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Review article

The neurocognition of alexithymia: evidence from neuropsychological and neuroimaging studies

Wingbermühle E, Theunissen H, Verhoeven WMA, Kessels RPC, Egger JIM. The neurocognition of alexithymia: evidence from neuropsychological and neuroimaging studies.

Objective: Alexithymia refers to an ineffective regulation and expression of emotions. It constitutes a major risk factor for a range of medical and psychiatric problems, including chronic pain, somatisation, anxiety and depression. Alexithymia is a multi-faceted concept, described in terms of cognitive and affective aspects. From a neuropsychological perspective, alexithymia can be defined as a disturbance in affective information processing and social cognition. As the growing literature on brain structures involved in alexithymia is fragmented and sometimes even contradictory, the aim of this article was to review findings on neural substrates with regard to their convergence.
Methods: A narrative review was performed, including both early neuropsychological and more recent imaging studies, in order to achieve a better understanding of the aetiology of alexithymia.
Results: Corpus callosum, cingulate cortex and insula are clearly involved in alexithymia. The amygdala and the orbitofrontal part of the cortex appear to be implicated as mediators, because of their broader involvement in emotional processing and executive control.
Conclusion: Notwithstanding the diffuse neural representation, the alexithymia construct can be usefully applied in the clinical and empirical studies of social cognition, particularly when adopting a dimensional neuropsychological approach.

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Summations

- Alexithymia may be considered a social-cognitive dysfunction which may underlie affective disorders and that may decrease quality of life.
- Corpus callosum and cingulate cortex are explicitly involved in alexithymia.
- Together with the study of cerebral structures, the further understanding of alexithymia requires a combined developmental, neuropsychological and biological perspective.

Considerations

- Reviewed articles have to date focussed on lesions, neurobehavioural parameters or on imaging research. The relative contribution of these sources to the aetiological understanding of alexithymia remains to be quantified.
- A further analysis of the methodology followed in the various studies, including axiomas on the dimensional or taxonic nature of alexithymia, would be necessary. Unfortunately, this would substantially enlarge the manuscript and distract readers from its focus.

The neurocognition of alexithymia

In 2004, Taylor and Bagby reviewed the relations between alexithymia and emotional processing as known until then, discussing the achievements of broad, interdisciplinary developments in alexithymia research (1). With rapid advances in technology and a still growing interest in social cognition, alexithymia research has continually expanded ever since without, however, definitive clarification. Both theoretical (top down) and empirical (bottom up) guidance is mandatory to further the understanding of the concept. Therefore, with a social-cognitive focus and evaluating both early neuropsychological and more recent imaging studies, this article reviews the evidence on the neural correlates of alexithymia.

Some conceptual issues with respect to the character and definition of alexithymia will be discussed first, followed by a short introduction to social-cognitive theory and a summary of widely used instruments to measure alexithymia. The neural correlates will be highlighted following primarily the lines of research history, moving from low-tech to high-tech experiments, from first indications of the involvement of large, hardly specified brain areas to identifying specific (parts of) structures and functional networks concerned with alexithymia. The article will end with a social-cognitive reappraisal of the alexithymia concept.

Alexithymia from 1973 to date

The alexithymia concept was first introduced by Sifneos in 1973, as an 'absence of words for emotions' (2). It refers to difficulties in identifying and describing emotions, to an externally oriented mode of thinking and to a restricted fantasy life. Disturbances in the processing of emotions may lead to psychosocial problems and even to severe psychopathology (3). Having difficulties in identifying feelings has been shown to be a significant predictor of psychopathology, e.g. major depression and anxiety disorders (4,5). With prevalence rates up to 10% in the general population and indications of diminished levels of quality of life in relation to alexithymia, the importance of disentangling the aetiology is important (6,7).

Alexithymia as a construct stems from clinical observations of patients with psychosomatic disorders. It is originally rooted in psychodynamics, in the beginning explained as a defence mechanism to repress unconscious conflicts (8–10). In the early 1960s, French psychoanalysts suggested a lack of fantasy and a proneness to practical and action-oriented thinking to be typical traits for patients with psychosomatic diseases. They called their style of communication 'la pensée opératoire', which can be seen as the precursor of the alexithymia concept of Sifneos. Five aspects emerged repeatedly: (a) a reduction or incapacity to experience emotions; (b) problems in verbalising emotions; (c) an inability to fantasize; (d) an absence of tendencies to think about or analyse one's emotions and (e) difficulty in identifying, primarily one's own, emotions (11).

With the rise of the Object Relations and Self Psychology concepts in the second half of the 20th century, the influence of the conflict model decreased, and another aspect of psychoanalytic theory was accentuated: 'failing ego functions' were introduced as the key problem in alexithymia. In this deficit model, an early disturbance in the parent-child relationship was suggested to predispose inadequate ego functions, resulting in deviances in the awareness, the experience, the regulation and the expression of emotions. Developmental principles were applied and alexithymia was theorised to be the result of a stagnation in the development of differentiation of emotions and in the shift of the so-called concrete operational to the 'formal' stages of thinking, according to the theories of Werner and Piaget (7,12–14).

