On Clinical Diagnostics of Social Cognition in Patients with Epilepsies*

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Summary

Patients with epilepsy may suffer from communication problems and interpersonal difficulties that have a significant bearing on their quality of life. Imaging and lesion studies have identified cerebral networks associated with social cognitive functions which are frequently affected in patients with temporal or frontal lobe epilepsies. Accordingly, recent studies have demonstrated impairments in social cognition in these patient groups using specific tasks involving emotional recognition and theory of mind (ToM). Within social cognition one can differentiate between more advanced social cognitive abilities, which require the understanding of complex mental conditions, and more basal processes such as the perception and expression of emotional information. The perception and expression of emotional information and ToM abilities have been investigated in numerous studies in a variety of patient groups and healthy persons using a number of experimental paradigms and tests. This paper broadly covers the most commonly used or representative tests of social cognition. Short descriptions and behavioural data from a variety of tests are presented in order to reveal their differences and to highlight recent developments and research perspectives.

Temporal lobe epilepsies (TLE) are often associated with behavioural disturbances such as psycho-social maladjustments and psychiatric co-morbidities including depression and social anxiety. However, since anxiety and distress related to epileptic seizures and their consequences, stigmatisation and discrimination as well as a lack of social support can be seen as causative variables in the development of psychiatric afflictions, it remains unclear to what extent psychosocial difficulties are caused by these factors and to what extent they are related to deficits in social cognitive functions and, accordingly, to lesions in structures associated with social cognition. The fact that psychosocial difficulties and psychiatric symptoms appear more often in mesial TLE compared to other chronic epilepsy syndromes supports the assumption of an association between mesial TLE and impairments in social cognition and offers an indication of a possible specific pathology associated with this epilepsy syndrome.

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Key words: Social cognition, temporal lobe epilepsy, theory of mind, emotion

Zur klinischen Diagnostik von Defiziten der sozialen Kognition bei Patienten mit Epilepsie

Patienten mit Epilepsie leiden häufiger an interpersonellen Problemen und kommunikativen Schwierigkeiten als Patienten mit anderen chronischen Erkrankungen. Heute können wir davon ausgehen, dass zumindest bei Patienten mit fokalen Epilepsien frontalen und temporalen Ursprungs Strukturen in ihrer funktionellen Integrität beeinträchtigt sind, die für die soziale Kognition eine grosse Bedeutung haben. Der Funktionsbereich der sozialen Kognition umfasst komplexe Fähigkeiten der interpersonellen Zuschreibung mentaler Zustände wie auch basalere Prozesse der Emotionserkennung. Der Artikel stellt von den Autoren favorisierte neuropsychologische Testverfahren zur Diagnostik sozialer Fähigkeiten vor. Im zweiten Teil werden spezifische Ergebnisse aus Studien zur sozialen Kognition bei Patienten mit Temporallappenepilepsien präsentiert, die eine erhöhte Vulnerabilität dieses Funktionsbereiches belegen.

Schlüsselwörter: Soziale Kognition, Temporallappenepilepsie, mentale Zustände, Emotion

Du diagnostic clinique de la cognition sociale chez les patients atteints d'épilepsie

Les patients atteints d'épilepsie souffrent plus souvent de difficultés d'interaction et de communication que les patients avec d'autres maladies chroniques. Aujourd'hui, nous pouvons partir du principe qu'en tout cas les patients avec des épilepsies focales d'origine frontale et temporale sont atteints dans l'intégrité de fonctionnalités qui sont d'une grande importance pour la cognition sociale. Le domaine fonctionnel de la cognition sociale englobe des facultés complexes d'attribution interpersonnelle d'états mentaux, ainsi que des processus plus basiques d'identification d'émotions. L'article présente des procédures de tests

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neuropsychologiques favorisés par les auteurs pour le diagnostic de facultés sociales. Dans la deuxième partie sont présentés les résultats spécifiques d'études de la cognition sociale sur des patients avec des épilepsies temporales qui corroborent une plus grande vulnérabilité de cette aire fonctionnelle.

Mots clés : Cognition sociale, épilepsie du lobe temporal, états mentaux, émotion

Introduction

Social neuroscience is an emerging interdisciplinary field aimed at investigating the fundamentals of human social and emotional behaviour, the quintessence of which is the relationship between the brain and social interaction. Studies on the impact of neurological, psychiatric, and psychological conditions on human social behaviour contribute to our understanding of the complexity of social interactions and highlight important social and affective symptoms in brain disorders such as epilepsies which continue to be overlooked in clinical practice.

In patients with epilepsy non-social cognitive functions including memory, language and executive functions have been studied for many years, whereas social cognitive abilities have received little attention [1]. This is quite astonishing in light of what we know about the remarkable overlap between structures associated with social cognition and anterior brain structures which are frequently affected in patients with epilepsy. The paucity of research becomes more understandable when one considers the lack of readily apparent social deficits in the majority of patients with epilepsies [2].

