Alexithymia and the brain potential P300

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Background: The P300 is an event-related potential occurring at about 300 ms post-stimulus. The P300 covaries in amplitude with the perceived significance of the stimulus as well as with its emotional valence. Alexithymia refers to severe reductions in the cognitive as well as affective components of the emotional experience. For these reasons the study into the P300 in alexithymic subjects is interesting. Two such studies have been published, one claiming results indicating lower P300 in alexithymics, one claiming the opposite result.

Aims: The aim of this study was to clarify the effects of alexithymia on the P300 response.

Method: High- and low-alexithymic individuals were drawn from a normal population (based on scores on the Bermond-Vorst Alexithymia Questionnaire) and participated in a visual oddball task while scalp EEG was recorded. The oddball task consisted of a series of non-target stimuli, intermixed with less frequent target stimuli, emotional stimuli, and neutral stimuli.

Results: P300 amplitudes were enhanced for emotional compared with neutral pictures. Females showed higher P300 amplitudes compared with males. High-alexithymic women showed smaller P300 amplitudes than low-alexithymic women, irrespective of stimulus category. Furthermore, female low-alexithymics showed enhanced amplitudes for electrodes over the left compared with the right hemisphere. Suggestive evidence indicated that P300 amplitude was higher in high- compared with low-alexithymic males. (*Netherlands Journal of Psychology*, 64, 65-77.)

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Sifneos (1973a) coined the term 'alexithymia' to label a complex of features, referring to severe reductions in both cognitive and affective components of the emotional experience.

It has been proposed that alexithymia enhances the probability of (psycho)-somatic complaints (Nemiah & Sifneos, 1970), and many publications support this notion (see Taylor, Bagby & Parker,

1997, for a review). Furthermore it has been proposed that alexithymia results in greater emotional physiological responses, or greater autonomic baseline levels, which may explain the relationship between alexithymia and psychosomatic complaints (Gross, 2002; Thayer & Brosschot, 2005). However, the relevant literature is equivocal. Several studies have demonstrated that alexithymia is related to higher baseline levels (Papciak, Feuerstein & Spiefel, 1985; Thayer & Brosschot, 2005; Wehmer, Brejnak, Lumley & Stettner, 1995; Fukunishi, Sei, Morita & Rahe, 1999; Spitzer, Brandl, Rose, Nauck & Freyberger, 2005), while other studies reported the contrary, e.g. lower baseline levels (Hyer, Woods, Summers, Boudewyns & Harrison, 1991; Newton & Cotrada, 1994). Still others even failed to find any effects at all (Roedema & Simons, 1999; Neumann, Soller, Thayer & Waldstein, 2004). The literature regarding alexithymia and autonomic responses to stress or negative affect is also equivocal. Some studies indicate that alexithymia is related to attenuated autonomic responses to stress or negative affect (Neumann et al., 2004; Wehmer et al., 1995; Linden, Lenz & Stossel, 1996; Friedlander, Lumely, Farchione & Doyal, 1997; Fukunishi et al., 1999, Roedema & Simons, 1999), while others found the opposite (Papciak et al., 1985; Martin & Pihl, 1986; Waldstein, Kauhanen, Neumann & Katzel, 2002), or no effect at all (Rabavilas, 1987).

The hypo-arousal model of alexithymia (Linden et al., 1996; Neumann et al., 2004) could explain the lower autonomic responses in alexithymics. This model proposes that alexithymics have limited affective reactivity and, thus, damped sympathetic responses. This is in line with the ideas of the founding fathers of the alexithymia concept, Nemiah and Sifneos, who have always stressed the importance of the affective components (e.g. reduced emotionalising and reduced fantasising) as important aspects of alexithymia (Nemiah & Sifneos, 1970; Sifneos, 1973b; Nemiah, 1977, 1996; Sifneos, 1991, 2000).

The P300 is an event-related potential occurring at about 300 ms post-stimulus. The P300 is sensitive to the ascribed importance of the stimulus in such a way that the higher the importance of the stimulus is for the subject, the higher the P300 amplitude in reaction to that stimulus will be. The P300 is also related to the evaluation of the stimulus in another sense, as higher evaluated emotional valences of the stimulus have been found to be related to higher P300 amplitudes (Cuthbert, Schupp, Bradley, Birbaumer & Lang, 2000; Schupp, Cuthbert, Bradley, Cacioppo & Lang, 2000). Moreover, studies recruiting several clinical groups report a relationship between P300 responses and altered capacities to process emotional stimuli. For instance, lower P300 amplitudes in case of psychopathy (Williamson, Harpure & Hare, 1991), and depression (Kayser, Bruder, Tenke, Steward & Quitkin, 2000), and higher ERP amplitudes in the P300 time window for subjects scoring high on dissociation compared with those scoring low on dissociation (de Ruiter, Phaf, Veltman, Kok & van Dyck, 2003), while the results of Blomhoff, Reinvang and Matt (1988) with posttraumatic stress disorder (PTSD) patients pointed to more complex relations between specific aspects of PTSD and event-related potentials.

The hypo-arousal model of alexithymia (Linden et al., 1996; Neumann et al., 2004) leads to the expectation of lower attributed valence to perceived emotional stimuli, and should therefore result in lower P300 amplitudes in alexithymic subjects. However, the two studies published present conflicting results: Heijman (1998) is claiming lower, whereas Franz, Schaefer, Schneider, Sitte and Bachor (2004) are claiming higher P300 amplitudes in alexithymics.

The aim of the present study is to study P300 responses in high-alexithymics and low-alexithymics. Since it has been proposed that alexithymia could be the result of a reduced functioning of the right hemisphere or a hyperactive left hemisphere (Weintraub & Mesulam, 1983; Taylor, 1984a, b; Voeller, 1986; Bear, 1983; Berenbaum & Prince, 1994), we analysed the data for possible laterality effects in P300 peaks as well. Finally, since there are indications for gender differences in neural underpinnings of alexithymia (Lumley & Sieky, 2000) attention was also paid to possible gender differences in P300 values.

