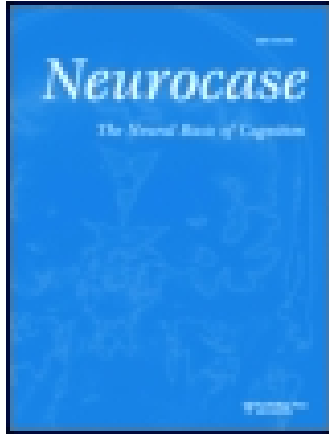


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Ralf Schäfer^a, Kerstin Popp^a, Silke Jörgens^b, Robert Lindenberg^b, Matthias Franz^a & Rüdiger J. Seitz^b

^a Institute of Psychosomatic Medicine and Psychotherapy, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany

^b Department of Neurology, University Hospital Düsseldorf, Düsseldorf, Germany

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Alexithymia-like Disorder in Right Anterior Cingulate Infarction

RALF SCHÄFER¹, KERSTIN POPP¹, SILKE JÖRGENS², ROBERT LINDENBERG², MATTHIAS FRANZ¹ and RÜDIGER J. SEITZ²

¹*Institute of Psychosomatic Medicine and Psychotherapy, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany*

²*Department of Neurology, University Hospital Düsseldorf, Düsseldorf, Germany*

The frontal midline structures have been demonstrated by functional neuroimaging to be involved in the affective control of human behavior. However, due to the rareness of diseases affecting this part of the brain little is known about behavioral abnormalities following damage to these brain areas. We present a patient with a right anterior cingulate infarct who presented with an alexithymia-like disorder. Event-related potentials revealed an abnormality of emotional face perception in the right cerebral hemisphere. We suggest that the anterior cingulate lesion induced a deficit of emotion processing including emotional face perception probably due to an interference in a critical node of a large-scale network subserving affective control of behavior.

Keywords: Stroke, anterior cingulate, face perception, emotion, self-control of behavior

Introduction

The anterior cingulate has been proposed to play an important role in controlling behavior due to the convergence of neural circuits related to motor control, cognitive control, and control of affect in this portion of the brain (Carter, Botvinick, & Cohen, 1999; Hines, Chiu, McAdams, Bentler, & Lipcamon, 1992; Paus, 2001). While the dorsolateral prefrontal cortex has been known to play a prominent role in the control of behavior by interspersed representations related to cognitive problem solving (Duncan & Owen, 2000; Fuster, 2000), the functional role of the frontal midline structures has been less well understood. As the frontal midline structures have enjoyed a massive phylogenetic development of size and width of the cortical layers in man as compared with non-human primates (Imagawa & Yamadori, 1996; Semendeferi, Armstrong, Schleicher, Zilles, & van Hoesen, 2001) and are densely interconnected with the dorsolateral prefrontal cortex (Petrides & Pandya, 1999), it may be assumed that they play a pivotal role in controlling human behavior. However, there are only few case studies in the open literature showing behavioral deficits related to lesions of the frontal midline structures. Most readily to assess are visible deficits of motor control such as akinesia, alien limb syndrome and bilateral disturbances of movement control resulting from infarctions or brain tumors that rarely affect these regions of the brain (Feinberg, Schindler, Flanagan, & Haber, 1992; Stephan

et al., 1999; Kumral, Bayukem, Evyapan, & Yunten, 2002). However, there are also a few reports showing alterations of emotional control of behavior ensuing brain lesions of the frontal midline structures (Eslinger & Damasio, 1985; Eslinger, 1998; Hornak et al., 2003; Shamay-Tsoory, Tomer, Goldsher, Berger, & Aharon-Peretz, 2004). In fact, these abnormalities may be so severe that they resemble sociopathy (Saver & Damasio, 1991; Damasio, Grabowski, Frank, Galaburda, & Damasio, 1994). More recently, accumulating evidence from functional neuroimaging suggests that the frontal midline structures play an important role in the motivational and affective self-control of human behavior (Frith & Frith, 2006; Northoff & Heinzl, 2006). In fact, a large meta-analysis revealed that the mediodorsal prefrontal and adjacent cingulate cortex are involved in guiding behavior with respect to internal personal standards such as moral, emotional categories and empathy (Seitz, Nickel, & Azari, 2006).

Here, we report on a patient presenting with an infarction in the right anterior cingulate and adjacent mesial prefrontal cortex. By neuropsychological testing we found severe impairments in emotional awareness and processing in this patient. Also, using psychophysical recordings of the electroencephalogram (EEG) we were able to show that the patient had an abnormality of higher order processing of body-related emotion similarly to patients with alexithymia. Thereby, this patient underscores the importance of the frontal midline structures for the subjective awareness of emotion and self-control of behavior.

This study was supported by the Bundesministerium für Bildung und Forschung (Brain Imaging Center West). The authors are grateful to Professor Dr Mödler, Institute of Diagnostic Radiology, University Hospital Düsseldorf, for providing the MR-images of the patient. The authors thank for the support of this investigation by the Deutsche Forschungsgemeinschaft (DFG) under FR 839/10-1.

Address correspondence to Dr R. J. Seitz, Department of Neurology, University Hospital Düsseldorf, Moorenstrasse 5, 40225 Düsseldorf, Germany. E-mail: seitz@neurologie.uni-duesseldorf.de

Case report

The 61-year-old, right-handed woman presented with a sudden onset of vertigo, unsteady gait and weakness of her left arm and leg. She had a 9-year school education, had three children and worked as a shop assistant until her retirement 2 years earlier. She lived together with her retired husband in a rented apartment. One month before admission arterial hypertension had been detected and oral treatment initiated. On admission the moderately overweight patient had a slight gaze paresis towards left. Finger movements were clumsy and slowed in her left hand, and her left leg would drop spontaneously when required to be held upright. Muscle tendon reflexes were symmetric and there were no pathological reflexes. Sensory examination was normal. There was a slight ataxia of stance and gait with a tendency to fall to the left. Blood pressure was moderately elevated to 150/80 mmHg. Speech and language functions were not impaired. The patient was cooperative, presented with even mood but with slowed psychomotor activity and reduced emotional responsiveness. The neuropsychological deficits are reported in detail below. Magnetic resonance imaging showed a large recent infarct in the right anterior cingulate and the adjacent corpus callosum (Figure 1). In addition, on one section there was a small infarct lesion in the posterior part of the corpus callosum. Magnetic resonance angiography showed a narrowing of the right pericallosal artery. But there were no stenoses of the intracranial arteries as detected with transcranial Doppler or of the extracranial arteries as found on doppler-sonography and Duplex. The cerebrospinal fluid was normal showing three cells per μl and 41 mg protein per 100 ml. The breathing pattern was normal as was the electrocardiogram and transthoracic echocardiogram. There was no patent oval foramen. Blood tests were unremarkable apart from an elevated cholesterolin (320 mg/l).