Nevertheless, comprehensive clinical studies have revealed that psychosocial maladjustment is a serious problem in many patients with chronic epilepsies [3]. To what extent these maladjustments are caused by social burdens, stigma, and risk factors of active epilepsy, and to what extent they are due to dysfunctional social cognition, remains an open question [4, 5]. However, the fact that psychosocial maladjustment and psychiatric comorbidity are more frequent in certain focal epilepsies compared with other epilepsy syndromes may reflect a specific pathological association [6].

In the past, psychiatry and neurology have used different terms and concepts and differed in their diagnostic approaches, research and treatment methods. Their focus converges to some degree within the framework of the modern neurosciences. As such, social and affective neuroscience provides insight into behavioural disorders in patients with epilepsy via new unifying concepts that can be investigated by means of behavioural tests, structural and functional imaging as well as by neuropsychopharmacological interventions. These opportunities allow us to advance our understanding of brain diseases, how they affect behaviour and raise the hope of new and more efficient therapeutic interventions.

Social cognition

Many patients with epilepsy suffer from communication problems and interpersonal difficulties that have a significant bearing on their quality of life. Imaging and lesion studies have identified cerebral networks associated with social cognitive functions which are frequently affected in patients with temporal or frontal lobe epilepsies. Accordingly, recent studies have demonstrated impairments in social cognition in these patient groups using specific tasks involving emotional recognition and theory of mind [7-11].

Social cognition is a complex and extensive concept that comprises a wide spectrum of sub-processes at different levels of brain functioning [12]. It includes the perception, encoding, organising and accessing of a variety of relevant social information.

Social cognition is based upon the exchange of signals, whereby the processing of these signals can take place at the automatic and controlled level and is influenced by motivational aspects [13]. It is noteworthy that these processes rapidly act in different modalities in parallel and draw on implicit as well as explicit memories. Therefore, it is reasonable to assume that lesions in one or more widely distributed independent components may lead to greater or less severe impairments in social cognition.

Adequate social interactions are a prerequisite for normal human development from an anthropogenetical as well as ontogenetical point of view. Social cognition encompasses any cognitive process that involves conspecifics, either as a group or an individual. It encompasses the ability to build representations about others, oneself, and the relationships between oneself and others, and to apply them flexibly to execute social behaviour [13]. Therefore, the success of social interactions depends upon the ability to understand the cognitive and emotional processes of others [14].

Basal social-cognitive processes

Within social cognition one can differentiate between more advanced social cognitive abilities, which require the understanding of complex mental conditions, and more basal processes such as the perception and expression of emotional information.

Processing of emotional information plays an important role in many aspects of cognition [15], including decision-making [16], memory, and attention [17]. Furthermore, understanding other people requires relevant information from different modalities which may provide social information about others including speech, facial expression, prosody, lexical information, gaze

direction, gestures and posture. Besides the predominant meaning gleaned from visual information, olfactory, auditory and tactile sensations can also influence processing of social signals [12]. However, the majority of studies have explored the processing of facial expressions because of longstanding research traditions and well established test materials [18].

Brain damaged patients who exhibit impaired emotional processing, but who are otherwise neuropsychologically intact, show marked deficits in social behaviour and in their interpersonal relationships [16]. Emotional agnosia, also called expressive or social emotional agnosia, can be seen as an emotion perception deficit and refers to a form of agnosia in which individuals are unable to perceive facial expressions, body language and intonation, thus making it impossible for them non-verbally to perceive people's emotions and limiting their social interactions. Social-emotional agnosias are commonly observed following amygdala and right cerebral lesions, particularly those involving the temporal lobe [19].

Although not a form of agnosia in the narrow sense of the word, alexithymia may be difficult to distinguish from, or even co-occur with, emotional agnosia. Whereas emotional agnosia refers to the inability to recognize affect in others (oriented towards others), alexithymia refers to the inability to recognize affect in oneself (oriented towards oneself). Peter Sifneos introduced the term to describe people who appeared to have impairments in understanding, processing, or describing their own emotions [20].

Despite the importance of emotional expression and processing of emotional information, there are only a few measures available to assess these functions, most of which are not standardised [21] or cross-culturally validated.

More detailed information about measures of basal social cognitive functions is provided in the following sections covering methodological issues and imaging.

Theory of mind (ToM)

Humans are by far the most talented species in reading the minds of others. This implies that we constantly make assumptions about the intentions and beliefs of others which form the framework of our complex interpretations of human behaviour in daily life. These mentalistic interpretations often seem trivial to us to the point that we fail to perceive them as meaningful, not to mention consider them part of an intuitive psychological theory. Nevertheless they represent a fundamental aspect of social cognition which has been coined theory of mind (ToM) [22]. ToM is thought to be the proximate mechanism enabling humans to find their way in complex, collaborative social networks.

The terms empathy, social intelligence, and perspective taking are, along with ToM, related abilities and concepts and were often used as equivalents in the literature as well as in everyday speech. Therefore, social cognition is not equivalent to ToM since there are a number of cognitive abilities which fall within the realm of social cognition which do not involve ToM operations in the narrow sense of the word, e.g. social reasoning and decision making, the recall of knowledge regarding social schemata and moral judgment [23].