Methods

Alexithymia

Alexithymia was measured by means of the Bermond-Vorst Alexithymia Questionnaire (BVAQ) (Vorst & Bermond, 2001). This questionnaire has five separate subscales, (8 items per subscale, 4 indicative and 4 contraindicative) for all alexithymia features as mentioned by Nemiah and Sifneos (1970) and Sifneos (1973a), who defined the concept of alexithymia by the following traits: reduced capacities for emotionalising, fantasising, identifying emotions, verbalising emotions and pensé opératoire (Marty & M'Uzan, 1963) or reduced analysing emotion. These original alexithymia features come back in early publications: Taylor, Ryan and Bagby (1985), Hendryx, Haviland and Shaw (1991), Bermond, Vorst, Vingerhoets and Gerritsen (1999). Thus, the BVAQ covers both the cognitive and the affective components of alexithymia. Further, the BVAQ has good psychometric properties (Vorst & Bremond 2001).

Subjects

Forty-two subjects selected out of the population of freshman psychology students ($n = 516$) at the University of Amsterdam on the basis of their BVAQ scores were willing to participate in the experiment. Selection criteria were: scoring in the 15 highest percentiles (high-alexithymia group) or scoring in the 15 lowest percentiles (low-alexithymia group). The cut-off scores for the selection criteria mentioned were calculated over the summed populations of freshman psychology students, covering several years ($n = 4901$). Two subjects were rejected due to a history of epilepsy, or use of antidepressants. Finally data of ten subjects were left out of the statistical analyses for the following reasons: missing too many targets (1), apparatus problems (2) and either too much drift or artefacts in data (7). The remaining subjects ($n = 31$) did not report a history of neurological, major medical or psychiatric disorders. This resulted in 16 high-alexithymic subjects (mean age = 20.9 years; $SD = 5.5$), and 15 low-alexithymic subjects (mean age = 21.8 years; $SD = 4.8$). Due to dropping subjects from further analysis, the groups are no longer well balanced for gender (high-alexithymics: 7 males, 9 females; low-alexithymics: 10 males, 5 females). However, this difference did not reach significance ($\chi^2 = 1.64$, $p = 0.200$).

All subjects had signed an informed consent form and received 7.50 euros for their cooperation.

The design was double-blind: neither the investigator nor the subjects knew the alexithymia scores. At the end of the study the selection scores were provided by a colleague, who was not further involved in this study.

Stimuli

The stimulus material consisted of four categories: targets (TAR), non-targets (NOT), emotional stimuli with negative valence (EMO) and neutral stimuli (NEU). The target was a cross with a diagonal of about 1.5 cm. The non-target was a circle with a diameter of about 1 cm. The emotional and neutral stimuli consisted of pictures selected from the International Affective Picture System[1] (IAPS, NIMH, centre for study of emotion and attention, University of Florida). These stimuli were not target stimuli. Hence, the subjects did not have to respond to these stimuli. Therefore, the P300 response to these stimuli would not be enhanced by target properties. Previous research with this picture set invoked a reliable electrodermic response (Tranel & Damasio, 1994; Lane, Chua & Dolan, 1999) and P300 amplitude concurring with the emotional intensity of the pictures (Cuthbert et al. 2000). The picture size was 9 x 12 cm. Examples of emotional pictures are war scenes, mutilations, spiders, snakes, insects and dead animals. Examples of neutral stimuli are coffee cups, buildings, towels and chess players. The IAPS pictures are not well controlled for physical properties, such as luminance. However, since this is an internationally widely used picture set, and further since it has been demonstrated before that this set invokes P300 amplitude concurring with the emotional intensity of the pictures, we opted for these pictures.

Procedure

Before the start of the actual experiment, subjects had to judge the emotional intensity of the EMO and NEU pictures. Subjects evaluated the pictures choosing from five scales by keyboard (1 = not emotional; 2 = somewhat emotional; 3 = emotional; 4 = quite emotional; 5 = very emotional). In order to avoid that the P300, in responses to emotional and neutral stimuli, would be influenced by novelty aspects, (which increase the P300 (Goldstein, Spencer & Donchin, 2002)), each picture was presented for 3 seconds during this picture evaluation period.

The experiment itself was an oddball design; stimuli were presented in three experimental blocks (lasting approximately 5 minutes). Each block constituted 160 trials, containing 16 targets, 16 emotional pictures, 16 non-emotional pictures, and 112 non-targets. All stimuli were presented centrally for 170 ms with a constant rate of one stimulus per 1305 ms. Trial presentation order was pseudo-randomised. No more than two stimuli out of one category succeeded each other. In between the stimuli, a fixation cross appeared. The importance of maintaining fixation was stressed throughout the trials. Subjects had to react to the targets by pressing a button. Reaction times, number of missed targets and false responses were registered. If subjects responded incorrectly (at non-targets, emotional and neutral stimuli), trials were omitted from further analysis. Therefore, motor potentials arising from false responses were removed prematurely. To sustain attention to the task, subjects received some feedback about their achievements during the periods between the experimental blocks. Prior to the first experimental block participants were given 20 test-trials to become familiarised with the experimental context.

Psychophysiological recording

Subjects were sitting in a dimly lit, sound-attenuated room. They sat comfortably in an easy chair with an eye-monitor distance of 80 cm. The EEG was recorded according to the 10-

1 *IAPS numbers: 2840, 5500, 5530, 5533, 5534 5800, 7000, 7002, 7004, 7006, 7009, 7010, 7020, 7025, 7030, 7031, 7034, 7035, 7040, 7050, 7060, 7080, 7090, 7100, 7130, 7140, 7150, 7175, 7180, 7190, 7217, 7224, 7233, 7234, 7235, 7490, 7491, 7500, 7550, 7560, 7700, 7950, 8010, 8311.*

20 system, with tin-electrodes embedded in an elasticised cap (Pivik, Broughton, Coppola & Davidson, 1993). Electrodes were placed at F3, Fz, F4; C3, Cz, C4; P3, Pz, P4; T5 and T6 and both mastoids. Horizontal eye movements (hEOG) were derived from two electrodes placed at the outer canthi. Vertical eye movements (vEOG) were derived from two electrodes placed one centimetre above and below the left eye. An electrode attached to the forehead was used as ground. The EEG was amplified by a Nihon-Kohden polygraph. The impedance of the electrodes was set below 8 kΩ. EEG gain was 10,000. A bandpass filter of 0.01-30 Hz was used. Data were digitised at 256 Hz sampling rate.

