NAVIGATING SOCIAL LIFE:
ON SOCIAL COGNITION IN HEALTH AND PSYCHOSIS

SUMMARY
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Social cognitive abilities underpin successful social functioning. They enable humans to fine-tune their behaviour to that of others and to guide behaviour within social relationships. Basic social cognitive abilities emerge during early childhood, but the more elaborate forms continue to develop into adulthood. Understanding how social cognition impacts upon social behaviour is crucial for the conceptualisation of social development and functioning in healthy populations, but also highly important for the understanding of atypical processes that are seen in schizophrenia and other psychopathologies.

The research presented in this thesis entitled ‘Navigating Social Life: On Social Cognition in Health and Psychosis’ had two objectives. The first part aimed to advance current knowledge regarding developmental aspects of social cognition and behaviour in the healthy population. Chapters 2 and 3 focussed on the associations between perspective-taking and trust and on how age-related changes in social cognition and behaviour are related to changes in brain function. The second part of this thesis investigated various aspects of social cognitive impairment and their impact on social functioning across the psychosis continuum. Chapters 4 and 5 examined the association between social cognitive functioning, functional outcome and quality of life of patients with non-affective psychosis. The study in Chapter 6 used a genetically sensitive design to study the aetiology of social cognitive dysfunction. Chapter 7 investigated the association between social cognitive functioning and the dynamics of social interactions across the psychosis continuum.

An introduction to the concept of social cognition is provided in Chapter 1. Various social cognitive functions, their development, their impact on social behaviour and their cortical instantiation (i.e. the social brain network) are discussed. Recent neuroimaging research associated the development of social cognition with changes in the ‘social brain’ and showed that these processes continue into adulthood. This insight increased the interest in the associations between social cognition and social functioning in the previously often neglected, but socially highly interesting and relevant period of adolescence. Adolescence is not only a phase of social change, but is also accompanied by an increased occurrence of schizophrenia, a disorder characterized by social problems. The second part of the introduction focuses on non-affective psychosis and its association with social cognitive disturbances and their possible underlying neural mechanisms and impact on social functioning. Finally, Chapter 1 introduces issues regarding the measurement of social cognition. The vast amount of research in the domain of social cognition, both in healthy populations
and populations with psychotic illness, has employed ‘offline’ measures to investigate social cognitive mechanisms. These studies yielded valuable insights into basic social cognitive constructs but could not capture the interactive character of real life social encounters. Recent advances that evolved from the fusion of behavioural economics and neuroscience, i.e. Neuroeconomics, now allow for the ‘online’ investigation of complex social interactions. These methods are discussed along with the associated research findings on the underlying cortical mechanisms of social interactions.

**Part I: Social Cognition in Health**

**Chapter 2** examines the association between social cognitive functioning in the domain of perspective-taking and the social mechanisms of trust and reciprocity during adolescence. Changes in social behaviour and increased social tendencies during this phase have been attributed to an increased sensitivity to the perspectives of others. We examined this hypothesis by means of two multi-round trust games that were played with two counterparts and an online perspective-taking task. In reality, but unknown to the participants, the counterparts were played by a computer that was pre-programmed with two probabilistic computer algorithms, one reflecting a cooperative and one reflecting a deceptive decision making style. The sample consisted of 50 healthy adolescents between 13 and 18 years of age who were divided into two groups; the first consisted of those with a strong tendency to take others viewpoints into account and the second consisted of those with a weak tendency to take others viewpoints into account. In both trust games participants were investors. They received a start endowment of £10 and in each game round they had to decide how much money they wanted to give to the other player. The shared amount was tripled and the counterpart then decided whether to share or to keep most or all of the money. High perspective takers demonstrated greater trust, as indicated by higher investments, both towards an anonymous interaction partner and during multiple interactions with a cooperative partner, but also decreased their trust more drastically in response to deception. These findings indicate that a greater sensitivity to the perspective of others is associated with specific mechanisms of trust and reciprocity, rather than a general and undifferentiated increase in pro-social behaviour towards others. The findings were not related to age. This is in line with other studies that indicate the most important changes in social behaviour and cognition during the transition phases from childhood to adolescence and from adolescence to adulthood and suggests that the social mechanisms during the currently investigated period of adolescence are based on earlier developed social cognitive skills.
Chapter 3 describes a functional magnetic resonance (fMRI) investigation of changes in the neural correlates of trust and cooperation between early adolescence and adulthood. A sample of 45 healthy males between 13 and 49 years played two multi-round trust games with anonymous counterparts (as described in Chapter 2). Participants were in the investor role. Age was associated with higher initial trust at the onset of anonymous social interactions and with increased levels of trust during interactions with a cooperative partner. With increasing age, participants also showed a stronger decline in trust during interactions with a deceptive partner. We used an event-related design to analyse the neural correlates of trust as function of partner reciprocity. Wholebrain correlational analyses were conducted between the different investment and condition combinations and age. The neuroimaging data demonstrated increased age-related activation in the temporo-parietal junction and the posterior cingulate gyrus and precuneus, brain regions implicated in mentalising. In interactions with a cooperative partner, the orbitofrontal cortex and caudate nucleus showed decreased activation with age. The anterior cingulate, moreover, showed age-related increases in activation in response to deception. Our findings demonstrate a positive age-related shift in social behaviour towards increased trust and cooperation. The increased sensitivity to others’ social signals may be driven by increased activation in mentalising related brain areas. Age was associated with reduced activation in reward related areas during social cooperation, which may reflect basic expectations of trustworthiness in older individuals. Finally, changed activation pattern in brain regions implicated in conflict monitoring may reflect the necessity to inhibit natural pro-social tendencies in the face of a partner’s actual levels of cooperation.