According to numerous findings, ToM is considered a specific cognitive domain that needs to be delineated from general intelligence and from executive functions. There are many studies in which social cognition has been shown to be dissociable from general intelligence. For example, Baron-Cohen and Jolliffe [24] showed that very high functioning adults (HFA) with autism or Asperger's syndrome (AS), despite being of normal or above average IQ, were nevertheless impaired on a subtle theory of mind test. A further example of this dissociation is seen in Down's syndrome where intellectual function is impaired, but individuals perform well on theory of mind tasks [25].

In another study, Baron-Cohen et al. [26] used a revised version of the "Reading the mind in the eyes Test" (Eyes Test) and administered this test to a group of adults with AS or HFA. Again, there was no significant correlation between IQ and the performance in the Eyes Test, confirming that this is independent of general (non-social) intelligence. Using the "Mind in the Voice" Task, which extends the aforementioned test into the auditory domain, Rutherford et al. [27] found that individuals with AS/HFA have difficulty extracting mental state information from vocalizations. Here, too, no significant correlation was found between verbal IQ and performance on the voice task for either the AS/HFA group or the noncollege control group.

Apart from theory of mind, memory, attention, executive functions (including planning of action), motivation and decision making equally contribute to the cognitive and behavioural outputs in social interactions. ToM should be considered a complex neuropsychological function that can be selectively disturbed, but which is correlated with distinct cognitive abilities, in particular executive functions [28].

The first precursors of ToM, including the imitation of intended actions [29] and the distinction between one's own and others' desires and their relation to emotions [30] can be observed already at the age of eighteen months. Also, the beginning of the pretend play [31], joint attention skills and the development of the ability to attribute wishes and emotions to others [32] can be considered as an important milestone in the development of a ToM.

By the age of about three to four years children gain the cognitive prerequisite for the comprehension of another person's belief (e.g. that he or she has a false assumption about a certain fact) and thereby the ability to represent mental conditions independent of reality and to derive action predictions from attributions of mental states. This ability requires a conceptual understanding

of the mental conditions of another human being [33].

The comprehension of false beliefs in children can be investigated with the help of so-called „first-order false belief tests", the most prominent of which include the „Sally-Anne Task" [34], the „Maxi-Task" [35] and the "Smarties-Task" [36]. The development of an understanding that someone can have a false belief about a false belief begins a bit later towards the age of 6 years [37], while the understanding of different perspectives appears between the ages of 12 and 17 [38].

The ability to attribute second-order or embedded mental states (e.g., he thinks that she thinks) is a very socially relevant achievement in the development of a theory of mind. Being able to represent what one person thinks about what a second person thinks allows us to understand not only another's belief about the world (a first-order belief) but also to understand that person's concern about yet another person's belief about the world (a second-order belief). This sort of reasoning is necessary for any sophisticated understanding of the subtleties inherent in social interactions. Perner [39] argued that it is at the level of second-order reasoning that social interaction can be understood as an interaction of minds where people are concerned about each other's mental states. Typical second-order false belief tasks are the Ice-Cream Van Task [37] or the second-order Sally-Anne Task [34].

Tests which go above and beyond simple attribution performances are also called „higher-order" or „advanced" ToM tests and require the understanding of complex mental states (what does X think or feel?) or also the comprehension of mental states in role-taking activities (e.g. does X also really mean what X says? Why does X behave thus?). The inferences one makes regarding others' mental states include knowledge regarding their thoughts and beliefs ("cognitive ToM component") as well as knowledge and empathic understanding of their emotional states and feelings ("affective ToM component").

Methodological issues

Testing social cognition

The perception and expression of emotional information and ToM abilities have been investigated in numerous studies in a variety of patient groups and healthy persons using a number of experimental paradigms and tests. The following list of selected tests is not intended to be exhaustive, but broadly to cover the most commonly used or representative tests. Short descriptions and behavioural data from a variety of tests are presented below in order to reveal their differences and to highlight recent developments and research perspectives.

Selected tests of basal processes of social cognition

Ekman faces

Test description.

Influenced by the work of the psychologist Sullivan Tompkins, Ekman was the first to apply quantitative methods in an effort to clarify the question of the biological basis of emotional facial expression. He showed that facial expressions of emotions are not culturally determined, but universal across human cultures and, thus, biological in origin. Expressions he found to be universal included anger, disgust, fear, joy, sadness and surprise. Ekman and Friesen [18] developed the Facial Action Coding System (FACS) to taxonomise every conceivable human facial expression. The FACS has since become the most widely used and validated series of photographs in facial expression research. These photographic representations have been applied in a variety of tests requiring identification, matching, sorting or rating of facial expression of emotions.

Behavioural data.

While initially the question of lateralisation of emotional facial expression perception was pursued [40], the amygdala has increasingly attracted attention with advances in imaging technology. Primarily it was assumed that the perception of fearful expressions depended on the structural and functional integrity of both amygdalae [41]. However, subsequent studies have shown that not only facial expressions of fear, but also the perception of other emotions, are affected after bilateral amygdalar lesions [42, 43] and that unilateral lesions can also result in deficits [44, 45]. Disturbances in the perception of emotions from facial expressions have also been reported in patients with Traumatic Brain Injury (TBI) [46], in frontotemporal dementia [47] as well as in patients with frontal and temporal lobe epilepsy [7, 9, 48, 49].