Data reduction

During off-line analysis the signal was divided into epochs of 1000 ms including a 100 ms prestimulus baseline. Data were subsequently scanned for A/D clips and flatlines. Ocular artefacts were controlled for according to Woestenburg, Verbaten and Slangen (1983). Trials containing artefacts or drifts exceeding 50 µV (per 12 ms) and 100 µV (per sweep of 1000 ms), respectively, were removed from further analysis. After inspecting their EEGs, we took a threshold of 60 µV and 150 µV, respectively, for some cases. According to Cohen and Polich (1997), we took a minimum threshold of 20 trials in each condition for averaging (mean number of trials: low-alexithymics: NON = 233.63; TAR = 35.81; EMO = 35.69; NEU = 36.19; high-alexithymics: NON = 273.07; TAR = 39.27; EMO = 40.20; NEU = 39.73).

Data analyses

P300 amplitude
P300 amplitude was defined as the amplitude modulation with positive deflection occurring in the period of 300 to 500 ms after stimulus presentation. This resulted in some missing data, either because the peak did not occur within the defined time window, or because there was no clear peak. No clear peak refers to the fact that in some cases the examined time window contained multiple peaks and, in terms of timing, it was not obvious which one was the P300. The analysis was based on an automated algorithm. However, the outcome of the algorithmic procedure was always examined visually and in case of doubt we entered missing values. Heijman (1998) measured the P300 responses in her alexithymic subjects over the whole scull, whereas Franz et al. (2004) measured the P300 over electrode sites: Fz, Cz, and Pz only. However, Franz et al. (2004) explained their results indicating higher P300 amplitudes in alexithymic subjects by assuming that alexithymics, due to their deficits concerning the cognitive emotional knowledge, need more effort and cognitive resources to process emotional information. If this explanation is correct then higher P300 amplitudes have to be expected at various electrodes sites. For these reasons analyses were performed in a repeated measurement model, (over all sites) containing the following factors: alexithymia (2) x gender (2) x stimulus category (4). Stimulus category was entered as a within-subject factor. Gender was entered as a factor because of hypothesised effects on P300 (Orozco & Ehler, 1998) and hypothesised differences in neural underpinnings of alexithymia (Lumley & Sielky, 2000). When repeated measures indicated significant effects for stimulus category, Helmert contrasts were calculated. When necessary we corrected using the Greenhouse-Geiser ϵ.

Laterality effects of P300 in alexithymia and P300 latency times

P300 latency time was defined as the time between stimulus onset and the peak of the P300.

In several comparable studies, tests of possible laterality effects have been based on the electrodes directly left and right of the midline (F3/C3/P3 versus F4/C4/P4), whereas P300 latency is usually measured over the central electrodes (Fz/Cz/Pz) only, since the P300 is typically maximal at the mid-line (see for instance, Donchin & Coles, 1988; Franz et al., 2004; Gasbarri, Arnone, Pompili, Pacitti, Pacitti & Cahill, 2007). We followed up these methods.

Results

Alexithymia

The mean BVAQ subscale scores (with corresponding standard deviations) for the low- and high-alexithymic subjects are presented in table 1. Since there turned out to be a clear significant interaction factor (alexithymia x gender) in P300 amplitudes (see below) these scores are also presented for females and males separately. Based upon BVAQ scores of clinical groups, Vorst (2007) established clinical BVAQ cut-off scores. The mean BVAQ sum total scores for all low-alexithymia groups fell within the non-alexithymic range, whereas the mean BVAQ sum total sores for all high-alexithymic groups fell within the alexithymic range.

Table 1 **Alexithymia subscale scores for the various groups (standard deviation in parentheses).**

	Verbalising	*Identifying*	*Analysing*	*Emotionalising*	*Fantasising*
Low-alexithymics	11.60 (1.88)	11.33 (3.64)	14.20 (3.71)	18.53 (3.40)	13.80 (4.50)
High-alexithymics	27.62 (5.24)	21.19 (3.49)	21.81 (5.62)	25.50 (4.91)	25.99 (5.79)
Male low-alexithymics	12.30 (1.49	14.40 (2.55)	13.00 (3.80)	19.30 (3.30)	12.90 (3.45)
Male high-alexithymics	25.00 (4.69)	19.29 (5.28)	22.43 (4.16)	28.57 (4.89)	24.71 (6.99)
Female low-alexithymics	10.20 (1.92)	13.80 (5.76)	11.00 (3.24)	17.00 (3.39)	15.60 (6.19)
Female high-alexithymics	29.67 (4.92)	23.78 (5.33)	20.22 (2.73)	23.11 (3.55)	25.22 (5.09)

Evaluation of stimuli

Pictures selected for their negative valence were evaluated as significantly more emotional [$F(1, 26) = 577.17$, $p = < 0.0001$] than pictures selected for their neutral valence. Moreover high- and low-alexithymics differed significantly in their judgment [$F(1, 26) = 4.90$, $p = 0.036$]. This effect was explained by a three-way interaction factor emotional value x gender x alexithymia [$F(1, 26) = 4.50$, $p = 0.044$]. An univariate ANOVA indicated that high-alexithymic men evaluated the pictures with negative valence ($M = 2.82$, $SD = 0.83$) significantly less emotionally [$F(1, 15) = 6.31$, $p \leq 0.025$] than low-alexithymic men ($M = 3.52$, $SD = 0.55$), while low-alexithymic men rated the pictures equally emotionally as both low-alexithymic ($M = 3.57$, $SD = 0.46$) and high-alexithymic females ($M = 3.63$, $SD = 0.34$). No differences were found between groups on the ratings of the neutral pictures (male high-alexithymics [$M = 1.27$, $SD = 0.35$]; male low-alexithymics [$M = 1.17$, $SD = 0.15$] female high-alexithymics [$M = 1.12$, $SD = 0.05$]; female low-alexithymics [$M = 1.16$, $SD = 0.12$]).

Missed targets

None of the subjects missed more than three targets in all the experimental blocks taken together, indicating that all subjects attended to the task accurately.

