently (Frith and Frith, 2008). We most often infer others' mental states online while engaging in social interactions. Thus, regions involved in implicit mentalizing might play a particularly important role for accurate social behavior and social functioning.

Neuroimaging studies that compare mentalizing related neural activity of typically versus atypically developed individuals can help to delineate the contribution of higher- and lower-level mentalizing processes for unimpaired social functioning (Kennedy and Adolphs, 2012). So far, few neuroimaging studies have addressed mentalizing deficits of individuals with ASD. Studies investigating explicit mentalizing with direct static tasks found reduced MPFC and TPJ activity in individuals with ASD compared to typically developed controls (e.g., Happe et al., 1996; Lombardo et al., 2011). More recently, studies using indirect measures (e.g. gaze tracking) or dynamic stimuli (e.g. shapes that move in a goal directed manner) have repeatedly linked abnormal social cognitive processes of individuals with ASD with aberrant amygdala and STS activation (e.g., Baron-Cohen et al., 1999; Critchley et al., 2000; Castelli et al., 2002; Pelphrey et al., 2011; Perlman et al., 2011; Kliemann et al., 2012)

While the social impairments of individuals with ASD have been closely associated with aberrant amygdala and STS activity, little is known about the particular contributions of these regions to mentalizing performance in typically and atypically developed individuals. This is because on the one hand, mentalizing has been mostly studied with static instead of dynamic stimuli, which recruit amygdala and STS activity to a higher extent (Wright et al., 2003; Adolphs, 2009). On the other hand, neuroimaging studies in social cognition have generally neglected the relationship between neural processing and accurate social behavior (Zaki and Ochsner, 2011). In the next section I will outline the neural networks involved in processing dynamic prosodic cues and how research on emotional prosody processing could potentially inform research on mentalizing in dynamic naturalistic settings. In the last section of this chapter I will outline findings that further underscore the important role of the amygdala and STS in the typical and atypical development of mentalizing skills and how the interplay between these regions might crucially contribute to mentalizing in real life social settings.

4.3.2. Neural processing of emotional prosody

According to the acoustic lateralization hypothesis suprasegmental speech signals (i.e. prosody, music processing) are predominantly encoded in right hemisphere structures, whereas segmental speech processing (i.e., phonemes, syllables) are processed in left areas (see Belin et al., 2004; Poeppel et al., 2004). This hypothesis was first put forward by Ross (1981), who assumed that prosodic information would be encoded within right-sided perisylvian regions. In particular, he proposed that the comprehension of prosodic cues was bound to the right superior temporal region (homologue of the left-hemispheric Wernicke's area, which supports speech comprehension). More recently, the acoustic lateralization hypothesis has been challenged by a series of studies, which consistently implicated the right STS and bilateral IFG in emotional prosody processing (Schirmer and Kotz, 2006; Wildgruber et al., 2006). Furthermore, based on a Dynamic Causal Modeling (DCM) approach (Ethofer et al., 2006), Wildgruber and colleagues (2006) proposed a hierarchical model of emotional prosody processing, which assumes that prosodic information is extracted and represented within the right STS and subsequently projected to the bilateral IFG, where information is explicitly evaluated (Ethofer et al., 2006). To date however, many studies have shown a stronger involvement of the right-sided IFG in the extraction of emotional significance, whereas the left-sided IFG has been more closely linked to semantic and linguistic processing (George et al., 1996; Buchanan et al., 2000; Mitchell et al., 2003; Schirmer and Kotz, 2006). Additionally, emotional prosody has been repeatedly shown to elicit amygdala and ventral striatum activity, possibly due to the emotional and motivational saliency of the stimuli (see Schirmer and Kotz (2006) for a review).

Emotional prosody is processed mostly implicitly in real life social communication. However, whether the emotional prosody network is modulated by processing type (implicit versus explicit) remains a matter of debate. To date, few studies investigated implicit emotional prosody processing. The most commonly used task to assess implicit processing of emotional prosody is to ask participants for the speaker's gender instead of asking them to label the emotion expressed in the voice (e.g., Grandjean et al., 2005; Sander et al., 2005; Bach et al., 2008; Fruhholz et al., 2012). In general, studies point at a difference between implicit versus explicit processing of emotional prosody. However, differences in processing type (explicit versus implicit) do not seem to modulate activity of core prosody regions, but rather to elicit differential activity of other frontal and subcortical regions, such as the anterior cingulate cortex (ACC) or the basal ganglia. (e.g. Sander et al., 2005; Bach et al., 2008).

In line with the notion that understanding social emotions requires a higher degree of mentalizing skills, neuroimaging studies reported increased activity of core mentalizing regions, such as the MPFC for social versus basic emotions (e.g., Moll et al., 2002; Takahashi et al., 2004; Takahashi et al., 2008; Alba-Ferrara et al., 2011). Thus, investigating prosody processing of social emotions might be instrumental to identify the neural mechanisms supporting mentalizing on the basis of naturalistic, dynamic social cues (Zaki and Ochsner, 2009). To date, however, only a handful of neuroimaging studies have investigated the neural mechanisms of emotional prosody processing with social emotions, and thus it remains unclear whether and to what extent processing social emotions recruits the mentalizing network in typically developed individuals.

Finally, the neural basis of impaired social communication, for instance in ASD, has received very little attention. The few studies investigating prosody processing in ASD found increased activity of the core prosody processing regions, bilateral STS and IFG (Wang et al., 2006), and increased activity of regions typically assigned to the mentalizing network (Eigsti et al., 2012). However, it is not clear whether and how such differences in neural processing of emotional prosody relate to the observed differences in social communication. Research in this field can help to delineate the role of prosody processing regions in real life typical and impaired social communication. There are several reasons why individuals with ASD constitute a highly appropriate clinical population for neuroimaging studies on emotional prosody processing. Firstly, dynamic subtle social cues, such as emotional prosody, can pick up the social deficits of individuals with ASD more sensitively than static stimuli (Golan et al., 2007). Secondly, the amygdala and the STS, two regions that support emotional prosody processing, have been tightly linked to the social deficits of individuals with ASD (see e.g., Pelphrey et al. (2011)). Finally, several researchers have proposed that ASD are characterized by aberrant connectivity between cortical brain regions (Koshino et al., 2005; Just et al., 2007). Investigating the functional coupling between prosody processing regions in individuals with ASD as compared to controls can enhance the understanding of how information processing between prosody processing regions supports accurate prosody recognition.

4.3.3. The role of the amygdala and the STS in typical and atypical social information processing

Two out of the four regions Brothers and colleagues (1990) originally assigned to the social brain show a particular sensitivity to dynamic social stimuli in primates and humans. In primates, neurons of the STS and the amygdala were found to be particularly responsive to dynamic social information, such as the direction of gaze, or dynamic social interactions of conspecifics (Brothers et al., 1990; Brothers, 1996). Similarly, in humans these regions have been consistently implicated in implicit lower-level social cognition, in particular, in orienting towards and tracking biological motion (see Allison et al. (2000) and Bahnemann et al. (2010)) for a review.

Furthermore, in humans both regions seem to support the development of mentalizing skills. The strongest support for amygdala involvement in the development of mentalizing abilities comes from lesion studies and studies investigating the social cognitive deficits of individuals with ASD (see Pelphrey et al. (2004) for a review). Patients who acquired amygdala lesions in early developmental stages showed mentalizing impairments, whereas patients who acquired amygdala lesions in adulthood did not differ in their mentalizing skills from healthy controls (Fine et al., 2001; Heberlein and Adolphs, 2004; Shaw et al., 2004). In the same vein, individuals with ASD show deficits in lower-level social cognitive processes (e.g., reduced focus on the eye regions, deficits in emotion recognition) that support the development of mentalizing (Senju, 2013) and these social deficits have been consistently associated with a dysfunctional profile of the amygdala (Baron-Cohen et al., 1999; Dziobek et al., 2010; Kliemann et al., 2012).

Similar to the amygdala, the STS has been strongly implicated in processing dynamic social information, such as biological motion (i.e., body movements or movements of body parts) (see Allison et al. (2000); Bahnemann et al. (2010) for a review) or emotional prosody (e.g., Schirmer and Kotz, 2006). Importantly, STS activity for biological motion is additionally modulated by whether or not particular movements signal a person's intentions (Allison et al., 2000; Pelphrey et al., 2011). Consequently, the observed deficits of individuals with ASD in inferring intentions from biological motion have been associated with less activation of the STS (Castelli et al., 2002; Pelphrey et al., 2004; Pelphrey et al., 2011).

Taken together, amygdala and STS have been implicated in dynamic social information processing in primates and humans (Brothers, 1996). In particular, both regions have been shown to support social cognitive skills that support the development of mentalizing (Adolphs, 2009). Given that both regions show a high sensitivity to dynamic social information, such as eye gaze shifts, or emotional prosody, both regions might support accurate implicit mental state inferences. To address this notion, there is a need to investigate mentalizing with naturalistic tasks. Similar to real-life situations, tasks including dynamic video stimuli require participants to track and integrate social information online, i.e., implicitly (Klin et al., 2002).

Another important step in understanding typical and impaired social information processing is to investigate connectivity between regions of the social brain (Adolphs, 2010a). In particular, connections between the STS and amygdala might be particularly important for implicit social information processing. The STS has been proposed to be the primary site for the integration of dynamic information in primates (e.g., Baizer et al., 1991) and humans (Wildgruber et al., 2006). Given that amygdala and STS are linked via reciprocal connections (Castelli et al., 2002), it is likely that dynamic information is projected from the STS to the amygdala, which encodes the social saliency of the particular information (Brothers, 1996). A substantial body of literature suggests that ASD is a disorder of connectivity between social brain regions (Gotts et al., 2012; von dem Hagen et al., 2013). Consequently, the functional connectivity between amygdala and STS might account for the social impairments of individuals with ASD.

5. Research questions and hypotheses

The overall aim of this dissertation was to advance the understanding of social information processing in real life social settings. In the three empirical studies of this dissertation, my co-authors and I developed and used a new set of dynamic video and audio stimuli to approximate real life social information processing. Furthermore, to identify processes that distinguish impaired from intact social functioning, we investigated typically developed individuals and individuals with ASD, the latter representing a model of impaired social cognition. The three empirical studies summarized in this thesis (Rosenblau et al., in revision; Rosenblau et al., submitted; Rosenblau et al., submitted) investigated the following five empirical questions.

Question 1: How can implicit and explicit social behavior be differentiated, and how do they contribute to social functioning in naturalistic settings? (Study 1)

To address this question, we sought to design two naturalistic, indirect and direct performance-based mentalizing tasks. The tasks mainly differed with respect to the answering format. After watching a social interaction scene, in the indirect task, participants were asked to solve a film puzzle by selecting the most likely continuation of the film scene out of four different film clip options. Importantly, there was no explicit prompt to infer mental states. Here, our conceptualization of implicit processes is narrower than that of most studies on implicit social cognition (e.g., Greenwald and Banaji, 1995). The indirect task includes the conscious evaluation of multiple answer options. However, it does not include explicit, verbal cues that prompt participants to infer mental states. In line with the definition of an indirect measure by (Fazio and Olson, 2003), the indirect task provides information about the construct of interest without asking the participant directly to report it. In contrast, in the direct task, after watching a film scene, participants were asked to select the most likely verbal explanation for the protagonists' emotional states. In both tasks accuracy and reaction times could be measured, thereby allowing for an objective comparison of intra- and interindividual performance differences.

In study 1, we investigated the tasks' validity, reliability and sensitivity to the social cognitive impairments of individuals with ASD. Specifically, we expected individuals with ASD to perform significantly lower than typically developed participants on both direct and indirect tasks. In accordance with the notion that individuals with ASD were more impaired in implicit mentalizing (Senju et al., 2009), we further expected them to show lower performance on the indirect than on the direct task. Finally, following the hypothesis that implicit and explicit mentalizing processes are distinguishable to some extent (Apperly and Butterfill, 2009), we expected performances on the direct and indirect task to be relatively independent of one another, and the performance on other established direct mentalizing measures to be higher correlated with direct than with indirect task performance.

Question 2: What are the neural mechanisms of mentalizing in naturalistic settings, and how do they support accurate mental state inferences? (Study 2)

To approximate spontaneous mentalizing in naturalistic settings, in study 2, we introduced a new functional magnetic resonance imaging (fMRI) task including dynamic videos of social interactions. In this task, ASD and typically developed participants were presented with film scenes depicting social interactions that were split into three consecutive film clips. During the mentalizing condition, participants were asked to make inferences about clip-by-clip changes in the protagonists' affective states. In real life, mentalizing occurs mostly implicitly while interacting with others (Frith and Frith, 2008). Thus, in a next step, we attempted to link neural mental state processing to accurate implicit mental state inferences measured with the indirect behavioral task, which was introduced in study 1. In line with a substantial body of literature linking both the amygdala and STS to dynamic social cognitive processing and the social deficits of individuals with ASD, we hypothesized that the ASD group would show reduced activation of the mentalizing network during spontaneous mentalizing, in particular of the amygdala and STS. Furthermore, we expected activity of both the amygdala and STS to predict accuracy on the indirect behavioral task, whereby in typically developed controls, the relationship between neural activity and behavioral accuracy would be higher than in individuals with ASD.

Question 3: What are the neural mechanisms of naturalistic prosody processing, and how do they support prosody recognition? (Study 3)

The emotional prosody processing network in typically developed individuals (which includes the right STS and bilateral IFG) has been consistently established across a variety of different tasks (Frith and Frith, 2008). To date, however, little is known about how this network is modulated by the social relevance of emotions (social versus basic emotions) and by the processing type (explicit versus implicit) in typically developed individuals. Furthermore, similar to the state of research on mentalizing, little is known about the relationship between activity of prosody processing regions and accurate emotion prosody recognition. In study 3 we introduced two newly developed emotional prosody tasks, a behavioral and an fMRI task. To approximate real-life social information processing, we included a larger number of speakers and social emotions than has been done by most studies. We first investigated the sensitivity of the behavioral task to the social communication deficits of individuals with ASD. In the subsequent fMRI study, we investigated the neural mechanisms of social versus basic emotional prosody assigned to either an implicit or explicit emotion processing condition. We hypothesized that the newly developed behavioral task would be sensitive to the social deficits of individuals with ASD. On the neural level, we expected individuals with ASD to show reduced activity of the prosody network, in particular in of the amygdala and the STS, when processing emotional versus neutral prosodic speech, especially for social versus basic emotions. Finally, we hypothesized that in typically developed individuals activity of the prosody processing network would be related to accurate emotion recognition performance and that this relationship between neural processing and behavior would be weaker in individuals with ASD.

Question 4: How does the coupling between social brain regions contribute to social cognition and social functioning? (Study 3)

Question 4 relates the coupling between brain regions during social information processing to typical social functioning. More specifically, in study 3 we investigated group differences in the functional connectivity between core prosody regions during emotional prosody processing. Given that individuals with ASD are characterized by social communication deficits (American Psychiatric Association, 2000) as well as by reduced connectivity between social brain regions (Lombardo et al., 2011), my coauthors and I hypothesized that the functional coupling between prosody regions for emotional versus neutral prosody, and more specifically for social versus basic emotional prosody, would be significantly reduced in individuals with ASD compared to typically developed controls.

Question 5: What are the particular roles of the STS and amygdala in naturalistic and dynamic social information processing? (Study 2 and Study 3)

In line with a substantial body of literature linking the amygdala and STS to processing dynamic social information (Adolphs, 2009) as well as to the social impairments of individuals with ASD (Pelphrey et al., 2011), we expected amygdala and STS activity to support dynamic social information processing in typically developed controls in the visual and auditory modality. Specifically, we expected a higher functional connectivity between the amygdala and the STS for social versus nonsocial dynamic information processing and that activity in both regions would predict accurate social behavior. We further expected that individuals with ASD would show reduced amygdala and STS activity for social versus nonsocial information processing in the visual and auditory domain. Finally, we hypothesized that the relationship between activity of these regions and social behavior would be significantly reduced in individuals with ASD.

6. General methodology

In the following section, I will briefly outline two of the most pertinent methodological aspects of the three empirical studies. I will first describe the development and validation of the naturalistic stimuli, and how they were implemented into the tasks. Subsequently, I will introduce the methodological approaches used in the studies to investigate the relationship between the social brain and social behavior. A complete description of each study’s methodology can be found in the respective methods section of the three studies.

6.1. Naturalistic assessment of social cognition

A shortcoming of most tasks for the assessment of social cognition concerns their abstract and mostly static stimulus material, which often lacks the required sensitivity to assess real life social cognitive skills in typically and atypically developed individuals (Zaki and Ochsner, 2009). In contrast, naturalistic tasks may be more difficult and thus have the potential to produce the required amount of variability in performance. This would facilitate research on individual differences in social cognition as well as on the social deficits of individuals with ASD that are more pronounced in unstructured real life (Volkmar et al., 2004).

We produced a set of naturalistic life-like stimuli within the framework of a comprehensive project, which aimed at developing new social cognitive test and training tools. The stimuli were recorded in cooperation with a total of 70 actors in a professional film studio of the Humboldt University Berlin, Berlin Germany in cooperation with its Computer and Media Service team (CMS). Actors were asked to portray 40 different emotional states (e.g. happiness, envy, anger or enthusiasm) through facial expression, prosody and short films of social interactions (see Figure 1 A). These particular emotions were pre-selected on the basis of their communicative frequency and thus relevance in real life social interactions (Hepach et al., 2011). In the following paragraphs I will outline the stimulus production and validation process for the auditory and video stimuli that constituted the basis for the experimental tasks used in the three empirical studies.

6.1.1. Videos of social interactions

The film scenes used in study 1 and study 2 displayed different social interactions between two or three protagonists. In total, 30 actors of varying ages participated in the scenes. We made sure to cover a wide range of different social contexts including friendships (e.g., friends having dinner, discussing wedding plans, or going to the theatre together), romantic relationships (e.g., couples having breakfast or discussing their plans for the week end) and work relationships (e.g., having a lunch break, getting promoted, working together on a presentation). The scripts for the scenes were written in cooperation with professional scriptwriters and included a variety of social emotions (e.g., gratefulness, forgiveness, jealousy, contempt) as well as traditional mentalizing concepts such as false belief, deception, sarcasm, and irony. Furthermore, the film scenes varied with respect to their focus on verbal communication. Film scenes contained more or less verbal communication, and some were explicitly nonverbal. In the nonverbal scenes, participants had to rely solely on facial expressions, gestures, and body language for their mental state inferences (see Figure 1 B).

The video-based items of the newly developed behavioral tasks introduced in study 1 were subjected to an initial validation study in a separate sample of healthy individuals (N = 28). Participants were first asked to rate the believability of the scenes. Second, in the indirect task, they provided a free text answer on how the scene might continue, and in the direct task, they were asked to report what a protagonist was feeling at the end of the scene. Finally, participants were asked to solve the multiple-choice items. Items of both tasks were rated as believable (indirect task mean believability = 4.4; SD = 0.34; direct task mean believability = 4.8; SD = 0.38; on a 6-point Likert scale; 1 = not believable to 6 = very believable). The items of the indirect task yielded a sufficient overall item difficulty of 0.76 (SD = 0.19), on the direct task, however, participants performed at ceiling. Almost all participants picked the right answer option and provided a very similar free answer. In consequence, we revised the item introductions of both tasks and the text answers of the direct task items to reduce ambiguity and increase item difficulty of the direct task. The final item sets of both direct and indirect tasks yielded good reliability (direct task: Cronbach's α = 0.82; indirect task: Cronbach's α = 0.84). For more details, please see the methods sections of the main manuscripts and the supplemental sections of studies 1 and 2.

Figure 1. Production of naturalistic stimuli

A: Documentation of the stimulus production with a professional actor in the film studio of the Humboldt University Berlin. Here, the actor is given directions by a project member. B: Screenshot of a film scene that has been included in the newly developed fMRI task.

6.1.2. Vocal emotional expressions

The audio stimuli of the behavioral and fMRI tasks introduced in study 3 were selected out of a large item pool comprising 2000 audios (50 professional actors of varying ages displayed 40 different emotions each). The actors were given semantically neutral sentence (e.g., I have a meeting this afternoon) that had to be spoken with varying emotional prosody or with neutral prosody. To facilitate the interpretation of the various emotional states, actors were given specific emotion inducing instructions, comprising a typical situation in which the respective emotion occurs (e.g. curiosity: "Your flat mate left an open love letter on the kitchen table"). Actors were also invited to remember a personal event in which they felt the respective emotion and to put themselves into that particular situation again. The emotion inducing scenarios were developed together with professional acting instructors.

Audio stimuli were validated in two steps. During stimulus production and postproduction (e.g., cutting, labeling, normalizing the audios), project members evaluated the ecological validity and preciseness of the emotional expressions for the first time. Based on this pre-selection, audios containing ambiguous emotional prosody were immediately excluded from the dataset. In a second step, a subset of 100 items was subjected to a validation study including expert ratings from 10 psychologists working in the field of social cognition that were not part of the team developing the items. The emotional prosody of the audios was recognized in 83.6% of the cases (SD = 10.3%) and they were rated as believable (mean believability = 4.1; SD = 0.49; 6-point Likert scale from 1 = not believable to 6 = very believable). 25 out of the validated 100 items were selected as task items for the behavioral prosody task. For a more detailed description of the stimulus production and validation procedures, please see the supplementary methods section of study 3.

6.2. Brain behavior relationship

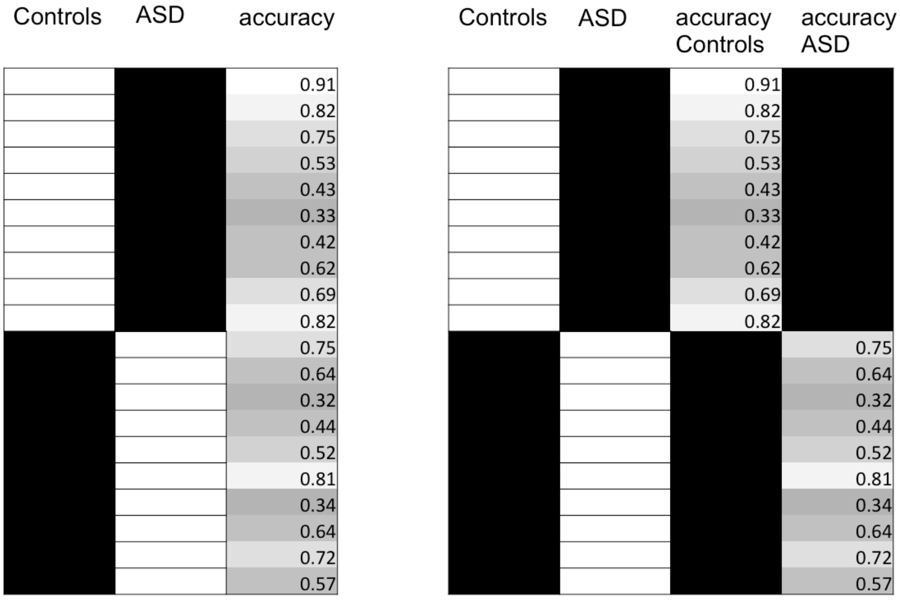
To investigate whether and how social brain networks were related to behavior (i.e. emotion recognition or mentalizing), my co-authors and I conducted two kinds of analyses: psychophysiological interaction (PPI) analyses and covariate analyses using accuracy on the independent behavioral mentalizing and prosody tasks as a covariate into the fMRI analysis. In the following two sections I will outline the general aim of these approaches and specify how they were used in the respective studies.

6.2.1. Covariate analysis

The aim of an fMRI covariate analysis is either to control for certain variables of no interest (i.e., regressor of no interest) or to specifically investigate the effects of a specific covariate on the neural activity (i.e., regressor of interest). For instance, in a model with a single group, one can control for performance related neural activity during a mentalizing task (contrast of interest: c = [1 0]; first column of the design matrix is the group, second column is the additional covariate). One can also be specifically interested in such performance related changes in neural activity (contrast of interest: c = [0 1]). For more than one group (e.g. controls and ASD individuals), however, the design matrix could differ depending on whether the covariate is of interest or of no interest. If the study's aim is to investigate group differences in neural activity during a mentalizing task and to additionally control for task performance, the respective design matrix could contain one regressor for typically developed controls, another one for individuals with ASD and a third regressor comprising the continuous covariate task performance. One would then compare the first two regressors and disregard the covariate (c = [1 -1 0] or c = [-1 1 0]). If, however, the aim is to investigate a group by performance interaction, which investigates whether controls and ASD participants exhibit different relationships between their Blood Oxygen Level Dependent (BOLD) activation during the mentalizing task and task accuracy, the design matrix must include one regressor for controls, one for ASD participants, and two separate regressors comprising the accuracy scores of the controls and ASD participants, respectively (see Figure 2). The contrast for the group by performance interaction would be c = [0 0 1 -1] or c = [0 0 -1 1] (see e.g., Poldrack et al. (2011) for more details)

In study 2 and study 3, we were interested in the relationship between neural activity and performance. Thus the covariates represented regressors of interest. We ensured that this analysis was not prone to potential non-independence errors by entering performance on the independently assessed behavioral tasks – not of the behavior in the fMRI task - as a covariate into the fMRI analysis.

