doi:10.1093/scan/nss048

Altered resting state connectivity of the default mode network in alexithymia

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Alexithymia is a trait characterized by a diminished capacity to describe and distinguish emotions and to fantasize; it is associated with reduced introspection and problems in emotion processing. The default mode network (DMN) is a network of brain areas that is normally active during rest and involved in emotion processing and self-referential mental activity, including introspection. We hypothesized that connectivity of the DMN might be altered in alexithymia. Twenty alexithymic and 18 non-alexithymic healthy volunteers underwent a resting state fMRI scan. Independent component analysis was used to identify the DMN. Differences in connectivity strength were compared between groups. Within the DMN, alexithymic participants showed lower connectivity within areas of the DMN (medial frontal and temporal areas) as compared to non-alexithymic participants. In contrast, connectivity in the high-alexithymic participants was higher for the sensorimotor cortex, occipital areas and right lateral frontal cortex than in the low-alexithymic participants. These results suggest a diminished connectivity within the DMN of alexithymic participants, in brain areas that may also be involved in emotional awareness and self-referential processing. On the other hand, alexithymia was associated with stronger functional connections of the DMN with brain areas involved in sensory input and control of emotion.

Keywords: alexithymia; connectivity; default mode network; fMRI; resting state

INTRODUCTION

Alexithymia has been conceptualized as a personality trait that is associated with difficulties in emotion processing (Taylor *et al.*, 1997). More specifically, alexithymia is characterized by difficulties in verbalizing one's emotions, diminished affect-related fantasy and imagery, difficulty to distinguish emotions from bodily sensations and a tendency to focus on external events rather than internal experiences (Sifneos, 1973; Taylor *et al.*, 1991). The prevalence was ~10% in a Finnish sample (Salminen *et al.*, 2007). Alexithymia has been associated with increased risk for psychosomatic complaints, anxiety disorders and depression (Taylor *et al.*, 1997) and the emotion regulation difficulties characteristic of alexithymia have been hypothesized to play a mediating role in these (Taylor, 2000; Waller and Scheidt, 2006). Unraveling the neurocognitive mechanisms underlying alexithymia may improve our understanding of this trait with possible clinical and societal implications.

In this study, we started from the observation that alexithymia is associated with difficulties in emotion processing, e.g. recognizing emotional facial expressions and deducing emotions of others from narratives (Swart *et al.*, 2009; Meltzer and Nielson, 2010), which may reflect a more general reduction of emotional awareness (Lane *et al.* 1997).The ability to recognize and experience emotions allows an individual to form a representation of his own emotions (Damasio *et al.*, 2003; Northoff *et al.*, 2006). Such self-referential emotional processing and imagery have been suggested to take place in a network of brain areas called the 'Cortical Midline Structures' (CMS) (Northoff *et al.*, 2006), which is a key part of the default mode network (DMN) (Gusnard and Raichle, 2001). Indeed, parts of the DMN have been associated with emotion processing in general (Kober *et al.*, 2008). The main regions within the DMN are the precuneus, posterior cingulate cortex (PCC), anterior cingulate cortex (ACC), inferior parietal lobule (IPL) and medial prefrontal cortex (MPFC) (Gusnard and Raichle, 2001). In a broader definition of the network, middle temporal gyrus (MTG), middle, superior and inferior frontal gyrus (MiFG, SFG and IFG), hippocampal formation and cerebellar regions are also included (He *et al.*, 2004; Buckner *et al.*, 2008). The DMN is also highly active during rest when self-referential processing apparently takes place (Gusnard and Raichle, 2001) and shows synchronized slow fluctuations across its brain areas (Gusnard and Raichle, 2001; Fransson, 2006). Schilbach *et al.* (2008) proposed in their review that brain activation of DMN regions during the resting state is related to self-consciousness and self-processing and may thus be relevant for introspection. Indeed, D'Argembeau *et al.* (2005) showed that activation in the anterior part of the DMN is correlated to self-referential thoughts.

Several studies have shown a relation between emotional awareness, which may be impaired in alexithymia, and DMN brain areas (Gusnard and Raichle, 2001; Northoff *et al.*, 2006). Lower activation of the ACC and its connectivity to other brain areas have been related to lower emotional awareness and alexithymia (Lane *et al.*, 1997, 1998). In alexithymic participants, the ACC and functionally related areas were less activated whereas the somatosensory cortex was more activated by emotionally valenced videos, emotional pictures, or imagery (Berthoz *et al.*, 2002; Kano *et al.*, 2003; Mantani *et al.*, 2005; Moriguchi *et al.*, 2006; Karlsson *et al.*, 2008). Likewise, a structural MRI study found lower ACC and precuneus volumes in alexithymic participants (Borsci *et al.*, 2008). Therefore, we hypothesized that alexithymic participants would show lower brain connectivity in areas implicated in emotional processing such as the ACC and higher somatosensory connectivity during rest, which may be related to less emotional awareness and a more action-oriented emotional coping style.