Reaction times to targets

Differences in reaction times to targets between high-alexithymic and low-alexithymic subjects turned out to be non-significant [$F(3, 27) = 0.03$, $p = 0.862$]. Neither was there a significant difference between the sexes [$F(1, 27) = 0.17$, $p = 0.685$].

P300 latency times

P300 latency times were analysed, and provided clear significant results regarding stimulus categories (target, emotional, neutral): {Fz [$F(3, 22) = 6.43$, $p < 0.003$]; Cz [$F(3, 22) = 11.94$, $p < 0.000$]; Pz [$F(3, 22) = 13.22$, $p < 0.000$]}.

Calculation of Helmert contrasts showed significantly slower P300 latencies for target compared with emotional and neutral pictures: {Fz [$F(1, 24) = 19.99$, $p < 0.000$]; Cz [$F(1, 24) = 34.45$, $p < 0.000$]; Pz [$F(1, 24) = 34.51$, $p < 0.000$]}.

There were no significant main effects of alexithymia, nor significant interaction effects with alexithymia, regarding latency times.

P300 amplitude and stimulus categories

Table 2 presents the P300 amplitudes (means, with corresponding standard deviations) for the various leads, stimuli, and groups.

As expected we found a significant effect of stimulus category: [$F(3, 299) = 254.25$, $p < 0.0001$]. Significant effects of stimulus category were found for all leads: Fz [$F(3, 22) = 14.86$, $p < 0.0001$]; Cz [$F(3, 22) = 47.48$, $p < 0.0001$]; Pz [$F(3, 23) = 54.17$, $p < 0.0001$]; P3 [$F(3, 22) = 39.07$, $p < 0.0001$]; P4 [$F(3, 22) = 35.58$, $p < 0.0001$]; T5 [$F(3, 21) = 28,29$, $p < 0.0001$]; T6 [$F(3, 21) = 15.80$, $p < 0.0001$].

Helmert contrasts revealed significantly greater P300 amplitudes [$F(1, 301) = 133.98$, $p < 0.0001$] for emotional stimuli compared with neutral stimuli. This was also found for all leads except T6: Fz [$F(1, 24) = 7.77$, $p = 0.010$]; Cz [$F(1, 24) = 18.87$, $p < 0.0001$]; Pz [$F(1, 25) = 24.32$, $p < 0.0001$]; P3 [$F(1, 24) = 20.30$, $p < 0.0001$]; P4 [$F(1, 24) = 13.43$, $p = 0.001$]; T5 [$F(1, 21) = 6.97$, $p = 0.015$]; T6 [$F(1, 23) = 2.06$, $p = 0.165$].

Table 2	**P300 amplitudes for low- and high-alexithymics.**											
Non-alexithymic		*Fz*	*Cz*	*Pz*	*F3*	*F4*	*C3*	*C4*	*P3*	*P4*	*T5*	*T6*
Males	NON	1.48 (2.25)	2.76 (2.07)	3.89 (1.56)	1.33 (2.00)	1.52 (2.71)	2.98 (1.58)	3.51 (2.33)	3.61 (1.15)	5.01 (1.01)	4.71 (1.16)	5.38 (1.81)
	TAR	11.62 (6.98)	19.56 (6.10)	24.27 (4.32)	10.00 (6.71)	10.19 (5.56)	16.84 (5.59)	17.57 (4.34)	19.77 (5.25)	19.23 (3.70)	13.72 (4.91)	12.94 (4.37)
	EMO	4.16 (5.86)	8.60 (5.37)	12.21 (4.06)	3.09 (6.60)	2.59 (6.99)	6.58 (3.61)	6.45 (4.29)	10.92 (4.16)	11.68 (6.55)	10.61 (2.84)	11.53 (5.57)
	NEU	3.29 (6.40)	6.00 (5.49)	9.58 (4.22)	1.41 (6.58)	1.44 (6.49)	5.73 (5.12)	4.71 (4.67)	9.18 (3.67)	9.41 (5.29)	9.11 (3.99)	11.10 (5.58)
Females	NON	3.26 (3.79)	5.31 (5.50)	6.40 (4.48)	3.21 (3.62)	2.92 (3.57)	5.73 (4.70)	5.98 (3.62)	8.23 (4.30)	10.00 (3.49)	8.15 (2.98)	9.15 (4.28)
	TAR	14.21 (8.77)	21.65 (9.48)	25.49 (9.77)	11.05 (6.07)	13.78 (8.55)	19.96 (8.54)	20.19 (8.33)	23.81 (11.20)	22.38 (7.36)	16.81 (6.27)	13.84 (4.83)
	EMO	11.62 (7.32)	17.02 (10.27)	17.79 (6.81)	11.20 (5.09)	9.46 (6.65)	16.19 (9.05)	13.49 (8.35)	17.55 (6.96)	15.63 (5.81)	14.43 (3.89)	11.59 (4.81)
	NEU	9.38 (5.60)	14.64 (7.58)	14.68 (7.24)	9.66 (5.67)	8.18 (6.58)	13.41 (6.61)	11.79 (7.50)	14.07 (7.29)	12.38 (5.37)	14.64 (3.94)	11.74 (4.89)
Males and females	NON	2.08 (2.85)	3.61 (3.60)	4.79 (3.04)	1.95 (2.68)	1.99 (2.97)	3.96 (3.19)	4.39 (2.98)	5.26 (3.43)	6.55 (3.08)	5.94 (2.55)	6.64 (3.27)
	TAR	12.48 (7.41)	20.26 (7.12)	24.67 (6.30)	10.35 (6.31)	11.39 (6.62)	17.88 (6.58)	18.45 (5.79)	21.12 (7.58)	20.28 (5.16)	14.75 (5.39)	13.26 (4.37)
	EMO	6.65 (7.12)	11.41 (8.10)	14.07 (5.59)	5.79 (7.15)	5.05 (7.44)	9.78 (7.33)	8.80 (6.60)	13.29 (6.04)	13.00 (6.39)	11.98 (3.64)	11.55 (5.12)
	NEU	5.47 (6.63)	9.09 (7.39)	11.40 (5.79)	4.35 (7.31)	3.85 (7.10)	8.47 (6.65)	7.24 (6.57)	11.06 (5.63)	10.47 (5.32)	10.81 (4.64)	11.37 (5.08)
High-alexithymic		**Fz**	**Cz**	**Pz**	**F3**	**F4**	**C3**	**C4**	**P3**	**P4**	**T5**	**T6**
Males	NON	2.81 (2.84)	4.82 (2.82)	5.08 (1.98)	2.58 (2.37)	2.51 (3.21)	4.12 (2.39)	4.60 (2.88)	5.55 (2.66)	5.36 (1.92)	5.32 (1.40)	5.93 (2.34)
	TAR	10.99 (7.99)	21.13 (10.32)	26.14 (9.71)	9.20 (8.10)	10.25 (6.97)	17.58 (8.53)	18.64 (7.96)	21.73 (8.04)	20.97 (9.08)	13.42 (5.30)	11.94 (4.63)
	EMO	3.45 (6.22)	10.47 (5.72)	14.64 (7.88)	2.66 (5.16)	3.60 (5.79)	7.71 (4.83)	8.62 (6.24)	13.43 (6.05)	12.33 (7.47)	11.04 (5.07)	9.69 (5.56)
	NEU	2.02 (5.75)	8.54 (4.20)	12.74 (5.82)	0.00 (4.77)	0.46 (6.03)	6.09 (3.48)	5.38 (5.85)	11.16 (5.36)	9.83 (4.63)	8.34 (3.34)	8.58 (4.50)