Comprehensive Affect Testing System (CATS)

Test description.

Most studies on social cognition have used visual stimuli, but it is clear that real-life social interactions necessarily draw on additional modalities. Audition provides important social signals in addition to language. Accordingly, the intonation of speech – prosody – can signal various emotions, and is recognised using some

of the same structures that we use for recognising facial expressions [50]. Froming et al. [51] took this issue into account and developed a computerised measurement of visual and auditory emotional processing of the six basic emotions (Comprehensive Affect Testing System, CATS). The CATS consists of thirteen subtests assessing facial identification, emotion matching with and without verbal denotation, emotional tone or prosodic processing with and without verbal denotation, and with conflicting or congruent semantic content.

Behavioural data.

The CATS has been administered to patients with Asperger's syndrome (AS) and comparisons between these patients and healthy controls on CATS subtest results revealed general impairments in the comprehension of facial and prosodic information in the AS group [51]. Recently, Rocca et al. [52] applied the CATS to a group of patients with schizophrenia and healthy controls and found that controls performed better on all subtests, the only exception being an affect discrimination task. Data collection is in progress with different groups of patients with brain damage.

Selected tests of theory of mind

Various experimental paradigms exist for evaluating ToM-skills. However a truly theoretically based differentiation of relevant aspects and dimensions of the ToM-construct and its test psychological considerations remain absent.

According to the conceptual classification of a "cognitive" and an "affective" ToM component (with overlaps with empathy), some tests require the attribution of epistemic mental conditions such as knowledge, attention or beliefs while other tests investigate the attribution of affective mental conditions e.g. "feel happy" or "want something" [53]. According to Shamhay-Tsoory and Aharon-Peretz [54], performance on second-order false belief tasks requires cognitive components of ToM while "higher-order" or "advanced ToM tests" such as the faux-pas test [55] require both components. The attribution of intention assumes the recognition of whether an action was executed intentionally or accidentally and can be considered as a further type of attribution, although its inclusion under the attribution of epistemic mental conditions seems to be reasonable as well.

Apart from the classification of ToM tests according to their type of attribution, they also differ with regard to the stimulus modality they employ. While some contain verbal material such as stories and subsequently demand adequate language comprehension, complex visual stimuli are applied in other tests (dynamic and non-dynamic); rarely have verbal and visual material been combined.

Moving Triangles

Test description.

Heider and Simmel [56] conducted an experimental study over 65 years ago that can be seen as the starting point of attribution theory research. In their experiment healthy subjects were asked to interpret a short film sequence (2.5 min) in which three geometric shapes (a big and a small triangle and a circle) move around at different speeds. Another shape in the field is a rectangle which also acts as door that can be opened and closed. All in all, Heider and Simmel's [56] study contained three experiments. In the first experiment subjects freely described what they saw after watching film sequences twice. In a second experiment, subjects were asked to interpret the movements of the figures as human actions and to answer structured interview questions after presentation of the film. In the third experiment the video was shown in reverse and subjects took part in a short, structured interview. The authors observed that people attributed intentions and desires to moving geometric shapes if these actions are of adequate complexity.

Behavioural data.

Klin [57] developed the Social Attribution Task (SAT), a new cognitive procedure based on Heider and Simmels's cartoon animation and applied it to a group of individuals with autism, with Asperger's syndrome (AS), and normally developing adolescents and adults. The SAT is adapted for presentation to developmentally disabled individuals by minimising factors thought to promote ToM task performance but that are absent in real-life social situations. Furthermore, it includes a coding system to examine and quantify different aspects of the subject's social cognitive responses. Both clinical groups showed significant deficits in making social attributions.

Based on the classic Heider and Simmel [56] paradigm, Abell et al. [58] aimed to design novel stimuli whose properties of motion would evoke mental state attributions. Protagonists of the new test were two shapes (a big red and a small blue triangle) moving around the screen, which on most trials contained an enclosure. Mental state attributions were restricted to pure movement and interaction in the absence of vocal or facial expression. In their study they presented three different types of animation sequences: random movement in which no interaction occurs (e.g. bouncing), goal-directed (G-D) interactions that elicit attributions of simple actions (e.g. fighting) and ToM interactions

that elicit attributions of mental states to the agents (e.g. tricking). The G-D and ToM condition consisted of four animations each, while the random condition had two animations. The computerised animations were presented to high-functioning children with autism, children with general intellectual impairment, normally developing 8-year olds and adults. The authors found that high-functioning children with autism frequently used inappropriate descriptions when characterising the ToM animations. Castelli et al. [59] used twelve silent animations, four of each of the three types of animations, and here as well the autism group gave fewer and less accurate descriptions of the ToM animations.

Finally, Heberlein and Adolphs [60] used a video of the original Heider and Simmel [56] film in a single case study and found that a patient who acquired bilateral focal damage during childhood failed to attribute social intent to the moving geometrical objects in the normative manner.

Cartoon task

Test description.