Since the DMN is highly active during rest and related to self-awareness, resting state analysis might, provide relevant information

Received 11 March 2011; Accepted 18 April 2012
Advance Access publication 3 May 2012
This work was supported by a EURopean Young Investigator award (N.W.O. number 044035001) awarded to A.A.

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about the neural background of alexithymia. Resting state functional connectivity is considered as a more natural measure of brain function than task-based fMRI (Raichle and Gusnard, 2005), because it reflects intrinsic brain interactions (Van de Ven *et al.*, 2004). These interactions may provide knowledge about overall brain function (Fox and Lancaster, 1994) and predict task performance or behavior (Fox and Raichle, 2007), without being biased by differences in task performance during the scanning (Calhoun *et al.*, 2001; Van de Ven *et al.*, 2004). If people with alexithymia in general devote less time to thinking about their feelings, this may have consequences for connectivity of relevant resting state areas, resulting in lower DMN connectivity.

Finally, alexithymia has been conceptualized as a disorder of emotion regulation, which warrants special interest for prefrontal areas known to be involved in emotion regulation (Taylor *et al.*, 1997; Ochsner *et al.*, 2002). Participants with alexithymia tend more to suppression of emotions than to use emotion reappraisal strategies (Swart *et al.*, 2009). In reappraisal, participants use cognitive–linguistic strategies to downregulate emotional responses to arousing stimuli (Goldin *et al.*, 2008; Reker *et al.*, 2009; Silani *et al.*, 2009). Effective control of emotions by reappraisal strategies has been related to activation of the medial and lateral prefrontal areas (Ochsner *et al.*, 2002; Phan *et al.*, 2005; Kim *et al.*, 2007; Wager *et al.*, 2008), which prevent excessive experience of negative emotions (Urry *et al.*, 2009; Abler *et al.*, 2010). Emotion regulation strategies such as suppression may involve right sided lateral frontal areas, but for a longer time period because suppression works on later stages of emotion processing than reappraisal (Ochsner *et al.*, 2002; Goldin *et al.*, 2008; Abler *et al.*, 2010). We hypothesize that participants with alexithymia may show higher connectivity in the right lateral frontal and lower connectivity in the ventromedial prefrontal cortex, related to hampered emotion regulation.

In this study, the resting state DMN connectivity of high- *vs* low-alexithymic participants was investigated. Since no such study has been conducted before, this study has an exploratory nature. We hypothesized that alexithymic participants would show diminished connectivity in areas implicated in awareness (DMN areas) and verbalizing of emotions (left frontal areas). In addition, we explored whether there might be higher connectivity in alexithymic participants of areas implicated in emotion control (lateral prefrontal areas) and action-oriented processing (sensory and motor areas).

METHODS

Participants

The study was approved by the local medical ethical committee and carried out in accordance with the latest version of the Declaration of Helsinki. A total of 493 right-handed students of different disciplines from the local university filled out the verbalizing subscale of the Bermond–Vorst Alexithymia Questionnaire (BVAQ). This subscale was chosen because reduced ability to verbalize emotions has been considered a central deficit of alexithymia (Aleman, 2005). Further details of the questionnaire are given in the next section. Subjects scoring at the upper and lower extremes (25%) of the verbalizing subscale of the BVAQ, i.e. showing high or low levels of alexithymia based on this measure, participated in the study.

All participants were normally functioning and showed no signs of psychiatric illness. Persons with a history of psychiatric or neurologic disorder for which they had received treatment were excluded from the study. Further exclusion criteria consisted of MRI incompatible implants, aged >50 years, pregnancy, claustrophobia, left-handedness and being a non-native Dutch speaker.

A total of 20 participants with high- and 18 participants with low-verbalizing score that fulfilled the inclusion criteria participated. All participants gave oral and written informed consent prior to testing after the procedure had been fully explained. An overview of the participant characteristics is given in Table 1. Groups did not differ in age (*t*-test; $T = -0.28$; $P < 0.78$). Since female participants may have stronger verbalizing skills, dissimilarity in general language skills due to different male/female ratios between groups might confound interpretation of findings and therefore our groups were matched on gender distribution (Chi-square test; $\chi^2 = 1.03$; $P < 0.16$).