The presenting neurological symptoms resolved completely within 2 weeks. Since no large-vessel or cardiac

abnormalities were detected, the patient was set on 100 mg acetylsalicylic acid per day. Blood pressure normalized upon antihypertensive treatment with 100 mg atenolol and 25 mg chlortalidon per day.

One month later, she was still slow in psychomotor behavior, had impaired attention, and showed a tendency to interrupt task performance when confronted with difficult questions.

Methods

Lesion analysis

To analyze the location of the brain infarction in this patient, her brain images were transformed into Talairach standard stereotaxic space (1988) and the lesion plotted onto the atlas sections as described in detail elsewhere (Binkofski et al., 1996). On a paramedian sagittal plane it can be seen that the patient's lesion affected the genu of the anterior cingulate and extended dorsally into the ventral parts of the superior frontal gyrus (Figure 2).

Neuropsychological testing

Neuropsychological testing was performed in the second week after the infarction and included tests for attention, memory, executive functions, visuoconstructive abilities and apraxia as summarized in Table 1. Handedness was assessed with the Edinburgh questionnaire (Oldfields, 1971). Neuropsychological testing involved tests of verbal fluency (Aschenbrenner, Tucha, & Lange, 2000), verbal and visual memory (VLMT, a german version of AVLT: Helmstädter, Lendt, & Lux, 2001; Rey Complex Figure Test: Meyers & Meyers, 1995; digit span and block span: Härting et al., 2000), attention (Testbatterie zur Aufmerksamkeitsprüfung; Zimmermann & Fimm, 1993), and executive functions (Behavioural Assessment of Dysexecutive Syndrome: Wilson, Aldermann, Burgess, Emslie, & Evans,

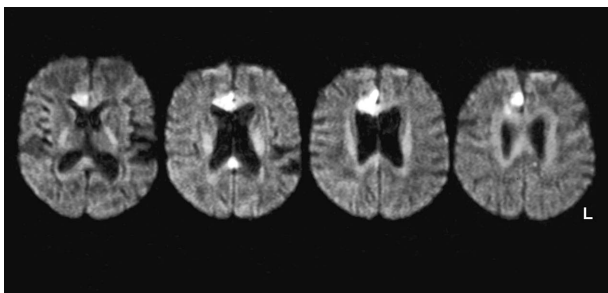


Fig. 1. Infarct lesion of the patient affecting the right anterior cingulate and the adjacent anterior corpus callosum in four adjacent image planes. Note the additional small ischemic lesion in the posterior portion of the corpus callosum. The images are three-dimensional trace maps obtained with diffusion weighted magnetic resonance imaging.

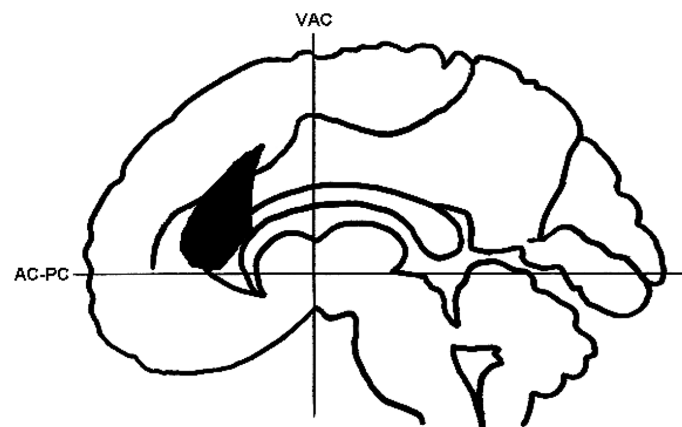


Fig. 2. Localization of the anterior cingulate cortex infarct in the stereotaxic atlas of Talairach and Tournoux (1988). Note that the lesion extends into the middle portion of the medial frontal cortex.

Table 1. Neuropsychological assessment of the patient

| Neuropsychological assessment | Performance | |
|--|--|---------------------------------|
| | Raw values | Percentiles |
| Attention (TAP, Zimmermann & Fimm 1993) | | |
| Tonic alertness (RT ms) | 579.0 | <1 |
| Phasic alertness | -0.162 | 16 |
| Selective attention (RT ms) | 654.0 | 8 |
| (errors) | 1 | <50 |
| Divided attention (RT ms) | 643.0 | 58 |
| (errors) | 12 | <1 |
| Memory | | |
| VLMT (German Version of AVLT) | | |
| DG 1 (Reproduction after 1st presentation) | 5/15 items | 30–45 |
| DG 5 (Reproduction after 5th presentation) | 9/15 items | 15 |
| I (Reproduction of Interferenz list) | 3 Items | <5 |
| DG 6 (Reproduction after Interferenz) | 8/15 Items | 20–25 |
| DG 7 (Reproduction after 30 min delay) | 7/15 Items | 15–20 |
| Recognition | 14- 5 false positives = 9 | 15 |
| Rey-Osterrieth complex figure (delayed) | 8.5 items | (normal range: 16.7+/-8.7 (SD)) |
| Digit span forward (WMS) | 7 | 35 |
| Digit span backward (WMS) | 5 | 31 |
| Block span forward (WMS) | 5 | 1 |
| Block span backward (WMS) | 5 | 24 |
| Executive functions (Wilson et al., 1996) | | |
| Behavioural Assessment of Dysexecutive Syndrome (BADS) | Score 15 | “Low average” |
| Verbal fluency (2 min “S”- words) | 11 words | 8 |
| Verbal fluency (2 min semantic “firstnames”) | 19 words | 1 |
| Five-point test (total) | 14 | (normal score: 37.7+/-9.7 (SD)) |
| Errors | 1 | (normal score: 1.9+/-2.8 (SD)) |
| Visuoconstructive abilities | | |
| Rey-Osterrieth complex figure (copy) | 22 items | (normal range: 33.2+/-4.0 (SD)) |
| Block design test | 6 points | 1 |
| Benton test (1990), Form C | 4 correct, 9 false | (severely impaired) |
| Florida Apraxia Screening | impaired bimanual coordination; mild signs of left-sided apraxia | |