Recent research in social cognitive neuroscience has begun to define subcomponents of ToM. One important differentiation is that of "affective" versus "cognitive" ToM, although different terms have been used to describe these and related concepts [61]. This differentiation was taken into account in the "Yoni" paradigm, which was introduced by Shamay-Tsoory et al. [62] and is based on a task previously described by Baron-Cohen and Goodhart [63]. It is a computer-controlled test for the assessment of cognitive and affective ToM-performances. In this test the mental state of the main character has to be inferred from the situational context on the basis of verbal cues, eye gaze and facial expression. There are three main conditions: cognitive, affective and physical, each requiring either a 1st or 2nd order inference. The cognitive and affective conditions require mental inferences, while the physical condition serves as a control condition and requires a choice based on the physical attributes of the character. In each of the 64 trials a face named Yoni is shown in the middle of a computer screen with four coloured pictures in each corner that either belong to a semantic category (e.g. animals, fruits) or show faces. In the upper range of the screen an incomplete sentence about what Yoni is referring to is presented and subjects are required to decide as quickly as possible which of the four stimuli in the corners best completes the sentence.

Behavioural data.

Using the Yoni-paradigm Shamay-Tsoory and colleagues [62] were recently able to demonstrate selective deficits in affective as opposed to cognitive ToM in various patients groups. In Shamay-Tsoory, Aharon-Peretz and Levkovitz's [64] study the performance of patients with schizophrenia was compared to that of patients with localised lesions in the ventromedial (VM) or dorsolateral prefrontal cortex (PFC), patients with non-frontal lesions, and healthy controls. The authors found that patients with schizophrenia and those with VM lesions were impaired on affective ToM tasks, but showed no difficulties in the cognitive ToM conditions. Support for a selective impairment in schizophrenia for the ability to attribute affective mental states comes from another study in which patients with schizophrenia made significantly more errors in the affective conditions as compared to healthy controls [62]. A modified version of the Yoni-paradigm which included additions to the ToM task of gloating, envy and identification trials ("fortune of others" emotion task) was used with patients with AS and HFA [65] as well as in patients with localised, well-defined brain lesions of various aetiologies [66]. The authors showed that, whereas individuals with AS and HFA had no difficulties with first- and second-order ToM tasks, they were impaired in their ability to identify envy and gloating.

In a study with patients with different localised lesions, Shamay-Tsoory and Aharon-Peretz [54] were able to demonstrate that affective and cognitive ToM processing depends in part on distinct anatomical substrates. While the ventromedial prefrontal cortex (VMPFC) seems to have a special role in processing affective ToM, cognitive ToM may involve both the VMPFC and dorsal parts of the prefrontal cortex. Furthermore, recognition of envy and gloating is impaired in patients with ventromedial prefrontal damage [66].

Reading the mind in the Eyes Test

Test description.

There are only a few tests which examine ToM skills in adults. So-called "higher-order" or "advanced ToM tests" go far beyond simple attributions and can only be used to study adolescents and adults of normal intelligence, e.g. "Reading the mind in the Eyes Test" (Eyes Test) [24, 26]. The subject's task is to choose which of four words best describes what the person in the picture, that shows only a pair of eyes, is thinking or feeling (e.g. terrified, upset, arrogant, annoyed) [26].

Behavioural data.

The Eyes Test has enjoyed wide use and has demonstrated reduced test performance in patients with psychiatric diagnoses including autism and AS [24, 26, 67] and in patients with schizophrenia [68].

Further, patients with unilateral or bilateral amygdalar lesions [44, 53], with frontotemporal dementia [69] as well as with frontal lobe epilepsy [48] have been found to have impaired performance in the Eyes Test. Farrant et al. [48], however, presume that the discovered deficits in the frontal variant of frontotemporal dementia (fvFTD) and FLE group are in fact caused by the emotional component rather than ToM itself.

All in all, findings from this widely used test show it to be sensitive for detecting specific ToM impairments in populations that have been found to have deficits in other ToM tests.

Faux pas Test

Test description.

The Recognition of Faux pas Test [55, 67] is another ToM test for adults and estimates the ability to recognise and understand a social faux pas. It was designed to evaluate mentalising abilities in individuals with high functioning autism who are able to pass second-order false belief tests. A faux pas is understood as a statement in which the speaker accidentally offends or insults another person. For example, person "A" complains to person "B" about a wedding present without realising that he is talking to the person from whom he received it. The Faux pas Test measures several ToM components by including deductions concerning epistemic mental conditions as well as affective mental conditions [53, 55]. As verbal materials, in the form of rather complex stories, are used in this task, it makes fairly high verbal demands of the individual.

Behavioural data.

Baron-Cohen et al. [67] administered an age-adapted version of the Faux pas Test to a group of younger subjects (mean age = 12 years old) with HFA/AS and found that they had difficulties using mental state knowledge and had difficulties in detecting the faux pas. Unlike the children with HFA/AS in the Baron-Cohen et al. study [67], adults with AS in Zalla et al.'s study [70] and the two adolescents with AS in Shamay-Tsoory et al.'s case-study [71] reported that something awkward or wrong was perpetrated in the faux pas stories; they were generally unable to provide correct justifications in terms of reasons and intentions and failed to attribute emotions to others.