In study 2 the covariate of interest was performance on the indirect mentalizing task, and in study 3, performance on the prosody recognition task. In both studies, we first investigated the relationship between BOLD signal change in the contrasts of interest and accuracy scores on an independent behavioral task in typically developed controls only (contrast c = [0 1]). Subsequently, we investigated group differences (Controls versus ASD participants) in the relationship between BOLD signal change and behavioral measures. Specifically, we were interested in identifying social brain regions, which would predict performance to a higher degree in controls than in individuals with ASD (contrast of interest: c = [0 0 1 -1]; see methods sections of study 2 and 3 for more details).



Controls	ASD	accuracy
□	■	0.91
□	■	0.82
□	■	0.75
□	■	0.53
□	■	0.43
□	■	0.33
□	■	0.42
□	■	0.62
□	■	0.69
□	■	0.82
■	□	0.75
■	□	0.64
■	□	0.32
■	□	0.44
■	□	0.52
■	□	0.81
■	□	0.34
■	□	0.64
■	□	0.72
■	□	0.57

Controls	ASD	accuracy Controls	accuracy ASD
□	■	0.91	■
□	■	0.82	■
□	■	0.75	■
□	■	0.53	■
□	■	0.43	■
□	■	0.33	■
□	■	0.42	■
□	■	0.62	■
□	■	0.69	■
□	■	0.82	■
■	□	■	0.75
■	□	■	0.64
■	□	■	0.32
■	□	■	0.44
■	□	■	0.52
■	□	■	0.81
■	□	■	0.34
■	□	■	0.64
■	□	■	0.72
■	□	■	0.57

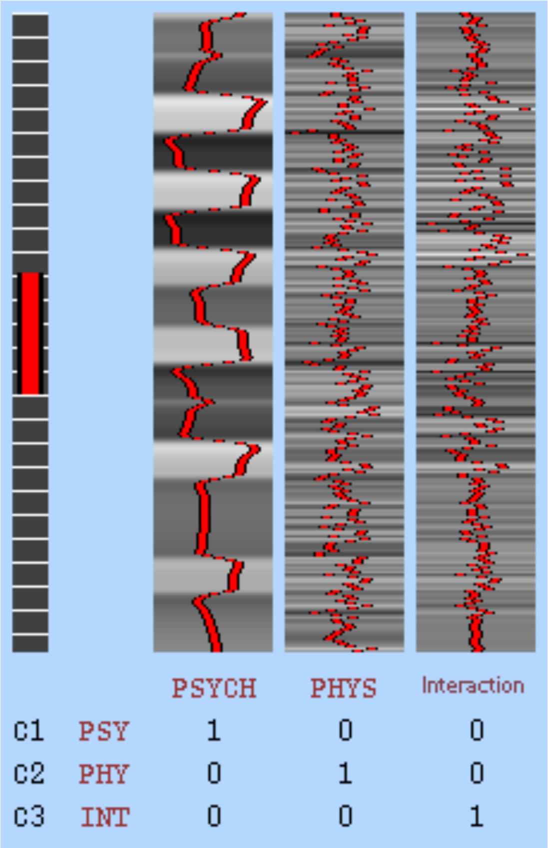
Figure 2. Design matrices when adding a continuous covariate.

The left panel demonstrates the model with only a main effect of performance (in this case % correct responses). The right panel illustrates the model with a performance / group interaction. The values represent the percentage of correct responses on the task (without mean centering; Figure adapted from Poldrack et al., 2011).

6.2.2. Psychophysiological Interaction analysis

A Psychophysiological Interaction (PPI) analysis reveals how the functional connectivity between a seed region and any other voxel in the brain is modulated by task condition (Friston et al., 1997; Rogers et al., 2007). The PPI thus represents the vector product of two factors: the psychological variable (PSY, which represents the task versus control task related BOLD responses) and the physiological factor (PHY, which contains the time-course of the seed region). The first step of the analysis is to determine an appropriate seed region and the task contrast of interest based on a priori hypotheses. There are several possibilities to choose an appropriate seed region. For example, one might have an a priori hypothesis about the functional connectivity between certain regions one can define from structural brain scans. Another possibility is to select a seed region based on functional activations in an initial general linear model (GLM) analysis. For instance, if the amygdala was more active during the task of interest versus the control task, in the PPI analysis one can investigate which regions have an increased functional connectivity with the amygdala during the task of interest versus the control task. After choosing an appropriate seed region and contrast of interest, the next step is setting up the single subject GLM analysis including the main factors PSY and PHY, as well as the interaction between both (see Figure 3). Finally, the interaction term is used as a contrast in a higher-level group analysis.

In study 3, we conducted a PPI analysis to identify potential group differences in the coupling between core prosody processing regions when processing emotional versus neutral prosody. Based on prosody processing model by (Wildgruber et al., 2006), we chose the right STS as the seed region for the analysis and investigated group differences in the coupling between right STS and bilateral IFG for emotional versus neutral prosody. Furthermore, we investigated whether changes in the coupling of prosody processing regions were distinctly modulated by emotion complexity (social versus basic emotions) in typically developed controls compared to individuals with ASD. Based on a priori hypotheses regarding the role of the STS in prosody processing (e.g., Wildgruber et al., 2006) and the prominent role of the amygdala and STS in social information processing in particular (Pelphrey et al., 2004), we chose the right STS as a seed region for this analysis and investigated significant group differences in the coupling between the right STS and the left and right amygdala for social versus basic emotional prosody. A detailed description of the respective hypotheses and PPI analyses can be found in the methods section of study 3.



		PSYCH	PHYS	Interaction
C1	PSY	1	0	0
C2	PHY	0	1	0
C3	INT	0	0	1

Figure 3. Design for a PPI single subject analysis.

Example design matrix contains the main factors and their interaction in FSL. PSY: Psychological factor, which represents the task of interest versus the task of no interest); PHY: Physiological factor, which contains the extracted time course from the seed region); INT: interaction of the psychological and physiological factors.

7. Summary of empirical studies

In this chapter, I will briefly outline the three empirical studies that form the basis of this dissertation (Rosenblau et al., in revision; Rosenblau et al., submitted; Rosenblau et al., submitted).

7.1. Study 1

Approximating implicit and explicit mentalizing with two naturalistic video-based tasks in typical development and autism

Recently, it has been proposed that individuals with ASD have greater impairments in implicit than in explicit mentalizing (Senju et al., 2009).

However, most previous studies assessed explicit mentalizing with static and abstract tasks that might lack sensitivity for the impairments of individuals with ASD (Baron-Cohen, 2001). Furthermore, tasks assessing implicit mentalizing lacked a direct measure of mentalizing performance (Zaki and Ochsner, 2011). Due to the differences in methodology, it has remained inconclusive how implicit and explicit mentalizing processes are to be distinguished and how they interact in typically developed individuals and in individuals with ASD. In study 1 my co-authors and I investigated implicit and explicit mentalizing with two naturalistic and comparable indirect and direct tasks, respectively.

Twenty-eight ASD participants and 23 typically developed controls, matched for age, gender and IQ, performed the newly developed indirect and direct mentalizing tasks. In both tasks participants first saw film scenes displaying social interactions. In the indirect task, they had to subsequently select the correct continuation of the film scene from four different options. Importantly, they were not explicitly asked to infer or label mental states, but instead they were told to simply solve a film puzzle. In the direct task, after they watched the film scenes, they were asked to infer how a protagonist was feeling at the end of the scene and to select the correct label and reasoning for his or her mental state from four different options (e.g., Sarah is angry, because her boyfriend forgot about their date). Both tasks allowed the tracking of accuracy and reaction times and thus an objective comparison of task performance between the direct and indirect conditions.

Both naturalistic tasks were reliable and produced the required amount of variability in the performance of control participants. Furthermore, ASD participants had significantly fewer correct responses than controls on both tasks, and accuracy scores of both tasks were negatively correlated with symptom severity, suggesting that more impaired individuals scored lower. Finally, the relationship between direct and indirect task performance differed significantly between ASD and control participants. In controls, performance scores on the direct and indirect tasks were not significantly correlated, whereas, in the ASD group they were highly intercorrelated. The group difference between the correlations was significant. These findings support the notion that implicit and explicit mentalizing processes can be differentiated to a certain degree by behavioral measures in typically developed controls, but not in individuals with ASD.

In sum, both the direct and indirect tasks were equally sensitive to the social impairments of individuals with ASD, suggesting that their pervasive social impairments concern implicit as well as explicit aspects of mentalizing. The results obtained by my co-authors and me underscore the importance of investigating implicit and explicit social cognitive skills, such as mentalizing, with naturalistic tasks that are more sensitive to the impairments of individuals with ASD. Furthermore, we were able to specify the relationship between explicit and implicit mentalizing processes in typically and atypically developed individuals. Our results suggest that in typically developed individuals implicit and explicit mentalizing processes can be distinguished to a certain degree, whereas in individuals with ASD they are closely linked.

7.2. Study 2

The role of the amygdala in implicit mentalizing while watching naturalistic social interactions

There is a substantial discrepancy between the way mentalizing is assessed in experimental settings (where participants have to explicitly infer mental states from mostly static and abstract stimulus material, such as comics or written stories (Saxe and Kanwisher, 2003; Walter et al., 2004), and mentalizing in real life social interactions (where individuals have to implicitly pick up and integrate dynamic, multimodal social cues (Zaki and Ochsner, 2009). This discrepancy hinders the understanding of the neural mechanisms of mentalizing in real life social settings, as well as of social impairments in psychiatric disorders, such as ASD. Another shortcoming of studies in the field of social neuroscience in general is the fact that they investigated social cognitive processes disregarding whether or not these processes supported accurate behavior. In consequence, the relationship between behavioral performance and neural processing has remained largely unclear. In this study, we investigated the neural mechanisms underlying naturalistic mentalizing, using a new video-based task that demands multimodal and more spontaneous processing of dynamic social stimuli in typically developed individuals and in individuals with ASD. In a next step, we aimed at investigating the relationship between social brain regions involved in spontaneous mentalizing and accurate implicit mentalizing performance.

Twenty individuals with ASD and 22 typically developed controls were matched for age, gender and IQ. This sample largely overlapped with the sample of study 1, and thus all except of one ASD participant had already completed the newly developed behavioral direct and indirect mentalizing tasks. In the fMRI experiment introduced in this study, participants watched film scenes comprising social interactions between two to three protagonists. The scenes were split into three consecutive film clips. During the mentalizing condition, participants were asked to make inferences about clip-by-clip changes in the protagonists' affective states, relying on affective mentalizing. Specifically, participants were asked to judge whether a protagonist was feeling "worse", "equally well", or "better" than in the previous clip. During the physical inference (PI) condition, participants saw the same film scenes, but the faces were blurred to reduce the social saliency of the clips and thus attentional demands. In the PI condition participants were asked to judge clip-by-clip changes in the protagonists' body movements (e.g. head-turning: Does Mrs. Hauser turn her head less often, equally often, or more often than in the last film clip?). Participants' eye movements were tracked during the experiment to ensure that controls and ASD individuals paid a similar amount of attention to the screen.

During spontaneously occurring mentalizing (while watching naturalistic social scenes in the mentalizing as opposed to the PI condition), typically developed controls showed higher activity of classical mentalizing regions (e.g., MPFC, STS and TPJ) and in addition of the insula and amygdala. Moreover, amygdala activity during spontaneous mentalizing predicted implicit mentalizing performance assessed with the behavioral indirect mentalizing task. Individuals with ASD showed less activity in the amygdala and in the STS during spontaneous mentalizing compared to controls and a reduced correlation between amygdala activity and performance on the indirect mentalizing task.

In conclusion, by investigating spontaneous mentalizing with a naturalistic and dynamic fMRI task, my co-authors and I revealed the crucial role of the amygdala and STS in naturalistic mentalizing and in the social impairments of individuals with ASD. Furthermore, we could relate spontaneous neural processing of mental states in naturalistic settings to accurate implicit mentalizing performance in typically developed controls. In individuals with ASD, reduced amygdala activation and the reduced correlation between amygdala activity and performance highlight the specific role of the amygdala for accurate implicit mental state inferences in typical development.

7.3. Study 3

Emotional prosody processing in Behavior and Brain Function: Insights from Autism Spectrum Disorder

Efficient social communication crucially depends on processing subtle nonverbal cues such as emotional prosody (Belin et al., 2004). Individuals with ASD are characterized by severe deficits in social communication, however, whether or not they are impaired in recognizing social emotional prosody remained underinvestigated. On the neural level, emotional prosody processing has been repeatedly shown to involve the IFG bilaterally and the right STS (e.g., Wildgruber et al., 2006), but to date, little is known about how this prosody processing network is modulated by the social relevance of emotions (social versus basic emotions), and how it relates to accurate prosody recognition and social functioning. For instance, the neural basis of the social communication deficits observed in ASD has remained elusive. In this study, my co-authors and I investigated emotional prosody processing and recognition with newly developed, naturalistic behavioral and fMRI tasks. The stimuli consisted of sentences spoken by a broad range of male and female speakers and included a wider range of social emotions than in previous studies. Specifically, we aimed at extending previous prosody processing models by investigating the relationship between the neural processing of emotional prosody and behavioral performance in typically developed individuals and in individuals with ASD.

Twenty-seven individuals with ASD and matched control participants (N=22) performed the behavioral prosody recognition task. In this task participants listened to semantically neutral sentences that contained emotional prosody. The majority of items comprised social emotions. Subsequently, participants were asked to label the emotional prosody from four different options. In a separate session, a sample of 20 ASD participants and 21 matched controls, largely overlapping with the initial behavioral sample, performed the emotional prosody fMRI task. In this task participants listened to semantically neutral audios spoken with emotional or neutral prosody and had to either indicate the speaker's gender (implicit condition) or the correct emotion label from two options (explicit condition). The emotional prosody sentences covered six basic and six social emotions, matched for valence and arousal levels as determined by pre-ratings.

Compared to controls, individuals with ASD were slower and less accurate at recognizing social emotions in the behavioral task. On the neural level, emotional prosody processing implicated a fronto-temporal network including the STS and IFG bilaterally over all participants. In individuals with ASD, however, the coupling between the core prosody regions, right STS and right IFG, was significantly reduced for emotional versus neutral prosody. When processing social versus basic emotions, individuals with ASD recruited the amygdala and STS to a lesser extent, and the functional connectivity between these two regions was significantly reduced in individuals with ASD compared to controls. Importantly, when processing social emotions, activity of core prosody regions, such as the bilateral STS and IFG, predicted accurate social emotion recognition on an independent task to a higher extent in controls than in individuals with ASD.

Taken together, the results of study 3 reveal the important role of the prosody processing network, including the IFG, STS and the amygdala, for accurate prosody recognition of social emotions. In contrast, the reduced functional connectivity between core prosody regions, along with a reduced relationship between activity in these regions and prosody recognition, may account for the pervasive impairments in social communication of individuals with ASD.

8. General discussion and future directions

In this chapter, I will first relate the findings of the three empirical studies, summarized in the previous chapter, to the general research questions of this dissertation. Second, based on the empirical results, I will propose a potential model of dynamic social information processing, and relate this model to previous research. In the third section, I will discuss how the proposed model could potentially guide future research and how it could be extended. Finally, I will discuss the potential implications of the empirical results and the proposed model for the development of social cognitive trainings and interventions.

8.1. Discussion of research questions

Question 1: How can implicit and explicit social behavior be differentiated and how do they contribute to social functioning in naturalistic settings? (Study 1)

To address this first question we developed two naturalistic performance-based tasks for the assessment of implicit and explicit mentalizing. In typically developed controls implicit and explicit mentalizing processes could be distinguished to a certain degree. Our results thus support the recently proposed distinction of two systems of belief reasoning in typically developed individuals (Apperly and Butterfill, 2009). Individuals with ASD showed similar impairments in both implicit and explicit mentalizing. This finding contradicts the notion that individuals with ASD are more impaired in implicit than in explicit mentalizing (see e.g., Senju (2013)). However, the study, which first proposed this distinction (Senju et al., 2009) did not use adequate methodological formats to objectively compare implicit and explicit mentalizing performance and investigated explicit mentalizing with classical false belief tasks that lack the required sensitivity to assess subtle mentalizing deficits in high-functioning adults with ASD (see Baron-Cohen (2001)). Finally, in contrast to typically developed controls, accuracy scores of individuals with ASD on the direct and indirect mentalizing tasks were highly intercorrelated.

This relationship suggests that common social impairments underlie both implicit and explicit mentalizing processes.

Taken together, implicit and explicit mentalizing processes are distinct to some degree in typically developed individuals, thus mediating distinct aspects of social cognition in naturalistic settings. In contrast, in individuals with ASD deficits in implicit and explicit mentalizing are closely connected.

Question 2: What are the neural mechanisms of mentalizing in naturalistic settings and how do they support accurate mental state inferences? (Study 2)

In order to address the second question, we developed a naturalistic movie-based fMRI task. To approximate spontaneously occurring mentalizing in naturalistic settings, participants watched movie-scenes of social interactions between two or three protagonists. In the subsequent analysis we compared neural activity while watching the movie-scenes in the mentalizing as opposed to the control condition. In typically developed controls, this contrast yielded higher activity of core mentalizing regions, such as MPFC, STS, IFG and TPJ, and furthermore of the amygdala and insula. Both the amygdala and insula have been tightly linked to emotion processing and empathy. Amygdala and insula are not thought to be involved in mental state inferences per se (Olsson and Ochsner, 2008), but rather in emotion processing and emotional engagement with to the particular task (Moll et al., 2002; Carr et al., 2003; Schilbach et al., in press). Compared to controls, individuals with ASD showed reduced amygdala and STS activity during spontaneous mentalizing. Both regions have been tightly linked to processing dynamic social information (Allison et al., 2000; Pelphrey et al., 2004; Adolphs et al., 2005), in particular when information signals intentions (Pelphrey et al., 2004). Furthermore, both regions have been repeatedly linked to the social impairments of individuals with ASD on a variety of tasks (Adolphs, 2010b; Pelphrey et al., 2011). Our results thus replicated previous findings and highlighted the important role of the amygdala for implicit mentalizing in naturalistic settings. In typically developed controls, amygdala activity during spontaneous mentalizing predicted implicit mentalizing performance on an independent behavioral task, whereas this relationship was significantly reduced in individuals with ASD.

To summarize, our results suggest that mentalizing in naturalistic settings recruits the classical mentalizing regions as well as the amygdala and insula – regions that are most likely involved in evaluating the social-emotional information within the context of our task. The amygdala in particular seems to play a prominent role for implicit mental state inferences in naturalistic settings. Importantly, amygdala activity during spontaneous mentalizing in naturalistic settings predicted implicit mentalizing performance. Individuals with ASD showed reduced activity of the amygdala and STS during spontaneous mentalizing in naturalistic settings and a reduced relationship between amygdala activity and performance. Given that both regions play a key role in decoding and evaluating dynamic social information, abnormal functioning of the amygdala and STS might be tightly linked to the social impairments of individuals with ASD.

Question 3: What are the neural mechanisms of naturalistic prosody processing and how do they support prosody recognition? (Study 3)

In the third study, my coauthors and I investigated prosody processing and recognition using a variety of male and female speakers and a wide range of social emotions. In typically developed controls, we replicated the well-established prosody-processing network (Wildgruber et al., 2006), including the right STS and bilateral IFG. Importantly, activity in frontal regions, including the right IFG, correlated with accurate explicit prosody recognition on the behavioral task. The right IFG has been repeatedly implicated in the emotional evaluation of prosody (Schirmer and Kotz, 2006). Our results thus extend previous findings by highlighting the role of the right IFG in accurate emotional prosody recognition. Individuals with ASD showed less activity of the amygdala and STS for social versus basic emotions. This finding underscores the importance of these regions in processing social information that signalizes intentions also in the auditory modality. Furthermore, the relationship between the prosody-processing network, including bilateral STS and IFG, and behavioral performance was reduced in individuals with ASD relative to controls. This suggests that the prosody-processing network supports accurate prosody recognition in particular.

In sum, activity within the well established prosody processing network supports accurate prosody recognition in typically developed individuals and to a much lesser extent in individuals with ASD. Furthermore, compared with controls, individuals with ASD showed reduced activity of the amygdala and STS when processing social versus basic emotions. This finding underscores the importance of the amygdala and STS in social information processing that requires mental state inferences.

Question 4: How does the coupling between social brain regions contribute to social cognition and social functioning?

In all three studies, my co-authors and I investigated typically developed participants and participants with ASD that substantially differ with respect to the level of social functioning. In the third study, in particular, we investigated how the coupling between social brain regions contributes to social information processing and thus to the level of social functioning. Specifically, we found that the functional connectivity between the right STS and IFG for emotional versus neutral prosody was significantly higher in controls than in individuals with ASD. The STS has been proposed to be primarily responsible for the perception and representation of prosodic information, which is supposed to be subsequently evaluated in the IFG (Ethofer et al., 2006). Our results extend this prosody processing model by showing that the coupling between the right STS and right IFG distinguishes typical from atypical emotional prosody processing. Furthermore, relatively to controls, individuals with ASD showed a reduced functional coupling between the STS and amygdala when processing social versus basic emotions. The STS and amygdala are linked via reciprocal connections (Allison et al., 2000) and both regions crucially support dynamic social information processing independent of modality (Pelphrey and Carter, 2008). Thus, dysfunctional connections between the amygdala and STS could account for the pervasive social deficits of individuals with ASD.

In conclusion, functional connectivity between social brain regions differs between individuals with low and high levels of social functioning. Individuals with ASD showed a significantly reduced functional coupling between social brain regions for emotional versus neutral prosody and for social versus basic emotions as compared to typically developed individuals. The reduced functional connectivity between social brain regions most likely leads to a reduced capacity of individuals with ASD to integrate social information.

Question 5: What are the particular roles of the STS and amygdala in naturalistic and dynamic social information processing?

Our results showed that STS and amygdala play important roles in processing naturalistic and dynamic social information in the visual and auditory modality. Both regions seem to be crucially involved in different stages of dynamic social information processing. The STS has been involved in extracting and representing dynamic information (Wildgruber et al., 2006), in particular when information signals intentions (Castelli et al., 2002; Wildgruber et al., 2006). In contrast, the amygdala has been associated with evaluating the social and emotional saliency of the information (Haxby et al., 2000; Adolphs, 2010b). As such, the interplay between these regions seems to support accurate implicit social information processing. Consistent with previous literature (Baron-Cohen et al., 1999; Baron-Cohen, 2001; Castelli et al., 2002), our results showed that individuals with ASD display reduced activity of the amygdala and STS in the visual and auditory modality and a reduced functional coupling between these two regions when processing social information in the auditory modality. Given that both the amygdala and STS have been tightly linked to the development of mentalizing abilities (Shaw et al., 2004), dysfunctional activations and connections between these regions could lie at the heart of the pervasive mentalizing impairments that concern explicit as well as implicit processes in individuals with ASD.

8.2. Model of dynamic social information processing

The proposed model outlines the different processing steps and the corresponding neural mechanisms that are at play when individuals process dynamic social information (see Figure 4).

In real life social settings, individuals are confronted with dynamic information, most of which reflects some kind of social intention (Zaki and Ochsner, 2009). Dynamic social information can be perceived visually as well as auditory. In all three studies of this dissertation, we investigated social information processing with dynamic video- or audio-based stimuli (in studies 1 and 2 we used video-based tasks and in study 3 the tasks comprised audios). The accuracy of social information processing determines the social response and thus the level of social functioning of an individual (Kennedy and Adolphs, 2012).

The majority of psychiatric and neurological disorders are characterized by impairments in social functioning (Kennedy and Adolphs, 2012). In the three studies of this dissertation the degree of social functioning has been dichotomized into typical and impaired social functioning. With respect to the latter category, my co-authors and I investigated individuals with ASD that represent a model of impaired social cognition and social functioning.

Dynamic social information is first decoded within the STS. The STS has been commonly implicated in extracting and representing dynamic information in the visual as well as in the auditory domain. With respect to face processing, Gobbini and Haxby (2007) have assigned the STS to the core system that deals with encoding of dynamic visual information, such as facial movements (changes in the direction of eye gaze or facial expression). In the auditory domain, using a DCM model, Ethofer and colleagues (2006) established that the STS is the input region of the prosody processing system, where information is extracted and represented. Furthermore, the STS seems to be particularly sensitive to social information that signals mental states and intentions (Bahnemann et al., 2010) and has thus been assigned to the core mentalizing network (Mar, 2011). In the same vein, aberrant STS activity has been tightly linked to the social impairments of individuals with ASD (Pelphrey et al., 2011). Our results extend the current literature by showing that the STS is crucially involved in processing dynamic social information in naturalistic settings. Typically developed controls showed higher STS activity compared to controls when spontaneously tracking others' intentions during social interactions (see study 2 for more details). Similarly, typically developed individuals recruited the STS to a higher degree than individuals with ASD when processing social emotions from speech, which involve mentalizing (see study 3 for more details).