SD, standard deviation.

1996, 5 Point Test: Lee, 1994). Also, we investigated apraxia with Florida apraxia screening (Rothi, Raymer, & Heilman, 1997) and the short time visual memory capacity (Benton, 1990). The general psychological impairment was assessed by the Symptom Check List 90R (Franke, 1995). Since the infarct lesion reached cortical areas which are essential for affect differentiation and emotional reflection we applied the Toronto-Alexithymia-Scale (TAS-20, Bagby, Parker, & Taylor, 1994). This questionnaire measures a difficulty of identifying and describing feelings associated with an externally oriented cognitive style (alexithymia). Finally, we applied scales of emotional experience (SEE; Behr and Becker, 2004).

Psychophysiological EEG-diagnostics (vERP)

To examine a possible deficit of emotional perception and processing which may be caused by the infarct lesion of the

right anterior cingulate cortex, the patient was tested in a dedicated test session 2 weeks after the infarction. Specifically human faces which are an important medium for the communication and expression of emotional information were used as stimuli. The patient was required to identify and name the affects in the faces shown to her. These data were noted by one experimenter, however, video recording of her performance was denied by the patient. Simultaneously the EEG was recorded and visual event related potentials (vERP) were determined as detailed elsewhere (Franz, Schäfer, Schneider, Sitte, & Bachor, 2004).

In short, we used an electrode placement according to the 10–20 system (Jasper, 1958). The stimulus material consisted of faces (neutral, sadness, anger, fear; taken from the set of Ekman & Friesen, 1976) and common objects (The International Affective Picture System, IAPS, photographic slides: Gainesville, Florida Center for Research in Psychophysiology, University of Florida; Lang, Öhman, & Vaitl, 1988).

The pictures were presented tachistoscopically in the right (rvhf) and the left visual half field (lvhf) for 225 ms, while the subject was asked to focus the center of the monitor screen (fixation cross). The vertical and horizontal electro-oculogram (EOG) was recorded to control motor artifacts and to control for the central fixation (low pass filter 35 Hz, time constant 5 s, amplification 20 $\mu\text{V}/\text{mm}$). For every stimulus category 30 episodes were averaged. Offline analyses were performed by commercially available software: Brain Vision Analyser[®] by Brain Labs inc.

Results

Neuropsychological testing revealed psychomotor slowing and cognitive deficits concerning divided attention, visual memory span and visuoconstructive abilities (Table 1). In addition, executive functions like verbal fluency and planning abilities were impaired. In the BADS, the patient showed a sum score in the lower range, but in subtests for planning complex actions like zoo map and six elements tests she failed. The main problem here was to follow given rules. Also deficits in visuoconstruction can possibly lead to her planning problems. Additionally bimanual coordination was impaired. Memory functions were in normal or near to normal range, but a proactive interference activity and a high rate of repetitions were observed in verbal memory. Psychopathological testing revealed no clinical psychological impairment (GSI of SCL-90R = 0.26) as depression or anxiety. In contrast, perception and processing of emotional information seemed to be impaired. The TAS-20 sum score was 62, which is below the clinical threshold of >61 (Bagby & Taylor, 1997, p. 62) and below the 66% percentile of the German population for women, which is 52 (Franz et al., in press). Corresponding to this, the SEE-scales indicated a reduced ability of the patient to make a cognitive connection between bodily sensations and emotional states. Furthermore the patient showed a reduced acceptance of affect related to own feelings and a reduced ability of bodily affect symbolization. These data are summarized in Table 2.

During the EEG session the patient was profoundly impaired in identifying and naming the affects shown to her.

Table 2. Patient's emotional experience (SEE)

| | <i>t</i> Value | Percent rank |
|--------------------------------------|----------------|--------------|
| Acceptance of one's own emotion | 26 | 4 |
| Experience of overflow of emotion | 31 | 2 |
| Experience of lack of emotion | 50 | 59 |
| Body oriented symbolizing of emotion | <24 | <1 |
| Imaginative symbolizing of emotion | 39 | 15 |
| Experience of regulation of emotion | 39 | 19 |
| Experience of self control | 72 | 72 |

Comparison to 254 healthy women older than 30 years (Behr & Becker 2004).

In the beginning of the test session she named less than 50% of the affects correctly but failed naming the affects after approximately half of the presentations altogether. The spontaneous EEG in general showed dominant beta activity interspersed with some theta waves which were more prominent over the right hemisphere but without focal accentuation. Remarkably, analysis of the vERPs revealed that there was no face specific N170 component on the parietal electrode positions P7 and P8. These electrode positions usually show the amplitude maximum of the N170 (Franz et al., 2004). Rather, the N170 was detected at an abnormal more dorsal location at the positions P5 and P6.