On the day of the MRI-session participants filled out the complete BVAQ and the Positive And Negative Affect Schedule (PANAS; Watson *et al.*, 1988).

Questionnaires

For assessment of alexithymia, we used the BVAQ. Several studies have supported the criterion validity of the BVAQ in clinical samples, e.g. for eating disorders (Deborde *et al.* 2008), alcoholism (Sauvage and Loas, 2006), autism spectrum disorders (Berthoz and Hill, 2005), schizophrenia (Van 't Wout *et al.* 2007) and high risk for schizophrenia (Van Rijn *et al.* 2011). However, because the BVAQ includes self-assessment, which may be compromised in certain clinical samples, its validity may be attenuated in clinical groups characterized by reduced insight in their psychological functioning. This is not a problem in the present study, because we investigated nonclinical participants.

The BVAQ is a validated 40-item self-report scale that consists of five subscales: verbalizing, fantasizing, identifying (cognitive component), emotionalizing and analyzing (emotional component) (Bermond and Vorst, 1993). Higher scores indicate a stronger degree of alexithymic characteristics. The scale measures alexithymic features as defined by Sifneos (1973). Previous studies have shown that the BVAQ has good psychometric properties (Berthoz *et al.*, 2000, 2007; Zech *et al.*, 1999).

The PANAS measures current affective positive and negative state (Watson *et al.*, 1988). Positive affect refers to the extent to which a person feels enthusiastic, active and alert, negative affect addresses distress. The scale consists of ten positive and ten negative items, which can be scored on a 5-point scale ($1 =$ certainly does not apply to me, up to $5 =$ certainly applies to me). The PANAS has shown good reliability and validity to measure positive (Cronbach's $\alpha = 0.89$) and negative ($\alpha = 0.85$) current mood states (Watson *et al.*, 1988).

Groups were tested on differences in the cognitive and emotional component of the BVAQ and the positive and negative subscale of the PANAS with a two sample *t*-test ($\alpha < 0.05$).

Behavioral data

Participants also performed a language processing task in the same fMRI session. We report the performance on this task to provide an indication of language processing differences between groups. The task (adapted from Aleman *et al.*, 2005) required participants to evaluate bisyllabic Dutch words for metrical stress followed by indicating the syllable that carried the metrical stress. In a second condition, participants rated the valence of a word (positive or negative).

Data acquisition

A resting state scan of 460 s was acquired at the end of an MRI session that additionally consisted of three tasks and an anatomical scan. During the resting state scan, participants were asked to close their eyes, relax and try to not fall asleep. There were no constraints on the content of their thoughts.

A 3 T Philips Intera MRI scanner (Best, The Netherlands) equipped with a eight-channel SENSE head coil was used to acquire 200 whole-brain echo-planar functional images (EPIs) with a TR of 2.3 s and TE

Table 1 Demographical data

Demographic characteristic	Low alexithymia, mean (s.d.)	High alexithymia, mean (s.d.)	*P*-value
Age (years)	22.3 (8.1)	21.6 (6.7)	0.77
Males/females	11/9	6/12	0.16
Cognitive component	42.9 (8.1)	63.2 (9.7)	< 0.0005
Emotional component	36.1 (8.1)	40.0 (9.7)	0.19
PANAS positive affect	33.8 (5.5)	30.5 (6.3)	0.059
PANAS negative affect	15.1 (3.5)	14.7 (4.1)	0.77

Mean and standard deviation of the demographic data of both subject groups, and the *P*-values of the *t*-test. The mean score on the BVAQ components and the two PANAS subscales are also shown. Subjects did differ significantly on the cognitive component of the BVAQ, but not on other subscales or demographic characteristics.

28 ms. The volumes contained 39 ($n = 3$ participants), 41 ($n = 29$) or 43 slices ($n = 4$); $3.8 \times 3.8 \times 3$ mm), interleaved, with a 0-mm slice gap and a 85° flip-angle (FOV = $220 \times 117 \times 220$ mm). The reason for a different number of slices is unspecified, but this is not expected to influence study outcome. A high-resolution, transverse T1 anatomical was also acquired for overlay of statistic images (160 slices; voxel size $1 \times 1 \times 1$ mm; FOV $256 \times 220 \times 256$ mm).