Subsequently, the dynamic information has to be further evaluated. Separable neural networks support lower-level implicit and higher-level explicit evaluation processes (Olsson and Ochsner, 2008).

The amygdala has been extensively implicated in implicit emotion processing that contributes to social behavior (Adolphs, 2009), in particular in coding the emotional saliency of stimuli (Whalen et al., 1998). With respect to social cognition, the amygdala supports the orientation towards socially salient stimuli, such as the eye region (Adolphs et al., 2005). In the same vein, amygdala response seems to be stronger for unknown as compared to familiar social stimuli (Gobbini et al., 2004; Leibenluft et al., 2004; Herry et al., 2007).

Dynamic social cues also contain important information about others' beliefs and intentions. Reasoning about others' mental states and intentions requires higher-level cognitive processes that have been tightly linked to the core mentalizing network comprising frontal, temporal and parietal regions such as the MPFC, IFG, and TPJ (Saxe and Kanwisher, 2003; Amodio and Frith, 2006; Mar, 2011). The MPFC has been prominently engaged in thinking about one's own mental state or that of another person. The TPJ has been closely related to imagining and attributing beliefs to someone else and the IFG has been consistently implicated in the explicit evaluation of emotional states (Schirmer and Kotz, 2006). Although a recent metaanalysis by (Mar,

2011) established the involvement of the IFG in mentalizing, its precise role has yet to be established.

In naturalistic settings, both implicit and explicit sets of processes are at play and interact with each other (Cunningham and Zelazo, 2007; Lieberman, 2007) depending on the nature of the social stimuli. Social information rarely requires exclusively explicit or exclusively implicit processing, but rather a combination of these two (implicit and explicit social cognition can be viewed as two poles of a continuum, (Cunningham et al., 2007). Thus, the networks mediating implicit and explicit processes interact with each other via reciprocal connections (Cunningham and Zelazo, 2007).

Processing naturalistic stimuli involved the amygdala as well as the MPFC, TPJ and IFG in typically developed individuals (see studies 2 and 3 for an exhaustive list of activated regions). Importantly, typically developed individuals showed a higher functional coupling than individuals with ASD between the STS and the IFG when processing emotional versus neutral prosody, and between the STS and amygdala when processing social versus basic emotions. This underlines the importance of the connections between the STS and the amygdala and between the STS and the IFG for unimpaired social information processing.

Furthermore, our results provide direct evidence of an involvement of the amygdala in implicit and of the IFG in explicit social behavior. In typically developed individuals, amygdala activity while watching naturalistic social interactions significantly predicted implicit mentalizing performance. Activity of prefrontal regions, including the right IFG, was significantly correlated with explicit emotion recognition (please refer to study 2 and 3 for more information). Thus, on the neural and behavioral level, both sets of processes can be distinguished to some extent in typically developed individuals (My co-authors and I established the behavioral distinction between the processes in study 1, and the distinction between neural networks that support implicit and explicit social behavior in study 2 and 3, respectively).

Finally, the empirical results of this dissertation support the notion that individuals with ASD are characterized by pervasive social impairments that are reflected on the behavioral and neural level and in the interplay between these levels. In line with a substantial body of literature linking the social deficits of individuals with ASD to aberrant amygdala and STS activity (e.g., Adolphs, 2009; Pelphrey et al., 2011), we found reduced activity of these regions in individuals with ASD in the visual and auditory modality. Furthermore, the functional connectivity between these regions was significantly reduced during social information processing compared to controls. Previous studies that investigated mentalizing with abstract stimuli and focused on higher-level social cognitive processes, such as inferring others' beliefs from written stories, found reduced activity of the TPJ and MPFC in individuals with ASD (Castelli et al., 2002; Lombardo et al., 2011). My co-authors and I did not find reduced activity of the higher-level social cognitive network in individuals with ASD. However, we did find a reduced relationship between this network and explicit social behavior as well as a reduced relationship between the amygdala, which mediates lower-level emotional processes, and implicit social behavior in individuals with ASD compared to controls. Taken together, individuals with ASD are characterized by severe impairments in social information processing that affect implicit and explicit processes to a similar degree (In study 1 my co-authors and I established that implicit and explicit mentalizing processes are impaired and closely related to each other).

In the following discussion section I will outline how components of the proposed model can be modulated to assess further research questions. For instance, instead of dichotomizing social functioning (e.g., impaired versus unimpaired social functioning), future studies could investigate the interplay between social functioning and social cognition over the course of development, and further address the question of how the neural development impacts the development of social cognition. Finally, I will discuss how the current empirical findings and the proposed model could help to refine social cognitive trainings and interventions.

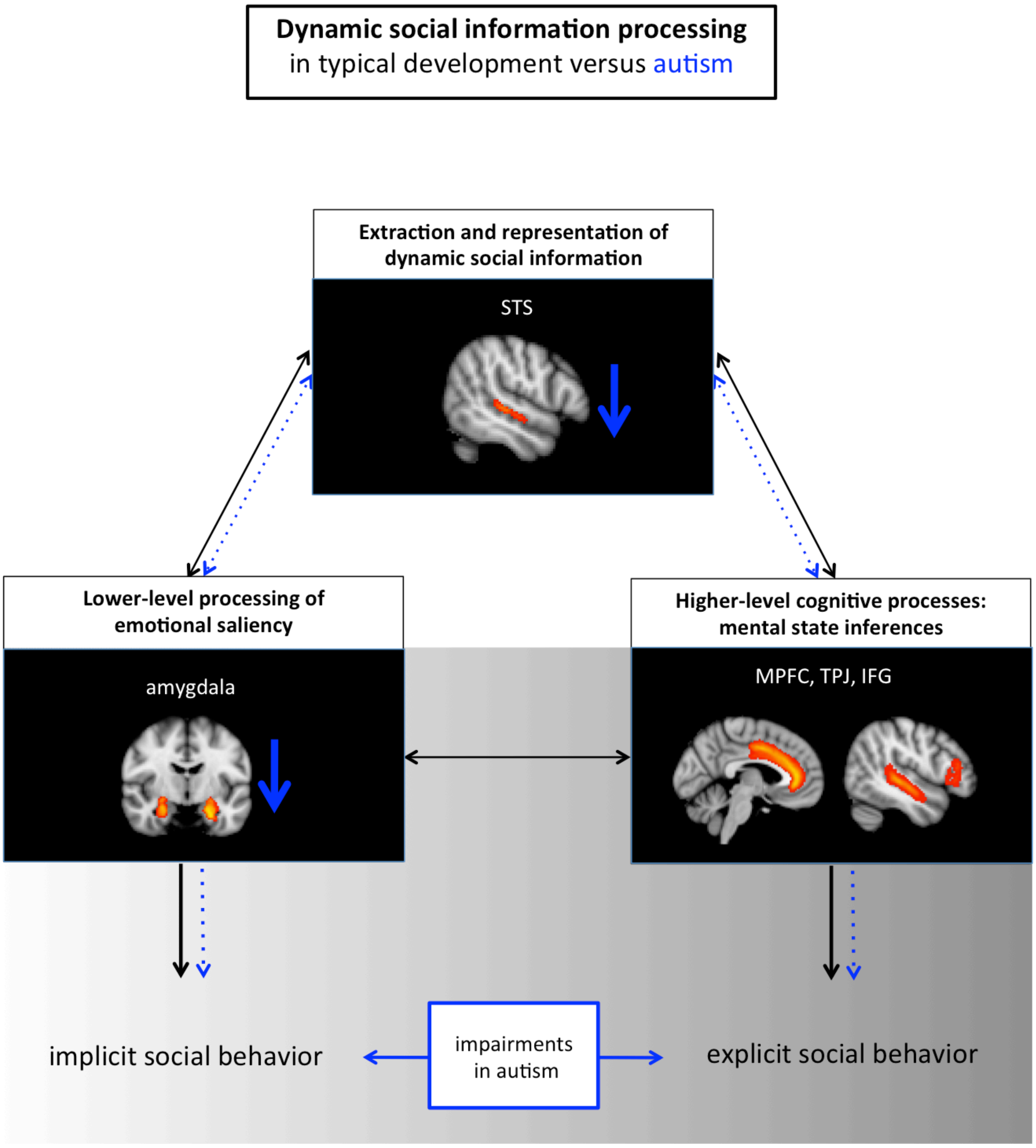


Figure 4. Potential model of dynamic social information processing in typical development versus autism.

Figure 4. Potential model of dynamic social information processing in typical development versus autism. (continued)

Dynamic social information involves lower-level emotional and higher-level cognitive processing. On the neural level, the STS is involved in the extraction and representation of social information. Subsequently, evaluating the social saliency of the respective information (lower-level emotional processing) recruits the amygdala. Higher-level cognitive processes, such as the explicit evaluation of mental states (thoughts, emotions, intentions) is mediated by a network encompassing the MPFC, TPJ and IFG. Functional connectivity between the STS and amygdala and STS and IFG (black arrows) ensures the integration of the different (emotional and cognitive) aspects of social information. Lower- and higher-level social information processing is directly linked to implicit and explicit social behavior, respectively. Amygdala activity predominantly supports implicit social behavior, whereas activity of cortical regions, such as the IFG, supports explicit social behavior, e.g., explicit emotion recognition (the relationship is symbolized by black arrows). Depending on the social information (whether it requires more or less explicit processing), more or less higher-level cognitive processing is needed (the continuum between implicit and explicit is represented by the gray shading).

Individuals with ASD are characterized by pervasive social deficits concerning implicit and explicit social information processing. (The blue arrows summarize the significant group differences between ASD individuals and controls, which were obtained in the three studies of this dissertation.) The impaired representation of dynamic social cues is related to reduced STS activity in individuals with ASD compared to controls (blue arrow pointing down). Impaired social information processing is associated with reduced functional connectivity between the STS and amygdala and STS and regions that support higher-level cognitive processing, such as the IFG, (blue dotted arrows). Subsequently, reduced amygdala activity when processing naturalistic social cues implies dysfunctional social saliency processing (blue arrow pointing down) and is related to impaired implicit social behavior (e.g., lower implicit mentalizing accuracy) in individuals with ASD (left panel: blue dotted line). Impaired explicit social behavior (e.g., explicit emotion recognition) is related to reduced activity of regions supporting higher-level cognitive processing, e.g., the IFG (right panel: blue dotted line).

8.3. Future directions for research and interventions

The research summarized in this dissertation and the proposed model of social information processing have several implications for future research and the development of social cognitive interventions.

First, our operationalization of implicit mentalizing in Study 1 differs from the conceptualization of implicit mentalizing in the field of developmental psychology. While developmental psychologists indirectly infer participants' implicit mentalizing abilities from their gaze patterns, without asking them explicitly to perform a certain task (see e.g., Onishi and Baillargeon (2005)), our operationalization of implicit is more narrow and direct. It involves the conscious consideration of multiple answer options without providing explicit prompts that instruct participants to infer others' mental states. The advantage of our indirect mentalizing task, however, is that it allows us to directly assess participants' performance and to relate it to explicit mentalizing performance. Aiming at a more precise characterization of implicit mentalizing processes, future studies should simultaneously investigate implicit mentalizing with gaze tracking and more direct measures, such as the newly developed indirect task, and subsequently investigate to what extent they capture the same processes.

Second, the proposed model of social information processing in naturalistic settings suggests bidirectional connections between regions belonging to different networks mediating social information processing (the extraction and representation of social information, lower-level emotional and higher-level social processing). This assumption is primarily based on the existence of anatomical connections between regions assigned to these different processing steps (Adolphs et al., 2005; Friederici, 2012; Iidaka et al., 2012) and on study 3 of this dissertation, which found task-based functional connectivity between regions assigned to the different information processing levels. To further specify the model, future studies could investigate the effective connectivity (i.e. causal or directed influence) between brain regions assigned to the proposed components of social information processing, using a DCM approach (Friston et al., 2003; Stephan and Friston, 2010).

Another possibility to extend the current model would be to investigate the relationship between social behavior and the underlying neural mechanisms over the course of development. Adolescence has been identified as a particularly interesting period to study this particular relationship (Blakemore and Mills, 2013). For instance, the development of mentalizing abilities as well as the structural and functional development of brain regions typically assigned to the mentalizing network extends beyond early childhood (Blakemore and Choudhury, 2006; Blakemore, 2012). Studies investigating structural changes from adolescence to adulthood found increasing cortical thickness in the temporal lobe and decreasing cortical thickness in medial frontal and lateral parietal lobes (Shaw et al., 2008), whereby these structural changes parallel changes in brain function (Blakemore, 2012; Cohen Kadosh et al., 2013). In adolescence, the recruitment of the MPFC in mentalizing decreases, while the recruitment of posterior temporal regions, such as the STS, increases with age (Blakemore et al., 2007). How the structural and functional development of social brain regions in adolescence might affect mental state understanding remains an open question (Blakemore, 2012).

Finally, the empirical results presented here and the proposed model of dynamic social information processing extend the literature on the social cognitive impairments of individuals with ASD. Given that a substantial number of psychiatric and neurological disorders are accompanied by impairments in social functioning (Kennedy and Adolphs, 2012), future research should investigate if and to what extent the proposed model of impaired social information processing in autism can be generalized to other psychiatric disorders, such as depression or schizophrenia.

A more practical implication of the empirical research conducted in the framework of this dissertation is that it highlights the importance of training social cognitive skills with dynamic and naturalistic stimuli. Previous studies (e.g., Dziobek et al., 2006) and the empirical studies summarized in this dissertation have shown that dynamic and naturalistic social stimuli represent a highly sensitive means to assess the social cognitive deficits of individuals with ASD. In consequence, they might also represent more sensitive training material. Most social cognitive trainings to date have comprised either abstract (e.g., Baron-Cohen et al., 2007) and static stimuli (e.g., FEFA, Bolte et al., 2006), or focused on specific social cognitive skills within a specific modality (e.g. emotion recognition from faces or voices, (Golan et al., 2006). Trainings that focus on the audio-visual integration of different types of social information (facial expressions, body language, semantics, the tone of voice and specific context information) may have the potential to produce training effects that can be generalized to real life social interactions.

9. Conclusion

This dissertation advances the understanding of dynamic social information processing in naturalistic settings by providing a framework that integrates different levels of description and analysis: the social brain, social cognition, social behavior, and social functioning. Specifically, dynamic social information processing in typically developed individuals requires the extraction and representation of social information within the STS. The subsequent evaluation of emotional and social saliency involves the amygdala and higher-level cognitive processing of mental states involves activity in core regions of the mentalizing network including the MPFC, TPJ and IFG. Activity in regions of the lower- and higher-level information processing components predicts accurate implicit and explicit social behavior, respectively, which can be dissociated to a certain degree. The model also incorporates insights into aberrant dynamic social information processing in individuals with ASD. The pervasive social impairments in ASD concern all levels of information processing: the social brain, social cognition, social behavior, and importantly the relationship between the social brain and social behavior. On the neural level, individuals with ASD show aberrant activation of the STS and amygdala during dynamic social information processing, and reduced functional connectivity between the STS and amygdala as well as between the STS and IFG. On the behavioral level, impaired social cognitive abilities are similarly visible in indirect and direct tasks, suggesting similar degrees of impairments in implicit and explicit social cognition. In contrast to controls, implicit and explicit processes in individuals with ASD are tightly linked. Finally, the direct relationship between activity in social brain regions, such as the amygdala and IFG, and accurate implicit and explicit social behavior is significantly reduced in individuals with ASD compared to controls. In sum, the current model could provide a fruitful basis for future research on dynamic social information processing.

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11. Research Articles

Study 1

Rosenblau, G., Kliemann, D., Heekeren, H.R., Dziobek, I. (in revision). Approximating implicit and explicit mentalizing with two naturalistic video-based tasks in typical development and autism. Journal of Autism and Developmental Disorders.

Study 2

Rosenblau, G., Kliemann, D., Lemme, B., Walter, H., Heekeren, H.R., Dziobek, I. (submitted). The role of the amygdala in implicit mentalizing while watching naturalistic social interactions. Journal of Neuroscience.

Study 3

Rosenblau, G., Kliemann, D., Dziobek, I., Heekeren, H.R. (submitted). Emotional prosody processing in Behavior and Brain Function: Insights from Autism Spectrum Disorder. Journal of Neuroscience.

Approximating implicit and explicit mentalizing with two naturalistic video-based tasks in typical development and autism

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Abbreviated title:

Approximating implicit and explicit mentalizing

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Abstract

Individuals with autism have been proposed to show greater impairments in implicit than explicit mentalizing. To test this proposition, we developed two naturalistic tasks for a performance-based approximation of implicit and explicit mentalizing in 28 individuals with autism and 23 matched typically developed (TD) participants. Both tasks were equally sensitive to the social impairments of individuals with autism. In TD participants, performance on the tasks did not correlate with each other, whereas in individuals with autism they were highly correlated. These findings suggest that implicit and explicit mentalizing processes are separable in typical development. In contrast, the close relationship between implicit and explicit mentalizing might indicate a lack of developmental specification of these processes in autism.

Keywords:

Autism Spectrum Disorder, cognition, mentalizing, behavioral assessment, implicit

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Acknowledgments

We thank Joerg Schulze, member of the Computer and Media Service team (CMS) at the Humboldt University, for his advice and support with the production and postproduction of the film stimuli and the actors. We also thank our student research assistants for their help with the stimulus production and data acquisition. In addition, we would like especially our participants on the autism spectrum for their participation in the study. This work was supported by a grant from the German Research Foundation (DFG; EXC 302).

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Abstract

Individuals with autism have been proposed to show greater impairments in implicit than explicit mentalizing. To investigate this notion, we developed two naturalistic tasks for a performance-based approximation of implicit and explicit mentalizing in 28 individuals with autism and 23 matched typically developed (TD) participants. Both tasks were equally sensitive to the social impairments of individuals with autism. In TD participants, performance on the indirect and direct task did not correlate with each other, whereas in individuals with autism they were highly intercorrelated. These findings suggest that implicit and explicit mentalizing processes are separable in typical development. In contrast, the close relationship between implicit and explicit mentalizing might indicate a lack of developmental specification of these processes in autism.

Keywords:

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The attribution of mental states to oneself and to others, also referred to as mentalizing, mental state attribution or theory of mind, represents one of the most important tools for successful social interaction (Premack and Woodruff, 1978). Using the false-belief test by Wimmer and Perner (1983) or similar simple tasks of mentalizing, researchers in developmental psychology established that around the age of 4 years typically developed children reach an important milestone in human development: they can explicitly differentiate between a false belief of another person and their own true belief (e.g. Perner et al., 2011). In contrast, the lack of false-belief recognition has been found to constitute a core deficit in autism spectrum disorders (ASD; Baron-Cohen et al., 1985; Leslie and Thaiss, 1992).

To date, a large number of studies have investigated explicit mentalizing deficits in individuals with ASD using direct tasks, i.e., asking participants directly to infer a protagonist's mental state from stories (Happe, 1993, 1994; Moran et al., 2011), photographs of persons' eye regions (Baron-Cohen et al., 2001) or from film scenes displaying social interactions (Dziobek et al., 2006). Such direct tasks prompt participants to infer others mental states, thus measuring explicit mentalizing processes.

Recently, the focus of interest in social cognitive research shifted from direct to indirect measures, i.e., the construct of interest is inferred indirectly from another behavior (De Houwer and Moors, 2010). In contrast to direct measures, indirect tasks aim at approximating implicit processes, which require less conscious control (Apperly and Butterfil, 2009). Here, we use the terms implicit and explicit to refer to social processes and social competencies and direct and indirect to refer to the types of measures.

Studies using indirect tasks provide increasing evidence for the notion that individuals with ASD show greater impairments in processing social cues implicitly, i.e., in the absence of direct prompts (see Senju, 2013 for a review). For instance, Kliemann et al., (2013) found that ASD participants showed greater deficits in implicit than in explicit facial emotion recognition, both assessed with comparable performance-based tasks. With regards to mentalizing, Senju et al., (2009) found that high-functioning individuals with ASD who did not show impairments on direct mentalizing tasks, showed a reduced spontaneous, i.e., more implicit, capacity for belief inference. Research using solely indirect measures, such as gaze tracking, report pronounced impairments of individuals with ASD in implicit social cognition. Studies using gaze tracking linked the social cognitive deficits of individuals with ASD with aberrant gaze patterns when looking at emotional faces (Kliemann et al., 2010) or naturalistic social scenes (Klin et al., 2002). Furthermore, using an indirect mentalizing task derived from game theory, Yoshida et al. (2010) found that the strategic behavior of individuals with ASD in a social cooperative game was less guided by implicit belief inference than in typically developed individuals.

Paralleling the observations of a differentiation between implicit and explicit mentalizing processes, Apperly and Butterfill (2009) have proposed a distinction between two systems of belief reasoning. The implicit system is postulated to be efficient but inflexible, while the explicit system is considered more flexible but also demanding more general cognitive resources. Up to now, it is largely unclear how implicit and explicit mentalizing processes can be distinguished and how they interact because previous studies either focused on only one of these processes or did not use comparable methodological formats that would allow unbiased comparisons (Frith and Frith, 2012; Nosek et al., 2011). Furthermore, the abovementioned indirect mentalizing tasks only assess implicit processes in terms of how participants respond to other minds and ignore how well they understand those minds. The accuracy of such implicit processes, however, is important, as the goal of everyday social cognition is to draw accurate inferences to guide social behavior (Zaki and Ochsner, 2011). Another shortcoming of most direct and indirect mentalizing tasks concerns their abstract and mostly static stimulus material. Abstract stimuli, such as written text or drawings, differ crucially from real life multimodal dynamic social cues that consist of visual and prosodic information embedded into a specific context that constrains our interpretations (Zaki and Ochsner, 2009). Due to the lack of complexity, some static mentalizing tasks have been reported to produce ceiling effects in adult populations (Baron-Cohen et al., 1997). In contrast, naturalistic movie-based tasks may have the potential to produce the required amount of variability in the performance of typically and atypically developed adults, making it possible to investigate individual differences in mentalizing. Since the deficits of individuals with ASD are more pronounced in unstructured real life social situations (Volkmar et al., 2004), naturalistic video-based tasks approximating real life scenarios are more sensitive in picking up mentalizing deficits of individuals with ASD than standard, static tasks (Dziobek et al., 2006).

To summarize, there is some evidence suggesting that individuals with ASD show greater impairments in implicit mentalizing, which is in line with the observation that ASD involves greater impairments in real life social settings (Volkmar et al., 2004), where mentalizing most often occurs implicitly (Frith and Frith, 2012). However, the interrelationships between implicit and explicit mentalizing processes in typical and atypical development remains unclear because of a lack of comparable indirect and direct tasks and because most standard mentalizing tasks to date are prone to ceiling effects in adults (Baron-Cohen et al., 1997), thus lacking sensitivity for a systematic comparison of implicit and explicit mentalizing processes in adult populations.

The aim of this study was to investigate implicit and explicit mentalizing processes in typically developed individuals and individuals with ASD. We thus designed two direct and indirect naturalistic movie-based tasks that allow the tracking of accuracy and reaction times and thereby a comparison of intra- and interindividual performance differences (see Kliemann et al., 2013 for a similar approach). The tasks mainly differ in their answering format. After watching a social interaction, in the indirect task, participants are asked to solve a film puzzle by detecting the most likely continuation of the film scene out of four different film clip options. Importantly, there is no explicit prompt to infer mental states. In contrast, in the direct task, the participants are asked to watch film clips and select the most likely verbal explanation for the protagonists' emotional states.

In order to systematically compare implicit and explicit mentalizing processes with the indirect and direct tasks respectively, we chose a more narrow conceptualization of implicit processes compared to studies using more indirect non-performance based measures, such as gaze tracking. Our indirect task involves the conscious evaluation of multiple answer options. Thus, our conceptualization of implicit mentalizing processes is not in line with the definition of implicit as a purely unconscious process (see e.g. Greenwald and Banaji, 1995). However, unawareness of the tested psychological construct is not always guaranteed and also not necessarily a criterion for an implicit process (Fazio and Olson, 2003; Nosek et al., 2011). In line with Fazio and Olson, (2003), our indirect task approximates implicit processes by seeking to provide information about the construct of interest without asking the participant verbally to report the desired information.

In this study we investigated the new tasks' sensitivity to atypical social cognition as well as possible dissociations between performance measured directly and indirectly. In line with previous studies, we expected the mentalizing impairments of individuals with ASD to be more pronounced in the indirect task. In order to investigate the tasks' validity and to further differentiate between mentalizing measured directly and indirectly, we included two widely established direct mentalizing measures, a performance and a self-report measure. We expected individuals with ASD to perform significantly lower than typically developed participants on both direct and indirect tasks. In accordance with the notion that implicit and explicit mentalizing processes are distinguishable, we expected the established direct mentalizing measures to be more strongly related to direct than to indirect task performance.