After stimulus presentation in the lvhf, an impressive deformation of the N170 occurred at the right hemisphere on position P6 for all stimulus categories but most prominent after presentation of emotional faces (Figure 3). A P100 potential was reduced for faces and even more for objects. In addition,

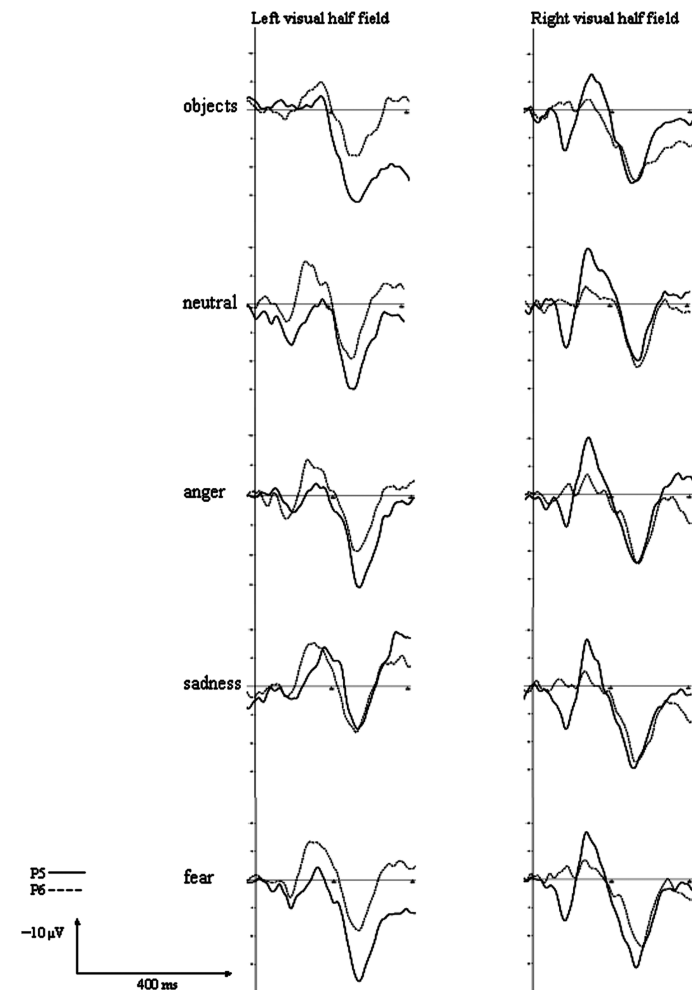


Fig. 3. Visually evoked potentials measured at position P6 (dotted line) and P5 (black line). Stimuli (objects and faces with neutral, anger, sadness and fear affect expression) were presented in the right visual half field (right column) and the left visual half field (left column).

transcallosal signal transduction into the left hemisphere led also to an abnormally broadened N170 potential measured on position P5. Apart from that, the typical differential response of the N170 amplitude to faces and objects was not affected showing a higher N170 potential after presentation of faces compared with objects. The later potential components were also reduced in amplitude over P6 as compared with P5. After stimulus presentation in the rvhf the left hemispheric response measured on position P5 showed nearly normal potential peaks, especially for face presentation.

Discussion

This patient with an infarction of the right anterior cingulate presented with a severe disorder of emotional processing with respect to external information such as facial expressions of emotions as well as to her own bodily sensations and emotional states. Psychopathological testing revealed that these abnormalities were of similar character and severity as in alexithymia (Franz et al., in press). In contrast, the patient did not suffer from depression or anxiety. We supplemented the behavioral observations with an ERP analysis during visual half field presentation of objects, emotional and neutral faces to investigate whether the patient's psychopathological abnormalities were related to changes of the N170 potential in the affected right hemisphere. We observed that visually presented faces but also objects induced an abnormal N170 response. Typically, recognition of a human face in an image induces a higher amplitude of the N170 potential as compared with recognition of an object (Franz et al., 2004). The greater amplitude of the N170 response to faces as compared to objects can also be observed in our data. However, the right hemispheric deformation of the N170 potential after face presentation suggests that the right anterior cingulate lesion disrupted a right hemispheric circuit which may be sensitive for face recognition and, in particular, the evaluation of facial affect expression. These observations accord with recent lesion studies in macaque monkeys which revealed that damage to the anterior cingulate result in abnormal social behavior and impairments of reward guided decision-making (Kennerley, Walten, Behrens, Buckley, & Rushworth, 2006; Rudebeck, Buckley, Walton, & Rushworth, 2006).

There are only few reports on the neurological and behavioral consequences of brain lesions of the frontal midline structures. Patients with lesions affecting the medial part of the left frontal cortex suffer from a lack of physical activity, mental animation, and impaired attention (Kumral et al., 2002). Those abnormalities were also present to some degree in our patient as demonstrated by neuropsychological testing. Further, lesions of the right anterior cingulate were found to induce the so-called alien limb phenomenon (Feinberg et al., 1992). It is characterized by the sensation that the contralateral limb feels strange and not belonging to the patient being frequently accompanied by spontaneous groping movements

of the left arm when occluded from vision. Moreover, as in our patient, lesions of the frontal midline structures including the corpus callosum have been shown to induce disturbances of bimanual coordination involving hand and finger movements (McNabb, Carroll, & Mastaglia, 1988; Stephan et al., 1999; Debaere, Swinnen, B eatse, Sunaert, Van Hecke, & Duysen, 2001; Serrien, Nirkko, & Wiesendanger, 2001; Serrien, Cassidy, & Brown 2003; Seitz et al., 2006). Also, anterior callosotomy has been shown to affect movement initiation in relation to self-referential cues and the bilateral coupling of synchronous movements or force control (Meyers et al., 1995; Eliassen, Baynes, & Gazzaniga, 2000; Franz, Waldie, & Smith, 2000; Kasow, Destian, Braun, Quintas, Kagetsu, & Johnson, 2000; Kennerley, Diedrichsen, Hazeltine, Semjen, & Ivry, 2002; Schmierer, Irlbacher, Grosse, Roricht, & Meyer, 2002; Diedrichsen, Hazeltine, Nurss, & Ivry, 2003). Most importantly, however, there are a few reports in the literature on patients with lesions in anterior cingulate and the adjacent medial frontal cortex showing that such patients exhibit significant changes in their subjective emotional state and their affective control behavior (Eslinger & Damasio, 1985; Eslinger, 1998; Hornak et al., 2003; Shamay-Tsoory et al., 2004). Right medial frontal cortex infarctions induce impaired expression of emotion in prosody and, to a lesser extent, repetition and comprehension of prosody (Heilman, Leon, & Rosenberg, 2004). Thus, these patients are affected in their spontaneity, emotional judgments, perception of their own bodily states, and social behavior. Apparently both cerebral hemispheres have to interact for the subjective control of behavior, since split-brain patients are impaired in the integration of planned action, moods and thoughts (Gazzaniga, Holtzman, & Deck, 1985). These observations in patients with focal brain lesions are supplemented by recent neuroimaging studies showing that the frontal midline structures mediate recognition and valuation of one's own actions and thoughts and inter-person communication (Frith & Frith, 2006; Seitz et al., 2006). In accordance with this neuropsychological deficits in action planning in our patient could be depending in problems of monitoring one's own actions.