Preprocessing

The raw images were converted to ANALYZE format and analyzed using Statistical Parametric Mapping (SPM5; Wellcome Department of Imaging Neuroscience, London, UK) running on Matlab 7.1. Images were first corrected for slice-time differences and realigned to the first functional image. The mean image created during realignment was co-registered to the anatomy, together with the functional images, and the anatomy and functional images were normalized to the T1 template of SPM (voxel size $3 \times 3 \times 3$ mm). Finally, images were smoothed with a 10-mm FWHM isotropic Gaussian kernel.

ICA procedure

Independent component analysis (ICA) is a data-driven method that can separate the fMRI signal into spatially independent networks (independent component; IC) that show shared temporal fluctuations (Calhoun *et al.*, 2001; Jafri *et al.*, 2008). An independent component consists of a time series and a spatial map per participant, which shows the contribution of every voxel in the brain to that time series, i.e. to that network (component). Those networks show a close correspondence to networks identified by activation studies (Smith *et al.*, 2009). The size and strength of the identified networks may differ between individuals and groups sharing a specific trait (Calhoun *et al.*, 2001; Van der Ven *et al.*, 2005), i.e. a smaller network could represent altered connectivity of (the brain areas within) the network.

Images of all participants were decomposed into a set of independent components by the Group ICA FMRI Toolbox (GIFT) using the Infomax algorithm (Calhoun *et al.*, 2001). We estimated the number of components by using the maximum likelihood and Akaike's criteria (Li *et al.*, 2006), to prevent splitting or merging of components (Smith *et al.*, 2009). The Infomax algorithm is a commonly used method to unmix the signal (Calhoun *et al.*, 2001). To perform group ICA, dimensionality of the data was first reduced using Principle Component analysis, and afterward the reduced subject data were concatenated over the time domain. Afterward, individual image maps were reconstructed from the aggregated data based on matrices stored during PCA. Resulting image maps and time courses were converted into *Z*-scores to normalize the signal. Though the overall architecture of the networks generated by spatial ICA is similar due to the separation based on spatial location, subtle differences between individuals may be present. These can be investigated in a voxel-wise group comparison (Calhoun *et al.*, 2001). Independent components were first sorted based on the white matter and gray matter masks of SPM for exclusion of components with artifacts. Artifacts will generally represented be by separate components, which give the additional advantage of noise reduction in the data (Calhoun *et al.*, 2001; Van der Ven *et al.*, 2004). Selection of the component(s) of the DMN was based on spatial overlap with an anatomical mask of the DMN created with the WFU pickatlas (http://www.nitrc.org/projects/wfu_pickatlas/; Maldjian *et al.*, 2003). The mask consisted of the PCC, precuneus, IPL, ACC, MPFC and MTG. See Supplementary Material for a figure of the mask. Components with a substantial overlap were visually inspected for DMN brain areas also described in the introduction. Stability of the components of interest, i.e. whether components had the tendency to split or merge with another component, was confirmed by running the ICASSO toolbox (Himberg and Hyvärinen 2003; Himberg *et al.*, 2004), which ran 20 iterations of the ICA. If the same component was identified during all iterations, this indicates the stable presence of that component in the data.

Group differences on questionnaires

Statistical analyses on questionnaires were performed using Statistical Package for Social Sciences (SPSS 16) and all tests were two tailed. The cognitive component: the sum of the verbalizing, identifying and analyzing subscale and emotional component: the sum of the emotionalizing and fantasizing subscales, of the BVAQ were calculated. A two-sample *t*-test was applied to test for significant differences between groups.

The positive and negative affect subscales of the PANAS were also calculated and compared between groups.

Group differences on behavioral data

Reaction time and accuracy on the language task were compared between groups. A two-way ANOVA was conducted separately on reaction times and accuracy, and separately for both task conditions. The analyses had reaction time or accuracy on the metrical stress or valence condition as independent variable, and group and gender as independent variables ($\alpha < 0.05$).

Statistical analysis of functional imaging data

The individual image maps of the identified components (networks) were entered into separate second level analyses of SPM5 per component, with a two sample *t*-test. First, a contrast was made of the main effect of interest, independent of group (FWE; $P < 0.05$; $k > 15$). Second, contrasts between both groups were made with a threshold of $P < 0.001$ uncorrected and a cluster-size threshold of 15 voxels. A mask of the contrast of the main effect of interest was used to restrict the analysis to DMN areas and to prevent false positive findings outside this area (inclusive mask; $P < 0.05$), as previously described (Garrity *et al.*, 2007).