Methods

Participants

Twenty-eight adults with ASD (18 men, mean age = 33.1) and 23 typically developed (TD) participants (17 men, mean age = 32.4) with no reported history of psychiatric or neurological disorders participated in the study. The ASD participants were recruited through the autism outpatient clinic of the Charité – Universitätsmedizin Berlin, Berlin, Germany, or were referred by specialized clinicians. All of the participants were diagnosed according to the DSM-IV criteria for Asperger syndrome and autism without mental retardation (American Psychiatric Association, 1994). Diagnosis included two instruments that are considered the gold standard for diagnosing autism: the Autism Diagnostic Interview - Revised (ADI-R; Lord et al., 1994), if parental informants were available (N = 15), and the Autism Diagnostic Observation Schedule (ADOS, Lord et al., 2002). For 25 ASD participants, the diagnosis of

Asperger syndrome was additionally confirmed with the Asperger Syndrome and High-Functioning Autism Diagnostic Interview (ASDI, Gillberg et al., 2001). The groups were matched according to gender, age, and verbal IQ (see Table 1), as measured by the Mehrfachwahl-Wortschatz-Test (MWT; Lehrl, 1989), a German vocabulary test. All of the participants gave written informed consent prior to their participation and received payment for participating. The study was approved by the ethics committee of the German Society for Psychology (DGPs).

###Table 1###

Materials

The Arena of Emotions Tasks. We developed two different tasks to assess mentalizing directly and indirectly: the video-based Arena of Emotions tasks, which approximate real-life settings more closely than text or photo-based tasks. Importantly, the tasks have a similar structure and use similar material. The items of both tasks consist of short film clips (mean duration: 21.6 s, SD = 5.2, range: 9-31 s) depicting everyday social interactions (e.g., colleagues taking a lunch break or friends discussing holiday plans), preceded by a short written introduction that describes the context (e.g., the relationship between the protagonists) and the setting of the interaction (e.g., the interaction takes place at work during a lunch break). We used independent film sets with similar content, design and the same actors for both the direct and the indirect task. The tasks were designed and programmed in cooperation with a digital agency (gosub communications gmbh, http://www.gosub.de/) to make the tasks graphically more appealing, increase the tasks' usability, and to facilitate their modification and distribution. The tasks can be accessed on a public webserver through any browser with the Flash Player plugin installed. Completing each task takes approximately 15 to 20 min. Although no time limits are set for the completion of either task, the participants are instructed at the beginning of each task to perform as quickly and accurately as possible.

In the 24-item indirect task, participants first watch a film scene and subsequently four short film clips (4 s) displaying different options for how the scene might continue. The participants then have to use the computer mouse to select the film clip that represents the most likely continuation and to place it into the target panel using a drag-and-drop function (see Figure 1). Thus, the indirect task instruction is to simply solve a film puzzle with no explicit information about the protagonists' emotional or mental states. The reaction times in this task represent the time to watch the four different video options and drag-and-drop the selected video option into the target field.

In the 25-item direct task, participants also first watch a film scene. In contrast to the indirect task, the direct task contains cues that explicitly direct the participants to infer others' mental states (e.g., How do Thomas and Anita feel?). That is, after having watched the initial film clip, participants are asked to select one of four text options that gives the best explanation for a protagonist's emotional state at the moment the film stops. Reaction times in the direct task are tracked from the time when the response options appear on the screen until the participants respond by making a selection via mouse click. Due to differences in task format reaction times differ systematically between the indirect task and the direct task (paired t-test on reaction times over all participants: t (1, 50) = 14.112, $p < 0.001$).

In both direct and indirect tasks, distractors were designed to represent three types of errors: (A) mental state inferences that are ''too excessive'', e.g., interpreting a mistake as intentional rather than accidental; (B) mental state inferences that are ''insufficient'', e.g., underestimating the consequences of disrespectful behavior; and (C) non-mental state inferences, i.e., the inferences are not directly related to the mental states of the protagonists in the previous interaction (for a similar approach, see Dziobek et al., 2006).

To ensure that both tasks are comparable with regards to the overall item difficulty and distribution, they were piloted in a separate validation study with an additional sample of TD participants (n = 28). Based on the results of the validation study, items that lacked sensitivity (i.e., produced ceiling or floor effects) were revised by changing the introduction information and/or the answer options. A detailed description of the stimulus production and validation processes is included in the appendix.

To assess the validity of the Arena of Emotions direct and indirect tasks and further differentiate between the assessed processes , we additionally included two established direct mentalizing measures into the study. The Reading the Mind in the Eyes Test (RMET, Baron-Cohen et al., 2001) is a performance-based measure that requires participants to label the mental state of a person based on the information conveyed in photographs of that person's eyes. Thus, the RMET aims at inferring and explicitly labeling mental states, similar to our direct task. We further assessed participants' awareness of their perspective-taking ability using the 'Perspective Taking' (PT) subscale of the 'Interpersonal Reactivity Index' (IRI) (German translation, Paulus (2006)). The PT subscale consists of 7 items answered on a 5-point Likert scale. The statements included in this scale, e.g. "I try to look at everybody's side of a disagreement before I make a decision", requires explicit insights into one's own perspective-taking abilities.

###Figure 1###

Procedure

The participants completed the Arena of Emotions direct and indirect tasks online through the project's website in testing rooms of the Freie Universität Berlin, Germany under the supervision of trained experimenters. The task order was counterbalanced across participants to control for possible order effects. Both direct and indirect tasks start with a few introduction slides that describe the procedure. Throughout the entire test, participants use the mouse only to read the introduction or solve and proceed to the next item.

The scores, e.g. accuracy scores and reaction times for each testing session are automatically saved to an online database for each of the two tasks independently. The datasheets can then be exported, downloaded, and further analyzed with a statistical program such as SPSS (IBM SPSS Statistics, Armonk, NY: IBM Corp.).

Furthermore, participants completed web-based versions of the MWT, IRI, both accessible through the project's website, and the computer-based RMET, presented using Presentation (Version 14.1, Neurobehavioral Systems Inc., Albany, CA).

Results

Reliability analysis

Both the direct and indirect tasks yielded good internal consistency (direct task: Cronbach's $\alpha = 0.82$; indirect task: Cronbach's $\alpha = 0.84$).

Tasks' Sensitivity to Atypical Emotion Recognition

Accuracy. We performed a repeated-measures ANOVA on accuracy rates with the within-subject factor condition (direct versus indirect task) and the between-subject factor group (TD versus ASD). On both tasks, the ASD group had significantly fewer correct responses compared with the TD group (main effect of group, *F* (1, 49) = 7.410, *p* = 0.009, η_p^2 = 0.131; see Figure 2). Overall, the participants showed comparable performance on the direct and indirect task; see Table 2 (*F* (1, 44) = 0.127, *p* = 0.723; interaction of group and condition, *F* (1, 44) = 0.161, *p* = 0.690). Furthermore, given recent evidence of gender differences in social cognition in ASD and a relatively large proportion of females in our sample, we analyzed gender differences within the ASD group in an exploratory fashion. As symptom severity and verbal IQ represent potential confounds, we included these as covariates into the analysis. Male participants scored significantly higher than female participants on both direct and indirect tasks (see Appendix).

Furthermore, the whole ASD group's performance on both tasks was negatively correlated with autism symptomatology, as measured by the ADOS (direct task: *r* = -0.387, *p* = 0.056; indirect task: *r* = -0.469, *p* = 0.018) and the ASDI (direct task: *r* = -0.379, *p* = 0.062; indirect task: *r* = -0.354, *p* = 0.083), indicating that more severely affected individuals scored lower on both tasks.

Reaction Times. Mean reaction times (RTs) for correct responses were calculated for each participant in both tasks and are referred to as RTs. Trials with incorrect responses were excluded from further analyses. There were no group differences in RTs for correctly solved items in either of the tasks (direct task: *t* (1, 34) = -1.061, *p* = 0.296; indirect task: *t* (1, 35) = 0.248, *p* = 0.806, see Table 2).

###Figure 2###

Correlation analysis

We analyzed correlations separately for the two groups because groups differed significantly in their performance on all social cognition measures (see Table 2).

###Table 2###

The relationship between direct and indirect task performance

The direct and indirect Arena of Emotions task performances were not correlated in the TD group (*r* = 0.345, *p* = 0.106), but significantly correlated in the ASD group (*r* = 0.829, *p* < 0.01). The correlations differed significantly between groups, reflecting differences in the relationship between implicit and explicit mentalizing processes in individuals with ASD and TD individuals (Fisher's r-to-z = 2.75, *p* < 0.01, see Figure 3).

###Figure 3###

The tasks' relationship with external measures

To investigate the tasks' validity and further differentiate between performance measured directly and indirectly, we correlated both direct and indirect task performances with scores from established direct social cognition measures, such as the RMET and the PT subscale of the IRI, which assess participants' explicit judgment of their perspective taking tendencies.

Among TD participants, Arena direct task performance correlated significantly with accuracy on the RMET ($r = 0.417$, $p = 0.048$). In contrast, the correlation between performance on the indirect task and performance on the RMET did not reach significance ($r = 0.303$, $p = 0.160$). However, the difference between the correlations was not significant (Williams' T_2: $t\,(20) = -0.493$, $p > 0.05$). In the ASD group, performance on both direct and indirect tasks was significantly correlated with performance on the RMET (RMET and indirect task: $r = 0.681$, $p < 0.001$; RMET and direct task: $r = 0.791$, $p < 0.001$).

PT correlated negatively with indirect task performance in the TD group ($r = -0.421$, $p = 0.045$), suggesting that participants with higher accuracy scores on the indirect task reported explicit perspective-taking tendencies less frequently. In contrast, PT was not significantly correlated with performance on the direct task ($r = 0.253$, $p = 0.245$). The difference between these correlations in the TD group was significant (Williams' T_2: $t\,(20) = -3.282$, $p < 0.01$). In the ASD group, PT did not correlate significantly with either indirect task performance ($r = 0.128$, $p = 0.517$) or direct task performance ($r = 0.280$, $p = 0.149$).

Discussion

In the current study, we developed two naturalistic, comparable tasks for a performance-based approximation of implicit and explicit mentalizing with an indirect and direct task, respectively. In typically developed participants, both tasks produced the required amount of variability in performance, showing that the naturalistic tasks are a sensitive means of assessing mentalizing in a typically developed adult population. The tasks were also sensitive to the social cognitive impairments of individuals with ASD. ASD participants gave significantly less correct responses and accuracy scores were negatively correlated with symptom severity, suggesting that more impaired individuals scored lower. Finally, the relationship between direct and indirect task performance differed significantly between groups. In the TD group, performance scores on the direct and indirect tasks did not correlate, indicating that the underlying processes are to some degree distinguishable. In the ASD group, performance scores on the direct and indirect task were highly intercorrelated, suggesting a lack of differentiation between implicit and explicit processes.

Individuals with ASD are characterized by atypical social cognition throughout development (e.g., Baron-Cohen, 2001) and thus constitute a highly appropriate clinical population for studies on implicit and explicit mentalizing processes, which have been proposed to differentiate early on in typically developed individuals (Low and Perner, 2012). As expected and in line with a great body of literature (Happe and Frith, 1996; Hill and Frith, 2003; Senju, 2013), individuals with ASD scored significantly lower on the direct and indirect task than the typically developed comparison group, with more impaired individuals scoring lower than less impaired individuals. In contrast to our expectations, we did not find an interaction between task and group, suggesting that individuals with ASD were not more impaired in implicit than in explicit mentalizing. A previous study by Senju et al. (2009) found that individuals with ASD had greater impairments in implicit, spontaneously occurring, than in explicit mentalizing. However, the tasks did not comparably assess performance differences between implicit and explicit mentalizing processing. Aberrant implicit mentalizing processing was inferred from a lack of visual attention anticipating where a protagonist would look for a hidden object. In contrast, the standard direct tasks used in this study assessed whether participants were able to pass standard false belief tests. Furthermore, the standard false belief tasks used, such as the Sally-Ann task by Baron-Cohen et al. (1985), have been shown to produce ceiling effects in participants with a mental age above 6 years (Baron-Cohen et al., 1997) and therefore may not have been sensitive enough to capture differences between groups. Thus, our results emphasize the importance of using more demanding, naturalistic mentalizing tasks that produce the required amount of variability to reliably assess mentalizing in both typically developed individuals and in populations with socio-cognitive impairments.

Exploratory analyses of gender differences in the autistic sample yielded significantly higher performance on both direct and indirect tasks of male ASD participants compared to females. Recently, a growing number of studies have reported gender differences within ASD on various behavioral measures including cognitive abilities (Bolte et al., 2011; Lai et al., 2011; Lord et al., 1982) and social cognition in particular (Carter et al., 2007; Golan et al., 2006; Golan et al., 2007; Sucksmith et al., 2013). In contrast to our results, previous studies have found higher facial emotion recognition performance in adult females with ASD compared to males (Golan et al., 2006; Sucksmith et al., 2013). However, in line with our results, Carter et al. (2007) found that parents reported higher social competences for boys with ASD than for girls and Golan et al. (2007) report higher performance on a naturalistic emotional prosody task in autistic males compared to females. Thus, in more complex naturalistic settings, such as inferring mental states from speech and videos, or interacting in real life situations, autistic males seem to have an advantage over females. Given that males have a higher tendency to systemize compared to females (Auyeung et al., 2012; Baron-Cohen et al., 2003) a possible explanation for this gender difference could be that autistic males benefit from higher systemizing skills in complex naturalistic settings. More specifically, males with ASD might use their systemizing skills to make sense of social cues by e.g. applying social norms, rather than processing them intuitively. Such strategies, however, require social stimuli to be relatively complex and thus might not be applicable to reduced static stimuli. In this study, we did not assess participants' potential task solving strategies and also we did not assess systemizing tendencies in our sample. To investigate this hypothesis, future studies should include larger samples of males and females with ASD and assess systemizing tendencies as well as performance on a wide range of basic and more complex social cognition measures.

With regards to the relationship between implicit and explicit aspects of mentalizing, accuracy scores on the direct and indirect tasks were not correlated in healthy individuals. These findings are in line with previous assumptions of a distinction between implicit and explicit social cognition (Adolphs, 2009; Low and Perner, 2012; Kliemann et al., 2013). In individuals with ASD, performance scores on the direct and indirect task were significantly intercorrelated. The correlations between indirect and direct task scores differed significantly between groups indicating group differences in the relationship between implicit and explicit mentalizing processes. However, typically developed individuals in our sample had a more restricted performance range than the ASD participants and this could at least partly explain the between group difference in the strength of correlations. By matching the groups for gender, age and verbal IQ, we controlled for demographic differences between groups, and thus believe that the greater variance in the performance of ASD participants reflects a wider spectrum of socio-cognitive abilities among individuals with ASD compared to the typically developed population.

In typical development implicit mentalizing develops during the first year of life (e.g., Kovács et al., 2010) and is seen as a precursor to explicit mentalizing, i.e., giving the correct reasoning for a person’s (false) belief (Low and Perner, 2012). Young infants, for example, track the beliefs of others (Kovacs et al., 2010; Onishi and Baillargeon, 2005) without necessarily being able to make correct explicit belief inferences (Ruffman et al., 2001).

During adulthood, implicit and explicit mentalizing processes seem to coexist mediating distinct features of social cognition. For example, Samson et al. (2010) reported that adults track another person's perspective, even when they are explicitly instructed to focus on their own perspective.

Our assessment of the relationship between the participants' performance on the newly designed tasks and established direct social cognition measures provides further evidence that implicit and explicit mentalizing processes can be differentiated to a certain degree by behavioral measures in typically developed individuals. The TD group's performance on the direct task correlated with the RMET test scores, suggesting that both measures might assess similar explicit processes. This result also provides an external validation of our newly developed direct task. In contrast, indirect task performance and RMET scores were not significantly correlated. However, the correlations between RMET and direct task performance and RMET and indirect task performance did not differ significantly from each other. This indicates that implicit and explicit processes, assessed with these newly developed tasks, are distinguishable but not completely independent of each other. In addition, TD participants' subjective judgment of their own perspective taking tendencies was negatively correlated with performance on the indirect task, but not with performance on the direct task. The significant difference between these correlations further indicates a distinction between the mentalizing processes assessed directly and indirectly. The lack of a positive correlation between direct task performance and the self-report perspective taking scale could be due to a discrepancy between objective test measures and subjective judgments of one's own tendencies. Subjective self-report measures are useful in detecting self-views but may not accurately reflect socio-cognitive abilities. Such a discrepancy between self-report and more objective performance tests have been already shown in the domain of social cognition (e.g., Brackett et al., 2006). The negative correlation between indirect task performance and subjective judgment of one's own perspective taking tendency suggests that the higher participants' awareness of how they infer someone else's mental state, the lower they scored on the indirect task. Our indirect task involves solving film puzzles. While watching film clips depicting complex social interactions participants infer protagonists' mental states spontaneously (Klin et al., 2002). Hence, individuals, who are less analytical and thus reflect less about their perspective-taking strategies, could perform better on a task that requires them to spontaneously track mental states while finding the matching film sequence.

In contrast, individuals with ASD show severe impairments in implicit social cognitive processes in early development. Young infants with ASD do not show a looking preference for humans as compared to objects (e.g., Swettenham et al., 1998) and do not share someone else's attention to an object, i.e. joint attention (Charman et al., 1997). Such implicit social cognitive tendencies have been identified as precursors to explicit knowledge about others' mental states (Low and Perner, 2012). Impairments in implicit mentalizing processes, such as joint attention, could thus lead to the observed impairments and delays in explicit mentalizing. The link between implicit and explicit mentalizing would thus reflect common pervasive socio-cognitive impairments underlying both implicit as well as explicit aspects of social cognition. To address this notion, there is a need for longitudinal investigations of implicit and explicit mentalizing in individuals with ASD with comparable performance based tasks.

In individuals with ASD, accuracy scores on the indirect and direct tasks correlated significantly with performance on the RMET and did not correlate with self-reported perspective taking tendencies. These findings provide further evidence of a lack of differentiation between implicit and explicit mentalizing processes as well as a lack of correspondence between subjective self-reported mentalizing abilities and objectively measured mentalizing in individuals with ASD, which is possibly due to a lack of introspection into their socio-cognitive deficits. For instance, self-reported symptom severity does not adequately differentiate autistic patients form other patient groups (Ketelaars et al., 2008) and does not correlate with scores on a standard diagnostic instrument, such as the ADI-R (Bishop and Seltzer, 2012).

Our findings support the notion that individuals with ASD have impairments in both implicit and explicit mentalizing and that therefore both processes deserve attention in therapeutic and intervention settings, such as social competence trainings (Frith and Frith, 2012). To date, existing social competence trainings are mainly direct, training individuals to label emotional facial expression or emotional prosody (e.g., Golan and Baron-Cohen, 2006). These training interventions mainly produce improvements on close generalization tasks that are very similar to the training material, without generalizing to other social-cognitive tasks or to everyday social functioning (Golan and Baron-Cohen, 2006; Hadwin, Baron-Cohen, Howlin, & Hill, 1997). It is possible that effects of social trainings that include indirect tasks and naturalistic stimuli that more closely approximate the complexity and dynamics of real-life social cues could generalize across a greater number of tasks and contexts.

In summary, we aimed to take a systematic approach towards comparing mentalizing processes measured directly and indirectly. To this end, we developed and carefully validated two comparable and sensitive tasks for a performance-based direct and indirect assessment of mentalizing. We showed that these tasks, comprising naturalistic video based stimuli, were sensitive to the impairments of individuals with ASD. Furthermore, assessing typically developed individuals and individuals with ASD with the direct and indirect tasks, we were able to further specify the relationship between explicit and implicit mentalizing processes in typical and atypical development. Our results suggest that implicit and explicit mentalizing processes seem to be distinct to a certain degree in healthy individuals, whereas in individuals with ASD implicit and explicit processes seem to be more closely linked. In conclusion, to address the pervasive mentalizing impairments of individuals with ASD, which concern both explicit and implicit mentalizing processes, direct and indirect tasks deserve equal attention in social cognitive test batteries, trainings and interventions.

Table 1 Demographical and symptom characteristics

	*ASD (*N = 28)				*TD (*N = 23)				
	N	*M*	*MD*	*SD*	*N*	*M*	*MD*	*SD*	*p Value*
Sex, F(N) /N	10/28	-	-	-	6/23	-	-	-	0.552
Age	28	33.07	33	8.45	23	32.43	30	8.86	0.795
MWT-IQ	28	112.68	107	16.40	23	108.39	104	12.91	0.313
ADOS	25	10.56	10	3.34	-	-	-	-	-
ASDI	25	42.00	43	4.76	-	-	-	-	-

Means (M), Median (MD), Standard Deviations (SD), and sample size (N) of group characteristics.

P-values: two-tailed significance-value for t- and χ^2-tests in ASD vs. TD participants.

Abbreviations: Autism Spectrum Disorders (ASD), Typical Development (TD), female (F), Mehrfachwahl-Wortschatz-Test (MWT), not applicable (-), Autism Diagnostic Observation Schedule (ADOS), Asperger Syndrome and High Functioning Autism Diagnostic Interview (ASDI).

Table 2 Social cognition measures in TD and ASD participants

	Arena of Emotion Implicit Task		**Arena of Emotion Explicit Task**		**RMET**$^{+}$	**PT (IRI)**
	Accuracy	*cRT (s)*	*Accuracy*	*cRT (s)*	*Accuracy*	*Mean rating*
TD (N = 23)						
M	0.68	21.73	0.67	10.10	0.71	25.70
MD	0.71	21.43	0.68	9.62	0.72	25.00
SD	0.11	4.46	0.13	3.56	0.10	3.91
ASD (N = 28)						
M	0.53	21.09	0.54	12.44	0.60	19.86
MD	0.54	19.97	0.60	9.31	0.64	20.00
SD	0.27	12.57	0.22	10.99	0.18	5.15
p Value	**0.010***	0.806	**0.014***	0.296	**0.011***	**10^{-5}*** **

Abbreviations: Reading the Mind in the Eyes Test (RMET), Perspective Taking Scale (PT), Autism Spectrum Conditions (ASD) Means (M), Median (MD), Standard Deviations (SD), and sample size (N).

P-values: two-tailed significance-value for t-tests ASD vs. Controls; *: significant difference between Controls and ASD ($p<.05$), ***: significant difference between ASD and Controls ($p<.001$). $^{+}$: Number of ASD participants differs for the RMET: N(ASD) = 24.

Conflict of interest declaration:

The authors declare that they have no conflict of interest.

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Figure 1

Ordnen Sie der Anfangs-Sequenz die richtige Folge-Sequenz zu.

What do Thomas and Anita feel?

They are surprised about having such little time.

They are angry because Dinah is being selfish.

They are irritated about Dinah's pushy behavior.

They are worried about Dinah having to pay a fine.

Ordnen Sie der Frage die richtige Antwort zu.

Fig 1 The Arena of Emotions Tasks

A: Example item for indirect task.

Each video item is preceded by a short written introduction, describing the context and setting of the interaction

Written Introduction: Julia and Tim have been a couple for three years. They are very happy and respectful with each other. It is Tim's birthday today and together with a friend he is waiting for Julia.

Film clip content: Tim's friend asks whether he has bought himself the new computer game he wanted. Tim replies that he did not. He states that he is sure Julia has bought him the game for his birthday. Julia comes in with a present. Tim opens it excitedly and discovers that she got him a pullover.

Task: Participants are asked to watch the 4 film clips and pick the best-suited option as to how the scene might continue.

Correct answer: Option 2; Tim's facial expression initially shows disappointment. Then, he smiles and thanks Julia for the gift.

B: Example item for direct task.

Each video item is preceded by a short written introduction, describing the context and setting of the interaction

Written Introduction: Dinah's friends are helping her to move out today. They do not know that she has to pay a fine if she is not done by noon. The three friends are in Dinah's apartment.

Film clip content: Dinah's friends take their time chatting about a vacation. Dinah urges them impatiently to stop talking and to start working instead.

Task: Participants are asked to pick one out of four text options that correctly describe what Dinah's friends are feeling at the moment when the film clip stops.

Correct answer: Option 3; "Thomas and Anita are irritated about Dinah's pushy behavior."