The psychopathological assessment of emotional functioning in our patient suggested impaired awareness and processing of emotional information. The enhanced scale values of the SEE indicated a deficit of body related emotional perception. In addition to that, the very high TAS-20 sum score indicated a deficit of identifying and describing feelings associated with an externally oriented cognitive style. The TAS sum score of 62 is beyond the 90th percentile of the general German population (Franz et al., in press).

Studies on evaluation and assessment abilities regarding emotional stimuli have proven performance deficits in alexithymics (Lane, 1996; Roedema & Simons, 1999). In neuroimaging studies a modified activation after emotional stimulation in alexithymics was found in the right anterior gyrus cinguli (Lane, Quinlan, Schwartz, Walker, & Zeitlin, 1990; Berthoz et al., 2002; Huber et al., 2002; Guendel et al., 2002), the left frontal cortex (Huber et al., 2002), the right

medial prefrontal cortex and in the amygdalae (Leweke et al., 2004) or the posterior cingulate cortex (Mantani, Okamoto, Shira, Okada, & Yamawaki, 2005). Further, in studies on verbal performance of recognition of emotional face expressions alexithymics showed increased error rates (Parker, Taylor, & Bagby, 1993; Pandey & Mandal, 1997; Jessimer & Markham, 1997). To detect, interpret and express facial emotional information the human brain engages a widespread specialized circuit involving subcortical pathways and cortical resources (Adolphs, 2002). An important relay node is the right superior temporal sulcus (STS) which seems to be specialized for the processing of changeable characteristics of the human face, like emotional expression or gaze direction (Allison, Puce, & McCarthy, 2000; Haxby, Hoffman, & Gobbini, 2002). Further, the temporobasal cortex is known to process more time stable facial characteristics like familiarity or identity. Using fMRI, Kanwisher and co-workers. (Kanwisher, McDermott, & Chun, 1997; Kanwisher, Stanley, & Harris, 1999), and Wojciulik, Kanwisher, and Driver (1998) identified the “fusiform face area” (FFA) as the critical structure. Other regions involved in the analysis of facially expressed emotional states are the amygdalae (Morris, de Bonis, & Dolan, 2002; Whalen et al., 1998), the orbitofrontal cortex (Nakamura et al., 1999; Hornak et al., 2003) and the anterior cingulate gyrus (Bush, Luu, & Posner, 2000).

This latter region of interest was affected by the right hemispheric infarction of our patient. The lesion site, taken together with the high alexithymia score in the TAS, led us to assume that our patient may also be impaired in face processing since this is a well known performance deficit in alexithymic subjects. In accordance, we found a seriously deformed N170 potential in the right hemisphere (Franz et al., 2004). We would like to suggest that our patient suffered from a functional disruption within the face processing network (Adolphs, 2002) resulting from the structural lesion in the right anterior cingulate. In view of the well-known reciprocal connections between visual areas 18 and 19 and the superior and inferior temporal cortex with the anterior cingulate (Pandya, van Hoesen, & Mesulam, 1981; Ban, 1986; Vogt & Pandya, 1987) and functional connectivity between these areas (Bodke et al., 2006), we speculate that our data accord with the notion of a top-down regulation from the anterior cingulate onto visual information processing in FFA and STS. In fact, early gamma oscillations recently have been shown to be larger for matched memory templates suggesting that memory sends feedback into perception systems (Herrmann, Lenz, Junge, Busch, & Maess, 2004). We speculate that the anterior cingulate lesion in our patient led to a disconnection of external stimuli from the corresponding internal somatic markers, leaving her insensitive to the consequences of her own emotions, to erroneous responses, and thus liable to abnormal social behavior (Swick & Turken, 2002; Gainotti, 2006).

The human face is crucial for inter-person communication. It is probably the most important “interface” to mediate and modulate social interaction between individuals and groups to organize survival and social success. In studies on verbal performance of recognition of emotional face

expressions alexithymics showed increased error rates (Parker et al., 1993; Pandey & Mandal, 1997; Jessimer et al., 1997). This alexithymic impairment in face recognition may contribute to psychological stress and the well-known enhanced risk of psychic and psychosomatic disorders. Due to this association of face recognition and psychological stress also neurological patients suffering from ischemic lesions within the face processing network (in particular anterior cingulum or temporal lobe) should be examined with respect to clinical performance of facial affect recognition. In the case of such a performance impairment one may also want to investigate the amplitude and latency of the N170-component of the visual event related EEG potential. In the case of a recognition impairment of affect and a deformed or delayed N170 one could speculate that neuropsychological training of emotional face recognition may be an effective therapeutic strategy which could be monitored by N170 recordings.

A limitation of this study is obviously that this deficit of affective processing was observed in only one patient. Since, however, infarcts in the anterior cerebral artery are so rare (Kumral et al., 2002), we thought it be justified to report this case. Further, we only had a clinical follow-up of 1 month, so we do not know whether the deficit resolved over a longer time period as clinically apparent for a number of post-stroke deficits. Finally, a more well educated patient might have reported spontaneously and more readily about subtle neuropsychological or psychopathological deficits which became apparent in our case by dedicated testing only.