In an additional analysis, PANAS and gender were entered as a covariate into the group analysis. The affect states were investigated to check for an effect of mood state on the group differences. Gender was controlled for because this might also have an effect on default mode connectivity (Bluhm *et al.*, 2008).

RESULTS

Questionnaire results

The scores on the two components of the BVAQ subscales and the positive and negative affect subscales of the PANAS are shown in Table 1. A two-sample *t*-test showed that groups differed significantly on the cognitive component [t (36) = 4.7, $P < 0.0005$], but not on the emotional component [t (36) = 1.3, $P = 0.19$]. Furthermore, there was a strong association between the cognitive component and the verbalizing scale used for selection ($r = 0.76$, $P < 0.0005$). Groups did not differ significantly on positive [t (36) = 1.9, $P = 0.059$] nor on negative affect [t (36) = 0.3, $P = 0.78$] as measured with the PANAS, although high-alexithymic participants had a higher negative and lower positive affect than the low-alexithymic participants.

Behavioral results

Reaction times and accuracy of the language task are presented in Table 2, separated for males and females. For the metrical stress condition, there was no significant effect of group [$F(1,34) = 0.11$, $P = 0.75$] or gender [$F(1,34) = 0.053$, $P = 0.82$] on reaction times, and also no interaction [$F(1,34) = 0.18$, $P = 0.68$]. There was also no significant effect on accuracy of group [$F(1,34) = 0.013$, $P = 0.91$], gender [$F(1,34) = 0.076$, $P = 0.79$] or interaction [$F(1,34) = 0.28$, $P = 0.60$].

For the valence evaluation condition, there was no significant effect or interaction of neither group nor gender on either reaction times or accuracy. The main effect of group on reaction times was $F(1, 34) = 0.56$, $P = 0.46$, the effect of gender was $F(1,34) = 0.003$, $P = 0.95$, and their interaction was $F(1,34) = 0.057$, $P = 0.81$. The effect of group on accuracy was $F(1,34) = 0.10$, $P = 0.96$, of gender $F(1,34) = 0.63$, $P = 0.43$, and their interaction $F(1,34) = 0.012$, $P = 0.93$.

Imaging results

After running the ICA, the DMN was unexpectedly represented in three separate components. The DMN was split in (i) an anterior part with ACC, medial frontal gyri and lateral frontal areas, (ii) a mainly middle/lateral part containing MTG, cingulate, insula, hippocampal formation and (iii) a posterior part containing mainly PCC, precuneus and IPL. We will refer to these subnetworks as (i) 'anterior' component, (ii) 'middle' component and (3) 'posterior' component (Figure 1). The anterior component had a spatial overlap of 21% with the DMN template while it contained mostly frontal areas but also some PCC, the middle component of 25% and the posterior component 27%. One additional component showed an overlap of 23% but this component contained blood vessel artifacts. These components of interest were entered in the group comparison.

The contrast of alexithymic *vs* non-alexithymic participants showed lower connectivity within the DMN for the following areas in alexithymic individuals; anterior component: cingulate gyrus, superior frontal gyri and right medial temporal gyrus (MTG); middle component: right MiFG; posterior component: left medial frontal gyrus (MeFG) and right SFG (Table 3 and Figure 2).

In contrast, higher connectivity with the DMN was observed for the following areas in alexithymic individuals; anterior component: occipital gyri and declive; middle component: precentral gyrus and right IFG; posterior component: precentral gyrus and right MiFG ($P < 0.001$; $k > 15$; Table 3 and Figure 2).

Table 2 Performance on metrical stress task

Performance measure	High alexithymia, mean (s.d.)		Low alexithymia, mean (s.d.)	
	Males	Females	Males	Females
Reaction time (s) metrical stress	1.53 (0.46)	1.45 (0.36)	1.44 (0.27)	1.46 (0.51)
Accuracy (%) metrical stress	78.1 (19)	76.4 (24)	75.3 (22)	80.8 (19)
Reaction time (s) valence evaluation	1.07 (0.43)	1.11 (0.47)	1.20 (0.16)	1.18 (0.42)
Accuracy (%) valence evaluation	78.1 (32.6)	68.4 (37.6)	87.4 (19.4)	80.0 (34.5)

Mean and s.d. of the reaction times and accuracy on the metrical stress task. Results are shown separately for males and females in both groups.

Adding gender, positive or negative affect as a covariate did not influence the outcome of the study. Thus group differences could not be explained by these variables.

