ERPs During Tonal and Phonetic Oddball Tasks in Patients Having Depressive and Anxiety Disorders

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Abstract

Differences have been reported between depressed patients with versus without an anxiety disorder in EEG alpha asymmetry and dichotic listening. The present study assessed the effects of having a depressive disorder, an anxiety disorder, or comorbidity of both disorders on ERPs recorded from 30 sites during oddball tasks using binaurally presented complex tones or syllables. ERPs of four groups were compared: (1) patients having a "pure" depressive disorder (n=58); (2) patients having an anxiety disorder alone (n=22); patients having comorbidity of these disorders (n=18); and (4) healthy controls (n=49). A principal components analysis with unscaled Varimax rotation derived five previously identified components: N1 (N100), N2 (N215), early P3 (P315), late P3 (P400) and a late positive slow wave. Early P3 was significantly smaller in depressed patients compared to non-depressed subjects. However, patients having comorbidity of depressive and anxiety disorders had a larger late P3 than the other groups. Task-dependent hemispheric asymmetries for N2 and P3 potentials replicated our prior findings (Kayser et al., 1998),i.e. larger ERP components of the N2-P3 complex over right frontocentral regions for tones and over left temporoparietal regions for syllables. There were no differences in these task-dependent asymmetries among groups. To the extent that N2 and P3 asymmetries in the tonal and phonetic oddball tasks reflect differential involvement in pitch (right frontotemporal) and phoneme (left temporoparietal) discrimination, these do not appear to differ in depressed patients, with or without an anxiety disorder, and healthy controls.

Introduction

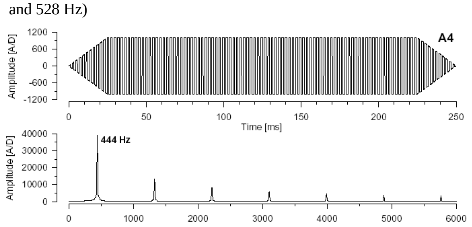
- Behavioral and electophysiologic studies have found evidence that anxiety disorders are associated with reduced left and greater right hemispheric activation (Davidson et al., 2000; Heller et al., 1995; Wiedemann et al., 1999).
- Depressed patients having comorbidity with an anxiety disorder showed EEG alpha asymmetry indicative of greater activation over right than left parietal sites, whereas patients having a "pure" major depression showed the opposite asymmetry (Bruder et al., 1997).
- This study examined the effects of having an anxiety disorder alone, a depressive disorder alone or comorbidity of these disorders on ERPs recorded during phonetic and tonal oddball tasks, which were previously shown to yield task-related asymmetries of N2 and P3 components (Kayser et al., 1998) .

Participants

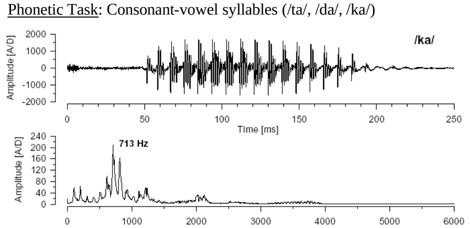
- Participants in four groups were assessed as part of the 2 X 2 factorial design: (1) 58 patients having a depressive disorder alone; (2) 22 patients having an anxiety disorder alone; (2) 18 patients having comorbidity of these disorders; (3) 49 controls without either disorder.
- Depressed patients met DSM-IV criteria for major depressive disorder or dysthymia and patients having anxiety disorders met DSM-IV criteria for panic disorder, social phobia, generalized anxiety disorder or obsessive-compulsive disorder.
- All participants were right-handed (Edinburgh Handedness Inventory) and were without hearing loss or neurological disorder.

Tonal and Phonetic Oddball Tasks

- ERPs were measured to binaural stimuli in two oddball tasks with 60 targets (20%) and 240 standards (80%).
- Tonal Task: Complex tones (fundamental frequencies between 264 Hz and 528 Hz)



- Phonetic Task: Consonant-vowel syllables (/ta/, /da/, /ka/)



- Subjects responded to infrequent targets as quickly as possible with a button press. Response hand was counterbalanced within subjects.