The adult version of this test has also been applied to patients with orbitofrontal and amygdalar lesions [53, 55], TBI [72], patients with mesial temporal lobe epilepsy [10], patients with Parkinson disease [73], patients with fronto-temporal dementia and patients with Alzheimer disease [69]; all of whom had difficulties recognising that a faux pas had been committed.

Strange Stories

Test description.

The Strange Stories Test is concerned with the comprehension of nonliteral statements in hedged expressions, metaphors, irony, sarcasm and bluff [74]. In this test subjects are confronted with a set of stories requiring the attribution of complex mental states. There are two conditions in this test consisting of two sorts of materials: social stories, which have to do with mental states and physical stories which have to do with physical behaviour. There are eight examples of each of these two sorts. Subjects were asked to read these stories and answer a question after each passage.

Behavioural data.

Happé [74] used such a set of stories to test able autistic, mentally handicapped and normal children and adults in their understanding of story characters' thoughts and feelings. Subjects with autism had difficulties understanding the protagonists' intentions and made context-inappropriate mental state attributions. By contrast, they had no difficulty understanding the physical events in the stories or understanding stories not involving mental states. These results were replicated in other studies of patients with HFA and AS [24, 75, 76].

Shaw et al. [77] reported deficits in a number of advanced ToM tests, including Happé's strange stories, in a group of subjects with early damage to the amygdala. These patients made significantly fewer fully accurate mental state attributions compared to a group of patients with late damage to the amygdala and healthy comparison groups.

Imaging of social cognition

Tasks which demand social cognitive abilities appear to activate a consistent set of brain regions. Experiments using imaging techniques have found underlying neural processes in different frontal and temporal localised brain regions [55, 78] including particularly the medial frontal cortex (MFC), inclusive the anterior cingulare cortex (ACC), the superior temporal sulcus (STS) at

the temporal parietal junction (TPJ), the temporal poles (TP) and the amygdala.

Medial frontal cortex (MFC) and anterior cingulate cortex (ACC).

For a better understanding of its role in social cognition, one can functionally divide the MFC into a posterior rostral region (prMFC, associated with cognitive processes) and an anterior rostral region (arMFC, associated with emotional processes), as well as into an orbital region (oMFC, associated with the monitoring of task outcomes). While the prMFC is thought to be engaged in monitoring the value of possible future actions, the oMFC guides behaviour regarding the evaluation of possible consequences. The arMFC appears to be activated by a wide range of social cognition tasks that involve thinking about the psychological attributes of people regardless of whether the person was the self, another person, or whether judgments pertained to dispositions or mental states [78]. Thus, activations of the arMFC and ACC were found for the perception of oneself as well as one's own mental conditions [79, 80] and for the thinking about the mental states of others [81]. Based on this knowledge and results which have revealed involvement of the ACC in the control of the attention [82], Gallagher and Frith [83] proposed that the activated parts of the ACC could govern the attention allocated to mental conditions. Thus, the ACC could correspond to the „decoupling" mechanism which was suggested by Leslie [84] and which differentiates hypothetical conditions from reality [85].

Superior temporal sulcus (STS).

Activation in the area of the STS has consistently and robustly been reported in many studies. It is assumed that the STS represents rather elementary processes involved in a variety of ToM tasks and that the posterior STS is particularly sensitive to biological motion [86]. Overall, the results point to the participation of the STS in the perception of purposeful actions and their attribution as self-caused or other-caused [87, 88].

Temporal parietal junction (TPJ). The TPJ appears to be involved in reasoning about the contents of another person's mind [89]. In particular, it has been proposed that the right TPJ is selectively involved in representing the beliefs of others [90]. However, this remains a controversial issue as this region has also consistently been activated during spatial reorienting of visual attention [91].

Temporal pole (TP).

The TP may be involved with the retrieval of memory contents, especially autobiographical memories and memories for faces [83]. Accordingly, the studies which presumably made only negligible demands on the memory or imagination of the test participant were unable to find any activation in the temporal pole [81, 92]. Olsen et al. [93] reviewed the literature in both non-human primates and humans and their findings indicated that the TP has some role in both social and emotional processes including face recognition and ToM.

Amygdala.

The amygdala-complex is considered to have a central role in the perception and processing of socially relevant information [94, 95], emotional learning [96] and memory [97]. The amygdala was shown to react to angry and fearful faces [98], be involved in gaze monitoring [99], and is crucial for the recognition of social emotions. Furthermore, there is converging evidence that amygdala structures and their connecting complex of neural systems are at the core of the ability to interpret the mental states of others [53, 100]. In their current overview of results from different functional imaging studies of the brain basis of ToM skills, Carrington and Bailey [101] found the amygdala to be less consistently activated. However, its influence on social and emotional reactions [102] clearly indicates involvement of the amygdala in certain ToM functions.

Task-related imaging.

Functional imaging studies on social cognition have used classical ToM tasks (introduced in the preceding section) as well as tasks involving the processing of faces.