Figure 2

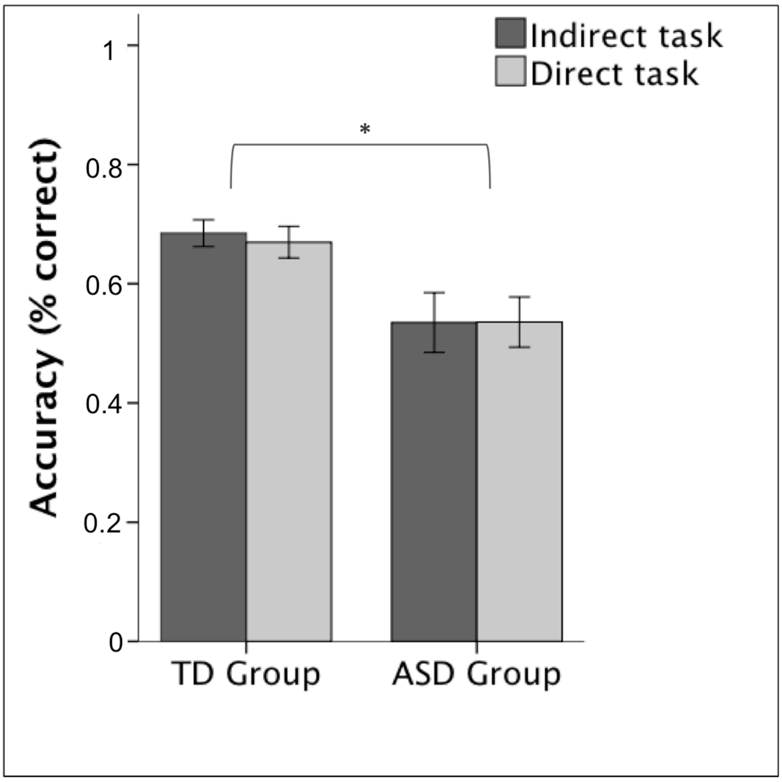

Fig 2 Accuracy scores of the direct and indirect tasks

Mean accuracy scores in the Arena of Emotions tasks in Controls and ASD

Accuracy scores in the indirect and direct Arena of Emotions tasks differ significantly between groups. *: significant difference between controls and ASD (p<.05); ASD: Autism Spectrum Disorder

Figure 3

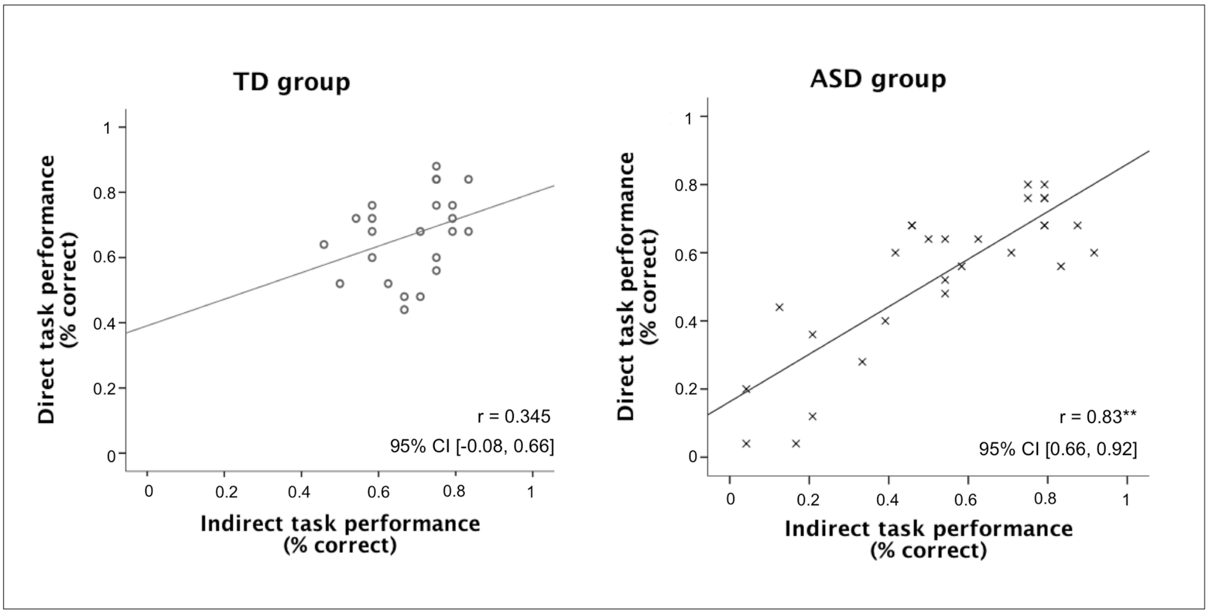

Fig 3 Relationship between the accuracy scores of the indirect and direct tasks

In the ASD group accuracy scores in the indirect and direct task are significantly correlated, in controls they are not correlated. The correlation coefficients differ significantly between groups. ASD: Autism Spectrum Disorder

Approximating implicit and explicit mentalizing with two naturalistic video-based tasks in typical development and autism

[app] Electronic appendix

Part 1: Stimuli production – page 2

Part 2: Task validation – page 2

Part 3: Gender differences within the ASD group – page 3

Methodological details

Stimuli production

First, we produced a new set of stimuli comprising 50 short film scenes (20-35s) displaying social interactions of 2 or 3 actors. After writing the scripts in cooperation with professional script writers, we produced the film clips in the film studio of the Humboldt University Berlin in cooperation with its Computer and Media Service team (CMS). A total of 23 professional actors (14 females) of varying age took part in the clips. The video stimuli aim at approximating a variety of real-life social settings and scenarios such as private family life or work environment. The interpersonal relationships between the protagonists in the film clips differ from that of strangers to very close friends or romantic partners. As a consequence, mental state inferences have to be made according to the respective social relation of the protagonists. Further, we incorporated traditional mentalizing concepts such as false belief, deception, sarcasm, and irony into the scenes and emphasized different modalities of human expression, by making film scenes more or less verbal and some explicitly nonverbal. In the nonverbal scenes, participants have to rely solely on facial expressions, gestures, and body language for their mental state inferences. The film scenes are independent from one another and thus so are test items.

Task validation

The tasks were subjected to a separate validation study in an additional sample of healthy individuals (N = 28; 14 male, age range: 19 – 47, mean age: 27.5, SD = 7.2). First, participants rated how believable the scenarios of the film scenes were on a 6-point Likert scale (1 = not believable to 6 = very believable). Second, they provided a free text answer for the protagonist’s next possible reaction in the indirect task and the protagonist’s feelings in the direct task, respectively. In a third step, they were asked to solve the multiple-choice items as described above. Items were labeled correct, if participants picked the right multiple-choice option and additionally provided a very similar free answer. For incorrect items, we additionally analyzed the content of the free answer to find out whether there existed a different plausible alternative to the correct option we designed. Ambiguous items were defined as items with an item difficulty lower than 0.50 or if more than 50% of free answers provided clearly differed from our correct option. Twenty-three items of the indirect task yielded a mean item difficulty of 0.76 (SD = 0.19) and mean believability rating of 4.4 (SD = 0.34). In the 26 items of the direct task, however, participants performed at ceiling (difficulty: .99 (SD = 0.02). Almost all participants picked the right answer option and also provided a very similar free answer. The believability ratings were similarly high as in the indirect task (believability: 4.8 (SD = 0.38)). The item analysis for the indirect task showed that alpha increased when item taken out for 5 items, which also showed high ambiguity.

After excluding these items, the indirect task showed a satisfactory reliability (Cronbach's a= 0.71).

Both tasks were revised with the aim of increasing test difficulty and reliability.

Gender differences within the ASD group

Male and female ASD participants did not differ with respect to symptom severity assessed with the ADOS (*t* (1, 23) = -1.256, *p* = 0.222) and ASDI (*t* (1, 23) = -0.897, *p* = 0.379). They also scored similarly on the verbal IQ measure (*t* (1,26) = -1.091, *p* = 0.285). To investigate the tasks' sensitivity to gender differences within the ASD group, we performed a repeated-measures ANOVA on accuracy rates with the within-subject factor condition (direct versus indirect task) and the between-subject factor gender (males versus females). ASD males and females showed comparable performance on the direct and indirect task (main effect of condition, *F* (1, 26) = 0.018, *p* = 0.894; interaction of gender and condition, *F* (1, 26) = 0.133, *p* = 0.718). On both tasks, females had significantly fewer correct responses than males (main effect of group, *F* (1, 26) = 6.609, *p* = 0.016, $\eta_p^2 = 0.203$). When entering ADOS, ASD and verbal IQ scores as covariates into the analysis, the group difference in performance between males and females remained significant (*F* (1, 17) = 4.581, *p* = 0.047, $\eta_p^2 = 0.212$).

The role of the amygdala in implicit mentalizing while watching naturalistic social interactions

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Abbreviated title: The role of the amygdala in implicit mentalizing

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Number of pages: 27
Number of words:
Abstract: 242
Introduction: 460
Discussion: 1231
3 Figures and 4 Tables

Acknowledgements

The data was in part presented at the Psychology and the brain conference 2012, Jena, Germany, June 8-10, 2012.

Conflict of Interest Disclosures: None of the authors have conflicts of interest.

Funding/Support: The study was funded by a grant from the German Research Foundation (DFG; EXC 302).

We gratefully acknowledge the actors, who participated in the film scenes and the members of the Computer and Media Service team (CMS) at the Humboldt University for their support with the production and postproduction of the film stimuli. We also thank our student research assistants for their help with the stimulus production and data acquisition and especially Alexander Hatri for his support with the eye tracking data analysis. In addition, we would like to thank our participants on the autism spectrum for their participation in the study.

Abstract

There is a substantial discrepancy between mentalizing in reduced laboratory settings, where humans have to explicitly infer mental states, and mentalizing in real life social interactions, which almost exclusively occurs implicitly. This hinders the understanding of the neural basis of real life social cognition, as well as of social impairments in psychiatric disorders. The aim of this study was to determine the neural mechanisms underlying naturalistic mentalizing using a new video-based functional magnetic resonance imaging (fMRI) task in 20 individuals with Autism Spectrum Disorder (ASD) and 22 matched healthy control participants. Eye movements of participants were recorded during the fMRI experiment. In healthy controls, beyond regions that have traditionally been implicated in mental state inferences (medial prefrontal cortex (MPFC), superior temporal sulcus (STS)), naturalistic mentalizing recruited the insula and amygdala. Moreover, amygdala activity predicted implicit mentalizing performance on an independent behavioral task. ASD participants showed reduced amygdala and STS activity compared to controls during the naturalistic mentalizing task and amygdala activity was not correlated with mentalizing accuracy on the behavioral task. In conclusion, mentalizing in naturalistic social settings recruits an extended social brain network including the amygdala and insula, which suggests emotional involvement when inferring others’ mental states in real life settings. In autism,

which represents a model for impaired social cognition, reduced amygdala activation and the reduced correlation between amygdala functioning and performance, highlight the specific role of the amygdala for the accuracy of implicit mental state inferences in typical development.

Introduction

A great number of psychiatric disorders involve severe impairments in the ability to infer thoughts, emotions or intentions, i.e., mentalizing or Theory of Mind (ToM) (Frith, 1989). The social cognition deficit of individuals with Autism Spectrum Disorder (ASD) is particularly prominent in real-life settings (Volkmar et al., 2004) that require the integration of multimodal information from faces, voices, body language, and social context (Zaki and Ochsner, 2009). In real-life, mentalizing involves both controlled explicit processes, such as consciously taking another person's perspective and – to a much greater extent - implicit processes, e.g., spontaneously inferring mental states without explicit prompts (Frith and Frith, 2008). Individuals with ASD seem to have more pronounced deficits in the latter set of processes (Senju et al., 2009).

Despite the importance of *implicit* mentalizing in *naturalistic* settings for effective social functioning, most studies have investigated explicit processes with often abstract and static stimuli such as written stories (Saxe and Powell, 2006) or cartoon tasks (Walter et al., 2004). Consequently, most current tasks lack the sensitivity to approximate aberrant behavior and brain function of individuals with impairments in real life.

A common network of brain regions has consistently been implicated in mentalizing (Mar, 2011), whereby different regions within the network seem to mediate explicit and implicit social cognitive processes (Olsson and Ochsner, 2008). The amygdala and the superior temporal sulcus (STS) have been implicated in lower-level implicit social information processing (Allison et al., 2000; Adolphs et al., 2005) and they have been tightly linked to the social cognitive impairments of individuals with ASD (Dziobek et al., 2010; Pelphrey et al., 2011). The precise role of these regions in mentalizing, however, has yet to be determined. Since both regions show a high sensitivity to dynamic, context dependent social stimuli (Wright et al., 2003), there is a need to study their role in mentalizing in naturalistic settings. Despite the crucial role of *accurate* social cognition for successful social functioning, the relationship between behavioral performance and neural processing has been widely neglected in the field of social neuroscience (Zaki and Ochsner, 2011). There is some evidence that the amygdala and STS are particularly important for accurate social cognition. For instance, lower performance in social cognition of individuals with ASD has been repeatedly linked to reduced amygdala and STS activation (see Pelphrey et al., 2011 for a review).

Here, we investigated spontaneously occurring mentalizing while watching videos of social interactions with a newly developed functional magnetic resonance imaging (fMRI) task in individuals with ASD and healthy controls. More specifically, we attempted to link neural mental state processing to performance in implicit mental state inferences measured with an independent behavioral task. We expected reduced activation of mentalizing regions, in particular in the amygdala and STS, in ASD during spontaneous and naturalistic mentalizing,

Methods and Materials

Participants

Twenty-eight adults with ASD (18 male, mean age = 33) and 22 control participants (16 male, mean age = 31) participated in the study. The ASD participants were recruited through the autism outpatient clinic for adults of the Charité – University Medicine Berlin, Germany or were referred to us by specialized clinicians. All of the participants were diagnosed according to the DSM-IV criteria for Asperger syndrome and autism without intellectual disabilities (American Psychiatric Association, 2000). Diagnostic instruments included the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2002) and the Autism Diagnostic Interview - Revised (ADI-R; Lord et al., 1994) if parental informants were available (N = 15). Diagnosis was confirmed using at least one of the gold standard instruments ADOS or ADI-R. Additionally, the diagnosis of Asperger syndrome was confirmed with the Asperger Syndrome and High-Functioning Autism Diagnostic Interview (ASDI; Gillberg et al., 2001). The two groups were matched according to gender, age, and verbal IQ (see Table 1), as measured by a German vocabulary test (Mehrfachwahl-Wortschatz-Test (MWT; Lehrl, 1989). Eight of the ASD participants met exclusion criteria for the fMRI experiment (i.e., claustrophobia: N = 3; no normal or corrected to normal vision N = 1, no current health insurance: N = 1; under psychotropic medication: N = 3). The remaining

20 ASD participants included into the fMRI experiment did not differ from the control group with respect to age, gender, and IQ (see Table 1).

All participants received payment for participation and gave written informed consent in accordance with the requirements of the ethics committee of the German Society for Psychology (DGPs).

Tasks and Material

We developed two new movie-based behavioral and fMRI mentalizing tasks, comprising naturalistic and dynamic stimuli, i.e., film scenes displaying social interactions between two or three professional actors.

Stimuli. The film scenes used in both the behavioral and fMRI experiments displayed different social interactions between two or three protagonists. The scenes' scripts were written in cooperation with professional scriptwriters and cover a variety of real-life social settings and scenarios such as a dinner with friends or waiting in line. The interpersonal relationships between the protagonists in the film clips vary from that of strangers to close friends or romantic partners. A total of 30 professional actors (18 females) of varying age took part in the film clips, which were produced in the film studio of the Humboldt University Berlin, Berlin Germany in cooperation with its Computer and Media Service team (CMS).

The *behavioral task, Arena of Emotions – indirect behavioral task (AE),* measures the capacity to implicitly infer others' mental states and has been introduced in a separate study

(Rosenblau et al., in revision). In a behavioral testing session participants performed the indirect behavioral task, which is a web-based application comprising 24 items. In the indirect task, participants first watch film scenes displaying everyday social interaction between two or three protagonists (range: 9 - 31s). Each film scene is preceded by a short written introduction, describing the context and setting of the interaction. After watching an initial film clip (e.g. a couple having breakfast), participants subsequently watch 4 short film clips (4 s) displaying different options for how the scene might continue (e.g., couple starts to argue, etc.) and are then asked to select the correct option. In order to pick the correct continuation, participants have to infer the protagonists' mental states. Importantly, mentalizing performance (comprising accuracy and reaction times (RT)) is assessed indirectly, i.e., participants are not explicitly instructed to infer others' mental states (see Figure 1).

fMRI task. In a separate session, participants performed the following fMRI experiment in two runs of 9 min 20 seconds each. The experiment was presented using Presentation (Version 14.1, Neurobehavioral Systems Inc., Albany, CA) and consisted of 16 blocks of two alternately presented conditions, a ToM condition (8 blocks) and a physical inference control condition (PI; 8 blocks). 8 independent film scenes were included into the fMRI task and presented twice, once in the ToM condition, and another time in the PI condition. A description of the social interaction in each film clip is displayed in the Table 2.

During the ToM condition, participants were asked to make inferences about changes in the protagonists' affective states, relying on affective mentalizing or cognitive empathy (see Walter, 2012 for a review). During the PI condition participants were asked to judge changes in the protagonists' body movements.

Each task block comprised film scenes that were split into three consecutive film clips (mean duration: 6.9s; SD = 1.7; range: 3.7s - 12.5s). Task blocks started with an introduction screen (6s), which contained information about the setting of the social interaction (e.g., Mrs. Hauser is going to the post office) and introduced the main protagonist (picture of the main protagonist with his/her name). The introduction screen was followed by a cue (4s) indicating the type of task participants had to solve in the respective block (ToM or PI). In ToM blocks, participants subsequently watched three consecutive film clips (i.e., video phases) and judged clip-by-clip changes in the affective states of the protagonists (i.e., Does the main protagonist feel "worse", "equally well", or "better" than in the previous clip?) similar to a previously published Cartoon paradigm (Walter et al., 2011). In PI blocks, participants were asked to judge clip-by-clip changes in the amount of different body movements of the protagonist (e.g. head-turning: Does Mrs. Hauser turn her head less often, equally often, or more often than in the last film clip?). After the second and third film clip, participants indicated changes in the affective state (ToM) or the amount of movement (PI) of the protagonist with a button press with the right hand (index finger for less, middle finger for more, index and middle finger simultaneously for equal affective state or movement). The respective answer phases had a fixed response duration of 6s (see Figure 2).

In each block participants were asked for two responses: i) indication of changes from the first to the second film clip (answer frame 1) and ii) indication of changes from the second to the third film clip (answer frame 2). Since a correct response in answer frame 2 partly depended on responding correctly in answer frame 1, we only included accuracy and RT for answer frame 2 into the analysis, if participants had answered correctly in answer frame 1.

To test whether participants paid an equal amount of visual attention to the screen between groups and conditions, we tracked participants' eye movements during the experiment (please refer to the section eye-tracking acquisition for more information).

To ensure that the PI and ToM conditions did not differ with respect to task demands, e.g., load related differences between the two conditions, we reduced the attentional demands as well as the social saliency of the PI condition by blurring the faces of the protagonists in the film clips. Thus, participants were less distracted by the affective content of the social scenes while counting body movements. To alternate in which condition the film scene would be presented first (ToM or PI) and to ensure a maximal distance between the same two film scenes (displayed once in the ToM and the other time in the PI condition), we presented the blocks in different predetermined sequences, which were counterbalanced across runs and participants.

For both tasks, the cue screen containing the task instruction preferentially allowed the participant’s tracking of mental states in the ToM condition and body movements in the PI condition. Given that we were specifically interested in capturing spontaneously occurring mentalizing in naturalistic settings, we modeled video (spontaneous menatlizing) and answer phases (explicit mentalizing) as separate regressors and only investigated mentalizing during the video phases.

Eye-tracking acquisition

To assess visual attention during the fMRI task, eye movements were recorded during scanning using a 1000 Hz embedded infrared camera (Eyelink 1000, SR Research). For each video we defined a rectangular region of interest (ROI) comprising the entire screen (1024x768). We subsequently analyzed the number of gaze points within that ROI and the total number of gaze points tracked by the eye tracker (valid gaze points) for the duration of the videos using a MATLAB algorithm (MathWorks, Natick, MA). The latter measure was used to assess data quality and as a baseline for further analysis. To assess the amount of visual attention on the screen, we divided the amount of gaze points within the screen ROI by the total number of valid gaze points for each video. Participants’ data were discarded if there were less than 50% valid gaze points per condition (ToM or PI) and run. As a result, we included 11 ASD (9 male) and 18 control participants (13 male) into the gaze duration analysis.

fMRI data acquisition

MRI data were acquired on a 3 Tesla scanner (Tim Trio; Siemens, Erlangen, Germany) using a 12- channel head coil. Functional images were acquired using an echo-planar T2*-weighted gradient echo pulse sequence (TR = 2000 ms, TE = 30 ms, flip angle = 70, 64 X 64 matrix, field of view = 192 mm, voxel size = 3 X 3 X 3 mm^3). A total of 37 axial slices (3 mm thick, no gap) were sampled for whole-brain coverage. The first two volumes at the beginning of each run were discarded to allow for T1 equilibration. Functional imaging data were acquired in two separate 280-volume runs of 9 min 20 s each. In the same scanning session, a high-resolution T1-weighted anatomical whole brain scan was acquired for each participant and was later used for registration of the fMRI data (256 X 256 matrix, voxel size = 1 X 1 X 1 mm^3).

fMRI data analysis

Preprocessing. fMRI data were preprocessed and analyzed using FEAT (FMRI Expert Analysis Tool) within the FSL toolbox (FMRIB's Software Library, Oxford Centre of fMRI of the Brain, www.fmrib.ox.ac.uk/fsl, Smith et al., 2004). Preprocessing included brain extraction, slice timing, motion correction and spatial smoothing (8-mm full width at half maximum (FWHM) Gaussian kernel). To remove low frequency artifacts, we applied a high-pass temporal filter (Gaussian-weighted straight line fitting, sigma = 100 s) to the data.

Functional data were first registered to individuals' T1-weighted structural image and then registered to standard space using the FMRIB Nonlinear Image Registration Tool.

fMRI single-subject analysis. We modeled the time series individually for each participant and run including nine epoch regressors, comprising the instruction, cue, video and answer phases (separate for the two experimental conditions ToM and PI), as well as one regressor for all button presses. Additionally, we included six regressors modelling head movement parameters. There were no differences between the two runs, conditions or groups and in the total amount of motion between functional volumes (mean relative displacement; run (run1 vs. run2): F (1, 40) = 1.56, p > 0.2; condition (ToM vs. PI): group: F (1, 40) = 0.31, p > 0.5). The regressors were then convolved with a Gamma hemodynamic response function (HRF). Contrast images were computed for each condition, each run and each participant. They were spatially normalized, transformed into standard space and then submitted to a second-order within-subject fixed-effects analysis across the two runs.

Group analysis. We performed higher-level mixed-effects analyses across participants with the between-subject factor group (ASD and Controls) using the FMRIB Local Analysis of Mixed Effects tool provided by FSL (FLAME, stage 1 & 2) based on single subjects' contrast images.. To identify the mentalizing network (see (Mar, 2011b) in healthy participants we contrasted ToM with PI video phases. Subsequently, we investigated group differences within the identified mentalizing network. We report clusters of maximally activated voxels that survived family-wise error correction for multiple comparisons at a statistical threshold of p < .05 and a z-value > 2.3. Activation differences between groups were cluster corrected within the ToM network of healthy controls.

To further visualize and characterize possible group by condition interactions for significantly activated clusters, we extracted and plotted the parameter estimates (PE) for each condition and group.

Covariate analysis. To determine whether amygdala and STS activation during mentalizing processing (ToM video phases versus PI video phases) correlated with implicit mentalizing performance in healthy controls, we performed a higher-level mixed-effects analysis for controls and ASD participants separately and added accuracy rates for the AE task as a covariate into the model. Crucially, we ensured that this analysis was not prone to potential non-independence errors by taking two measures. Firstly, we entered performance on an *independent* behavioral task as a covariate into the fMRI analysis. Secondly, we used anatomical masks of the amygdala and STS for the cluster corrections (see cluster correction details above). To further investigate whether individuals with ASD and controls exhibit different relationships between changes in individual BOLD responses of the STS and amygdala and accuracy scores in the behavioral task (group by accuracy interaction), respectively, we included individual accuracy scores as a covariate into the higher-level model for each group separately.

To visualize the strength and direction of the correlations between changes in neural activity and the behavioral covariate we extracted parameter estimates from the activated clusters identified in the contrast of interest.