Data Analysis

- ERPs were computed for each task (tonal/phonetic), condition (target/nontarget), and response hand (left/right), and submitted to an *unrestricted* principal components analysis (PCA) derived from the covariance matrix, followed by *unscaled* Varimax rotation (Kayser & Tenke, 2000), using an expanded data set (N=157; see poster #47).
- PCA factor scores were submitted to a repeated measures ANOVA for targets only:

Between-Group Factors	Within -Subjects Factors
Depressive Disorder (yes/no)	Task (tonal/phonetic)
Anxiety Disorder (yes/no)	Site (13 symmetric electrode pairs)
Gender (female/male)	Hemisphere (right/left)
	Response Hand (right/left)

PCA Factor Loadings

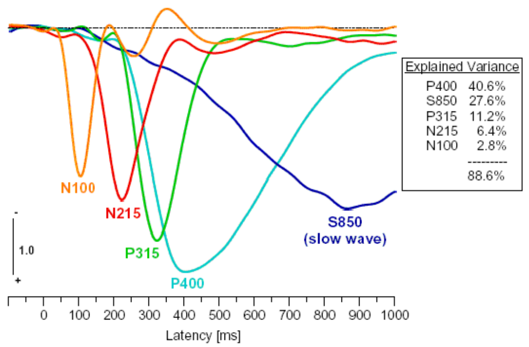


Figure 1. Varimax rotated (unscaled) factor loadings plotted over time for six orthogonal factors extracted by covariance-based principal components analysis (PCA). Factor labels were chosen to reflect both the time course of the factor loadings and the polarity of the associated ERP component. PCA factors may be interpreted as a measure of weighted time window amplitude. Note that the percentage of explained variance largely depends on the time period and the number of electrode locations covered by a factor.

Targets at Cz

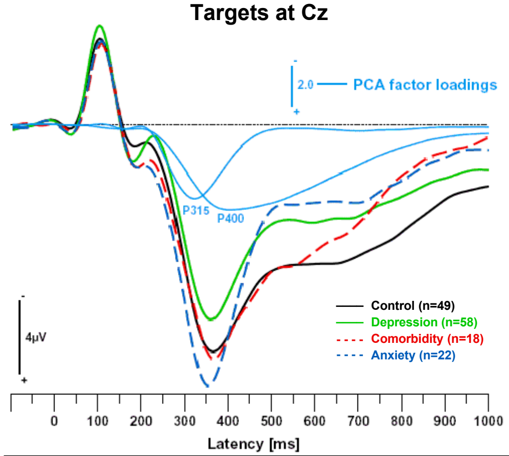


Figure 3. Grand average event-related potential (ERP) waveforms at electrode site Cz (vertex) for **58 patients** having a **depressive disorder alone**, **22 patients** having **anxiety disorder alone**, **18 patients** having **comorbidity of both disorders**, and **49 healthy control adults** (averaged across task, response hand, and gender). PCA factor loadings indicate that factor P315 captures the early portion of the P3 potential, whereas factor P400 reflects broader P3 activity, primarily after the P3 amplitude peak. Note that P3 amplitude is reduced in **patients** having a **depressive disorder alone**, but enhanced in **patients** having an **anxiety disorder alone**.