Non-alexithymic		*Fz*	*Cz*	*Pz*	*F3*	*F4*	*C3*	*C4*	*P3*	*P4*	*T5*	*T6*
Females	NON	2.24 (1.71)	2.24 (3.10)	4.28 (3.61)	1.80 (1.60)	1.51 (1.80)	2.94 (2.34)	2.82 (2.65)	6.04 (3.25)	6.08 (2.00)	5.90 (1.96)	7.05 (1.70)
	TAR	12.72 (9.20)	21.78 (9.23)	27.45 (8.00)	10.74 (10.17)	10.69 (7.19)	19.04 (8.39)	18.36 (6.28)	21.98 (7.41)	22.19 (7.05)	15.34 (5.19)	13.57 (4.85)
	EMO	5.95 (12.70)	12.32 (13.21)	16.58 (10.09)	2.98 (12.21)	3.68 (11.64)	9.12 (11.68)	9.91 (10.60)	14.44 (8.51)	15.45 (8.59)	12.60 (5.46)	14.24 (5.13)
	NEU	3.80 (10.72)	9.40 (10.64)	12.55 (8.35)	2.29 (10.21)	2.04 (9.75)	6.82 (9.20)	7.49 (8.73)	11.65 (6.51)	12.63 (7.30)	10.40 (4.16)	12.80 (4.48)
Males and females	NON	2.48 (2.18)	3.27 (3.17)	4.63 (2.95)	2.13 (1.92)	1.91 (2.41)	3.41 (2.35)	3.53 (2.79)	5.82 (2.92)	5.76 (1.93)	5.65 (1.71)	6.56 (2.02)
	TAR	11.97 (8.45)	21.50 (9.38)	26.87 (8.50)	10.06 (9.06)	10.50 (6.86)	18.40 (8.20)	18.48 (6.81)	21.87 (7.42)	21.66 (7.74)	14.50 (5.15)	12.88 (4.67)
	EMO	4.88 (10.15)	11.58 (10.59)	15.73 (8.95)	2.84 (9.50)	3.65 (9.26)	8.56 (9.32)	9.39 (8.86)	14.00 (7.32)	14.08 (8.02)	11.97 (5.18)	12.25 (5.64)
	NEU	3.02 (8.68)	9.03 (8.23)	12.64 (7.13)	1.29 (8.13)	1.35 (8.12)	6.50 (7.08)	6.57 (7.45)	11.44 (5.84)	11.40 (6.25)	9.50 (3.85)	10.96 (4.85)

Standard deviation in parentheses, NON = non-targets, TAR = targets, EMO = emotional stimuli, NEU = neutral stimuli.

Alexithymia and P300 amplitude

The grand means for both male and female high- and low-alexithymics are presented in figure 1.

Overall analysis over all electrode sites revealed a non-significant main effect for alexithymia [$F(1, 301) = 0.695$, $p = 0.405$]. However, a significant main effect for gender was found [$F(1, 301) = 14.34$, $p < 0.0001$]. Females showed significantly higher P300 amplitudes than males. Furthermore, a significant interaction effect for alexithymia x gender [$F(1, 301) = 8.34$, $p = 0.004$] was found. Such significant interaction factors were not found for any of the separate electrodes.

Overall analysis for males-only provided suggestive evidence [$F(1, 153) = 3.35$, $p = 0.069$] for increased P300 amplitudes in high-alexithymic males, compared with low-alexithymic males. The same analysis for females-only provided a clear significant result [$F(1, 148) = 4.89$, $p = 0.029$] demonstrating that high-alexithymic females show smaller P300 amplitudes compared with low-alexithymic females. This effect was not different for emotional stimuli compared with neutral stimuli. These results are presented graphically in figure 2.

Laterality effects of P300 in alexithymia

The interaction effect of laterality x gender x alexithymia turned out to be significant [$F(1, 82) = 5.51$, $p < 0.022$]. Further testing (laterality x alexithymia) revealed that, in contrast to female high-alexithymics, female low-alexithymics demonstrated greater P300 amplitudes over the left compared with the right hemisphere [$F(1, 40) = 1.98$, $p = 0.04$]. Furthermore testing for contrasts (differences between neutral and emotional stimuli) provided a non-significant result [$F(1, 40) = 1.98$, $p = 0.168$], indicating that the effect mentioned above is not emotion specific.

Finally, left to right hemisphere analysis (laterality x alexithymia) in P300 amplitudes provided a clear non-significant result for males [$F(1, 42) = 0.14$, $p = 0.709$].

These results are presented graphically in figure 3.