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References

- Adolphs, R. (2002). Recognizing emotion from facial expressions: Psychological and neurological mechanisms. *Behavioral Neuroscience Review*, *1*, 21–62.
- Allison, T., Puce, A., & McCarthy, G. (2000). Social perception from visual cues: role of the STS region. *Trends in Cognitive Science*, *4*, 267–78.
- Aschenbrenner, S., Tucha, O., & Lange, K. W. (2000). *Regensburger Wortflüssigkeitstest (RWT)*. Göttingen: Hogrefe.
- Bagby, R. M., & Taylor, G. J. (1997). Measurement and validation of the alexithymia construct. In G. J. Taylor, R. M. Bagby, & J. D. A. Parker (Eds), *Disorders of affect regulation: Alexithymia in medical and psychiatric illness* (pp 46–66). Cambridge: Cambridge University Press.
- Bagby, R. M., Parker, J. D. A., & Taylor, G. J. (1994). The Twenty-Item Toronto Alexithymia Scale, I. Item selection and cross-validation of the factor structure. *Journal of Psychosomatic Research* *38*, 23–32.
- Ban, T. (1986). Cortical neurons projecting to the posterior part of the superior temporal sulcus with particular reference to the posterior association area. An HRP study in the monkey. *Archives of Italian Biology*, *124*, 95–109.
- Behr, M., & Becker, M. (2004). *SEE. Skalen zum Erleben von Emotionen. Manual*. Göttingen: Hogrefe.