Part II: Social Cognition in Psychosis

Chapter 4 presents a systematic review and meta-analysis on the associations between neurocognitive and social cognitive functioning and different types of functional outcome in non-affective psychosis. Relevant studies on associations between neurocognition, social cognition and functional outcome in individuals with non-affective psychosis were retrieved by means of literature searches of MEDLINE and PsycINFO and reference lists from identified articles. Of 285 identified studies, 52 studies comprising of 2692 subjects met all inclusion criteria for the analysis. Forty-eight independent meta-analyses were conducted on associations between 12 a-priori identified neurocognitive and social cognitive domains and four domains of functional outcome. Neurocognitive and social cognitive impairment were both substantially and consistently associated with functional outcome with small to medium range effect sizes. Social cognition was more strongly related to community
functioning than neurocognition. The social cognitive domains could explain 16% of the variance in community functioning, while neurocognition explained 6%. Comparisons between the separate cognitive domains showed that this effect was specifically due to stronger associations with theory of mind. Thus, despite likely neurocognitive underpinnings, social cognition does explain unique variance in outcome. This highlights the importance of social cognition, and in particular theory of mind as a target for treatment interventions aimed at functional outcome.

Chapter 5 presents research on the association between social and neurocognitive functioning and quality of life. The sample consisted of 1032 patients, 1011 of their siblings, and 552 healthy controls from the Dutch Genetic Risk and Outcome in Psychosis (GROUP) study. Participants completed a battery of cognitive tests, including social cognitive tests on theory of mind (Hinting Task) and emotion perception (Degraded Facial Affect Recognition Task). Quality of life was assessed with the World Health Organization QoL Assessment-BREF. Patients’ symptoms were assessed with the Positive and Negative Syndrome Scale (PANSS). Social cognitive performance was significantly worse in patients than in siblings and healthy controls. Patients also had the poorest quality of life compared to siblings and controls and quality of life in healthy controls was better than in siblings. In contrast to the expectations, patients’ theory of mind was negatively associated with quality of life but no associations were present with emotion perception or neurocognition. In addition, there was a significant interaction between theory of mind and symptom severity, showing that higher symptoms were associated with a worse quality of life in those with better theory of mind. The findings suggest that in more severe schizophrenia better social cognitive functioning is associated with a lower quality of life. A possible explanation for the findings could be insight and the fact that more severely ill patients with a relatively unimpaired theory of mind may be more aware of the effects of their illness on their social environment.

Chapter 6 presents research on the association between social cognitive impairments and psychotic symptoms across the psychosis continuum. The study used a genetically sensitive cross-trait cross-sibling design to investigate the nature of the overlap between symptoms and social cognitive deficits in a sample of 1032 patients, 1017 of their healthy siblings and 579 control subjects (GROUP study). As in Chapter 5, social cognition was assessed with the Hinting Task (theory of mind) and the Degraded Facial Affect Recognition Task (emotion perception). Again, the PANSS was used to assess patients’ symptoms. Within siblings, symptoms were assessed with the Structured Interview for Schizotypy-Revised. Patients showed impaired social
cognition. There were significant associations between social cognitive performance and disorganized and, albeit to a lesser degree, negative symptoms. The associations between positive symptoms and social cognition were significant but smaller. Suggestive of a shared aetiology, both social cognitive functions, theory of mind and emotion recognition clustered within families. The associations between patients’ theory of mind and subclinical symptoms in siblings were not significant, showing that the overlap within patients is due to individual rather than shared familial factors. However, suggestive of a common familial substrate emotion recognition impairment overlapped significantly with disorganized and positive symptoms of siblings.

Chapter 7 examines the dynamics of social interactions across the psychosis continuum. A multi-round trust game of 20 consecutive real time social interactions was played by a sample of 29 patients with non-affective psychosis, 24 first-degree family members and 35 healthy controls in the investor role and 176 students as trustees. Patients with psychosis and healthy first-degree relatives showed lower initial trust as compared to healthy controls, i.e. they sent less money towards an unknown interaction partner. Compared to controls and relatives, patients did not show increased trust in response to positive information about the trustworthiness of their interaction partner, i.e. they did not increase their investments in response to contextual information on the benevolent nature of the game partner. Also they did not modify their behaviour towards the same amount of cooperative social interactions in response to positive behavioural feedback of the interaction partner. Within patients and relatives, less trust was associated with (subclinical) positive, but not negative symptoms. The behavioural flexibility in response to socially relevant information is a critical determinant of the success in establishing and maintaining social relationships and a lack thereof could be one of the driving factors in the progression from subclinical symptoms to a full-blown psychosis.

Chapter 8 is an integrative summary and discussion of the main findings presented in the Chapters 2 to 7. Clinical implications are discussed and directions for future research are given.