Alexithymia, in the last decade redefined as an impairment in affective information processing, has triggered neuroscientists to search for a neural basis. Neuropsychological research in this area may build upon theories of social cognition, i.e. the ability to construct representations of the relations between oneself and others, and to use these representations flexibly for guiding social behaviour (15). Social-cognitive skills encompass (a) the perception of social-emotional stimuli, such as facial expressions or verbal reactions of others, or interoceptive information about the state of one's own body, (b) the evaluation of these stimuli and (c) the modulation and regulation of social-emotional behaviour (16). Although alexithymia primarily describes problems in the experience and expression of one's own feelings, it often co-occurs with impairments in the recognition of emotions in others, in mentalising and empathising abilities, resulting in problems in social interactions (17). Studies of psychosocial functioning in psychiatric diseases such as schizophrenia and autism illustrate the close relation of the alexithymia concept with social-cognitive constructs. It is well known that patients with schizophrenia have higher levels of alexithymia. Apart from these problems in affective responsiveness to one's own emotional experiences, patients with schizophrenia are characterised by impairments in emotion perception and in perspective taking (18). In autism too, impairments are obvious in the interpersonal domain as well as in the intrapersonal or self-referential domain: autistic features are associated with poor mentalising capacities and with increased levels of alexithymia.

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In fact, the ability to understand our own feelings modulates empathic behaviour, and disturbances in both qualities may share the same functional cortical impairment (19,20).

A recurrent issue in alexithymia research is the question whether it should be considered a primary and permanent condition, caused by a structural deficit in the regulation of emotions, or rather a secondary, state-dependent phenomenon. Alexithymia is more prevalent after head injury; state-dependent alexithymia induced by head trauma is often referred to as 'acquired' or 'organic' alexithymia (21–23). However, people with severe physical illnesses or post-traumatic stress disorder (PTSD) may also manifest alexithymic features as a state-bound reaction, mostly understood as a way of dealing with profound stress (24–26). Others describe alexithymia as a constant disposition or personality trait, relatively independent from fluctuating stress levels (27–30). The time window is essential in defining a characteristic to be state- or trait-like. While not completely trait-like, alexithymia cannot be regarded as entirely state-like either (31).

Although the state-versus-trait discussion has received much academic attention, both the theoretical and clinical relevance of differentiating alexithymia on this basis can be debated. With respect to susceptibility to change, the state-trait differentiation has in fact not been very helpful so far. While it is clear that absolute levels of alexithymia may vary within persons over different situations, no prospective studies have been conducted focussing on the (in)stability of relative differences between persons over shared situations (e.g.: is the degree to which soldiers display differences in alexithymic features equal before and after a joint mission?).

If the ultimate aim is to understand alexithymia, it should probably be considered the result of cumulative and complex brain-behaviour-environment interactions. Interestingly, this is not discordant with earlier theories, which is illustrated by the study of Swart, Kortekaas and Aleman, who showed that alexithymic people use less efficient emotion-regulation strategies and are characterised by suppressive rather than reappraisal strategies (32). This neuropsychological interpretation again highlights the original psychodynamic background of the construct.

Measuring alexithymia

Alexithymia is a conceptually diverse concept. This diversity is also reflected in the variety of instruments that are being used to measure the construct. The latest version of the Toronto Alexithymia Scale (TAS-20) is internationally accepted as the gold standard to evaluate alexithymia. The TAS-20 is a self-report questionnaire consisting of three subscales: Difficulties in Identifying Feelings (DIF), Difficulties in Describing Feelings (DDF) and Externally Oriented Thinking (EOT). Although the reliability and validity of the TAS-20 have been shown to be sufficient, the scale has been criticised for ignoring affective aspects of the alexithymia concept (33).

A more differentiated operationalisation of alexithymia can be found in the 40-item self-report Bermond-Vorst Alexithymia Questionnaire (BVAQ), covering both affective and cognitive aspects. This questionnaire contains five subscales: Emotionalizing, Fantasizing, Identifying, Analyzing and Verbalizing emotions. Emotionalizing refers to the degree to which a person is emotionally aroused by emotion-inducing events, and Fantasizing to the degree to which someone is inclined to fantasize, imagine and daydream. Identifying, Analyzing and Verbalizing respectively refer to the degree to which one is able to define, explain and describe one's own arousal states and emotional reactions (34).

Bermond extensively studied alexithymia from a neuropsychological point of view and suggested a distinction into two main subtypes, following two neural mechanisms (35). Type I alexithymia, understood as a dysfunction of the right cerebral hemisphere, is characterised by the absence or constriction of the emotional experience and, consequently, by the absence or constriction of cognition accompanying the emotion. A decreased physiological arousal would cause this type of alexithymia. Type II alexithymia, understood as a dysfunction of the corpus callosum, is defined by a selective deficit of emotional cognition (i.e. Identifying, Analyzing and Verbalizing emotions), accompanied by an intact emotional experience and a normal physiological arousal. That is, due to a callosal disconnection syndrome, emotional arousal (supposedly a right-hemisphere function) cannot be transferred to the left hemisphere and be verbally interpreted (i.e. conscious awareness).

According to this disconnection model, the emotional information present in the right hemisphere cannot be transferred to the left hemisphere, resulting in physiological arousal that cannot be reduced by cognitive ways of coping. Consequently, in type I, both the affective and the cognitive components of emotion regulation are disturbed, whereas in type II the affective aspects are spared while the cognitive ones are impaired. In case of type I alexithymia, all subscale scores of the BVAQ are expected to be lowered, whereas in type II alexithymia subscale scores on Emotionalizing should be normal.