Results

Behavioral results

Arena of Emotions – indirect behavioral task performance. The behavioral results have been previously reported in a separate study and we refrain from restating them here (Rosenblau et al., in revision). In summary, the indirect task was reliable and sensitive to the mentalizing impairments of individuals with ASD. The total ASD group (N=28) had significantly fewer correct responses than the control group and the ASD group's performance on the task was negatively correlated with autism symptomatology. Please refer to results section of the respective manuscript for more information.

fMRI task – behavioral data. To test whether the two experimental conditions (ToM and PI) were comparable with regards to task difficulty across all participants, we performed repeated measures ANOVAs separately for accuracy rates and correct RT with the within subject factor condition (ToM / PI) and the between subject factor group (Controls / ASD). There were no significant differences in accuracy rates (condition: $F (1, 40) = 2.22, p > 0.1$) or correct RT (condition: $F (1, 40) = 0.76, p > 0.1$) between the two conditions. Furthermore, the ASD group showed a trend for lower accuracy on the fMRI task in general (group: $F (1, 40) = 2.97, p < 0.10, \eta_p^2 = 0.07$), but no differences in RT (group: $F(1, 40) = 0.38, p > 0.5$). There was no significant interaction between group and condition (ToM / PI) for accuracy rates and reaction times (accuracy: condition by group interaction: $F (1, 40) = 0.58, p > 0.50$;

correct RT: condition by group interaction: F (1, 40) = 0.14, p > 0.50; see Table 3). The lack of a significant group by condition interaction suggests that both groups tracked changes in the protagonists' emotional state to a similar extent. Thus, between group differences in BOLD activation during the ToM condition reflect differences in processing mental states and cannot be accounted for by group differences in task difficulty.

Eye-tracking analysis

To test whether in both groups participants paid equal amount of attention to the screen in both runs and both conditions, we performed a repeated measures ANOVA on eye gazes with the within subject factors run (run1 vs. run2) and condition (ToM vs. PI) and the between subject factor group (controls vs. ASD). In both runs (F(1, 27) = 2.45, p > .10) participants paid an equal amount of attention to both conditions (F(1, 27) = .01, p > .90). Furthermore, there was no significant difference in visual attention to the screen between groups (F(1, 27) = .321, p > .50) and no significant interactions between the factors.

fMRI results

Mentalizing related neural activity. The contrast ToM versus PI video phases yielded robust activations (p < .05, z = 2.3, cluster corrected) of mentalizing regions including the medial prefrontal cortex (MPFC), the left temporo-parietal junction (TPJ), the left STS, the bilateral temporal poles (TP), the bilateral inferior frontal gyrus (IFG), the insula, and bilateral amygdala (Figure 3A, in red, see also Table 4).

Differences in mentalizing related neural activity between ASD and controls. Within the previously identified mentalizing regions, we found significantly increased activation of the left amygdala and STS in the control compared with the ASD group ($p < .05$ cluster corrected). Furthermore, the left superior temporal gyrus (STG) and hippocampus were more activated in controls than in individuals with ASD (Figure 3B and Table 4).

<u>*Brain behavior relationship:*</u>

Magnitude of amygdala activation correlates with performance on the indirect behavioral mentalizing task. To identify regions within the ToM network that predict implicit ToM performance, we investigated the relationship between performance on the behavioral AE task and changes in BOLD signal during the video phases in the ToM versus PI condition. Activation in the left amygdala was positively correlated with performance on the behavioral task in healthy controls ($x = -26$, $y = -2$ $z = -24$, peak Z score = 4.07, 78 voxels; cluster corrected within anatomical mask) but not in individuals with ASD. Furthermore, a smaller cluster within the previously identified left amygdala correlated more strongly with performance on the AE task in controls than in ASD participants ($x = -26$, $y = -2$ $z = -24$, peak Z score = 3.06, 21 Voxels; cluster corrected within anatomical mask (see Figure 3C). No significant correlation was found between STS activation and performance on AE task in either group.

Discussion

The goal of this study was to identify neural mechanisms of naturalistic, spontaneously occurring mental state inferences with a naturalistic task in typical and impaired social cognition. In addition, we investigated the relationship between neural processing and accuracy of mentalizing. Using dynamic and naturalistic stimuli, our task revealed activity of regions within the well-established mentalizing network (see e.g. Mar, 2011) and in addition of the amygdala and insula. This suggests greater emotional engagement during the watching of naturalistic scenes. The study further revealed the crucial role of the amygdala and the STS during spontaneous on-line mental state processing in controls compared to individuals with ASD. Strikingly, amygdala activation significantly predicted accurate implicit mental state inferences on an independent task in controls but not in individuals with ASD.

Spontaneous mentalizing, while watching complex social interactions, robustly activated regions assigned to the mentalizing network in healthy controls. Besides activations in the classical mentalizing regions such as the MPFC, TPJ, STS, TP, and the IFG (Mar, 2011), more spontaneous mentalizing yielded activity of the bilateral insula and amygdala, regions strongly implicated in affective processing and empathy, e.g. (Carr et al., 2003). The simultaneous engagement of these regions in mentalizing has been previously observed during judgments of others' affective states (Baron-Cohen et al., 2000; Schnell et al., 2011) or processing of highly dynamic and context-dependent stimuli (Adolphs, 2010). Amygdala and insula activation during spontaneous mentalizing is most likely due to a combination of both inferring the protagonists' affective states and processing dynamic naturalistic stimuli, which requires a multisensory integration of social information. As Schilbach et al. (in press) point out, the amount of emotional engagement with the task (passive observer reads about others' mental states versus observer engages emotionally into a social interaction) fundamentally changes the social cognitive processes as well as the underlying neural networks. Our study thus extends previous research by showing that amygdala and insula are involved in spontaneous mental state processing in emotionally engaging naturalistic settings.

As previously described (Rosenblau et al., in revision), our indirect behavioral task sensitively reflected the social deficits of individuals with ASD in implicit mentalizing. In the fMRI adaptation of the task both groups showed a comparable amount of visual attention as measured via eye-tracking and no differences in accuracy scores. Thus, differences in neural activation between groups represent differences in mental state processing only and cannot be attributed to more general load related differences.

As expected, healthy controls showed greater changes in BOLD signal in the amygdala and the STS during spontaneous mental state processing than individuals with ASD. Our results are in line with a vast body of literature linking both the amygdala and the STS to implicit processing of dynamic social information (see Adolphs et al., 2005) and

(Allison et al., 2000) for a review) and to the typical development of mentalizing abilities (Heberlein and Adolphs, 2004; Pelphrey et al., 2011). Our findings crucially extend the literature by showing that amygdala and STS not only support the development of mentalizing, but also underlie mental state inferences in complex, unstructured social settings. Importantly, the social deficits of individuals with ASD have also been tightly linked to aberrant amygdala and STS activation (e.g., Pelphrey et al., 2011). In this study we further specified the role of these brain regions for the pervasive mentalizing deficits of individuals with ASD in naturalistic settings. Furthermore, we found greater changes in BOLD signal in the hippocampus and STG in controls than in individuals with ASD. The latter region has been closely linked to mentalizing or related processes such as speech and prosody perception (Amodio and Frith, 2006; Schirmer and Kotz, 2006), which represent important social cues in our video-based task. In line with our findings, Boddaert and colleagues (Boddaert et al., 2003) found reduced activation of the STG in individuals with ASD during speech perception. Greater hippocampus activation in controls, in contrast, might reflect between group differences in mentalizing related memory processes (Spreng et al., 2009) and emotion processing (Critchley et al., 2000).

In contrast to previous studies that asked participants to make explicit judgments about others' mental states (e.g., (Lombardo et al., 2011), we did not find group differences in TPJ and MPFC activation. Those studies used abstract stimuli such as shapes or stories, which possibly requires higher-level explicit ToM processes that are mediated by the MPFC and TPJ (Amodio and Frith, 2006; Saxe and Powell, 2006; Olsson and Ochsner, 2008; Yoshida et al., 2010). In contrast, processing naturalistic stimuli as in the current study relies to a much larger extent on the implicit integration of a variety of sources of social information including facial expressions, prosody, and biological motion (Zaki and Ochsner, 2009), which recruits the amygdala and the STS. In sum, the naturalistic tasks have proved to be a sensitive means for the assessment of spontaneous real life mentalizing in healthy controls and individuals with ASD on the behavioral and neural level.

Finally, our results highlight the specific role of the amygdala in implicit social cognitive processing by showing that in typical development amygdala activation is related to the accuracy of social inferences, whereas in autism, which represents a model for reduced mentalizing accuracy, this relationship is reduced. This finding is in accordance with previous studies, which found that the magnitude of amygdala activation was related to the implicit judgment of another person’s intention as deceptive or not (Grezes et al., 2004) as well as to accurate emotion recognition (Derntl et al., 2009). The significantly reduced correlation between amygdala activation and accurate implicit mental state judgments in individuals with ASD points to a reduced relationship between social behavior and social brain regions in this clinical population. Our study thus provides evidence for the crucial role of the amygdala for accurate implicit mental state inferences in typical development and in the pathophysiology of autism, which could potentially be extended to other psychiatric disorders characterized by social impairments.

That being said, we cannot rule out that increased amygdala activation during the ToM versus PI condition in controls as well as between group differences in amygdala activation could also be partly explained by the fact that the stimuli included in the ToM and PI condition differ with regards to the degree of social saliency (the protagonists’ faces were blurred in the PI but not in the ToM condition). On the other hand, in every-day social settings facial affect recognition represents an important part of understanding intentions (Zaki and Ochsner, 2009) and that again makes it difficult to disentangle these processes in general. Also, the correlation between amygdala activation and accuracy on the external behavioral task in the control group may be in part explained by the fact that facial affect recognition plays an important role in both the behavioral mentalizing task and the fMRI ToM condition. It is somewhat unlikely, however, that the correlation between performance on an external mentalizing task and group differences in mental state processing, both assessed with naturalistic social stimuli including facial expressions, body language, tone of voice and specific context information, merely reflect differences in facial affect recognition.

In conclusion, the pervasive deficits of individuals with ASD in spontaneous mental state inference are associated with aberrant amygdala and STS activation, two brain regions that play a crucial role in the development of mentalizing abilities. While in typically developed controls amygdala activation during spontaneous mentalizing mediates accurate implicit mental state inferences on an independent task, in atypical development this coupling between brain response and behavior is significantly reduced. Our results thus highlight the important role of the amygdala for implicit mental state inferences in naturalistic settings and point to the important role of this region for disorders characterized by social cognitive deficits. Finally, our study stresses the importance of investigating mentalizing with accuracy-based naturalistic tasks in typical development as well as in clinical disorders characterized by social cognitive deficits.

Table 1. Demographical and symptom characteristics

	Controls			*ASD* total sample				*ASD* fMRI sample			
	N	*M*	*SD*	*N*	*M*	*SD*	*p Value*	*N*	*M*	*SD*	*p Value*
Sex, F(N) /N	6/22	-	-	10/28			.525	6/20			.845
Age		31.3	8.5		33.1	8.5	.471		31.8	9.3	.878
MWT-IQ		110.8	14.8		110.8	14.8	.342		110.8	14.8	.352
ADOS	-	-	-	24	10.6	3.4	-	19	10.4	3.5	-

Means (M), Standard Deviations (SD), and sample size (N) of group characteristics. P-values: two-tailed significance-value for F- and χ^2-tests in ASD vs. Controls; Abbreviations: ASD: Autism Spectrum Conditions; F: female; MWT: Mehrfachwahl-Wortschatz-Test; not applicable (-); ADOS: Autism Diagnostic Observation Schedule; fMRI: functional magnetic resonance imaging.

Table 2. List of Theory of Mind scenarios included in the scanner task

Film Scenes	Film Clip 1	Film Clip 2	Film Clip 3
Scene 1 Standing in line	Mrs. Hauser goes into the post office. Although there are people cuing, she hurries to the front of the line.	The other people are upset and tell Mrs. Hauser that they are waiting too.	Mrs. Hauser explains desperately that her sick child is waiting for her in the car. The other people still urge her to go to the end of the line.
Scene 2 Vegetarian dinner	Lisa has been invited for dinner at her friend's house and now looks forward to the meal.	Lisa takes a bite but then stops chewing disgusted. She asks her friend if the dish contains meat.	Lisa's friend asks apologetic whether Lisa does not eat any meat. Lisa is upset and and replies that she expects her friend to know that she is a vegetarian.
Scene 3 Meeting a friend	Mr. Martin is doing his weekly shopping when an old friend comes along. He asks her how she is doing.	His friend tells him that she has not been happy recently because her marriage is not going well.	Mr. Martin seems shocked and says that he is very sorry to hear that. His friend replies that she does not think the relationship will last.
Scene 4 Dating	Ana waits for her boyfriend in the park.	Ana cannot see that her boyfriend tries to play a trick on her: He sneaks up behind Ana and scares her with a loud noise. Ana gets very frightened.	Ana then turns around. When she realizes that it is her boyfriend she looks relieved.

Scene 5 Waiting room	Mrs. Meier reads a book in the waiting room. A man walks in and takes the seat next to her.	The man also reads something and starts laughing loudly. Mrs. Meier feels disturbed and turns away from him.	The man continues laughing without noticing that Mrs. Meier feels disturbed. In the end she gets angry at him.
Scene 6 Language exam	Helga is upset because she did not receive a high score on her exam. She shows her exam to a friend.	Helga's friend makes fun of her bad result.	Helga gets very angry with her friend.
Scene 7 Job interview	Kurt waits anxiously for his girlfriend, who is having a job interview.	His girlfriend arrives and looks disappointed. Kurt is worried and asks her whether the job interview did not go well.	Kurt's girlfriend starts smiling and tells him that she actually got the job.
Scene 8 Final exam	Dina is excited because her and her friend just received the results of their final exam. Her friend looks worried.	Dina opens the folder and finds out that she passed all exams and is very happy about it.	Dinah then looks at her friend who finds out that he did not pass, which he is very disappointed about.

Table 3. fMRI task performance

	Controls			*ASD fMRI sample*		
	N	*M*	*SD*	*N*	*M*	*SD*
	22			20		
Accuracy ToM		0.72	0.18		0.66	0.18
Accuracy PI		0.67	0.14		0.59	0.17
Correct RT ToM		1.25	0.37		1.34	0.61
Correct RT PI		1.21	0.34		1.26	0.42

Abbreviations: Accuracy in the ToM condition (Accuracy ToM), Accuracy in the PI condition (Accuracy PI), Reaction times for correctly solved items in the ToM condition in seconds (Correct RT ToM), Reaction times for correctly solved items in the PI condition (Correct RT PI).

Table 4. Significant activations in videos phases

	Side	Cluster size (Voxel)	Peak voxel MNI coordinates (mm)			Peak Z score
			x	y	z	
ToM Videos > PI Videos in Controls						
Cluster 1		10932				
STS	L		-48	-28	-4	7.69
Middle temporal gyrus	L		-52	-2	-20	6.27
Temporal pole	L		-52	4	-22	6.06
TPJ	L		-54	-44	8	5.83
Cluster 2		8812				
Superior temporal gyrus / Heschl's gyrus	R		44	-30	8	6.28
Amygdala	R		30	0	-26	4.76
Temporal pole	R		52	14	-36	4.69
Cluster 3		4720				
MPFC	R/L		2	54	28	5.78
			-2	58	22	5.45
Superior frontal gyrus	R/L		6	58	32	5.39
			-6	24	62	5.26
Left IFG	L		-46	26	-8	4.81
Amygdala	L		-20	-6	-14	3.90
Right IFG	R		42	30	-14	3.75
Insula	L		-32	-28	10	3.72
ToM Videos > PI Videos in ASD						
Cluster		2696				
Temporal pole	L		-46	10	-38	3.98
Inferior frontal gyrus	L		-38	24	-22	3.79
STS	L		-60	-40	6	3.71
			-52	-12	-10	3.65
ToM Videos > PI Videos in Controls > ASD						
Cluster		2327				
Hippocampus	L		-24	-34	-6	3.42
Superior temporal gyrus	L		-50	-20	0	3.28
Amygdala	L		-12	-6	-20	3.21
STS	L		-52	-20	4	3.14

All reported clusters are family-wise error (FWE) cluster corrected for multiple comparisons at $p < 0.05$ and $z = 2.3$. Abbreviations: Superior temporal sulcus (STS), temporoparietal junction (TPJ), medial prefrontal cortex (MPFC), inferior frontal gyrus (IFG).

Figure 1. Arena of Emotions indirect task: Example screen of one task item.

Each video item was preceded by a short written introduction, describing the context and setting of the interaction (here: a couple having breakfast, boyfriend is often jealous). After watching the first film scene (here: girlfriend finds out that her ex-boyfriend won the lottery, boyfriend is jealous again, see upper left hand side), participants were asked to watch the 4 film scenes below and pick the best suited option as to how the scene might continue.

Figure 2

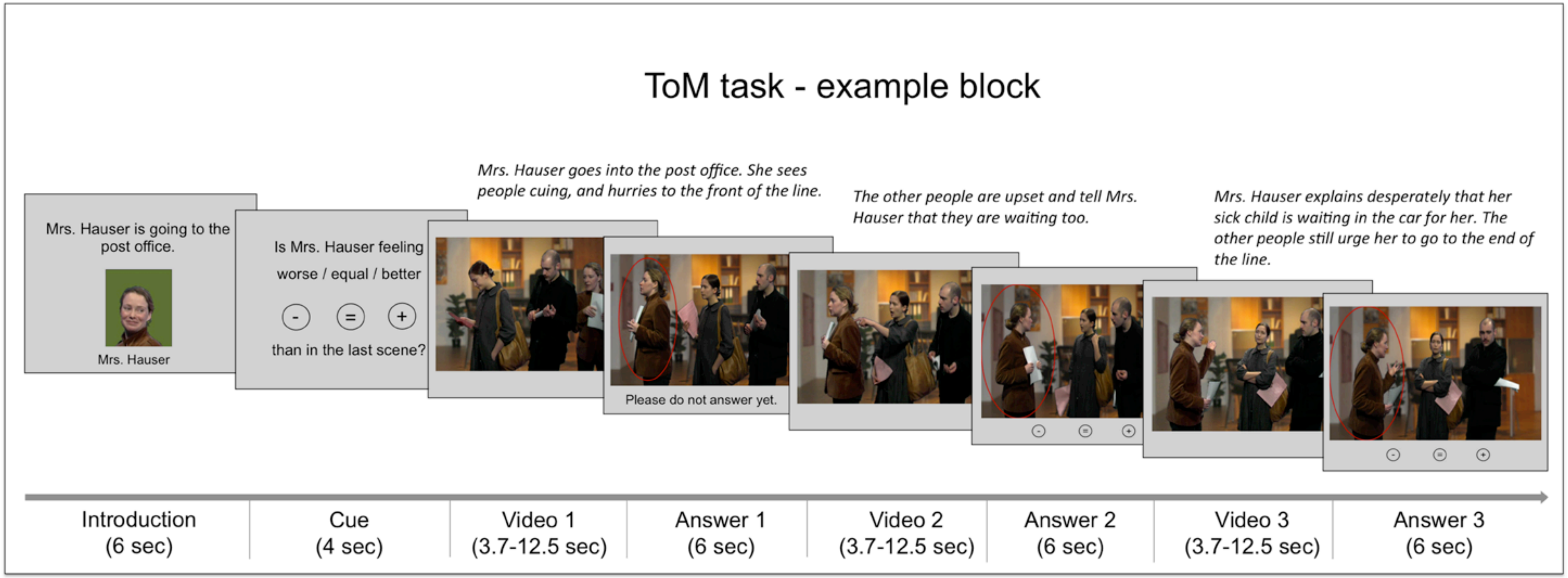
ToM task - example block
Mrs. Hauser is going to the post office.
Mrs. Hauser
Is Mrs. Hauser feeling
worse / equal / better
-
=
+
than in the last scene?
Mrs. Hauser goes into the post office. She sees people cuing, and hurries to the front of the line.
Please do not answer yet.
The other people are upset and tell Mrs. Hauser that they are waiting too.
Mrs. Hauser explains desperately that her sick child is waiting in the car for her. The other people still urge her to go to the end of the line.
Introduction (6 sec)
Cue (4 sec)
Video 1 (3.7-12.5 sec)
Answer 1 (6 sec)
Video 2 (3.7-12.5 sec)
Answer 2 (6 sec)
Video 3 (3.7-12.5 sec)
Answer 3 (6 sec)

Figure 2. Theory of mind (ToM) paradigm: Example of a ToM block

In ToM blocks, participants judged clip-by-clip changes in the affective states of the protagonists. Participants first saw an introduction comprising the setting of the social scene and presenting the main protagonist. The following cue indicated the type of condition (theory of mind (ToM) or physical inference (PI)). In ToM blocks, participants subsequently watched three consecutive film clips (i.e., video phases). After the first video phase participants did not have to make a judgment in the following answer phase. In the second and third answer phase, participants were asked to judge changes in affective state of the main protagonist between two consecutive video phases with a button press. Specifically, they were asked to indicate whether the main protagonist felt worse, equally well or better than in the previous film clip.

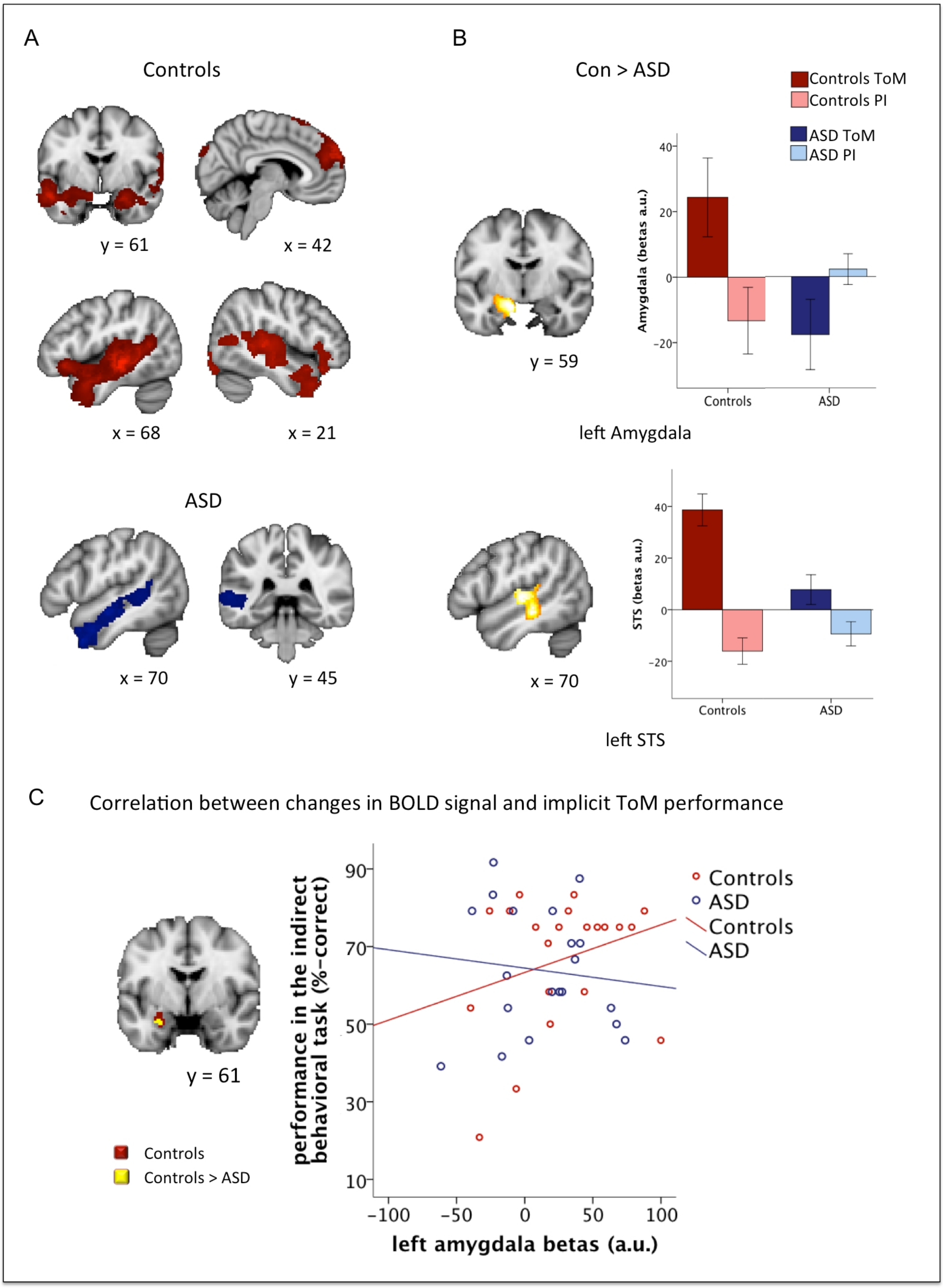
A
Controls
y = 61
x = 42
x = 68
x = 21
ASD
x = 70
y = 45
B
Con > ASD
Controls ToM
Controls PI
ASD ToM
ASD PI
y = 59
Amygdala (betas a.u.)
40
20
0
-20
Controls
ASD
left Amygdala
x = 70
STS (betas a.u.)
40
20
0
-20
Controls
ASD
left STS
C
Correlation between changes in BOLD signal and implicit ToM performance
y = 61
Controls
Controls > ASD
performance in the indirect behavioral task (%-correct)
90
70
50
30
10
-100
-50
0
50
100
left amygdala betas (a.u.)
Controls
ASD
Controls
ASD

Figure 3. ToM related BOLD signal and the relationship between BOLD signal changes and implicit ToM performance.