DISCUSSION

The aim of this study was to investigate differences between alexithymic and non-alexithymic participants in default mode connectivity. Participants with high levels of alexithymia showed lower connectivity of DMN areas, including the cingulate gyrus, MeFG and MTG. In contrast, they showed higher connectivity to sensory areas and right lateral frontal areas. These group differences were not caused by differences in affect or gender distribution. Moreover, participants showed no difference in performance on a language task involving semantic emotional evaluation and stress placement, indicating that differences in such skills were not confounding interpretation of group differences. Networks identified with a resting state analysis have been shown to converge with networks resulting from task-induced activation (Fox and Lancaster, 1994; Smith *et al.*, 2009). However, analysis of resting state networks is not biased by differences in task performance between groups (Van der Ven *et al.*, 2004).

The high- and low-alexithymic group showed no effect of positive or negative affect on imaging results. The TAS-20, measuring a trait, often shows a relation with negative affect, which is a state characteristic (Lane *et al.*, 1997). Since the TAS-20 may also tap aspects of affective state, the use of the BVAQ and the absence of an effect of the PANAS on our results may indicate that this study specifically measured trait alexithymia.

The two groups were initially selected based on the verbalizing subscale of the BVAQ. However, the high- and low-alexithymic group differed strongly on the cognitive component at the day of scanning. Thus, selection based on the verbalizing item of the BVAQ was considered adequate for creating two rather extreme groups. Interestingly, the cognitive component has shown a high correlation with the TAS-20 (Zech *et al.*, 1999; Berthoz *et al.*, 2000, 2007), thus this selection may be comparable to selection with the TAS-20.

The DMN was split into three subnetworks, while a test for component stability (ICASSO) showed a good stability of selected components. We did not expect the DMN to split into separate components. However, different components containing part of the DMN have been described by other studies as well, e.g. (Damoiseaux *et al.*, 2006; Garrity *et al.*, 2007; Jafri *et al.*, 2008). Indeed, our identified networks may fit the DMN model of Laird *et al.* (2010) and three subdomains described by Kim (2010). The part containing MTG quite closely resembles the 'action subnetwork' defined by Laird *et al.* (2010) and is involved in salience according to Kim *et al.* (2010). The anterior component (Laird: 'emotion subnetwork') could be the core domain of the DMN involved in cognitive emotional processing, and the posterior component (Laird: 'perception subnetwork') could be involved in monitoring of external cues and top–down memory (Laird *et al.*, 2009; Kim, 2010).

A key finding in the group comparison was that the alexithymic participants showed lower connectivity in anterior parts of the DMN, including cingulate gyrus, medial frontal regions and MTG (Gusnard and Raichle, 2001; Buckner *et al.*, 2008). This finding is in accordance with our hypothesis of decreased emotional awareness in alexithymia (Lane *et al.*, 1997), and is consistent with earlier approaches (Lane *et al.*, 1998).

The DMN is believed to reflect the baseline 'idling' state of the brain that diminishes during specific goal-directed behaviors (Raichle *et al.*, 2001). It has functions related to attending internal versus external