Factor analyses of the BVAQ items have indeed provided support for a two-factor structure, differentiating an affective dimension (including

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Emotionalizing and Fantasizing) from a cognitive dimension (including Identifying, Analyzing and Verbalizing) (34,36). The scales making up the cognitive dimension of the BVAQ correlate significantly ($r = 0.80$) with the corresponding factors of the TAS-20 (33).

Subtyping alexithymia has been helpful in understanding schizophrenia. Patients with schizophrenia display specific impairments in the cognitive components of emotion regulation (type II), coexistent with a disposition for higher levels of subjective emotional arousal. Difficulties in identifying and expressing their own emotions may very well contribute to the deficits in social functioning observed in patients with schizophrenia (37).

Other, less frequently employed instruments in the measurement of alexithymia are the Levels of Emotional Awareness Scale (LEAS), the Beth Israel Psychosomatic Questionnaire (BIPQ) and the Observer Alexithymia Scale (OAS). BIPQ and OAS, unlike TAS-20, BVAQ and LEAS, are observer-based questionnaires. As self-report inherently demands reflection on one's own emotions, precisely the quality under measurement, one would expect observer ratings to be used more often in alexithymia studies to counterbalance for potential bias. An extensive overview of alexithymia questionnaires can be found in the study by Kooiman (38).

Neural substrates

Involvement of the right cerebral hemisphere and the corpus callosum will be first discussed, as these two brain areas have historically been linked to alexithymia and they have been studied most extensively in this area of research. Subsequently, evidence for the involvement of other, more specific subcortical and cortical structures traditionally linked to emotional processing will be discussed: the amygdala, as well as the cingulate, insular and orbitofrontal cortices.

Hemispheric and interhemispheric structures

Right cerebral hemisphere. The right hemisphere is well known for its involvement in the perception and coordination of emotional behaviour (8,39,40). Bermond indeed described several clinical studies of patients with right-hemisphere lesions, who showed mixed alexithymic features, presenting combined affective and cognitive deficiencies (35). Moreover, the ability to recognise facial expression of emotions is reduced in alexithymic patients (41–46).

Jessimer and Markham indirectly explored the involvement of the right hemisphere in healthy participants with high and low levels of alexithymia by chimerical tasks (42). The chimeras consisted of pictures of faces made of conjoined emotive and non-emotive halves, as well as asymmetrically distributed stars and whole faces, expressing different emotions. Results indicated that participants with high levels of alexithymia had less leftward perceptual preference, suggesting reduced right hemisphere responding, although only the asymmetry scores on one task (sad/neutral chimerical photographs) reached the level of statistical significance. In addition, they were worse in recognising facial expressions of emotions than subjects with low levels of alexithymia. Differences were not emotion-specific.

An imaging study using positron emission tomography (PET) analysed brain activity in a non-clinical sample of 12 participants with and 12 without alexithymia according to the TAS-20, while these participants were viewing a range of emotional face expressions. The alexithymia group exhibited lower regional cerebral blood flow in the right hemisphere than the non-alexithymia group. In addition, the alexithymics showed higher regional cerebral blood flow in the left hemisphere when compared with the non-alexithymic participants (43).

Some authors have suggested that sex differences exist with respect to left- and right-hemisphere involvement in alexithymia (47–49). In stroke patients with right unilateral lesions in various regions, high TAS scores were more frequent in men than in women, despite the variety in lesion localisation. In women, both a left-hemisphere and a right-hemisphere stroke resulted in higher levels of alexithymia (49). A recent event related potential (ERP) study also showed sex differences regarding lateralisation in alexithymia. Females showed higher P300 amplitudes compared with males. Moreover, females with low levels of alexithymia showed enhanced amplitudes for electrodes over the left compared with the right hemisphere in a scalp electroencephalography (EEG) performed to record the P300 response. The results suggest that, at least in some women, the left hemisphere is involved in alexithymia (47).

In sum, most findings underline the idea of substantial right-hemisphere involvement in alexithymia, at least in males. Still, regarding the aetiology, these findings are not very specific, neither with respect to location nor to function. Moreover, many of these lateralisation findings need replication. If there is a reduced activity in the right hemisphere in a male alexithymic, then *how* does this explain the alexithymic features? As a consequence of the non-specificity of the contribution of the right hemisphere to alexithymia, both type I and type II aspects may be associated with dysfunctions of this brain area. In terms of social cognition, main problems may be expected with regard to the perception or

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interoception of social-emotional signals, but certainly not exclusively.

Corpus callosum. Adequate interhemispheric communication is required for adequate regulation of emotions. When it is impeded, type II alexithymic features can emerge (35). The left hemisphere is known to be more specialised in a verbal, conscious and analytic mode of information processing, whereas a non-verbal, unconscious and more holistic mode of information processing is predominantly associated with the right hemisphere (39,40,50). To consciously experience and verbalise emotions, perceptual information of the right hemisphere has to be transferred to the left hemisphere. The corpus callosum accounts for this transfer of information.