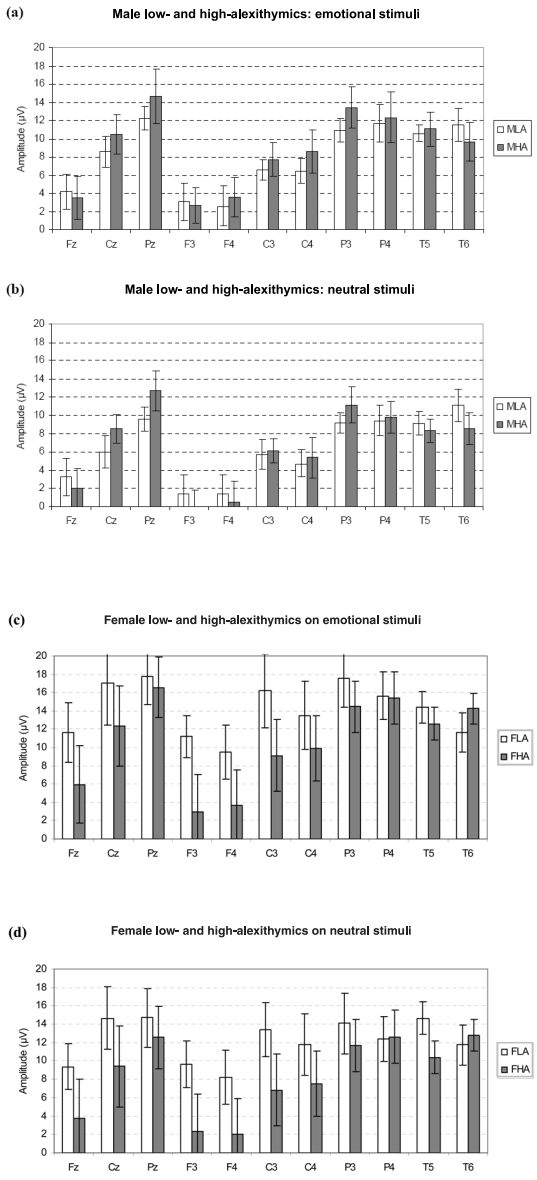

Figure 1
Grand totals.

P300 latency times

Analysing P300 latency times provided clear significant results regarding stimulus categories (target, emotional, neutral, and target) {Fz [$F(3, 22) = 6.427$, $p < 0.003$]; Cz [$F(3, 22) = 11.937$, $p < 0.000$]; Pz {$F(3, 22) = 13.220$, $p < 0.000$]}.

Calculation of Helmert contrasts showed slower P300 latencies for target compared with emotional and neutral pictures {Fz [$F(1, 24) = 19.986$, $p < 0.000$]; Cz [$F(1,24) = 34.449$, $p < 0.000$]; Pz {$F(1, 24) = 34.51$, $p < 0.000$]}.

There were no significant main effects of alexithymia, nor significant interaction effects with alexithymia, or interaction effects with gender regarding latency times.

Discussion

High-alexithymics evaluated emotional pictures significantly less emotionally than low-alexithymics. However, most significantly, this effect was limited to male subjects, whereas the result for females was clearly non-significant.

As expected, there was a significant overall P300 main effect for stimulus types, and this was also found for the various leads.

Calculation of contrasts (emotional pictures versus non-emotional pictures) also provided the expected results: overall P300 amplitudes in response to emotional stimuli being larger than those in reaction to neutral stimuli. This was also found for all leads except T6. Moreover, the results demonstrated a clear significant main effect for gender (females showing higher P300 amplitudes than males). This result is in line with data demonstrating that females show higher P300 amplitudes to emotional stimuli compared with men (Gasbarri et al., 2007). It is further in line with the fact that, in general, females score more favourably on emotionalising (Vorst & Bermond, 2001). Although the selection criteria for males and females in this study were the same (subjects scoring in the 15 highest or lowest percentiles on the BVAQ sum total) gender differences hold for the subjects in our study as well. Both low- and high-alexithymic females scored more favourably on the BVAQ subscale Emotionalising than the corresponding male groups (2.30 and 5.46 BVAQ points, respectively). Whereas low- and high-alexithymic women scored a little less favourably on the other BVAQ subscales compared with the male groups. Thus, if the hypo-arousal model of alexithymia (Neumann et al., 2004) is correct then the higher P300 amplitudes as found for females could also be explained by the fact that the women in our study scored more favourably on the BVAQ subscale Emotionalising. The results also demonstrated a clear, significant gender x alexithymia effect in overall P300 amplitudes. Further testing provided suggestive evidence (trend) for an overall larger P300 in high-alexithymic males than in low-alexithymic males. This effect was reversed, and clearly significant for females. Low-alexithymic women showed higher overall P300s than high-alexithymic women. The results concerning males are unexpected, especially since male high-alexithymics rated the pictures with negative valence less emotionally than male low-alexithymics, whereas this was not observed in females. Thus, according to the hypo-arousal model of alexithymia, lower P300 amplitudes had to be expected for male high-alexithymics, and not for female high-alexithymics. Against this expectation our results point precisely to the opposite. Still, our results indicate that high-alexithymic males process information differently than high-alexithymic females.