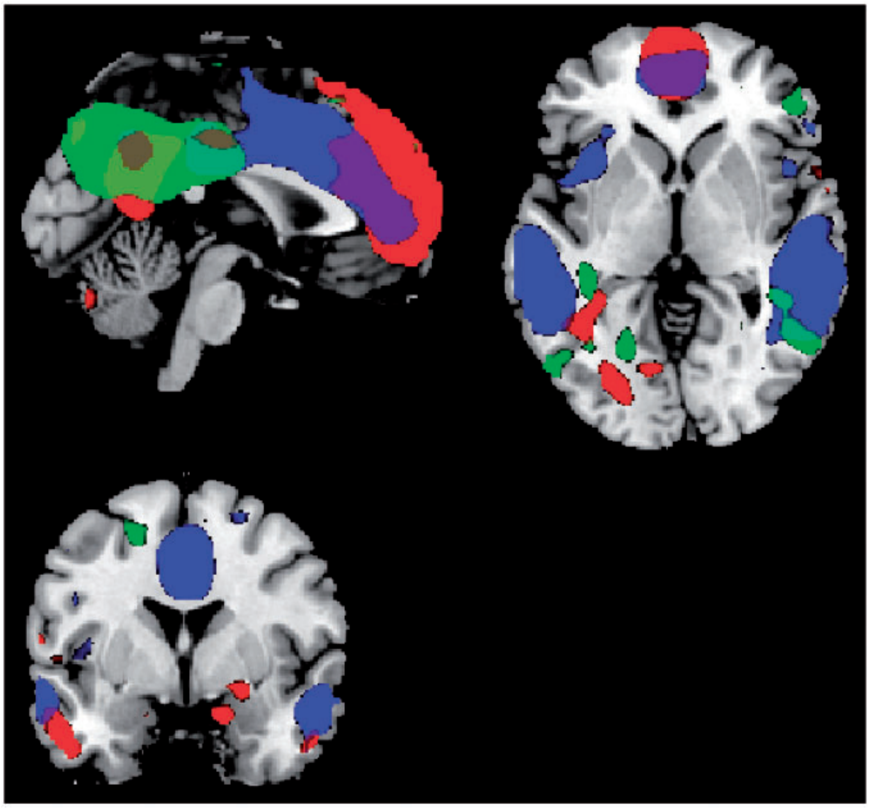

Fig. 1 The three networks identified, the whole network is shown irrespective of group. All main areas of the default mode network are visible, including the anterior cingulate, posterior cingulate, medial middle/MTG, prefrontal cortex, precuneus and IPL. The anterior component is indicated in red, the middle DMN component in blue and the posterior component in green.

Table 3 Results of group comparison

Voxels	*T*	*Z*	*x*	*y*	*z*	Area
High *vs* low alexithymia						
Anterior						
36	5.23	4.48	−33	−84	24	L superior occipital gyrus
87	5.22	4.47	39	−81	27	R superior occipital gyrus
22	4.08	3.67	−27	−75	−27	L declive
Middle						
44	5.66	4.75	−36	−15	36	L precentral gyrus
37	4.83	4.21	−6	−9	60	L precentral gyrus
27	4.55	4.02	33	0	30	R IFG
Posterior						
30	3.93	3.56	−6	−9	60	L precentral gyrus
20	3.83	3.48	57	0	45	R MiFG
Low alexithymia *vs* high alexithymia						
Anterior						
47	4.93	4.28	0	24	39	Cingulate gyrus
23	4.59	4.05	27	36	24	R SFG
16	4.33	3.86	−30	63	3	L SFG
33	4.21	3.77	39	−3	−36	R MTG
Middle						
42	4.61	4.06	30	27	27	R MiFG
Posterior						
16	4.34	3.87	−9	66	18	L MeFG
15	4.04	3.65	15	66	−6	R SFG

Overview of clusters showing connectivity differences between groups ($P < 0.001$; $k > 15$, inclusive mask at $P < 0.05$). The first part of the table shows areas that are more connected in alexithymia, and the second half areas of decreased connectivity. Anterior, middle and posterior refer to the different components of the DMN (L = left, R = right).

state and consciousness (Raichle *et al.*, 2001; Spreng *et al.*, 2009). Slow-wave fluctuations of the brain have shown to be related to short gaps of inattentiveness during task performance, which could be interpreted as a transient more internally oriented focus (Singh and Fawcett, 2009). Resting state fluctuations of the DMN may thus be related to the degree to which persons engage in introspective thinking (Singh and Fawcett, 2009), which may be less pronounced in alexithymia. In a similar vein, research on subjects with meditation experience showed increased connectivity within attentional networks, as well as between attentional regions and medial frontal regions (Hasenkamp and Barsalou, 2012). The authors suggested that these neural relationships may be involved in the development of cognitive skills, such as maintaining attention and disengaging from distraction, that are often reported with meditation practice. Thus, prolonged mental training or habits may have lasting influences on resting state networks.

Interestingly, lower DMN connectivity has also been shown in ASD (Assaf *et al.*, 2010), implying that it may reflect a trait characteristic associated with socioemotional difficulties. Furthermore, lower connectivity of the MTG may relate to impaired ability to link external events to self-referential mental activity (Laird *et al.*, 2009). Like the anterior cingulate, prefrontal regions and temporal areas have also been implicated in language aspects of emotions (Anderson *et al.*, 2010; Hesling *et al.*, 2010), disturbances in these areas may also reflect more specific difficulties to put feelings into words (Aleman *et al.*, 2005).