A, Network of brain regions showing significantly greater activation during theory of mind (ToM-videos) video phases compared to physical inference (PI-videos) video phases in controls (red) and in individuals with ASD (blue). B, Higher amygdala and superior temporal sulcus (STS) activations in controls than in individuals with ASD during ToM-videos compared to PI-videos. Parameter estimates extracted from the amygdala and STS are illustrated in bar graphs. Error bars indicate standard error of mean. C, Changes in BOLD signal in the left amygdala during ToM-videos compared to PI-videos were correlated with implicit ToM performance on an independent behavioral ToM task in controls (red). Changes in BOLD signal of a cluster within the left amygdala (yellow) and implicit ToM performance were higher correlated in controls than in individuals with ASD. The correlation plot displays the strength and direction of correlation between parameter estimates (a.u.: arbitrary units) extracted from the left amygdala (yellow) and accuracy on the independent behavioral ToM task.

Emotional prosody processing in Behavior and Brain Function: Insights from Autism Spectrum Disorder

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Number of pages:

Number of words:

Abstract: 250

Introduction: 591

Discussion: 1574

3 Figures and 4 Tables

Acknowledgements

Conflict of Interest Disclosures: None of the authors have conflicts of interest.

Funding/Support: The study was funded by a grant from the German Research Foundation (DFG; EXC 302).

We gratefully acknowledge the actors, who participated in the audio recordings and the members of the Computer and Media Service team (CMS) at the Humboldt University for their support with the production and postproduction of the audio stimuli. We also thank our student research assistants for their help with the stimulus production and data acquisition. In addition, we would like to thank our participants on the autism spectrum for their participation in the study.

Abstract

Social communication crucially depends on efficient processing of subtle nonverbal cues such as emotional prosody. Individuals with Autism Spectrum Disorder (ASD) are characterized by severe deficits in social communication, whereby specific impairments in emotional prosody processing have yet to be specified. Here, we investigated emotional prosody processing in individuals with ASD and matched control participants on the behavioral and neural level. New naturalistic behavioral and imaging tasks were developed that comprised a wider range of social emotions and more speakers than in previous studies. Compared to controls, individuals with ASD showed reduced performance in the behavioral task comprising mostly social emotions, such as jealousy. Emotional prosody processing recruited a fronto-temporal network including the superior temporal sulcus (STS) and the inferior frontal gyrus (IFG) bilaterally in both groups. Crucially, functional coupling between the right STS and right IFG was significantly reduced for emotional versus neutral prosody in ASD. In addition, individuals with ASD recruited the amygdala and STS to a lesser extent for social versus basic emotions than controls and functional connectivity between these regions was significantly reduced in ASD. Importantly, for social emotions activity of core prosody regions such as the bilateral STS and IFG predicted accurate emotion recognition on the behavioral task to a greater extent in controls than in ASD. In sum, these results provide evidence for dysfunctional emotional prosody processing in individuals with ASD on

the behavioral and neural level and highlight the crucial role of the relationship between brain function and behavior for unimpaired emotional prosody processing.

Introduction

Emotional prosody, i.e., the speaker's tone of voice, conveys important information about the speaker's communicative intention and in everyday social communication it is processed mainly implicitly (i.e., in the absence of explicit verbal cues) (Wildgruber et al., 2006). In contrast to basic emotions (e.g., joy, anger) that involve universal, highly stereotypical physiological reactions (Ekman and Friesen, 1971; Ekman, 1992; Zinck and Newen, 2008), understanding social emotions (e.g., gratitude or jealousy) requires a higher degree of mental state inference or mentalizing (Burnett et al., 2009).

Although Autism Spectrum Disorder (ASD) has been associated with abnormal emotional prosody production and processing (Tager-Flusberg, 1981; Baltaxe and D'Angiola, 1992; McCann and Peppe, 2003), to date empirical research produced mixed results. Some studies reported aberrant prosody processing of basic and social emotions in individuals with ASD compared to controls (Hobson et al., 1988; Baron-Cohen et al., 1993; Loveland et al., 1995; Deruelle et al., 2004; Golan et al., 2007; Kuchinke et al., 2011), whereas other studies did not find such group differences (Loveland et al., 1997; Boucher et al., 2000; Chevallier et al., 2011). These inconsistencies most likely reflect substantial differences in methodology between studies (see McCann and Peppe, 2003). Studies investigating emotional prosody processing with a limited number of mostly basic emotions (e.g., Boucher et al., 2000; Paul et al., 2005), including few speakers and answer options (e.g., Chevallier et al., 2011), might lack the sensitivity to detect subtle impairments in prosody processing in high-functioning individuals with ASD.

Across various tasks, emotional prosody processing involves activity of the right superior temporal sulcus (STS) and the bilateral inferior frontal gyrus (IFG) (Schirmer and Kotz, 2006; Wildgruber et al., 2006). A current prosody processing model proposes that the right STS is involved in extracting acoustic information, which is subsequently evaluated within the bilateral IFG (Ethofer et al., 2006; Wildgruber et al., 2006). Additionally, processing the emotional saliency of the stimuli recruit the amygdala and the ventral striatum (Schirmer and Kotz, 2006).

The neural processing of emotional prosody in ASD has remained an under-researched topic with inconclusive results. There is the notion that individuals with ASD show increased and more wide spread neural activity during prosody processing compared to controls (Wang et al., 2006; Eigsti et al., 2012). Interestingly, with respect to the visual domain, impaired recognition of social emotions, which relies on mentalizing abilities, and mentalizing impairments have been consistently linked with dysfunctional activity of the amygdala and the posterior STS (Baron-Cohen et al., 1999a; Castelli et al., 2002; Pelphrey et al., 2011). Given the fact that understanding social emotions requires mentalizing abilities (Heerey et al., 2003), processing processing impairments of social emotions in individuals with ASD might involve aberrant amygdala and STS activity.

In this study, we aimed at extending the current model of emotional prosody processing to naturalistic settings. Thus, we investigated emotional prosody processing in individuals with ASD and healthy controls with newly developed behavioral and fMRI tasks. To increase ecological validity, the tasks comprised a variety of social emotions, speakers, as well as implicit and explicit task conditions. Specifically, we aimed at relating neural prosody processing with behavioral prosody recognition in an independent task. We expected individuals with ASD to score lower than controls on the behavioral prosody recognition task, which would be associated with aberrant neural activity of the prosody processing network and a reduced relationship between activity of prosody processing regions and prosody recognition performance. Finally, we hypothesized that processing social versus basic emotions would involve the amygdala and STS to a lesser extent in individuals with ASD than in controls.

Materials and Methods

Participants

Twenty-seven adults with ASD (18 male, mean age = 33) and 22 control participants (16 male, mean age = 32) with no reported history of psychiatric or neurological disorders were matched according to gender, age, and verbal IQ as measured with a vocabulary test (Mehrfachwahl-Wortschatz-Test (MWT), Lehrl, 1989) (see Table 1). ASD participants were recruited through the autism outpatient clinic for adults of the Charité – University Medicine Berlin, Germany or were referred to us by specialized clinicians. ASD participants were diagnosed according to the DSM-IV criteria for Asperger syndrome and autism without intellectual disabilities (American Psychiatric Association, 2000). Diagnoses were confirmed by at least one of the two gold-standard diagnostic instruments: the Autism Diagnostic Observation Schedule (ADOS, Lord et al., 2002) and the Autism Diagnostic Interview - Revised (ADI-R; Lord et al., 1994), if parental informants were available (N = 15). Additionally, the diagnosis of Asperger syndrome was confirmed with the Asperger Syndrome and High-Functioning Autism Diagnostic Interview (ASDI; Gillberg et al., 2001). Seven of the 27 ASD participants met exclusion criteria for participation in the fMRI experiment (claustrophobia: N = 2; no normal or corrected to normal vision N = 1, no current health insurance: N = 1; psychotropic medication: N = 3). Two of the 22 controls did not want to participate in the fMRI experiment (one male and one female), and for one female participant we only acquired fMRI data. The fMRI sample thus comprised 20 ASD and 21 control participants matched for age, gender and IQ (see Table 1).

All participants received payment for participation and gave written informed consent in accordance with the requirements of the ethics committee of the German Society for Psychology (DGPs).

Tasks and Material

We developed two emotional prosody tasks, a behavioral and an fMRI task. Both tasks comprise semantically neutral sentences spoken with emotional prosody. Emotional prosody conveys either basic (e.g. happy, sad) or social emotions (e.g. thankful, embarrassed). Social emotions were defined here as emotions that rely on the interpretation of a social context or another's mental state (Burnett et al., 2009; Chevallier et al., 2011). To improve the tasks' sensitivity to real-life social information processing, we included a larger number of speakers and emotions than has been done by most studies. Based on a previous study, we selected emotions that had been rated to occur with high frequency in real life (Hepach et al., 2011).

Stimulus production and validation. The audio stimuli were recorded within the context of a comprehensive project to produce a new set of ecologically valid video and audio stimulus material, comprising a total set of 40 different emotional states as well as neutral expressions. The selection of 40 emotions was based on a previous study that classified emotional words based on the classic valence and arousal dimensions and furthermore regarding their communicative frequency and thus relevance in everyday life (communicative frequency, see, Hepach et al., 2011). The recordings took place at the film studios of the Humboldt University Berlin, Berlin Germany in cooperation with its Computer and Media Service team (CMS) and included 50 professional actors of varying age (18-65 years). The actors were given specific emotion inducing instructions, comprising for example situations in which the respective emotion usually occurs (e.g. jealous: “You have found a love letter directed to your partner on his/her desk”). Actors were further invited to remember a personal event in which they felt the respective emotion and put themselves into that particular situation again. The emotion inducing instructions were developed together with professional acting instructors.

Stimuli were validated in two steps. First, the quality of expression (e.g. preciseness and believability) was evaluated by the project members during stimuli production and postproduction steps (e.g., cutting, labeling, normalizing the audios). Audios containing ambiguous emotional prosody were immediately excluded from the dataset. In a second step, we selected 100 audios spoken by a total of 20 actors (10 males) for a validation study including expert ratings from 10 psychologists working in the field of social cognition that were not involved in the project (4 male, mean age = 29.6 years, SD = 4.3). Emotional prosody of the audios was correctly recognized in 83.6% of the cases (SD = 10.3), and was rated as overall naturalistic (6-point Likert scale from 1 = not believable to 6 = very believable). The rated level of believability (mean = 4.1, SD = 0.49) was significantly above the mid-point of the scale (one-sample t-test: t(9) = 4.13, p = 0.003). Out of the validated audio stimulus set, we selected 25 items for the behavioral prosody recognition.

Behavioral prosody task. The newly developed behavioral voice task comprises 25 semantically neutral sentences (e.g. They were all invited to the meeting) spoken by a total of 16 professional actors (6 male, varying age (20-50 years)). All sentences (mean length = 5.1 seconds, SD = 0.9,) were spoken with emotional prosody. In sum, the task covers four basic (angry, sad, happy, surprised) and 21 social emotions (interested, frustrated, curious, passionate, contemptuous, furious, confident, proud, desperate, relieved, offended, concerned, troubled, expectant, confused, hurt, bored, in love, enthusiastic, lyrical, shocked). After listening to the audio exerpt, participants are explicitly asked to select the correct emotion label out of four different options and drag and drop it into the target panel (see Figure 1 for an example). Distractor labels consist of i) two emotions of the same valence, one resembles the correct option more closely with respect to emotional arousal than the other one and ii) one emotion of the opposite valence. There is no time limit to solve each item, but participants are instructed to perform as fast and as accurately as possible. No trial and thus no target emotion is repeated and also no feedback is provided about whether the items have been solved correctly or not. Items are presented in randomized order across participants. The prosody task was designed and programmed as a web-based application in cooperation with a digital agency (gosub communications GmbH, www.gosub.de).

fMRI prosody task. In the block-design fMRI task participants are presented with semantically neutral sentences (mean length: 2.9s, SD = 0.01) spoken with emotional or neutral prosody by 10 different actors (5 male). Participants have to either indicate the speaker's gender (implicit condition) or the correct emotion label from two options (explicit condition). Each fMRI task block (30s) starts with a cue screen (2s), which indicates the condition ('gender' for implicit blocks; 'emotion' for explicit blocks), followed by four trials comprising an audio (4s) and an answer screen (3s). Note that we reduced the answering options for the prosody recognition task to reduce task demands and thus possible load-related between group differences in BOLD signal change. Eight blocks contain audios with neutral prosody (4 in each condition) and 24 blocks contain audios with emotional prosody (12 audios in each condition (implicit or explicit) either covering basic (3 blocks) or social emotions (3 blocks)). Positive and negative emotions are presented in different blocks. Blocks of audios are counterbalanced with respect to the type of emotion and speaker's gender across runs and conditions. There is no overlap between sentences used in the behavioral and fMRI task.

Based on the ratings obtained by (Hepach et al., 2011), the six basic emotions (happy, surprised, fearful, sad, disgusted, angry) were matched for valence (Wilcoxon signed-ranks: $p = 0.753$) and arousal (Wilcoxon signed-ranks: $p = 0.917$) with six social emotions (jealous, grateful, contemptuous, shocked, concerned, disappointed). In the fMRI session, the task was presented using Presentation (Version 14.1, Neurobehavioral Systems Inc., Albany, CA) in two runs of 10 min 34 seconds each.

Procedure

In the behavioral session, participants completed the behavioral prosody task online through the project's website in testing rooms of Freie Universität Berlin, Germany under the supervision of trained experimenters. Participants read a few introduction slides before completing the task. Completing the task took approximately 15 minutes. Throughout the entire task, participants used the mouse to navigate through introduction screens and solve the 25 task items.

The fMRI experiment took place in a different session at the DINE (Dahlem Institute for Neuroimaging of Emotion, Freie Universität Berlin, Germany; http://www.loe.fu-berlin.de/dine/index.html).

fMRI data acquisition

MRI data were acquired on a 3 Tesla scanner (Tim Trio; Siemens, Erlangen, Germany) using a 12-channel head coil. Functional data were acquired using an echo-planar T2*-weighted gradient echo pulse sequence (TR = 2000 ms, TE = 30 ms, flip angle = 70, 64 X 64 matrix, field of view = 192 mm, voxel size = 3 X 3 X 3 mm^3). A total of 37 axial slices (3 mm thick, no gap) were sampled for whole-brain coverage. Functional imaging data were acquired in two separate 310-volume runs of 10 min 34 s each. Both runs were preceded by two dummy volumes to allow for T1 equilibration. For each participant, a high-resolution T1-weighted anatomical whole brain scan was acquired in the same scanning session, which was later used for registration of the fMRI data (256 X 256 matrix, voxel size = 1 X 1 X 1 mm^3).

fMRI data analysis

Preprocessing. fMRI data were preprocessed and analyzed using FEAT (FMRI Expert Analysis Tool) within the FSL toolbox (FMRIB's Software Library, Oxford Centre of fMRI of the Brain, www.fmrib.ox.ac.uk/fsl, Smith et al., 2004). After brain extraction, slice timing, and motion correction, volumes were spatially smoothed using a 8-mm full width at half maximum (FWHM) Gaussian kernel. Low frequency artifacts were subsequently removed with a high-pass temporal filter (Gaussian-weighted straight line fitting, sigma = 100 s).

Functional data were first registered to individuals’ T1-weighted structural image and then registered to standard space using the FMRIB's Linear Image Registration Tool (FLIRT, Jenkinson and Smith, 2001).

fMRI single-subject analysis. We modeled the time series individually for each participant and run including ten epoch regressors (representing the factor levels for the three factors emotion *complexity* (social and basic prosody), *valence* (positive, negative and neutral prosody) and *condition* (implicit and explicit condition)), as well as one regressor for all button presses that occurred during the experiment. Additionally, we included six regressors modelling head movement parameters. The regressors were then convolved with a Gamma hemodynamic response function (HRF). Contrast images were computed for each condition, run, and participant. They were spatially normalized, transformed into standard space and then submitted to a second-order within-subject fixed-effects analysis across the two runs.

fMRI group analysis. Contrast images were subjected to higher-level mixed-effects analyses using the FMRIB Local Analysis of Mixed Effects tool provided by FSL (FLAME, stage 1 & 2). We report clusters of maximally activated voxels that survived family-wise error (FWE) cluster correction for multiple comparisons at a statistical threshold of $p < .05$ and a z-value of 2.3.

To identify a *common emotional prosody network* across both groups, we contrasted emotional with neutral prosody over all participants. In the subsequent between group analyses, we investigated *group* (controls versus ASD) differences in emotional prosody processing and whether the emotional prosody network was distinctly modulated by *condition* (explicit versus implicit) and *emotion complexity* (social versus basic) in controls versus ASD participants. Since the aim of the study was to investigate modulations of the emotional prosody network by the three factors group, condition, and emotion complexity, we restricted the analysis to the common emotional prosody network. By doing so we avoided the problem of biasing the selection of voxels to either of the three factors. In order to investigate the notion that processing social emotions recruits mentalizing related regions, such as the medial prefrontal cortex (MPFC), to a higher extent than basic emotion processing in controls (see e.g., (Alba-Ferrara et al., 2011)), we performed a whole brain analysis for this contrast in controls only. Consistent with the previous analyses, we report clusters of maximally activated voxels that survived FWE cluster correction for multiple comparisons at a statistical threshold of $p < .05$ and a z-value of 2.3.

To investigate whether and how potential group differences in neural processing of emotional prosody were related to behavior (i.e., emotion recognition), we conducted two kinds of analyses: a psychophysiological interaction (PPI) analysis and a covariate analysis using accuracy on the independent behavioral prosody task as a covariate into the model.

Psychophysiological Interaction (PPI). The PPI analysis reveals how the coupling of a seed region and any other voxel in the brain changes with task condition (Friston et al., 1997; Rogers et al., 2007). Here, we conducted a PPI analysis to identify potential group differences in the coupling between core prosody processing regions when processing emotional versus neutral prosody. We restricted the PPI analysis to a-priori-defined regions of interest (ROIs), which comprised right STS and bilateral IFG (see Wildgruber et al., 2006)). ROIs were defined by drawing a 10mm sphere around the peak-activated voxels of respective regions within the common prosody network over all participants. In accordance with the dynamic causal modeling (DCM) study by Ethofer et al. (2006), in which the right STS has been identified as the input region within the prosody processing network, we selected the right STS as the seed region for the PPI analysis, bilateral IFG represented the target regions. Thus, on the single-subject level, the general linear model (GLM) analysis comprised three regressors: the first regressor (physiological regressor) was the demeaned time course from the seed region (right STS), the second regressor represented the psychological condition (emotional versus neutral prosody) and the third regressor was the vector product, i.e., the psychophysiological interaction, of the first two regressors. In the subsequent group analysis we investigated significant differences in the amount of changes in coupling between right STS and bilateral IFG for emotional versus neutral prosody at a statistical threshold of $p < .05$ and a z-value of 2.3 FWE cluster corrected for multiple comparisons.

Furthermore, we investigated whether changes in the coupling of prosody processing regions were distinctly modulated by emotion complexity (social versus basic emotions) in controls versus individuals with ASD. The single-subject general linear model (GLM) analysis comprised the demeaned time course from the seed region (right STS), the psychological condition (social versus basic emotional prosody) and the psychophysiological interaction, of the first two regressors. Given our a priori hypotheses on group differences in STS and amygdala activity for social compared to basic emotions, in the subsequent group analysis we investigated significant differences in the amount of changes in coupling between right STS and left and right amygdala for social versus basic emotional prosody at a statistical threshold of $p < .05$ and a z-value of 1.7 FWE cluster corrected for multiple comparisons.

Covariate analysis. The aim of this analysis was to investigate whether BOLD signal change within the common prosody processing network correlated with explicit prosody recognition of social emotions in healthy controls and individuals with ASD. We ensured that this analysis was not prone to potential non-independence errors by entering performance on the independent behavioral prosody task as a covariate into the fMRI analysis. Furthermore, we investigated whether the correlations between brain activity and performance on the behavioral prosody task differed significantly between groups. Following the same rationale as for the fMRI group analysis we restricted the analysis to the common prosody network over all participants and to a statistical threshold of p < .05 and a z-value of 2.3 FWE cluster corrected for multiple comparisons.

To visualize the strength and direction of the correlations between neural activity and the covariate (i.e., the accuracy scores of the behavioral prosody task), we extracted parameter estimates from the activated clusters identified in the contrast of interest.

Results

Behavioral results: Emotional prosody recognition

Performance measures for both tasks comprised accuracy scores (percentages of correct answers) and reaction times (time to choose the correct emotion label) for correctly solved items.

Behavioral prosody task. To avoid the repetition of basic emotion in the task, the majority of items convey social emotions (21 out of 25 task items). Due to this difference between basic and social emotions, we refrained from analyzing group differences in basic emotion recognition and from comparing basic and social emotion recognition in the behavioral task. Independent sample t-tests revealed that controls were more accurate and faster than individuals with ASD (accuracy: t (1, 41) = 2.72, p = 0.006; RT: t (1, 47) = -2.23, p = 0.03; see Figure 1B and 1C). In the ASD group accuracy scores correlated negatively with autism symptomatology, as measured by the ADOS (r = -0.448, p = 0.028) and the ASDI (r =

-0.478, *p* = 0.018). The negative correlation between task accuracy and autism symptomatology indicates that more severely affected individuals scored lower on the task.

fMRI task. The number of blocks containing basic and social emotions in the fMRI prosody task was equal, and thus we compared emotion recognition of social versus basic emotions by adding the within-subject factor emotion complexity to the analysis. Repeated measures ANOVAs with the within subject factor complexity (social versus basic emotions) and the between subject factor group (Controls versus ASD) were performed for accuracy rates and RT separately. Over all participants, basic emotions were recognized more accurately and faster than social emotions (accuracy: $F(1, 39) = 47.9$, $p < 0.01$, $\eta_p^2 = 0.551$; RT: $F(1, 39) = 55.93$, $p < 0.01$, $\eta_p^2 = 0.589$). The groups showed comparable emotion recognition performance for basic and social emotions (accuracy: $F(1, 39) = 0.43$, $p = 0.516$; RT: $F(1, 39) = 0.18$, $p = 0.667$). Furthermore, there was no significant group by complexity interaction for accuracy rates ($F(1, 39) = 0.61$, $p = 0.441$) and RT ($F(1, 39) = 2.05$, $p = 0.161$; see also Table 2)

fMRI results

Common emotional prosody network over all participants

Contrasting emotional with neutral prosody revealed a previously described fronto-temporal network including bilateral STS, IFG, temporal poles, left insula and right amygdala (see

Figure 2 B and Table 3). There were no between group differences in overall emotional prosody processing.

Condition and emotion complexity effects within the emotional prosody network

In controls, explicit versus implicit emotional prosody processing yielded increased activity of prosody processing regions including the core regions right STS and bilateral IFG. Implicit versus explicit prosody processing in controls recruited bilateral temporal regions, such as the superior temporal gyrus, and the insula to a higher extent. With respect to group differences, however, there was no significant condition by group interaction (see Table 3).

With regards to emotion complexity, processing social versus basic emotions did not modulate activity of prosody processing regions or other brain regions not included in the network in controls. There was, however, a significant interaction of group and emotion complexity. Compared with the ASD group, controls showed significantly increased activity of the right STS, amygdala, planum temporale and superior temporal gyrus (STG) for social versus basic emotions (see Figure 3A and Table 3).

Brain behavior relationship

PPI results

The PPI analysis revealed that emotional prosody-dependent changes in connectivity between right STS and the right IFG differed between groups. Controls showed a significantly higher coupling between the right STS and right IFG for emotional versus neutral prosody compared to ASD participants. Furthermore, during processing of social versus basic emotional prosody, controls showed a higher functional connectivity between the right STS and the left amygdala compared to the ASD group (see Table 4).

Covariate analysis.

To identify regions within the emotional prosody network that support accurate recognition of social emotions, we investigated the relationship between accurate recognition of social emotions in the behavioral prosody task and BOLD signal changes when processing social emotions versus neutral prosody. In controls, the right IFG, temporal pole and middle frontal gyrus were positively correlated with performance on the behavioral task (see Figure 3B, red color and Table 4). Compared to controls, individuals with ASD showed a reduced relationship between activity of core prosody processing regions, including the bilateral IFG and bilateral STS, and accurate emotional prosody recognition (see Figure 3B, yellow color and Table 4).

Discussion

The aim of the current study was to further characterize behavioral emotional prosody processing and associated neural mechanisms in individuals with ASD and healthy controls. Over all participants, emotional prosody processing implicated a fronto-temporal network including the STS and IFG bilaterally. In individuals with ASD, the coupling between the core prosody regions, right STS and right IFG, was significantly reduced compared to controls. Importantly, between-group differences in processing and recognizing emotional prosody were particularly pronounced for social emotions. Compared to controls, individuals with ASD were slower and less accurate in recognizing social emotions. On the neural level, individuals with ASD recruited the amygdala and STS to a lesser extent when processing social versus basic emotions and the functional connectivity between these two regions was significantly reduced compared to controls. Strikingly, when processing social emotions, activity of core prosody regions, such as the bilateral STS and IFG, predicted accurate social emotion recognition in an independent task in controls but not in individuals with ASD.

