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Normalization of P300 Amplitude following Treatment in Dysthymia

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Introduction

Studies in major depression have revealed "state" dependent smaller amplitude of P300 event related potential (ERP) (Blackwood et al 1987; Gangadhar et al 1993). Whether it is true in dysthymia remains untested. In the study by Shagass et al (1985), neurotic patients were vaguely assumed to have a dysthymic disorder and the study included evoked potentials but not cognitive ERPs. Giese-Davis and Miller (1987) studied mismatched negativity in dysthymics (DYs), whereas Yee and Miller (1988) studied the emotional information processing with respect to modulation of fear, and did not address the P300 ERP abnormalities *per se* in DYs. Likewise, Yee et al (1992) have studied in DYs ERP components earlier to P300. Bruder et al (1995) found reduced amplitude and hemispheric asymmetry of P300, using dichotic complex tone test, in 44 depressives (five DYs dysthymics). In the present study we compared the P300 ERP in DYs, depressives with melancholic features (DMs), normal controls, and included a follow-up to examine if P300 abnormalities persist upon improvement.

Methods

The DY group consisted of 15 adult (18–50 years of age, mean ± SD = 30.6 ± 9.9 years) outpatients (eight men), with DY confirmed on international classification of diseases (ICD) 10 Diagnostic Criteria for Research checklist (WHO 1992). They had to be without any other psychiatric disorder (especially major depressive disorder), with at least 7 years of schooling, and not on any psychotropic medications during the last 1 month. There were two control groups: (1) 15 patients (mean: ± SD age = 35.7 ± 9.8 years; six men) having a depressive episode with somatic symptoms (DM), confirmed as above and meeting other recruitment criteria as in the DY group; (2) 15 normal controls matched for age (mean: ± SD = 30.8 ± 5.6 years) and sex (eight men) to the DY group, who never had any psychiatric disorder and scored less than 2 on General Health Questionnaire (GHQ 12) (Goldberg 1972).

All in the DY group and nine in the DM group were taught Sudarshana Kriya Yoga (SKY) (Yoga research group 1995), which they practiced as their sole treatment as part of an open trial. SKY treatment, found to be effective, consisted of daily practice of three successive components of specified rhythms of breathing for about ½ hour and continued for 3 months. In the DM group, six patients received electroconvulsive therapy (ECT) or antidepressants. Hamilton Rating Scale for Depression (HRSD) Hamilton 1960, Beck's Depression Inventory (BDI) (Beck et al 1961), and Clinical Global Impression scales (CGI) (Guy 1976) were administered before the first P300 recording and at 1 and 3 months.

P300 Event Related Potential Recording

Auditory oddball P300 ERP was recorded as detailed elsewhere (Jyoti Rao et al 1995). There was however, one difference; when there were two identifiable peaks in the P300 latency range (in eight recordings), the later peak was chosen for measurements. P300 ERP recording was done in a sound attenuated room from 1200–1600 hours (after lunch) using Neuropack-8 (Nihon

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Table 1. Mean (SD) HRSD, BDI, and CGI Severity Total Scores at Pretreatment, 1 month, and 3 months

HRSD score	Pretreatment	1 month	3 months	RM ANOVA
Dysthymics	12.27 (3.15)	5.6 (3.14)	3.73 (2.58)	$F = 61.1$, df 2,28, $p < 0.001$
Depressives	24.60 (6.3)	7.20 (7.25)	4.93 (5.68)	$F = 91.9$, df 2,28, $p < 0.001$
BDI score	**Pretreatment**	**1 month**	**3 months**	**RM ANOVA**
Dysthymics	27.53 (11.31)	13.93 (9.31)	8.07 (7.61)	$F = 57$, df 2,28, $p < 0.001$
Depressives	40.27 (9)	18.53 (17.18)	12.47 (15.35)	$F = 32.1$, df 2,28, $p < 0.001$
CGI Severity	**Pretreatment**	**1 month**	**3 months**	**RM ANOVA**
Dysthymics	3.1 (0.3)	2.1 (0.6)	1.3 (0.5)	$F = 69.2$, df 2,28, $p < 0.001$
Depressives	4.7 (0.9)	2.1 (1.2)	1.5 (0.9)	$F = 81.5$, df 2,28, $p < 0.001$

[a]The dysthymics had smaller scores than depressives on HRSD ($t = 6.8$, $p < 0.001$), BDI ($t = 3.4$, $p < 0.01$), and CGI ($t = 6.5$, $p < 0.001$).