Using positron emission tomography (PET) Morris and his colleagues [103] were the first to document a specific activation of the amygdala during the presentation of faces with systematically varied expressions (Ekman Faces). Thus, a modulation of the neural activation took place depending on the valence and intensity of the emotion. The left amygdala registered significantly more neuronal activity looking at fearful faces than looking at happy faces. Whalen and his colleagues [104] were able to confirm this finding. They also noticed a significantly stronger activation looking at fearful faces in comparison to neutral or angry ones. Baron-Cohen et al. [67] was even able to show, using fMRI, that patients with autism and Asperger's Syndrome (AS) did not show amygdalar activation in comparison to healthy controls while making mentalistic inferences from the eyes (Eyes Test). These results are in accordance with histopathological studies demonstrating gray matter abnormali-

ties in the amygdala and surrounding temporal areas [105].

Functional imaging has also been used to study the detection of mental state information in Heider and Simmel's [56] animations of moving geometric shapes. Castelli et al. [88], using positron emission tomography, presented an animated sequence in which two triangles interacted with each other. The more strongly the observers attributed mental conditions to the triangles, the stronger the activity in the MPFC, temporal pole and STS. Schultz et al. [106] utilised an analogous task and noticed activations in the same areas when using fMRI. In both of these studies where mentalising was determined by the movements of abstract shapes, the activity in the temporal pole extended into the amygdala and some activity could also be seen in the fusiform gyrus. Each study required explicit mentalising whenever the test persons were asked to characterise the mental states of another person or to make decisions according to the mental states of others. The only exceptions were studies using passive viewing of animations.

To our knowledge there is only one study to date which has linked structural abnormalities to impaired social cognitive abilities using faux pas tasks [107]. Herold et al. [107] used voxel-based morphometry (VBM) to compare data of patients with schizophrenia to healthy individuals and found that the poor faux pas performance of patients with schizophrenia correlated with gray matter reduction in the left OFC and right TP. These results correspond to those recently found in a study by Shamay-Tsoory et al. [108] who revealed that the pattern of ToM deficits in patients with schizophrenia resembled those seen in patients with ventromedial PFC lesions.

A PET study of ToM in autism [109] employed a story comprehension task (Strange Stories), replicating a prior study in normal individuals [110]. The authors found displaced and diminished mPFC activation in subjects with autism. However, due to small sample size (six subjects with autism) and relatively poor spatial resolution of PET imaging, these results should be considered preliminary.

Social cognition in temporal lobe epilepsy

Mesial temporal lobe epilepsy (MTLE) is the most prevalent focal epilepsy. It is characterized by recurrent seizures which originate from mesial temporal structures, most frequently within the hippocampus. Therefore, hippocampal sclerosis represents the most common pathological substrate in MTLE [111]. Neuropsychological examinations often uncover memory impairments which are usually material-specific to the side of ictal onset [112]. Resective surgery can be highly effective in obtaining seizure freedom in medically intractable patients with MTLE, but bears a significant risk of memory and language impairments. Accordingly, performances on measures of memory, language, and executive functions have been studied extensively pre- and postoperatively in this patient group. But despite knowledge that cerebral networks associated with social cognitive functions are frequently affected in patients suffering from temporal lobe epilepsies, investigations into social cognitive abilities have been scarce [1]. This paucity of research could be due to the lack of readily apparent social deficits in temporal lobe epilepsy patients [2].

At the same time, TLE is often associated with behavioural disturbances such as psycho-social maladjustments and psychiatric co-morbidities including depression and social anxiety [3]. However, since anxiety and distress related to epileptic seizures and their consequences, stigmatisation and discrimination as well as a lack of social support can be seen as causative variables in the development of psychiatric afflictions [4, 5], it remains unclear to what extent psychosocial difficulties are caused by these factors and to what extent they are related to deficits in social cognitive functions and, accordingly, to lesions in structures associated with social cognition. The fact that psychosocial difficulties and psychiatric symptoms appear more often in MTLE compared to other chronic epilepsy syndromes [6] supports the assumption of an association between MTLE and impairments in social cognition and offers an indication of a possible specific pathology associated with this epilepsy syndrome. Of course, there are other epilepsy syndromes, such as frontal lobe [48] or juvenile myoclonic epilepsy [113], which may also be at risk of social cognitive impairments, but these have only rarely been investigated and we therefore focus below on TLE.

Several studies of basal aspects of social cognition suggest that the recognition of basic emotions in facial expressions is frequently impaired in TLE-patients [7-9, 11, 49]. In particular, patients with early seizure onset within the right, non-speech dominant, hemisphere showed pronounced difficulties in the recognition of fearful faces [7, 9]. Also, the early-onset right MTLE-HS patients in Hlobil et al.'s [114] study were impaired in their ability to recognise fear when compared to other MTLE patients and control subjects, indicating that age of damage is an important factor determining this ability.

Moreover, impairments in the recognition of basic emotions with negative valence have also been reported in temporal lobectomy patients with amygdala damage on the basis of facial and vocal expressions [115]. The patients in Shaw et al.'s [49] study who underwent a left anterior temporal lobectomy for medically intractable epilepsy which incorporated the entire amygdala, evaluated fearful facial expressions in a more normative manner. By contrast, in right-sided MTLE patients the operation did not have any effect on the level of impairment.