Processing emotional prosody robustly activated the well-replicated prosody network over all participants (Schirmer and Kotz, 2006; Wildgruber et al., 2006). There were no differences in overall prosody processing between groups. In controls, however, the coupling between the core prosody regions, right STS and right IFG, was significantly stronger for emotional versus neutral prosody than in individuals with ASD. According to the DCM model of emotional prosody processing by (Ethofer et al., 2006) the connection between STS and IFG ensures that perceived prosodic information encoded in the right STS is transferred via parallel projections to the bilateral IFG, where the information is evaluated. Our results extend the respective model by showing that the functional connectivity between the right STS and right IFG distinguishes typical from atypical emotional prosody processing in ASD. Given that the right IFG is more strongly implicated in the explicit evaluation of emotional prosody (Ross, 1981; Heilman et al., 1984; Starkstein et al., 1994; Buchanan et al., 2000; Mitchell et al., 2003), the reduced coupling between the right STS and right IFG in individuals with ASD might further account for observed impairments in prosody recognition and social communication. However, reduced task-based functional connectivity between cortical regions in individuals with ASD has been consistently reported across a wide range of cognitive tasks including sentence processing (Just et al., 2004), executive functions (Koshino et al., 2005; Just et al., 2007), and mentalizing (Koshino et al., 2005). Thus, our finding of reduced functional connectivity between cortical regions during prosody processing might reflect general deficits of individuals with ASD in integrating information across cognitive domains (Just et al., 2004).

Individuals with ASD showed lower performance on the newly developed prosody recognition task compared to controls. Accuracy rates were negatively correlated with symptom severity in individuals with ASD, with more impaired individuals scoring lower.

Along with basic emotional expressions, the newly developed task covers a wide range of social emotions portrayed by a large number of male and female speakers. The higher degree of complexity and ecological validity of the task most likely increased its sensitivity to the subtle impairments of our sample of high-functioning ASD participants. Our results are in line with studies showing emotion recognition difficulties of individuals with ASD from voices (Hobson, 1986; Hobson et al., 1988; Baron-Cohen et al., 1993) and in particular for complex social emotions (Golan et al., 2007). Given that emotion recognition requires mental state processing (Hoffman, 2000; de Vignemont and Singer, 2006; Decety and Jackson, 2006), the impaired recognition of social emotions in individuals with ASD may reflect their core deficit in understanding others' mental states (Baron-Cohen et al., 2001). We did not find between group differences in the simpler fMRI version of the task, which comprised a very limited number of emotions (six basic and six social emotions) with only two answer options. Similarly, some studies that also used a more limited number of speakers, emotions or answer options report no differences in emotional prosody recognition between individuals with ASD and controls (Loveland et al., 1997; Boucher et al., 2000; Chevallier et al., 2011). Our study thus stresses the importance of using more naturalistic tasks than previously done to sensitively assess the subtle social cognitive impairments of high-functioning individuals with ASD.

On the neural level, individuals with ASD recruited the amygdala and STS to a lesser extent than controls when processing social compared to basic emotions. In the visual domain, both the amygdala and STS have been tightly linked to the social cognitive deficits of individuals with ASD (Critchley et al., 2000; Castelli et al., 2002; Dziobek et al., 2010; Kliemann et al., 2012), in particular to deficits in inferring others' mental states (Baron-Cohen et al., 1999b; Pelphrey et al., 2011). Our findings extend the literature by showing that aberrant amygdala and STS activity underlies the social deficits of individuals with ASD also in the auditory modality. In typically developed individuals both structures have been implicated in social cognitive processes that precede and support the development of mentalizing abilities (Allison et al., 2000; Adolphs et al., 2005) as well as in mental state inferences per se (Mar, 2011). Consequently, in controls, social emotions require a higher degree of mental state inferences –associated with higher amygdala and STS activity – than in individuals with ASD.

In contrast to previous studies (Takahashi et al., 2004; Alba-Ferrara et al., 2011), we did not find increased activity of core mentalizing regions such as the MPFC in controls for social versus basic emotional prosody. The lack of a modulation by emotion complexity in typically developed controls suggests that in intact prosody processing and recognition, basic and social emotions might be comparably salient and thus elicit comparable activity of prosody processing regions.

Importantly, functional connectivity between STS and amygdala was significantly reduced for social versus basic emotions in individuals with ASD compared to controls. Our results extend previous findings by showing that individuals with ASD are characterized by both aberrant activity and reduced connectivity between social brain regions. Given that the STS and amygdala are anatomically linked via reciprocal connections (Allison et al., 2000), greater functional connectivity between these regions might be associated with better performance at detecting or decoding social cues (Bickart et al., 2012). Both amygdala and STS crucially support social cognitive processes independent of modality (Pelphrey and Carter, 2008). The disruption of these connections could account for the pervasive social deficits of individuals with ASD.

In line with previous studies (e.g., Grandjean et al., 2005; Sander et al., 2005; Bach et al., 2008; Fruhholz et al., 2012), we found a modulation of the emotion prosody network by task condition (implicit versus explicit) in controls. Explicit evaluation of emotional prosody processing produced increased activity of the right STS and bilateral IFG, regions assigned to the core prosody network. In accordance with previous studies our results thus provide evidence of greater involvement of the core prosody regions (right STS and bilateral IFG) in directing attention to emotional prosody (explicit condition) versus away from emotional prosody (implicit condition) (Buchanan et al., 2000; Wildgruber et al., 2005; Bach et al., 2008; Ethofer et al., 2009). Implicit compared to explicit emotional prosody processing in controls yielded activity of bilateral temporal regions (including the STG and Heschl’s gyrus) and the insula. In accordance with the literature, our study suggests that implicit and explicit prosody processing are mediated by distinct neural networks in controls (e.g., Bach et al., 2008; Fruhholz et al., 2012). However, we did not find group differences in explicit versus implicit prosody processing within the emotional prosody network.

Importantly, changes in fMRI signal in prosody regions, while processing social emotions, significantly predicted social emotion recognition on an independent prosody task in controls. This relationship was significantly reduced in individuals with ASD. These results highlight that an increased sensitivity of the prosody processing network supports accurate explicit emotion recognition in typically developed individuals compared to ASD individuals. In controls, the network included the right IFG, temporal pole and middle frontal gyrus, confirming the important role of the right IFG in explicit emotion recognition (e.g. Schirmer and Kotz, 2006). The frontal poles have also been shown to play an important role in emotion recognition. Lesions of the temporal pole and insula were closely associated with lower emotion recognition accuracy (Leigh et al., 2013). Furthermore, in controls changes in activity of core prosody regions, including the STS and IFG bilaterally, were more highly correlated with prosody recognition of social emotions than in individuals with ASD. The significantly reduced correlation between changes in activity in these regions and accurate recognition of social emotions in individuals with ASD suggests a reduced relationship between performance and social information processing in autism, which could potentially be extended to other psychiatric disorders characterized by social impairments.

In sum, our study provides important insights into typical and atypical prosody processing that most likely have important implications for typical and impaired social communication in real life social settings. Lower recognition rates of emotional prosody conveying social emotions in individuals with ASD were associated with reduced amygdala and STS activity, suggesting the importance of these regions for social cognition across modalities. Finally, our study highlights the crucial role of the interplay between behavioral emotional prosody recognition and neural processing of emotional prosody in social communication. The reduced functional connectivity between core prosody regions along with a reduced relationship between neural prosody processing and behavioral prosody recognition may account for the pervasive impairments in social communication of individuals with severe social impairments such as autism.

Table 1. Demographical and symptom characteristics

	Total sample							*fMRI sample*						
	Controls			*ASD*				*Controls*			*ASD*			
	N	*M*	*SD*	*N*	*M*	*SD*	*p Value*	*N*	*M*	*SD*	*N*	*M*	*SD*	*p Value*
Sex: N(F)/N	6/22	-	-	9/27			.760	6/21			6/20			.595
Age		31.8	8.5		33.1	8.7	.600		31.9	9.3		31.8	9.3	.970
MWT-IQ		108.6	13.2		112.9	16.7	.330		108.3	13.6		113	17.3	.335
ADOS	-	-	-	24	10.5	3.4	-				19	10.4	3.5	-

Means (M), Standard Deviations (SD), and sample size (N) of group characteristics. P-values: two-tailed significance-value for F- and χ²-tests in ASD vs. Controls; Abbreviations: ASD: Autism Spectrum Disorders; F: female; MWT: Mehrfachwahl-Wortschatz-Test; not applicable (-); ADOS: Autism Diagnostic Observation Schedule; fMRI: functional magnetic resonance imaging.

Table 2. Emotional prosody recognition performance

	Controls			*ASD*		
	N	*M*	*SD*	*N*	*M*	*SD*
Behavioral task						
	22			27		
Accuracy		0.69	0.10		0.58	0.18
RT total scale (s)		11.4	3.26		13.9	4.44
fMRI task						
	21			20		
Accuracy basic emotions		0.79	0.16		0.79	0.13
Accuracy social emotions		0.64	0.15		0.60	0.14
RT basic emotions (s)		1.48	0.23		1.57	0.31
RT social emotions (s)		1.78	0.30		1.76	0.30

Abbreviations: ASD: Autism Spectrum Disorders; Reaction times for correctly solved items (RT). seconds (s).

Table 3. Significant activations in the contrasts of interest

	Side	Cluster size (Voxel)	Peak voxel MNI coordinates (mm)			Peak Z score
			x	y	z	
Emotional Prosody > Neutral Prosody over all participants						
Cluster 1		9458				
Superior Temporal Sulcus	R		48	-18	-8	5.33
Inferior Frontal Gyrus	R		44	32	-2	5.10
			46	30	4	4.95
			56	20	14	4.76
			50	18	14	4.76
			56	26	0	4.76
Cluster 2		4898				
Superior Temporal Sulcus	L		-62	-28	8	5.02
			-52	-22	-4	4.50
			-50	-18	-14	4.22
Temporal Pole	L		-52	4	-22	4.91
Superior Temporal Gyrus	L		-46	-22	-2	4.56
			-46	-14	-4	4.25
			-50	-18	-14	4.22
Cluster 3		1886				

Frontal Orbital Cortex	L	-32	28	-10	3.61
Inferior Frontal Gyrus	L	-52	18	24	3.61
		-44	20	20	3.60
		-50	28	6	3.56
		-60	22	16	3.47
Insular Cortex	L	-32	22	-4	3.40
Cluster 4	1781				
Intracalacarine Cortex	R	18	-70	6	4.41
	R	16	-64	6	3.85
	L	-12	-76	16	3.48
	L	-12	-72	8	3.37
	L	-16	-70	8	3.33
Lingual Gyrus	L	-18	-58	-2	3.40
Amygdala	R	30	-6	-18	2.85

Explicit > Implicit Emotional Prosody in Controls

Cluster 1		5552				
Superior Temporal Sulcus	R		54	-32	-6	5.62
			50	-32	-2	5.28
			52	-36	-2	5.22
Inferior Frontal Gyrus	R		46	24	8	5.18
			56	26	6	5.00
Cluster 2		1042				
Inferior Frontal Gyrus	L		-42	12	20	3.92
			-48	30	-10	3.31
Frontal Orbital Cortex	L		-30	28	-10	3.21
			-38	26	-14	3.18
			-32	24	-8	3.15
			-38	24	-10	3.13
Cluster 3		589				
Temporal Pole	L		-48	4	-26	4.72
			-50	14	-28	3.54

			-46	14	-30	3.51
Middle Temporal Gyrus			-52	-10	-20	3.50
Implicit > Explicit Emotional Prosody in Controls						
Cluster 1		832				
Superior Temporal Gyrus	L		-54	-8	-2	6.06
			-66	-16	10	5.79
Planum Temporale	L		-56	-20	8	5.36
Planum Polare	L		-44	0	-10	4.59
Insula	L		-44	-2	-6	4.16
			-36	-14	-8	4.01
Cluster 2		581				
Heschl's Gyrus	R		54	-14	4	5.41
			52	-8	4	4.46
Planum Polare	R		44	-10	-6	4.82
			46	-14	-4	4.23
			42	-20	-4	4.15
Planum Temporale	R		58	-26	14	3.68

Social > Basic Emotional Prosody in Controls > ASD

Cluster 1		1886				
Planum Temporale	R		40	-32	12	4.24
			42	4	-20	3.04
Superior Temporal Gyrus	R		46	-14	-4	3.41
			64	-10	-4	3.05
			64	-10	-4	3.05
			48	-12	-10	3.03
Superior Temporal Sulcus	R		54	-38	4	3.19
			50	-42	8	3.12
Amygdala	R		30	-4	-20	2.77
Cluster 2		1427				
Heschl's Gyrus	L		-46	-20	4	3.75
Temporal Pole	L		-44	6	-12	3.33
Superior Temporal Gyrus	L		-62	-6	-2	3.30
			-66	-14	8	3.27
			-66	-36	8	3.25
Planum Polare	L		-46	-4	-10	3.10

All reported clusters are family-wise error cluster corrected for multiple comparisons (FWE) at a statistical threshold of $p < .05$ and a z-value of 2.3.

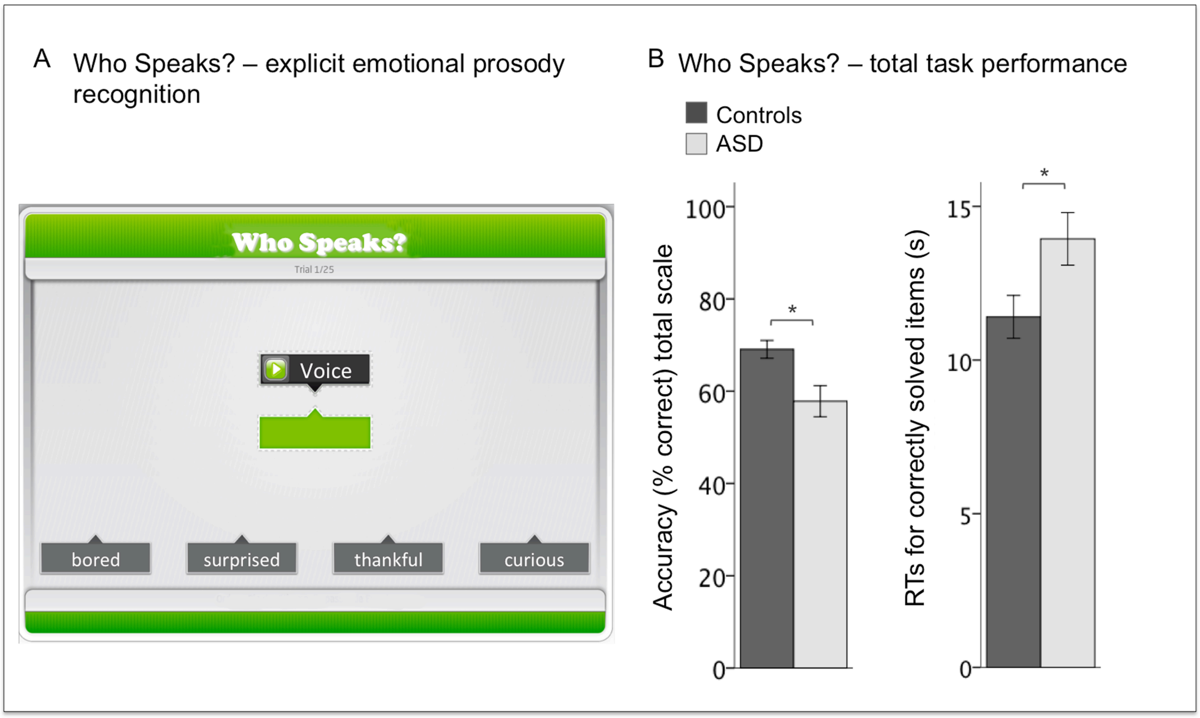

Figure 1. The behavioral emotional prosody task. A, Example item. Participants were presented with semantically neutral sentences spoken with emotional prosody and then had to chose one emotional label out of four different options. B, Mean accuracy scores (in percent, left) and reaction times (in seconds, right) for correctly solved items in controls and ASD participants. *: significant difference between controls and ASD (p<.05). Abbreviations: ASD: Autism Spectrum Disorder; Reaction time (RT); seconds (s). . Error bars represent standard error of the mean.

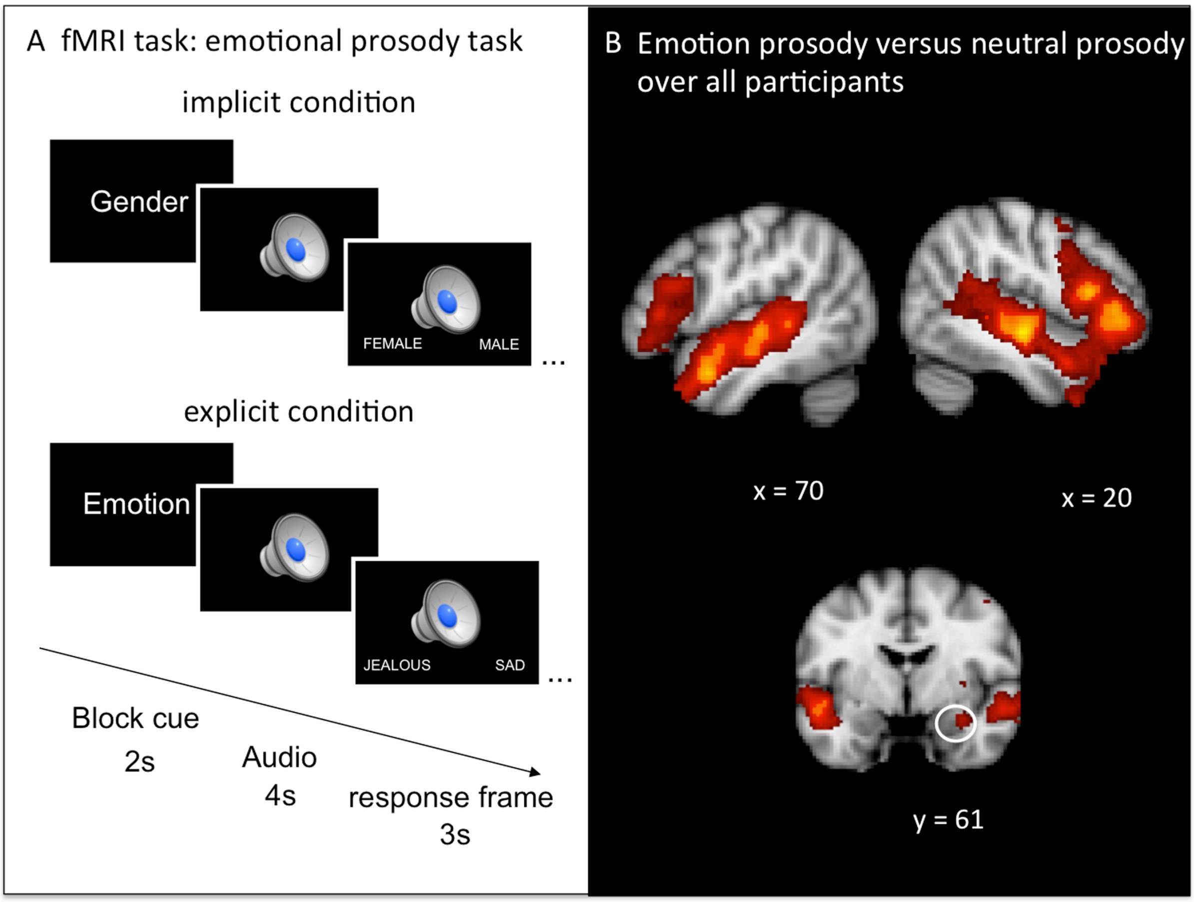

Figure 2. The fMRI emotional prosody task. A, The task comprised blocks of semantically neutral sentences spoken with emotional (basic or social) or with neutral prosody. Participants had to indicate the speaker's gender (implicit condition) or the correct emotion label (explicit condition) from two options. B, Brain regions showing significantly greater activation during emotional compared to neutral prosody processing over all participants (N = 41) at a statistical threshold of $p < 0.05$ and $z = 2.3$ family-wise error (FWE) cluster corrected for multiple comparisons.

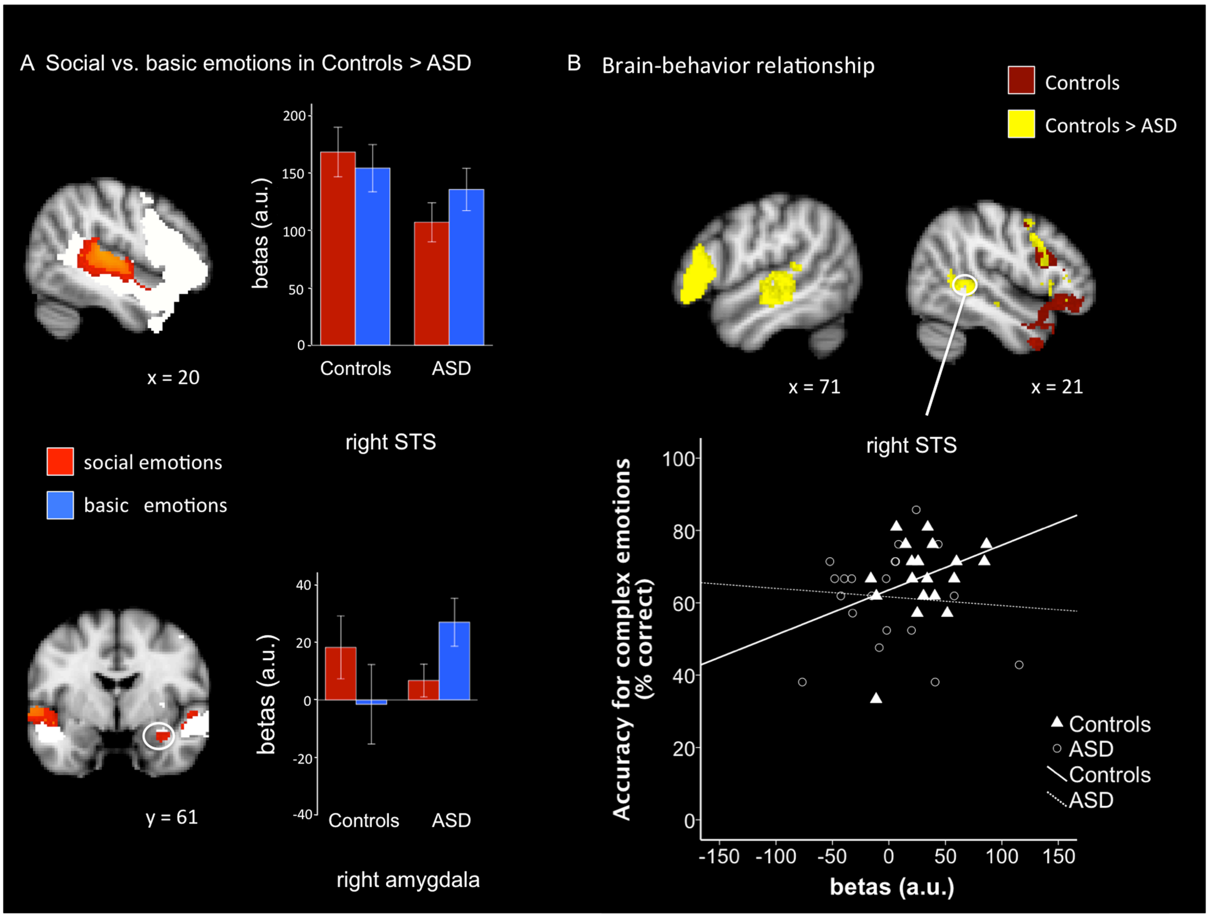

Figure 3. A, Brain regions within the emotional prosody processing network (main effect, emotional > neutral prosody over all participants, white) with significantly greater activation during social > basic emotions in controls compared to ASD. Parameter estimates extracted from the amygdala and STS are illustrated in bar graphs. Error bars indicate standard error of the mean. B, BOLD signal changes in regions of the emotional prosody processing network (white) when processing social emotions were correlated with prosody recognition accuracy for social emotions on an independent behavioral task in controls (red) and to a higher extent than in individuals with ASD (yellow). The plot displays the strength and direction of the correlation between parameter estimates extracted from the right STS (yellow) and accuracy on the independent behavioral prosody recognition task. All clusters

are significant at $p < 0.05$ and $z = 2.3$ family-wise error (FWE) cluster corrected for multiple comparisons. Abbreviations: Autism Spectrum Disorders (ASD); a.u. (arbitrary units); Superior Temporal Sulcus (STS); Blood Oxygen Level Dependent signal (BOLD signal).

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