Kohden). Stimuli consisted of pure tones of 50 mseconds duration presented once every 2 seconds binaurally at a level not causing discomfort, but clearly audible (about 30 dB above subject's threshold). The frequency of target tones was 1.5 KHz and nontarget 1 KHz. The target and nontarget ratio was 1:4 and the order of the former was pseudorandom. Subjects identified the target by depressing a counter switch. A practice session of about 10 minutes was allowed to "train" the subjects to identify correctly 80% or more of the targets. This was followed by two test sessions with an interval of 10 minutes. Subjects identified 80% or more targets correctly in both sessions. Electroencephalogram (EEG) was recorded from F_z, C_z, P_z sites referenced to linked mastoids and electroculography (EOG) from right infraorbital and outer canthus. The electrode impedence was less than 10 KΩ. EEG was amplified from 0.5–30 Hz with a 50 Hz notch filter. Artifact rejection switch was enabled during the recording. The averager rejected epochs having EEG amplitude exceeding 75 μV in any of the channels. EEG epochs of 700 mseconds following the tone were collected for averaging. Thirty epochs each following the target and the preceding nontarget tones were averaged in each test session. An average of these two sessions was obtained for waveform analysis. P300 was identified as a positive wave occurring from 250–600 mseconds following target tone, with larger amplitude in central or parietal leads than frontal, not detectable in the average following nontarget tone, and with no waveform of similar latency occurring on the EOG channel with target tone. The latency (msecond) was measured by moving the cursor to the peak of the P300. The amplitude (μV) was measured from a superimposed isoelectric line. All measurements were obtained only for the C_z recording channel. Patients (DY and DM groups) were tested three times, before treatment, at 1 month, and 3 months. P300 was recorded only once in the normal control group. The measurements were obtained from coded ERPs without knowledge of clinical details.

Results

The mean HRSD, BDI, and CGI severity scores were significantly higher in the DM group than in the DY group initially, but decreased significantly at 1 and 3 months in both groups (Table 1). The mean P300 amplitudes but not latencies, of both the patient groups were significantly smaller than the normal controls (Table 2). In the patients ($n = 30$), pretreatment P300 amplitude did not correlate with total HRSD scores (Pearson's

Table 2. Mean (SD) P300 Amplitudes (μV) and Latencies (msec) at Pretreatment, 1 month, and 3 months

P300 Amplitude (μV)	Dysthymics	Depressives	Normals[a]	ANOVA
Pretreatment	8.1 (4.5)	6.8 (3.6)	14.4 (3.9)	$F = 15.3$, df 2,42, $p < 0.01$[b]
1 month	10.7 (5.0)	10.0 (4.2)	14.4 (3.9)	$F = 4.3$, df 2,42, $p < 0.02$[b]
3 months	14.7 (4.8)	14.3 (5.2)	14.4 (3.9)	$F = 0.4$, df 2,42, $p = .96$
2 Way RM ANOVA (DY versus DM): group F = 0.3, df 1,28, $p = 0.6$; session F = 44.3, df 2,56, $p < 0.01$;[b] group × session F = 0.14, df 2,56, p = 0.9				
P300 Latency (msec)	**Dysthymics**	**Depressives**	**Normals[a]**	**ANOVA**
Pretreatment	353.1 (38.9)	357.3 (27.2)	344.1 (29.8)	$F = 0.6$, df 2,42, p = 0.5
1 month	351.1 (20.7)	348 (28.8)	344.1 (29.8)	$F = 0.3$, df 2,42, p = 0.8
3 months	338.5 (22.2)	340.2 (32)	344.1 (29.8)	$F = 0.2$, df 2,42, p = 0.9
2 Way RM ANOVA (DY versus DM): group F = 0.14, df 1,28, $p = 0.7$; session F = 2.6, df 2,56, $p = 0.08$; group × session F = 0.64, df 2,56, $p = 0.5$.				

[a]Normals were tested only once but the same values were used for ANOVA at 1 and 3 months.
[b]Significant.

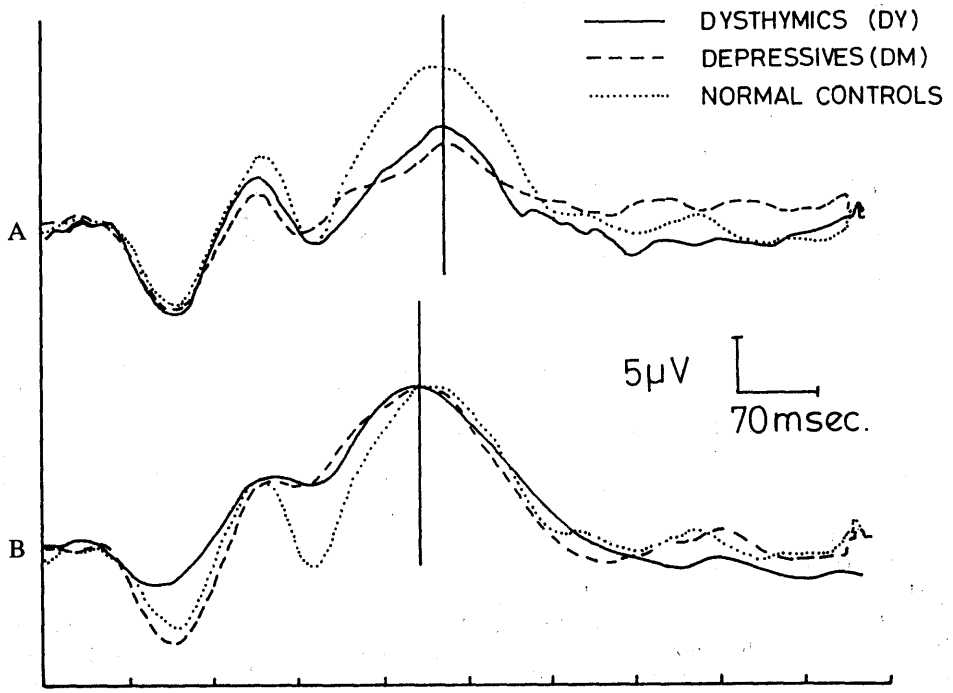

Figure 1. Grand average P300 ERP records pretreatment (*A*) and at 3rd month (*B*) (normals had one recording, the same is given in both).