An interhemispheric communication deficit as a neural explanation for alexithymia stems from observations in split-brain patients, who had been treated for severe types of epilepsy for which they underwent complete cerebral commissurotomy (8). Hoppe and Bogen studied 12 patients before and after split-brain surgery and showed that after surgery all were highly alexithymic according to the BIPQ and that they experienced problems with the verbal expression of emotions. In addition, there was a decrease in their ability to fantasize, to symbolise and to dream (51). Ten Houten, Hoppe, Bogen and Walter performed a similar study with eight patients who underwent commissurotomy and eight matched controls (52). Participants were shown a 3-min film with the purpose to evoke emotions and fantasies by symbolically representing death and loss. After watching the film, the participants were asked to give comments, verbally and in writing, and answer questions about the film. The results of the study clearly indicated that the patients used fewer affect-laden words and fewer adjectives in their descriptions of the film, compared with their matched controls. In short, patients were more alexithymic than the controls in this study. Unfortunately, only the use of language was taken into account in this study, while the subjective emotional experience was not examined.

In a corpus callosum agenesis case study of Buchanan, Waterhouse and West, the patient showed severe alexithymia as measured by the BIPQ (53). Another corpus callosum agenesis case study, using the TAS-20, showed that the adolescent patient, who also had chronic pain, appeared to have flat affect, a restricted fantasy life and was unable to recall dreams, all characteristics of alexithymia (54).

Additional support for the interhemispheric communication deficit hypothesis of alexithymia was provided by Zeitlin, Lane, O'Leary and Schrift, who used a tactile finger localisation task to assess the efficiency of interhemispheric communication in participants without neurological damage (55). In such a task, the researcher simultaneously touches one, two, three or four fingers of the participant with a pencil. Then, he or she has to state which fingers were touched, by touching them again with the thumb of the same hand (uncrossed condition) or with the thumb of the other hand (crossed condition). For the crossed condition, interhemispheric communication is required. Interhemispheric communication of patients with and without alexithymia (TAS-20) suffering from PTSD secondary to combat in Vietnam was compared with the interhemispheric transfer of control subjects without alexithymia. The results indicated a strong association between alexithymia and an interhemispheric communication deficit. In addition, the deficit in interhemispheric communication was bidirectional. It was concluded that at least some forms of alexithymia may be mediated by a functional disconnection of both hemispheres. The reason for this prudent conclusion is the fact that the localisation task measures the transfer of sensorimotor information, but not necessarily the transfer of emotional information.

Dewaraja and Sasaki used a visual lateralisation matching task with linguistic (words) and non-linguistic (line drawings) emotional stimuli as variables (56). Right-handed university students were identified as either alexithymic or non-alexithymic with the Schalling-Sifneos Personality Scale, an incidentally used 20-item self-report questionnaire with suboptimal psychometric properties (7,57). Differences in ipsilateral and contralateral hand reaction times were used to indicate speed of callosal transfer. The alexithymic group was significantly slower than the non-alexithymic group in the interhemispheric communication of non-linguistic information, but the groups did not differ in the speed of transferring linguistic information. Only a right-to-left relationship between alexithymia and interhemispheric communication was found, in contrast with the findings of Zeitlin et al. (55), who found a bidirectional relationship.

Parker, Keightley, Smith and Taylor tried to replicate Zeitlin's findings in a non-clinical sample (58). The efficiency of interhemispheric communication was assessed in 14 alexithymic and 15 non-alexithymic right-handed, male students using the tactile finger localisation task. The non-alexithymic participants were significantly more efficient at transferring information between the cerebral hemispheres than the alexithymic subjects in a bidirectional way. These findings suggest that an alexithymic cognitive style reflects poor integration of the information processing of both hemispheres. Lumley and Sielky also used the tactile finger localisation task to assess the interhemispheric

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communication in a non-clinical sample of 47 men and 58 women (48). Among the men, the TAS-20 scales 'difficulty identifying emotions' and 'difficulty describing emotions' were correlated with reduced interhemispheric transfer of information. However, among the women, alexithymia was completely unrelated to interhemispheric functioning. The authors concluded that deficiencies in interhemispheric communication may contribute to alexithymia in men, but not in women. Again, in both studies note that the tactile finger localisation task involved the transfer of sensorimotor information only.

In 2008, after more than 30 years of research on the interhemispheric transfer deficit in alexithymia, more direct evidence was provided by a transcranial magnetic stimulation study (59). Functional differences were found in transcallosal interactions in 16 high alexithymic as compared to 16 low alexithymic male and female students, according to the Italian version of the TAS-20. This supports the conclusion of Bermond et al., that although not unequivocal, experimental results suggest that 'alexithymia could be related to a "functional commissurectomy"' (36).

In conclusion, there is supporting evidence for the hypothesis of an interhemispheric communication deficit underlying alexithymia, particularly in alexithymic men. According to Bermond's subdivision (35), this deficit would result mainly in type II alexithymia, implying that the cognitive aspects of alexithymia would be impaired, whereas emotional arousal ought to be present. In social-cognitive terms, mainly the facets modulating and regulating social-emotional information may be implicated in callosal dysfunction. That is, the conscious awareness and expression of emotions is impaired because of the inability to verbally interpret the right-hemisphere arousal. Nevertheless, none of the aforementioned studies has yet revealed the precise nature and directionality of the transfer deficit sufficiently (60).