- Benton, A. L. (1990). *Der Benton-Test. Handbuch. 6., unveränderte Auflage*. Bern: Verlag Hans Huber.
- Berthoz, S., Artiges, E., Van De Moortele, P. F., Poline, J. B., Rouquette, S., Consoli, S. M., & Martinot, J. L. (2002). Effect of impaired recognition and expression of emotions on frontocingulate cortices: An fMRI study of men with alexithymia. *American Journal of Psychiatry*, *159*, 961–67.
- Binkofski, F., Seitz, R. J., Arnold, S., Claßen, J., Benecke, R., & Freund, H.-J. (1996). Thalamic metabolism and integrity of the pyramidal tract determine motor recovery in stroke. *Annals of Neurology*, *39*, 460–70.
- Bokde, A. L., Lopez-Bayo, P., Meindl, T., Pecher, S., Born, C., Faltraco, F., Teipel, S. J., Moller, H. J., & Hampel, H. (2006). Functional connectivity of the fusiform gyrus during a face-matching task in subjects with mild cognitive impairment. *Brain*, *129*, 1113–24.
- Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Science*, *4*, 215–22.
- Carter, C. S., Botvinick, M. M., & Cohen, J. D. (1999). The contribution of the anterior cingulate cortex to executive processes in cognition. *Reviews in the Neurosciences*, *10*, 49–57.
- Damasio, H., Grabowski, T., Frank, R., Galaburda, A. M., & Damasio, A. R. (1994). The return of Phineas Gage: Clues about the brain from the skull of a famous patient. *Science*, *264*, 1102–105.
- Debaere, F., Swinnen, S. P., Béatse, E., Sunaert, S., Van Hecke, P., & Duysen, J. (2001). Brain areas involved in interlimb coordination: a distributed network. *NeuroImage*, *14*, 947–58.
- Diedrichsen, J., Hazeltine, E., Nurss, W. K., & Ivry, R. B. (2003). The role of the corpus callosum in the coupling of bimanual isometric force pulses. *Journal of Neurophysiology*, *90*, 2409–18.
- Duncan, J., & Owen, A. M. (2000). Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends in Neuroscience*, *23*, 475–83.
- Ekman, P., & Friesen, W. V. (1976). *Facial action coding system: A technique for the measurement of facial movement*. Palo Alto, CA: Consulting Psychologists Press.
- Eliassen, J. C., Baynes, K., & Gazzaniga, M. S. (2000). Anterior and posterior callosal contributions to simultaneous bimanual movements of the hands and fingers. *Brain*, *123*, 2501–11.
- Eslinger, P. J. (1998). Neurological and neuropsychological bases of empathy. *European Neurology*, *39*, 193–99.
- Eslinger, P. J., & Damasio, A. R. (1985). Severe disturbance of higher cognition after bilateral frontal lobe ablation: Patient EVR. *Neurology*, *35*, 1731–741.
- Feinberg, T. E., Schindler, R. J., Flanagan, N. G., & Haber, L. D. (1992). Two alien hand syndromes. *Neurology*, *42*, 19–24.
- Franke, G. H. (1995). *SCL-90-R. Die Symptom-Checkliste von Derogatis – German Version*. Göttingen: Beltz.
- Franz, E. A., Waldie, K. E., & Smith, M. J. (2000). The effect of callosotomy on novel versus familiar bimanual actions: A neural dissociation between controlled and automatic processes? *Psychology Science*, *11*, 82–5.
- Franz, M., Schäfer, R., Schneider, C., Sitte, W., & Bachor, J. (2004). Visual event-related potentials in subjects with alexithymia: Modified processing of emotional aversive information? *American Journal of Psychiatry*, *161*, 728–35.
- Franz, M., Popp, K., Schäfer, R., Sitte, W., Schneider, C., Hardt, J., Schmutzer, G., & Brähler, E. (in press). Alexithymia in the German general population. *Social Psychiatry and Psychiatric Epidemiology*.
- Frith, C. D., & Frith, U. (2006). The neural basis of mentalizing. *Neuron*, *50*, 531–34.
- Fuster, J. M. (2000). Executive frontal functions. *Experimental Brain Research*, *133*, 66–70.
- Gainotti G. (2006). Brain lesions and emotional disorders. *Future Neurology*, *1*, 323–34.
- Gazzaniga, M. S., Holtzman, J. D., Deck, M. D., & Lee, B. C. (1985). MRI assessment of human callosal surgery with neuropsychological correlates. *Neurology*, *35*, 1763–766.
- Guendel, H., Lopez, A., Deus, J., Cardoner, N., Mittag, B., von Rad, M., & Pujol, J. (2002). Anatomical variability of the anterior cingulate cortex in relationship to alexithymia. *Psychosomatic Medicine*, *64*, 110.
- Härting, C., Markowitsch, H. J., Neufeld, H., Calabrese, P., Deisinger, K., & Kessler, J. (Hrsg.) (2000). *WMS-R (Wechsler Gedächtnistest- revidierte Fassung- deutsche Adaptation)*. Bern: Verlag Hans Huber.
- Haxby, J. V., Hoffman, E. A., & Gobbini, M. I. (2002). Human neural systems for face recognition and social communication. *Biology Psychiatry*, *51*, 59–67.
- Heilman, K. M., Leon, S. A., & Rosenberg, J. C. (2004). Affective aprosodia from a medial frontal stroke. *Brain and Language*, *89*, 411–16.
- Helmstädter, C., Lendt, M., & Lux, S. (2001). *VLMT: Verbaler Lern- und Merkfähigkeitstest*. Göttingen: Beltz.
- Herrmann, C. S., Lenz, D., Junge, S., Busch, N. A., & Maess, B. (2004). Memory-matches evoke human gamma-responses. *BMC Neuroscience*, *5*, 1–8.
- Hines, M., Chiu, L., McAdams, L. A., Bentler, P. M., & Lipcamon, J. (1992). Cognition and the corpus callosum: Verbal fluency, visuospatial ability, and language lateralization related to midsagittal surface areas of callosal subregions. *Behavioural Neuroscience*, *106*, 3–14.
- Hornak, J., Bramham, J., Rolls, E. T., Morris, R. G., O'Doherty, J., Bullock, P. R., & Polkey, C. E. (2003). Changes in emotion after circumscribed surgical lesions of the orbitofrontal and cingulate cortices. *Brain*, *126*, 1691–712.
- Huber, M., Herholz, K., Habedank, B., Thiel, A., Muller-Kuppers, M., Ebel, H., Subic-Wrana, C., Kohle, K., & Heiss, W. D. (2002). Different patterns of regional brain activation during emotional stimulation in alexithymics in comparison with normal controls. *Psychotherapy and Psychosomatic Medicine in Psychology*, *52*, 469–78.
- Imagawa, M., & Yamadori, T. (1996). Phylogenetic development of brain and brain sulci in primates. *Kobe Journal of Medical Science*, *42*, 61–72.
- Jasper, H. H. (1958). The ten-twenty electrode system of the international federation. *Electroencephalography in Clinical Neurophysiology*, *10*, 371–75.
- Jessimer, M., & Markham, R. (1997). Alexithymia: a right hemisphere dysfunction specific to recognition of certain facial expressions? *Brain and Cognition*, *34*, 246–58.
- Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: a module in human extrastriate cortex specialized for face perception. *Journal of Neuroscience*, *17*, 4302–311.
- Kanwisher, N., Stanley, D., & Harris, A. (1999). The fusiform face area is selective for faces not animals. *Neuroreport*, *10*, 183–87.
- Kasow, D. L., Destian, S., Braun, C., Quintas, J. C., Kagetsu, N. J., & Johnson, C. E. (2000). Corpus callosum infarcts with atypical clinical and radiologic presentations. *American Journal of Neuroradiology*, *21*, 1876–880.
- Kennerley, S. W., Diedrichsen, S., Hazeltine, E., Semjen, A., & Ivry, R. B. (2002). Callosotomy patients exhibit temporal uncoupling during continuous bimanual movements. *Nature Neuroscience*, *4*, 376–81.
- Kennerley, S. W., Walten, M. E., Behrens, T., Buckley, M. J., & Rushworth, M. F. S. (2006). Optimal decision making and the anterior cingulate cortex. *Natural Neuroscience*, *9*, 940–47.
- Kumral, E., Bayukem, G., Evyapan, D., & Yuntun, N. (2002). Spectrum of anterior cerebral artery territory infarction: Clinical and MRI findings. *European Journal of Neurology*, *9*, 615–24.
- Lane, R. D. (1996). Impaired verbal and nonverbal emotion recognition in alexithymia. *Psychosomatic Medicine*, *58*, 581–81.
- Lane, R. D., Quinlan, D. M., Schwartz, G. E., Walker, P. A., & Zeitlin, S. B. (1990). The Levels of Emotional Awareness Scale: a cognitive-developmental measure of emotion. *Journal of Personal Assessment*, *55*, 124–34.
- Lang, P. J., Öhman, A., & Vaitl, D. (1988). *The international affective picture system [photographic slides]*. Gainesville, FL Center for Research in Psychophysiology, University of Florida.
- Leweke, F., Stark, R., Milch, W., Kurth, R., Schienle, A., Kirsch, P., Stingl, M., Reimer, C., & Vaitl, D. (2004). Neuronale Aktivitätsmuster auf