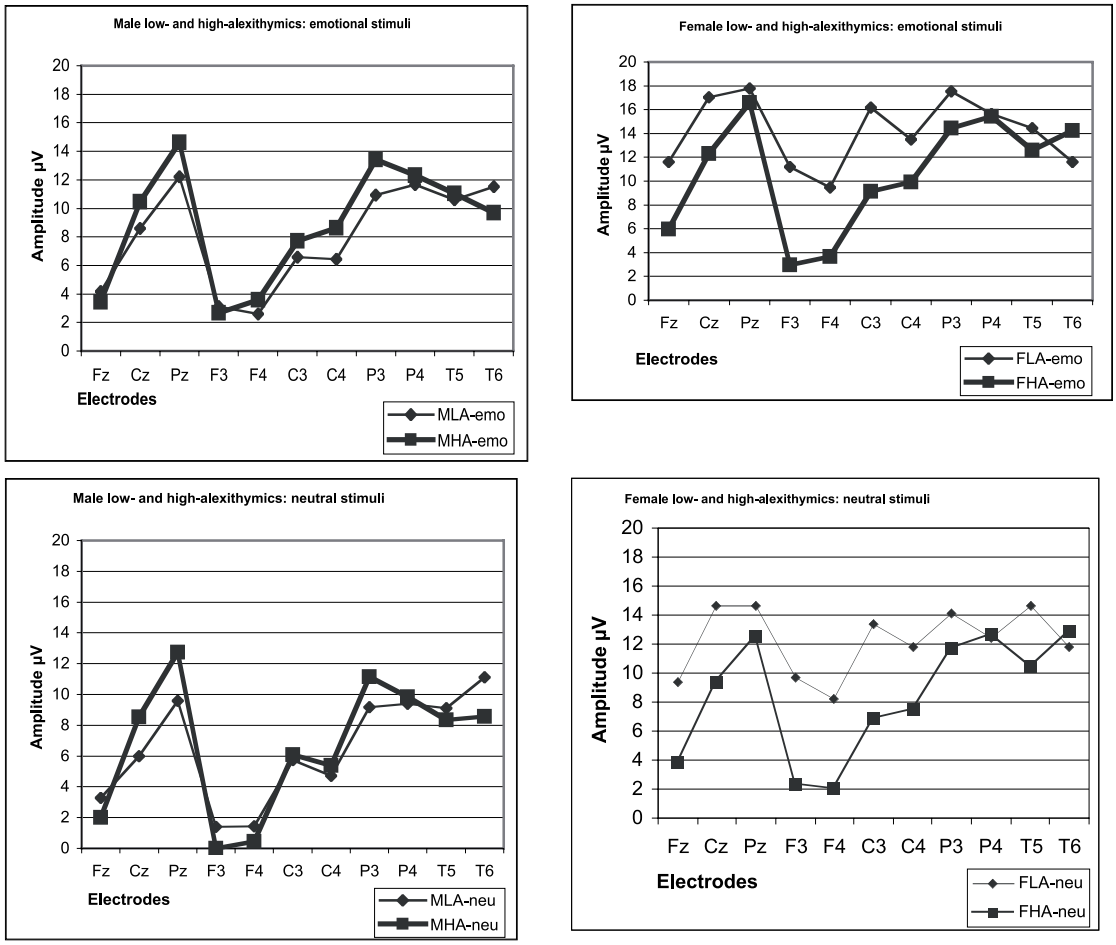

Figure 2
Graph: difference alexithymia x emotional / neutral stimuli. Differences between high- and low-alexithymics on emotional and neutral stimuli.

As stated in the Methods section, Franz et al. (2004) explain their results, pointing to higher P300 amplitudes in alexithymics, by assuming that alexithymics, due to their deficits concerning the cognitive emotional knowledge, need more effort and cognitive resources to process emotional information. This explanation could also hold for our results regarding males, but seems to be in conflict with our results regarding females. If the explanation by Franz et al. (2004) is correct, then the results for females force us to assume that alexithymic women invest less effort and cognitive resources in their processing of emotional information. We will discuss this possibility later in this discussion.

Our results further demonstrated that low-alexithymic females showed greater P300 amplitudes over the left than the right hemisphere, a phenomenon that was not observed in high-alexithymic females. This result is in conflict with results indicating that alexithymia is related either to a reduced functioning right hemisphere or an overactive left hemisphere (Parker, Taylor & Bagby, 1992; Lane, Kivley, DuBois, Shamasundara & Schwartz, 1995; Jessimer & Marham, 1997; Lumley & Sielky, 2000; Spalletta, Pasini, Costa, De Angelis, Ramundo, Paolucci & Caltagirone, 2001; Bermond, Bleys & Stoffels, 2004). However, these results fit with indications for gender differences in the neuro-anatomical basis of alexithymia. For instance, alexithymia in males is related to a reduced right hemisphere function and to right hemisphere lesions, whereas in women the selective importance of the right hemisphere could not be demonstrated (Lumley & Sielky, 2000; Spalletta et al. 2001). It has further been demonstrated that the size of the right anterior cingulate correlates with alexithymia in males, whereas such a correlation could not be demonstrated in females (Gündel et al., 2004). The combined results of Lumley and Sielky (2000), Spalletta et al. (2001), and Gündel et al. (2004) suggest that alexithymia in males is mainly related to malfunction of the right hemisphere, whereas in females alexithymia is also related to malfunction of the left hemisphere. This could explain the literature pointing to the selective importance of malfunctioning of the right hemisphere (see above). If alexithymia in males is mainly due to malfunctioning of the right hemisphere whereas in females it could be due to malfunctioning of either hemisphere, and if the data of males and females are not analysed separately, then the conclusion will be that the