Subcortical structures

Amygdala. The subcortical brain structure that is best known for its contribution to emotion processing is the amygdala. The amygdala receives, together with the prefrontal cortex (PFC), highly processed sensory information from all modalities. It has extensive reciprocal connections with a large number of other brain structures, such as the ventromedial frontal cortices, the hypothalamus and the hippocampus, whose functions can be modulated by emotion. The amygdala is considered to be a part of what was described by McLean as the limbic system, a functionally interconnected set of subcortical and cortical structures involved in emotional processing, motivation and emotional association with memory (61). It is particularly known for its involvement in the evaluation of valence of emotions in social situations, such as those related to reward and fear. Furthermore, the amygdala is important in emotional conditioning and in the consolidation of emotional memories (62–65).

Many studies have indicated that the amygdala is involved in evaluating emotional significance (66–70) and in the recognition of facially communicated threat (71–73), two features associated with alexithymia. Surprisingly, studies directly examining whether the amygdala is involved in alexithymia are scarce. Results tend to reveal no differences between alexithymic and non-alexithymic participants with respect to brain activity in limbic structures in general (43,74,75).

As the amygdala is important in the detection of emotional significance, as well as in the recognition of emotions in facial expressions, it could be hypothesised that the alexithymia features 'Emotionalizing' (type I) and 'Identifying' (type II) may be compromised in people with amygdala lesions. Concerning the magnitude and frequency of emotions, Anderson and Phelps found no differences between patients with unilateral and bilateral amygdala lesions and controls (76). Patients with amygdala lesions were able to report emotional feelings of normal intensities, pleading against involvement of the amygdala in affective aspects of alexithymia (type I).

In sum, the amygdala is undisputedly an essential structure with regard to emotional processing, but there is no convincing evidence that it is dysfunctional in alexithymia. Specific research of amygdala functioning in alexithymic subjects is however still lacking.

Cortical structures

Anterior cingulate cortex. The anterior cingulate cortex (ACC) appears to be involved in initiation, motivation and goal-directed behaviour and is also recognised to have a function in attention processing, pain, response selection, as well as maternal and skeletomotor behaviour (77). In 1937, Papez was the first to propose involvement of the ACC in the regulation of emotions (78). In the 1940s and 1950s, animal and human studies on the ACC clearly showed the involvement of the cingulate cortex in motor and autonomic control. Lesions in the ACC have also been related to changes in affect and personality. Patients with ACC lesions have been described as indifferent after making mistakes (79,80). Hornak et al. described patients with ACC lesions whose subjective emotional experiences changed and who developed deficits in the recognition of emotional face expressions (81).

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The ACC has been further subdivided into a dorsal 'cognitive' part, engaged in response selection associated with motor activity, and an anterior-ventral 'affective' part, dedicated to autonomic activity and internal emotional responses. The cognitive subpart has strong reciprocal interconnections with the lateral PFC and motor areas, while the affective subpart is connected to the amygdala, hypothalamus, hippocampus and the orbitofrontal cortex. Regarding alexithymia, it is important that these two subparts show reciprocal suppression and that cognitive and emotional information may be processed separately (77,82). However, rather than considering the subregions of the ACC as two separable entities, Critchley et al. advocated an integrative approach in explaining the functions of this structure (83). The authors showed integration of mental and bodily processes in the ACC and suggested that the production of autonomic responses that signal the requirement for adaptive control of behaviour is the core task of the ACC: the ACC as an autonomic, executive regulator.

There is supporting evidence for a dysfunction of the ACC in relation to alexithymia. Lane et al. observed significantly deviant activation of the ACC in response to watching emotion-inducing films (84). In their PET study, they explored the neural correlates of emotional experience in 12 healthy women. They measured regional cerebral blood flow during film- and recall-induced emotion and correlated changes in the blood flow attributable to emotion with the scores on the LEAS. The LEAS measures the level of emotional awareness, varying from awareness of physical sensations to complex emotions in social situations. Their findings imply that the degree to which the ACC is activated during emotion varies across individuals. Positive associations between LEAS scores and regional cerebral blood flow in the ACC were found during film-induced negative emotions.

Kano et al. found similar results in the PET study described already in the discussion of the involvement of the right cerebral hemisphere (43). They showed that people with alexithymia showed less ACC activation compared to the volunteers without alexithymia, as a response to angry faces. Berthoz et al. conducted a functional magnetic resonance imaging (fMRI) study in eight men with alexithymia and eight men without alexithymia (74). They observed stronger ACC activation in men with alexithymia than in men without alexithymia in response to highly positive emotional pictures, and they found reduced activation in the left ACC in men with alexithymia in response to negative emotional pictures. An fMRI study confirmed this once more (85). Twenty-six patients with PTSD and 16 trauma-exposed controls completed a trauma script imagery task. In the PTSD group as well as in the controls, TAS-20 scores correlated negatively with activation in the ACC. More recently, Karlsson, Näätänen and Stenman found alexithymia to be related with less activation in the ACC, in their PET study with 10 TAS-20-alexithymic adult female students, watching emotion-inducing films with positive, neutral or negative valence (86). With respect to structural differences, a magnetic resonance imaging (MRI) study of Gündel et al. showed a significant positive relation between the size of the right ACC and the extent of alexithymia in male university students, as measured by the TAS-20 (87). In women, a prominent ACC was associated with a tendency to withdrawal behaviour (harm avoidance). The authors suggested the ACC to be involved in a suppression mechanism that pushes unwanted associations out of awareness. This explanation is consistent with the findings of Bush et al. (82), in which the cognitive and emotional parts of the ACC show reciprocal suppression.