$r = -0.07$, $p > 0.2$). The P300 amplitudes of both the patient groups increased comparably at 1 and 3 months with the symptomatic improvement and were comparable with the normals at 3 months (Table 2, Figure 1).

Discussion

Several safeguards were taken against the known confounding factors. Patients were studied for 3 months to ensure stable improvement (asymptomatic for more than 2 months). Bipolars were avoided to ensure homogeneity of the sample in the DM group. Subjects older than 50 years were excluded to avoid age-related confounding factors. Only literates were chosen to exclude people who may have mental subnormality. Subjects on psychotropic medications were excluded and none smoked. To avoid seasonal effects, the controls were tested in the same month as the patient's initial recording. The P300 ERP recording procedure was designed to overcome several methodologic problems identified in the earlier studies (Polich 1992).

In the present study, the smaller P300 amplitudes in the DY group was comparable with the previous studies that used the same P300 paradigm in major depression (Blackwood et al 1987; Gangadhar et al 1993). The mean: ± SD years of formal education in the control group (15.8 ± 4.4) was significantly higher than in both the patient groups (DY = 8.7 ± 3.2; DM = 9.3 ± 3.8). This is unlikely to have contributed to smaller P300 amplitude, as at recovery the DY groups had P300 amplitudes comparable to normals. This study also confirmed earlier findings that P300 amplitude normalizes with clinical recovery in major depression (Blackwood et al 1987; Gangadhar et al 1993). Since normalization in DY occurred similar to that in DM, smaller P300 amplitude in depressed patients may be a nonspecific indicator of mood state unrelated to diagnosis. Absence of differences either in P300 latency within or across groups is in keeping with other published literature (Blackwood et al 1987; Gangadhar et al 1993).

Conclusions

In summary, the pretreatment P300 amplitude in the DY group was significantly lower than in the normal control group but did not differ from the DM group. The P300 amplitude increased with the symptomatic improvement of DY and normalized at 3 months, as was the case in the DM group. There was no significant difference in P300 latency either among the three groups or across the occasions.

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References

Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J (1961): An inventory for measuring depression. *Arch Gen Psychiatry* 4:561–571.

Bruder GE, Tenke CE, Stewart JW, Towey JP, Leite P, Voglmaier M, Quitkin FM (1995): Brain event-related potentials to complex tones in depressed patients: relation to perceptual asymmetry and clinical features. *Psychophysiology* 32:373–381.

Blackwood DHR, Whalley LJ, Christie JE, Blackburn IM, St Clair DM, McInnes A (1987): Changes in auditory P3 event related potential in schizophrenia and depression. *Br J Psychiatry* 150:154–160.

Gangadhar BN, Ancy J, Janakiramaiah N, Umapathy C (1993): P300 amplitude in non-bipolar, melancholic depression. *J Affective Dis* 28:57–60.

Giese-Davis J, Miller GA (1987): Stimulus mismatch effects on anhedonia and dysthymia (abstract). *Psychophysiology* 24:2: 590.

Goldberg DP (1972): *The Detection of Psychiatric Illness by Questionnaire.* Maudsley Monograph No. 21. London: Oxford University Press.

Guy W (1976): *ECDEU Assessment Manual for Psychopharmacology.* Rockville: NIMH, pp 217–222.

Hamilton M (1960): A rating scale for depression. *J Neurol Neurosurg Psychiatry* 23:56–62.

Jyoti Rao KM, Ananthanarayanan CV, Gangadhar BN, Janakiramaiah N (1995): Smaller auditory P300 amplitude in schizophrenics in remission. *Neuropsychobiology* 32:171–174.

Polich J (1992): On the clinical application of P300 (editorial). *Biol Psychiatry* 31:647–649.

Shagass C, Roemer RA, Straumanis JJ, Josiassen RC (1985): Combinations of evoked potential amplitude measurements in relation to psychiatric diagnosis. *Biol Psychiatry* 20:701–722.

World Health Organization (1992):ICD-10: *Classification of Mental and Behavioural Disorders.* Geneva: Diagnostic Criteria for Research.

Yee CM, Miller GA (1988): Emotional information processing—modulation of fear in normal and dysthymic subjects. *J Abnorm Psychol* 97:54–63.

Yee CM, Deldin PJ, Miller GA (1992): Early stimulus processing in dysthymia and anhedonia. *J Abnorm Psychol* 101:230–233.

Yoga research group (1995): *Treating Depression with Sudarshana Kriya Yoga* (video cassette). Bangalore: NIMHANS.