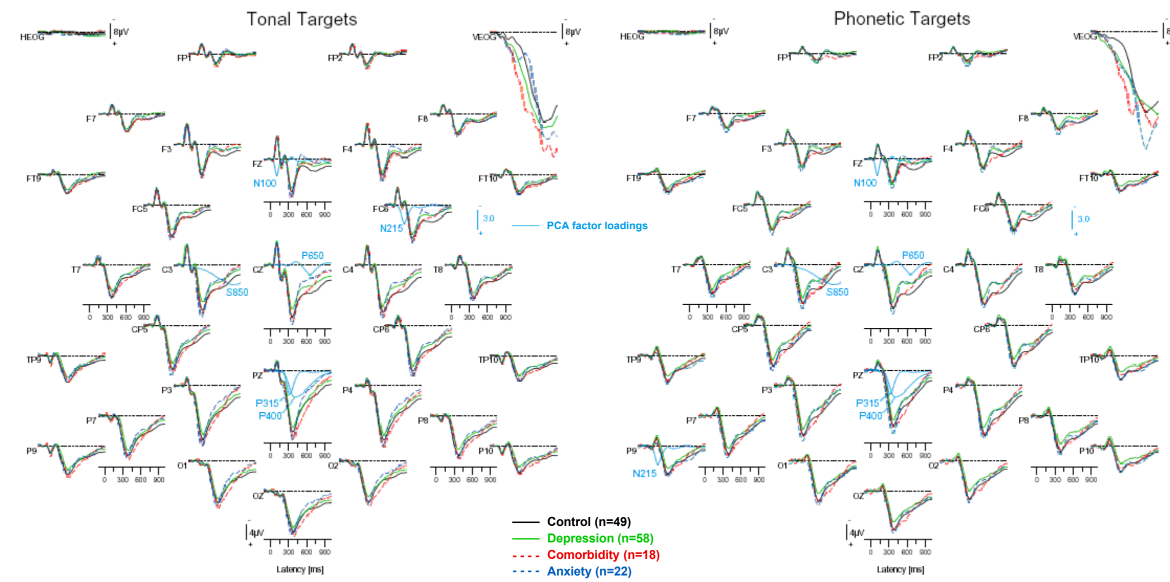


Figure 2. Grand average event-related potential (ERP) waveforms at all 30 recording sites for tonal and phonetic target stimuli, comparing **58 patients** having a **depressive disorder alone**, **22 patients** having **anxiety disorder alone**, **18 patients** having **comorbidity of both disorders**, and **49 healthy control adults** (averaged across response hand and gender). Distinct ERP components closely corresponded to the extracted PCA factors, as is evident from the time course of the PCA factor loadings shown at selected sites. Horizontal (HEOG) and vertical (VEOG) electrooculograms are shown at a smaller scale before eye blink correction.

Topographies of P3 Amplitude

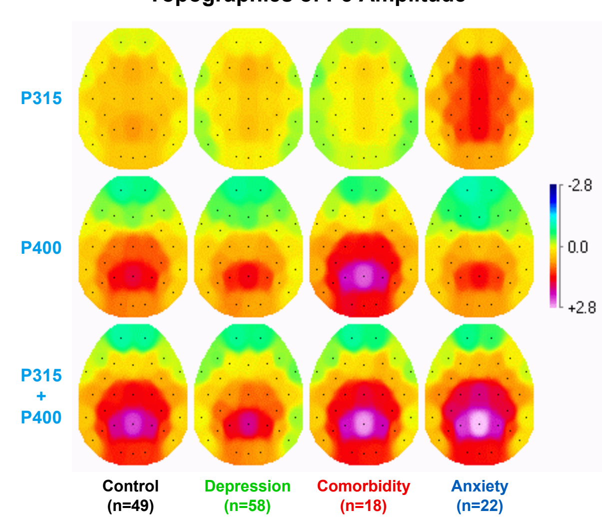


Figure 4. Topographies of PCA factor scores at 30 electrode sites (top view, nose upwards) corresponding to early (Factor P315) and late (Factor P400) P3, and the sum of both P3 factors (i.e., P315-plus-P400), comparing the four groups included under study (averaged across task, response hand, and gender). The factor scores (i.e., the weights of each PCA component) reflect the removal of the grand mean ERP waveform for a covariance-based PCA. Note that P315 amplitude is reduced in depressed patients but increased in patients having an anxiety disorder alone. Also, P400 amplitude is increased in the comorbid patients.