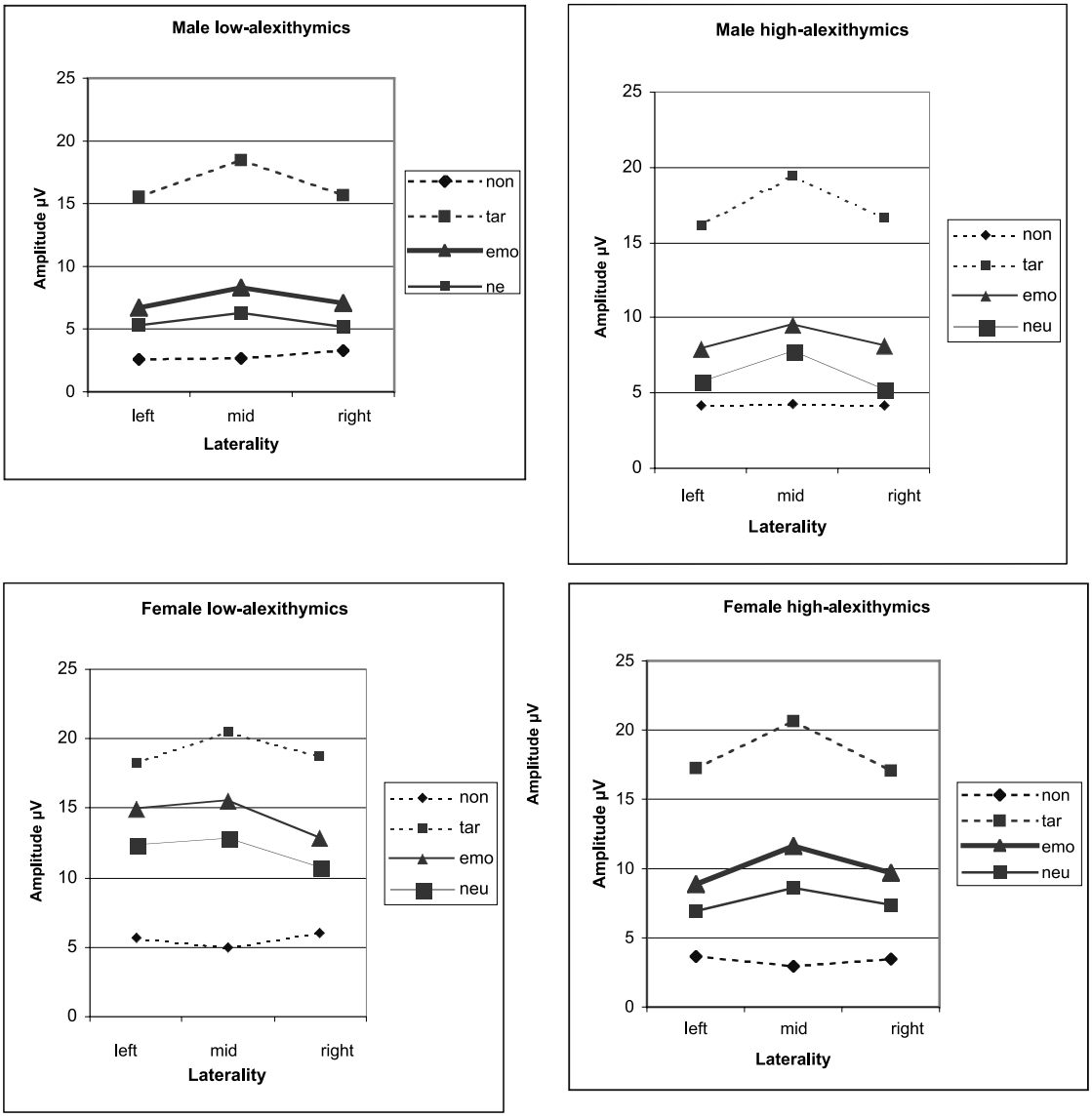

Figure 3
Lateralisation: average P300 amplitudes at left, midline and right electrodes.

right hemisphere is most important. The idea of the greater importance of the left hemisphere in females fits with recent results indicating that, for the processing of emotional information, the left hemisphere is more important in females, whereas the right hemisphere is more important in males. Reviewing the relevant literature, Cahill (2005) presents data demonstrating that (non-alexithymic) women show, in reaction to emotional stimuli, more activation in the left amygdala, and left hemisphere (among which higher P300 amplitudes), compared with the right hemisphere and amygdala, whereas the reverse holds for males. The recent study by Gasbarri et al. (2007) confirmed the idea that the P300 amplitude in women is larger over the left hemisphere compared with the right hemisphere. This fits perfectly with the results of our study, concerning low-alexithymic women, whereas our findings concerning high-alexithymic women are in conflict with these results. Our results, therefore, suggest that at least in some alexithymic women the left hemisphere is malfunctioning. They therefore process information in both hemispheres more equally.

This could also explain our results demonstrating the lower P300 amplitudes in high-alexithymic females when compared with low-alexithymic females. The idea that, compared with the right hemisphere, the left hemisphere is far more involved in cognitive analytical processes is generally accepted. Gazzaniga (1995) even concludes that the human inferential system is limited to the left hemisphere, and he states: 'The left hemisphere, on the other hand, is constantly, almost reflexively, labelling experiences, making inferences as to cause, and carrying out a host of other cognitive activities.' Thus since, in contradistinction to males, reduced left hemisphere function can be the basis of alexithymia in females it is conceivable that female alexithymics activate, in comparison with non-

alexithymic women, less (left hemisphere) cognitive modules while processing emotional information, resulting in lower overall P300 amplitudes.

Our results for women-only are in line with Heijman (1998). She studied the P300 in 12 alexithymics (5 females and 7 males) and 11 controls (10 females and 1 male). Her results indicated that alexithymics show lower P300 amplitudes. However, Heijman's results could be due to the fact that the percentage of females in her control group (90%) was much higher than in her alexithymia group (42%), as our results demonstrated that females in general show higher P300 amplitudes compared with males.

Our results for males-only are in line with the results of Franz et al. (2004), who studied the P300 in 20 alexithymics and 20 controls and present results indicating higher P300s in alexithymic subjects. However, our results regarding females-only are clearly contradictory to those of Franz et al. (2004). Broadly speaking, the methodologies of the two studies mentioned are comparable; however, they deviate in three important respects. 1) Franz et al. selected their subjects with the aid of the German version of the TAS-20. Although this scale measures the cognitive component (reduced capacity for verbalising, identifying and analysing emotions) correctly, it ignores the affective alexithymia component (emotionalising and fantasising) completely (Bagby, Parker & Taylor, 1994; Vorst & Bermond, 2001). Thus, in the two studies, subjects were selected for alexithymia in qualitatively different ways. 2) Franz et al. selected their low-alexithymic subjects by scores below the 33rd percentile, while their high-alexithymic group consisted of subjects scoring the above 66th percentile. In our study, scores above the 85th percentile selected high-alexithymics, and scores below the 15th percentile of the population selected low-alexithymics. In other words, selection criteria were far more stringent in our study. Although both 1) and 2) could possibly provide explanations for the difference in results regarding females, the third difference in methodology could be more important. 3) The alexithymia group as well as the control group in the study by Franz et al. were balanced for gender, and probably for this reason these authors did not include gender as a variable into the statistical analyses, which could have masked possible gender effects.

As stated in the section methods, the IAPS pictures are not well controlled for physical properties, such as luminance. This could have influenced the P300 amplitudes. Thus, it is possible that the overall higher P300 amplitudes in response to emotional compared with neutral stimuli could be the result of the physical properties of the pictures used. However, since our results concerning alexithymia and P300 amplitudes are overall effects (not emotion specific) this possibility is not a problem in the interpretation of these results.

It is evident that, due to dividing the groups into males and females, our results are based upon small samples. Furthermore we did not measure handedness; thus, it remains possible that there were more right-handed low-alexithymic women than high-alexithymic women, which, if so, could also explain the laterality effect demonstrated. For both reasons replication is necessary.

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