In conclusion, the ACC takes part in emotion regulation processes and less ACC activation is associated with negative emotions. Furthermore, the ACC has been linked to affective as well as cognitive aspects of alexithymia. Thus, dysfunction of the ACC may result in type I alexithymia. From a social-cognitive perspective different aspects can supposedly be affected by ACC dysfunction, including the evaluation, modulation and regulation of social-emotional stimuli.

Posterior cingulate cortex. The posterior cingulate cortex (PCC) can be differentiated from the ACC on the basis of cell architecture and patterns of projection, as well as function. The ACC has been characterised as 'executive' in function, whereas the PCC would be fitted for 'evaluative' purposes (88). The PCC has shown to be involved in both memory and emotion processing. Emotional stimuli have been reported to consistently activate this area, and it is speculated that the PCC is active in the modulation of episodic memory (89). The PCC does indeed have strong reciprocal connections with regions engaged in memory processing, such as the hippocampus and the thalamus. It also has reciprocal projections to the ACC and the orbitofrontal cortex (75).

Based on fMRI findings, Mantani et al. were the first to propose the PCC to play a crucial role in alexithymia, especially in alexithymia-related imagery disturbance (75). People with alexithymia are known to have limited ability to fantasize. The regional cerebral activation of 10 participants with and 10 without alexithymia according to the TAS-20 was compared during various imagery conditions. Participants were

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instructed to image a past and future happy event, a past and future sad event and a past and future neutral event. The results revealed significantly reduced activation of the PCC in alexithymic people during happy imagery. Given the projections of this brain structure, this result may be related to a dysfunction of episodic memory retrieval during happy imagery in subjects with alexithymia. The authors suggested that while people without alexithymia can easily use memories of emotional events to imagine future events, this process is compromised in individuals with alexithymia. Why the reduced activation in the PCC was specific for the future happy event remained uncertain, but the authors suggest that the specific difficulty of imagining future happy events could reduce motivation and hope. In line with these findings with respect to PCC involvement in alexithymia, the before mentioned fMRI study of Frewen et al. showed not only decreased activity of the ACC in alexithymic patients performing a trauma imagery task but also positive correlations between TAS-20 scores and increased activation in the PCC (85). Although Miyake et al. reported covariation of PCC activation and alexithymia levels, their findings did not equivocally replicate those of Frewen et al. and Mantani et al. (75,85,90).

Maddock, Garrett and Buonocore conducted an fMRI study to determine if activation of the PCC by emotional stimuli can be attributed to the memory-enhancing effects of non-emotional stimulus features (91). In a valence-decision task, pleasant and unpleasant words were matched with neutral words on non-emotional features known to influence memory. They reported heightened activation of the PCC in healthy participants during the processing of emotional words; these results confirmed that the PCC mediates interactions of emotional and memory-related processes. Although alexithymia was not a variable in this study, the results suggest that a dysfunction of the PCC may contribute not only to the diminished affect-related imagery in alexithymia but also to problems in verbalising emotions. Subsequently, Aleman proposed that compromised interactive processing in hippocampal-amygdala circuits during the development of associations between affective states and words may underlie the problem of verbalising feelings in alexithymia (92). In their recent fMRI study, Swart et al. showed alexithymia, in particular difficulties with verbalising emotions, to be positively related to a catechol-O-methyltransferase (COMT)-genotype variation (COMT Val158Met polymorphism), which in turn results in a decrease of neural activation in the PCC. As PCC is one of the cortical midline structures, they therefore suggested PCC functionality to be connected with self-awareness (93).

Thus, the PCC takes part in alexithymia-related (self) imagery disturbances, as well as in emotional learning and in problems in verbalising emotions. Dysfunction of the PCC can be expected to result in type I alexithymia, as problems in imagining and fantasizing may constrict emotional experience, including emotional awareness. According to the description of social-cognitive processes of Adolphs, the evaluative or interpretative aspect of social cognition may be impeded in alexithymia associated with PCC malfunction.

Anterior insular cortex. The insular cortex is the part of the cerebral cortex situated in the centre of the brain, folded within the lateral sulcus; it can be divided into a smaller posterior part posterior insular cortex (PIC) and a larger anterior part anterior insular cortex (AIC). The AIC, also referred to as the 'interoceptive cortex', is involved in a bottom-up process, mapping internal body states and integrating them in conscious representations of feeling states, as Damasio first suggested in 1994 (94–98). It is often studied because of its involvement in the social-cognitive processes of empathy, in particular pain-related empathy. However, to affectively share feelings of other people, intact cognitive capacities to make self-other distinctions are mandatory. Shared network models of empathy suggest that the neural networks involved in the representations of one's own feelings are the same as those underlying the representations of feelings of others (98).

In the already cited study of Kano et al., alexithymic participants displayed decreased insular activity in response to angry faces (43). The same research group found heightened activity in the right insula of TAS-20 alexithymics in response to visceral stimulation (99), as did Frewen et al. in response to trauma imagery (85).

The before-mentioned PET study of Karlsson, Näätänen and Stenman also showed higher levels of activation in the (left) insula and in sensory and motor cortices, in alexithymic women watching films that evoked empathic reactions. The authors suggested this overactivation of 'bodily brain regions' as an explanation for the tendency of alexithymic patients to experience physical symptoms rather than emotions, supporting the hypothesis of somatosensory amplification in alexithymia (86).