In addition, the alexithymic group showed stronger connectivity to areas implicated in sensory input, namely the precentral gyrus and occipital areas. One could speculate that higher connectivity with sensory areas is consistent with the action-oriented tendencies of

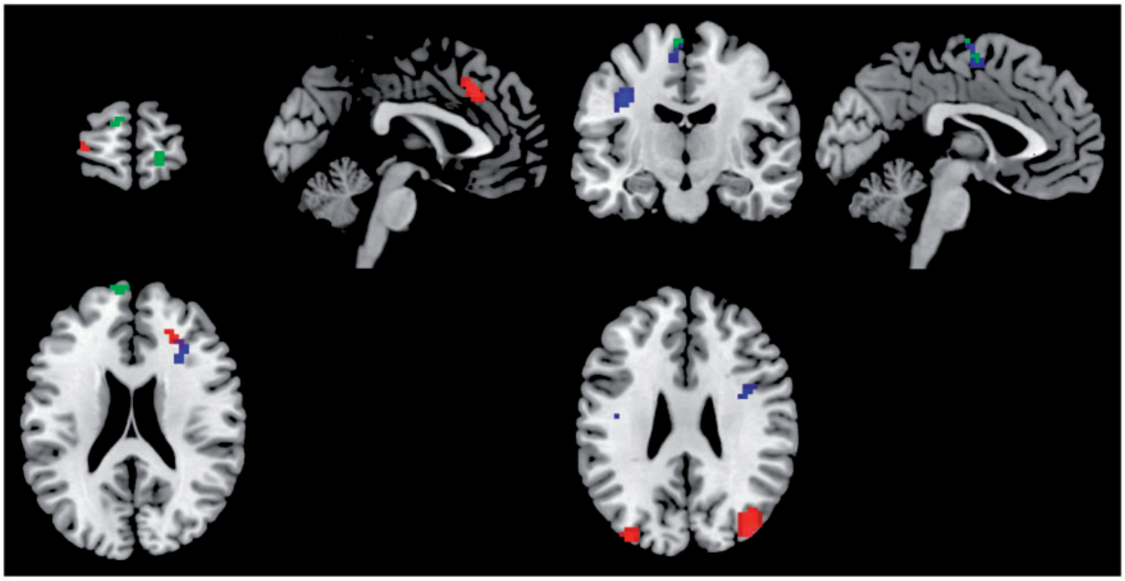

Fig. 2 Left: brain regions that show decreased connectivity in subjects with high alexithymia compared to low alexithymic subjects. Different components are indicated in different colors. Green: anterior part, red: middle part; blue: posterior part. Right: brain regions that show increased connectivity in subjects with alexithymia compared to control subjects. Different components are indicated in different colors. Green: anterior part; red: middle part; blue: posterior part.

alexithymic people and a tendency toward strong bodily expressions of emotions (Sifneos, 1973; Taylor *et al.*, 1991; Taylor *et al.*, 1997). Supporting our findings, alexithymic participants showed higher activation in sensory and motor areas (Karlsson *et al.*, 2008) and altered activation of visual areas (Mantani *et al.*, 2005; Karlsson *et al.*, 2008) during viewing of emotional pictures. Participants with lower emotional complexity showed higher activation in action-oriented brain areas, such as the precentral gyrus, during animated 'social' interactions (Tavares *et al.*, 2010).

The alexithymia group also showed higher connectivity in right-sided prefrontal regions. These areas have been implicated in emotional control including suppression (Goldin *et al.*, 2008; Reker *et al.*, 2009; Silani *et al.*, 2009). Ochsner (2002) hypothesized that cognitive reappraisal may involve verbalizing strategies resulting in more left sided activation whereas other emotion regulation strategies such as suppression—more often used by alexithymic persons (Swart *et al.*, 2009)—may lead to right sided frontal involvement (Ochsner *et al.*, 2002). Of note, it has been shown that reduction of emotional arousal by affect labeling is mediated by the right vLPF (Lieberman *et al.*, 2005, 2007), which does not fit our hypothesis. However, this topic should need further investigation in relation to alexithymia.

On a final note, some brain areas that showed altered connectivity in our study were not core parts of the DMN. Supporting our results, He *et al.* reported that these areas, such as precentral gyrus and lateral frontal areas, show a synchronized activation with the DMN (He *et al.*, 2004).

In conclusion, the alexithymic group demonstrated a higher connectivity with right-sided prefrontal regions and sensory areas. These areas have been associated with emotion suppression and a more action-oriented focus. However, the high alexithymic group showed less connectivity with frontal areas of the DMN. We suggest that such distinct patterns of connectivity may be related to the diminished emotional awareness of alexithymic people.

FUNDING

This work was supported by a EURopean Young Investigator award (N.W.O. number 044035001) awarded to A.A.

CONFLICT OF INTEREST

None declared.

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