- affektinduktive Reize bei Alexithymie. *Psychotherapy and Psychology in Medicine*, 54, 437–44.
- Mantani, T., Okamoto, Y., Shirao, N., Okada, G., & Yamawaki, S. (2005). Reduced activation of posterior cingulate cortex during imagery in subjects with high degrees of alexithymia: a functional magnetic resonance imaging study. *Biological Psychiatry*, 57, 982–90.
- McNabb, A. W., Carroll, W. M., & Mastaglia, F. L. (1988). “Alien hand” and loss of bimanual coordination after dominant anterior cerebral artery territory infarction. *Journal of Neurology Neurosurgery Psychiatry*, 51, 218–222.
- Meyers, J., & Meyers, K. (1995). *The Meyers scoring system for the Rey complex figure and recognition trial: Professional Manual*. Odessa, FL: Psychological Assessment Resources.
- Morris, J. S., de Bonis, M., & Dolan, R. J. (2002). Human amygdala responses to fearful eyes. *Neuroimage*, 17, 214–22.
- Nakamura, K., Kawashima, R., Ito, K., Sugiura, M., Kato, T., Nakamura, A., Datano, K., Nagumo, S., Kubota, K., Fukuda, H., & Kojima, S. (1999). Activation of the right inferior frontal cortex during assessment of facial emotion. *Journal of Neurophysiology*, 82, 1610–614.
- Northoff, G., & Heinzel, A. (2006). First-person neuroscience: A new methodological approach for linking mental and neuronal states. *Philosophy and Ethics in Humanitarian Medicine*, 1, 1–10.
- Oldfields, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, 9, 97–113.
- Pandey, R., & Mandal, M. K. (1997). Processing of facial expressions of emotion and alexithymia. *British Journal of Clinical Psychology*, 36, 631–33.
- Pandya, D. N., van Hoesen, G. W., & Mesulam, M. M. (1981). Efferent connections of the cingulate gyrus in the rhesus monkey. *Experimental Brain Research*, 42, 319–30.
- Parker, J. D., Taylor, G. J., & Bagby, R. M. (1993). Alexithymia and the recognition of facial expressions of emotion. *Psychotherapy and Psychosomatics*, 59, 197–202.
- Petrides, M., & Pandya, D. N. (1999). Dorsolateral prefrontal cortex: Comparative cytoarchitectonic analysis in the human and the macaque brain and corticocortical connection patterns. *European Journal of Neuroscience*, 11, 1011–36.
- Paus, T. (2001). Primate anterior cingulate cortex: Where motor control, drive and cognition interface. *Nature Review*, 2, 417–24.
- Rudebeck, P. H., Buckley, M. J., Walton, M. E., & Rushworth, M. F. S. (2006). A role for the macaque anterior cingulate gyrus in social valuation. *Science*, 313, 1310–312.
- Roedema, T. M., & Simons, R. F. (1999). Emotion-processing deficit in alexithymia. *Psychophysiology*, 36, 379–87.
- Rothi, L. J. G., Raymer, A. M., & Heilman, K. M. (1997). Limb praxis assessment. In L. J. G. Rothi & K. M. Heilman (Eds), *Apraxia: The neuropsychology of action*. (pp. 61–73). Hove, UK: Psychology Press.
- Saver, J. L., & Damasio, A. R. (1991). Preserved access and processing of social knowledge in a patient with acquired sociopathy due to ventromedial frontal damage. *Neuropsychologia*, 29, 1241–249.
- Schmierer, K., Irlbacher, K., Grosse, P., Roricht, S., & Meyer, B. U. (2002). Correlates of disability in multiple sclerosis detected by transcranial magnetic stimulation. *Neurology*, 59, 1218–224.
- Seitz, R. J., Nickel, J., & Azari, N. P. (2006). Functional modularity of the medial prefrontal cortex: Involvement in human empathy. *Neuropsychology*, 20, 743–51.
- Semendeferi, K., Amstrong, E., Schleicher, A., Zilles, K., & van Hoesen, G. W. (2001). Prefrontal cortex in humans and apes: A comparative study of area 10. *American Journal of Physical Anthropology*, 114, 224–41.
- Serrien, D. J., Nirkko, A. C., & Wiesendanger, M. (2001). Role of the corpus callosum in bimanual coordination: A comparison of patients with congenital and acquired callosal damage. *European Journal of Neuroscience*, 14, 1897–905.
- Serrien, D. J., Cassidy, M. J., & Brown, P. (2003). The importance of the dominant hemisphere in the organization of bimanual movements. *Human Brain Mapping*, 18, 296–305.
- Shamay-Tsoory, S. G., Tomer, R., Goldsher, D., Berger, B. D., & Aharon-Peretz, J. (2004). Impairment in cognitive and affective empathy in patients with brain lesions: Anatomical and cognitive correlates. *Journal of Clinical and Experimental Neuropsychology*, 26, 1113–127.
- Stephan, K. M., Binkofski, F., Halsband, U., Dohle, C., Wunderlich, G., Schnitzler, A., Tass, P., Posse, S., Herzog, H., Sturm, V., Zilles, K., Seitz, R. J., & Freund, H.-J. (1999). The role of ventral medial wall motor areas for bimanual coordination: A combined lesion and activation study. *Brain*, 122, 351–68.
- Swick, D., & Turken, A. U. (2002). Dissociation between conflict detection and error monitoring in the human anterior cingulate cortex. *Proceedings of The National Academy of Sciences of the United States of America*, 99, 16354–6359.
- Swinnen, S. P., Walter, C. B., Lee, T. D., & Serrien, D. J. (1993). Acquiring bimanual skills: Contrasting forms of information feedback for interlimb decoupling. *Journal of Experimental Psychology and Learning Memory and Cognition*, 19, 1328–344.
- Talairach, J., & Tournoux, P. (1988). *A stereotactic atlas of the human brain*. New York: Springer.
- Vogt, B. A., & Pandya, D. N. (1987). Cingulate cortex of the rhesus monkey: II. Cortical afferents. *Journal of Comparative Neurology*, 262, 271–89.
- Whalen, P. J., Rauch, S. L., Etcoff, N. L., McInerney, S. C., Lee, M. B., & Jenike, M. A. (1998). Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. *Journal of Neuroscience*, 18, 411–18.
- Wilson, B. A., Aldermann, N., Burgess, P. W., Emslie, H., & Evans, J. J. (1996). *Behavioural Assessment of the Dysexecutive Syndrome (BADS)*. Bury St. Edmunds: Thames Valley Test Company.
- Wojciulik, E., Kanwisher, N., & Driver, J. (1998). Covert visual attention modulates face-specific activity in the human fusiform gyrus: fMRI study. *Journal of Neurophysiology*, 79, 1574–578.
- Zimmermann, P., & Fimm, B. (1993). *Testbatterie zur Aufmerksamkeitsprüfung (TAP)*, Version 1.02c, Psytest.