Others have found deviant activity levels in the AIC in alexithymic participants as well. In an fMRI study with Asperger patients watching emotion-inducing pictures, Silani et al. showed low levels of emotional awareness, i.e. high TAS-20 and BVAQ-scores, to be correlated with hypoactivity in the anterior insula (100). Support for the shared role of the insular cortex in both alexithymia and empathy was

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confirmed by the work of Bird et al., who performed an fMRI study with an 'empathy for pain paradigm' in 18 males with autism spectrum conditions and 18 controls, matched on TAS-20 scores, sex, age and IQ. They found an increased activation of the left AIC in reaction to the observation of pain in closely related others. The strength of the signal was predictive of the degree of alexithymia in both autistic patients and controls (20). In sum, the interoceptive cortex, especially that of the left anterior insula, is associated with alexithymia. The ability to reflect on one's own emotions modulates empathic brain responses, in which the insula is involved as well. One would expect type I alexithymia to occur in focal injuries of the insula, or redefined in social-cognitive terms, the processes of both perceiving and evaluating social-emotional information.

Orbitofrontal cortex. The PFC is the part of the cortex that is situated in front of the motor and premotor cortices in the frontal lobe. The PFC can be divided into the lateral, medial and the orbitofrontal cortex (101). This area of the brain is thought to be involved in higher cognitive and emotional functions, such as decision-making, planning complex cognitive behaviours, moderating appropriate social behaviour and impulse control (102–104). Involvement of the PFC in alexithymia has predominantly been studied in patients with head trauma, as acquired brain injury often involves damage to the PFC.

In the 1940s, Freeman first introduced the transorbital method, a surgical procedure in which the orbitofrontal parts of the PFC were isolated from the rest of the brain, with the purpose to reduce suffering in patients with overwhelming emotions (105). In 1970, Trigg described several cases of patients who underwent frontal lobotomy (106). Generally, after removing the PFC, patients reported fewer complaints, they experienced a flatness of affect and an absence of spontaneous emotional reflection, known as features of alexithymia. However, emotional cognitions remained unchanged. This type of surgery could also induce a disinhibition of emotional behaviour, resulting in short periods of violent emotional behaviour.

The orbitofrontal part of the PFC is especially important in the regulation of emotions. This brain region is involved in emotion-related learning and in the regulation of facial expressions (102,104). It projects to the hypothalamus and has strong reciprocal connections with the amygdala (36,103,107,108). Lesions in the orbital PFC can impair voice and facial expression identification (81,101). Furthermore, they may lead to a reduction in emotionalising and to deficiencies in emotional decision-making, whereas the emotional cognitions may still be intact (103,107). Patients with frontal lesions may lack the internal drive to reflect upon their emotional cognitions, but they will do so if stimulated by others (109). This lack of spontaneous reflection may underlie the disrupted emotion decision-making.

In a case study of Angrilli et al., the orbital PFC proved to play an important role in retrieval of emotional information, particularly information with a negative valence (102). The patient, who had a right orbitofrontal lesion, showed reduced recall of unpleasant stimuli. During a task focusing on imagery of emotional situations, facial expressions to unpleasant imagery scripts were impaired. Hence, orbitofrontal lesions may be related to alexithymia, because people with alexithymia are known to have constricted imaginative capacities and impaired recognition of facial expressions. Constricted imagination and a reduction in facial expressions have been found repeatedly in patients with prefrontal lesions (11,110,111). The results of the study of Angrilli et al. are in line with the view that the orbital PFC is important in integrating past emotional physiological patterns, reactivated by the amygdala and the hippocampus, and current or 'online' information, kept in the working memory situated in the frontal cortex. The integration of information from these two systems is in turn essential for adequate decision-making and planning.

To date, only a few studies have directly addressed the role of the PFC in alexithymia. The PET study of Kano et al. showed that alexithymic subjects exhibited decreased activation in the inferior and superior frontal cortex and the orbital PFC of the right hemisphere, in reaction to negative emotional stimuli (43). Frewen et al. found conflicting results in their fMRI study with 26 PTSD patients and 16 controls, who completed a trauma script imagery task with negative emotional stimuli (85). In the controls, TAS scores correlated positively with activation in the bilateral medial PFC, suggesting alexithymia to be related to increased activation in these parts of the PFC. Mantani et al. observed no differences between persons with and without alexithymia in activation of the orbital PFC (75).

Although most research focuses on the orbital part of the PFC, Bermond suggested involvement of the dorsolateral part in 'pseudo-alexithymia' (35). The dorsolateral PFC has a function in motivational aspects of emotion regulation, such as planning, initiating and adapting behaviour to the demands of the environment. Selective lesions in this area may therefore prevent a person from reflecting upon their feelings and from actively responding to them, while the emotional experience and emotional cognition per se are intact.

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In conclusion, there is general agreement about the contribution of the PFC, particularly the orbital part, to the experiencing of emotions, but the relation with alexithymia is more inconclusive. PFC dysfunction may be related to the features 'Emotionalizing' (the orbital PFC as a thermostat, initiating or inhibiting emotions with a certain intensity), 'Fantasizing' (imagery, memory and emotion) and 'Analyzing' (integrating, reflecting on emotions, making decisions). The orbital PFC may especially be involved in the affective aspects of alexithymia (type I), including problems in perceiving and evaluating emotions, while the dorsolateral part has been associated with pseudo-alexithymia.