Apart from impairments in the recognition of basic emotions (considered to be a prerequisite for a ToM),

deficits in emotional memory [116] and in ToM abilities [10] have been associated with MTLE.

Abnormalities in higher-order social cognition were directly attributed to MTLE in a study by Schacher et al. [10]. The authors compared patients with MTLE to patients with epilepsy not originating within the MTL and healthy controls in their ability to detect a social faux pas. They used a shortened version of the Faux pas Test [53], consisting of three short prose passages, and found that MTLE patients performed significantly worse in this test than patients with epilepsy other than MTLE (extra MTLE) and healthy controls. This finding was not accounted for by variables such as age, age at seizure onset, duration of epilepsy, text comprehension or IQ and, thus, corroborate earlier findings that ToM abilities are mainly independent of other cognitive functions [85]. Considering that the epilepsy control group exhibited no impairments in the ToM task, the authors concluded that the observed deficit comprised a specific impairment in focal epilepsies with lesions in the ToM-network.

The question of the role of the amygdala and the affective functions which it mediates is still under debate [77]. The amygdala has been associated with ToM processes in numerous studies [94], whereby it appears to be of particular importance in the attribution of affective mental states [14]. To detect a social faux pas, as required in Schacher et al.'s [10] study, one has to be able to understand the emotional condition of another person. In patients with MTLE, the amygdala are often part of the epileptogenic zone and in about a quarter of patients with hippocampal sclerosis (HS), the ipsilateral amygdala shows volume reduction or even atrophy [117, 118]. Furthermore, neuropathological findings in temporal lobe epilepsy patients point to variable degrees of neuronal cell loss and astrogliosis in the amygdala [119, 120].

Disagreement remains as to what degree the amygdala merely supports the development of ToM abilities [77, 85, 121] or whether it additionally represents an important part of the neural network which underlies ToM processing abilities [53, 122-124]. The majority of authors agree with the latter supposition, which receives support in particular from lesion studies that indicate a clear connection between uni- and bilateral lesions of the amygdala and deficits in ToM [53, 125].

Apart from these behavioural studies, imaging studies have also been conducted that have detected amygdalar dysfunctions. Using an animated fearful face-paradigm in their fMRI study, Schacher et al. [126] showed that ipsilateral amygdala functioning is impaired in the majority of patients with mTLE. In contrast, the paradigm resulted in symmetrical bilateral amygdala activation in healthy volunteers.

Bonelli et al. [127] used a fearful face paradigm to study the role of the amygdala in the processing of emotions in patients with mTLE and to examine whether this may be a potential preoperative predictive marker for emotional disturbances following surgery. Healthy control subjects looking at photographs of fearful faces demonstrated left lateralised amgydala activation, while right-sided TLE patients showed bilateral amygdala activations. Left-sided TLE-patients, however, had significantly reduced activations of either the left or right amygdala in comparison to the control group and the right-sided TLE-patients. During scanning, subjects in Bonelli et al.'s [127] study were instructed to make judgments of whether photographs of faces were pleasant or unpleasant, a task in which patients with right-sided MTLE were previously shown to have impairments as compared to left-sided MTLE patients and healthy controls [7, 9]. In Bonelli et al.'s [127] study, the left-sided MTLE patients displayed on average bilaterally reduced fMRI amygdala reactivity. Inspections of scatter plots revealed, however, considerable interindividual variability in the asymmetry of amygdalar responses, even in patients with left-sided MTLE.

Structure-function analyses have also shown an association between impairments in the recognition of facial expressions, especially of fear [9], and reduced fMRI activity in patients with early onset right-sided TLE [7]. In addition, an association has been observed between fear recognition deficits and the duration of epilepsy as well as the amount of decrease in amygdalar volume [128, 129].

In sum, the majority of studies suggest that the degree of impairment and which aspects of social cognition are impaired is influenced by amygdalar pathology in addition to mediating factors such as the age at which and side of which a lesion was acquired, age at seizure onset, the expansion of the symptomatogenic zone as well as the functional deficit zone.

Conclusions

Today, we remain unsure as to whether we should consider deficits in social cognition as defining symptoms of the MTLE syndrome. However, the current state of research convincingly demonstrates that a considerable number of patients with MTLE demonstrate impairments in social cognition. These impairments may have a devastating impact on interpersonal relationships, social functioning and quality of life and may promote the occurrence of the frequently reported comorbid symptoms of depression and anxiety. Yet, aspects of social cognition are not often part of the psychiatric or neuropsychological assessment of patients with epilepsies. We strongly recommend the expansion of cognitive assessment batteries to include tests of social cognition. As acute difficulties in social cognition are not necessarily evident in brief interactions between physician and patient; and these symptoms are often subclinical in nature and, therefore, psychometrically difficult to ascertain, it is important to develop sensitive and standardised instruments to analyse social cognition in different modalities. Identifying deficits in social cognition would allow for the development more specific treatment strategies aimed at improving social-cognitive abilities in terms of training or within the scope of postoperative rehabilitation. As intact social-cognitive skills are of everyday relevance in that they allow for adequate social functioning in interpersonal relationships as well as in wider society, further insights into social cognition in epilepsy patients are required.

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