Alexithymia redefined as an impairment in social cognition

Alexithymia is considered a neuropsychological concept, which means that it has a neural basis, but is expressed through and measured by social-emotional behaviour. It can be defined as a disturbance in affective information processing, but as it is inherently linked with social impairments, it may be considered a disturbance in social-cognitive functioning as well and, consequently, as a disturbance in social-cognitive functions.

Traditional approaches as BVAQ type I and type II alexithymia reflect no absolute or dichotomous entities. Problems in affective and cognitive aspects seem to occur in different degrees. This is in line with the recent findings of Bagby et al., who performed confirmatory factor analyses and model-based cluster analyses on a large BVAQ database, showing that a decomposition into two types of alexithymia is not a just representation of the alexithymia construct. They state that the latent structure of alexithymia is dimensional rather than taxonic and they advocate the development of measures that use a continuous scale (112). Theoretically, Bermond et al. suggested dimensionality as well. They considered it possible that, due to experiences in childhood, the system for emotion regulation becomes fixated at different stages of maturity of the brain, resulting in extreme or intermediate personality types with respect to tendencies in emotionalising and expressing feelings (36). Affective-neuroscientific research concerning brain plasticity in early childhood provides confirmation for such a developmental explanation. The neural circuits of emotion (i.e. hippocampus, amygdala, PFC) might, as a result from plasticity, be influenced by stressful life events, which in turn shape patterns of emotional reactivity and change the risk for psychopathology later in life (108).

According to Adolphs, social-cognitive skills can be subdivided into the aspects: (a) perceiving, (b) evaluating and (c) modulating and regulating social-emotional stimuli (16). Theoretically, alexithymia has been subtyped in an affective (I) and cognitive (II) factor (35). Considering this distinction in the light of Adolphs' interpretation of social cognition, type I alexithymia would be the result of constrictions in the perception of social-emotional situations and/or in the experience of emotions (a + b), while type II alexithymia can be regarded as a disturbance in expressing emotions (c).

Roughly, two neurocognitive 'models' regarding hemispheric and interhemispheric disturbances have been extensively described to account for alexithymia. The first postulates a non-specific dysfunction of the right cerebral hemisphere, resulting in equally non-specified alexithymia (type I + II). Considering the contemporary state of knowledge, the right-hemisphere model with its broadband character is in fact of limited use in modern alexithymia research. Nevertheless, lateralisation is still an important variable in unravelling sex differences in alexithymia. The second influential model identifies the corpus callosum as dysfunctional, assuming an interhemispheric communication deficit, associated predominantly with impairments in the cognitive, expressive aspects of alexithymia (type II). Although this may be the best-studied structure with respect to the origins of alexithymia, the nature and directionality of the functional transfer deficit have not been cleared up in detail yet. In fact, the amount of literature on hemispheric and callosal structures, as compared with the other structures, may erroneously suggest their greater involvement in alexithymia. This, however, may be the reflection of a historical bias caused by the development of neuroscientific methods over the last decades.

For instance, since the development of imaging techniques, more structures have been pinpointed for their implications in alexithymia. The cingulate cortex takes part in emotion regulation processes, with the ACC being especially equipped for experiencing and controlling emotions (I + II), and the PCC specifically fit for imagery-related aspects of emotion (I). Findings with respect to the role of the cingulate cortex in alexithymia are not completely unambiguous, but a double dissociation between a diminished activation of the ACC together with an increased activation of the PCC does provide support for its involvement. The insular cortex is crucial in the representation of feeling states of the self and of others. Furthermore, the amygdala is obviously involved in affective information processing, but not evidently responsible for alexithymia. Likewise, the orbitofrontal PFC undoubtedly contributes to emotional experience, but it is not clearly involved in alexithymia per se, although it does seem to mediate affective aspects of alexithymia. Some brain

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structures probably derive their share in alexithymia from their projections to other brain structures, making them important, but not crucial.

With respect to the differentiation of alexithymia, the reputed clinical subdivision cannot be downsized to strictly separable cerebral roots. However, corpus callosum and prefrontal cortical structures, in particular the ACC and AIC, seem to be implicated more prominently.

Conclusion

Alexithymia is associated with a diffuse neural substrate, in which the corpus callosum and the cingulate and insular cortex seem to be explicitly involved, whereas the amygdala and (orbito)PFC are involved as mediators of the affective process in general. The relative contribution of these brain areas to the aetiological understanding of alexithymia remains to be quantified. A further analysis of the methodology followed in the various studies, including axiomas on the dimensional or taxonic nature of alexithymia, would be necessary. For future studies, the inclusion of more observer-based alexithymia questionnaires should be encouraged.

Refining our knowledge of the neural substrates is important, but adopting a contextual perspective is essential for furthering our understanding of alexithymia. In fact, alexithymia should be considered a social-cognitive impairment, in the explanation of which developmental, neurobiological, neuropsychological and behavioural theories have to be combined to enable a better understanding of the construct. This, in turn, is a prerequisite for the development of targeted interventions to prevent or diminish complaints and to enhance the quality of life in people with alexithymia.

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