Topographies of N2/P3 Amplitude

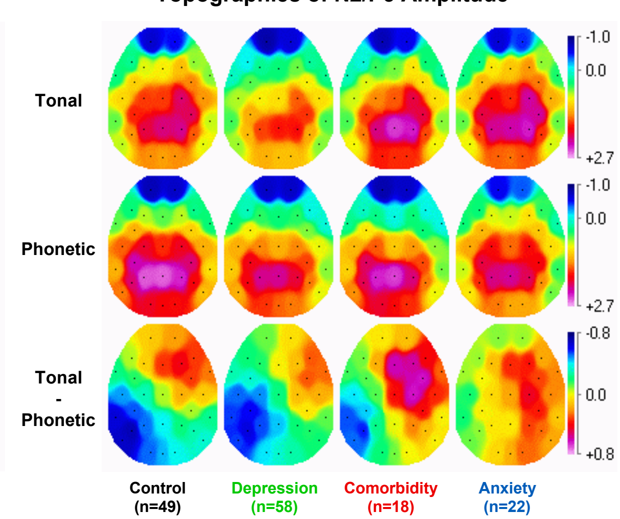


Figure 5. Topographies of N2/P3 amplitude (differences of PCA factor scores, i.e., P315 + P400 – N215) for each group (averaged across gender and response hand). Maps were calculated for tonal and phonetic target stimuli, and for the corresponding tonal-minus-phonetic differences. Note on the bottom row, the relatively greater N2/P3 amplitude over left hemisphere regions in the phonetic task (blue-green regions) was largest for the depressed only group and smallest for the anxiety only group.

ERP Recording

- ERPs recorded from 4 midline and 26 homologous scalp placements using an electrode cap and a nose reference
- EEG data were collected in two different laboratories with different acquisition settings [.01-30 Hz band pass (-6dB/octave), 100 samples/sec, *versus* .1-30 Hz band pass (-6dB/octave), 200 samples/sec]. Parameters were digitally equated off-line (1,280 ms epochs at 200 samples/sec via spline interpolation, 200 ms pre-stimulus baseline). Differences in data acquisition were not related to any of the reported findings.
- ERP averages low pass filtered at 12.5 Hz (-24dB/octave)
- Horizontal and vertical EOGs (bipolar)
- EEG and horizontal EOG data artifacted at ±100 µV after blink correction (linear regression)

Main Findings

- Early P3 (P315) was smaller in depressed subjects when compared to non-depressed subjects, i.e., healthy adults and patients having anxiety disorders alone, $F_{[1,139]}=10.1$, $p=.002$ (see Figures 3 and 4).
- Late P3 (P400) was *larger* in patients having comorbidity of anxiety and depressive disorders when compared to patients having either disorder alone or healthy controls (see Figure 4). This is supported by a Depressive x Anxiety Disorder interaction, $F_{[1,139]}=8.50$, $p=.004$.
- Task-dependent hemispheric asymmetries of the N2/P3 complex for subjects having a depressive disorder differed from those for non-depressed subjects, as indicated by a Depressive Disorder x Task x Hemisphere interaction, $F_{[1,139]}=4.23$, $p=.04$. This difference reflects the greater hemispheric asymmetry for depressed subjects than non-depressed subjects in the phonetic task, but not in the tonal task (see Figure 5).

Summary and Conclusions

- The results showed task-dependent hemispheric asymmetries for the N2-P3 complex, which replicated those in our prior study (Kayser et al., 1998).
- N2/P3 asymmetry in the phonetic oddball task was greater for depressed subjects than non-depressed subjects, which is in accord with prior findings of larger left hemisphere advantage for dichotic words in depressed adolescents and adults (Pine et al., 2000).
- Patients having an anxiety disorder alone had the smallest task-related N2/P3 asymmetries, with little evidence of greater N2/P3 over left parietotemporal sites in a phonetic oddball task.
- There was a difference in P3 subcomponents among groups. The early P3 subcomponent (P315) was smaller in depressed patients when compared to non-depressed subjects. Also, patients having comorbidity of depressive and anxiety disorders had larger late P3 subcomponent (P400) amplitude than the other groups.
- The difference in P3 subcomponents among groups underscores the importance of taking comorbidity with anxiety into account when comparing ERPs of depressed patients and other groups.

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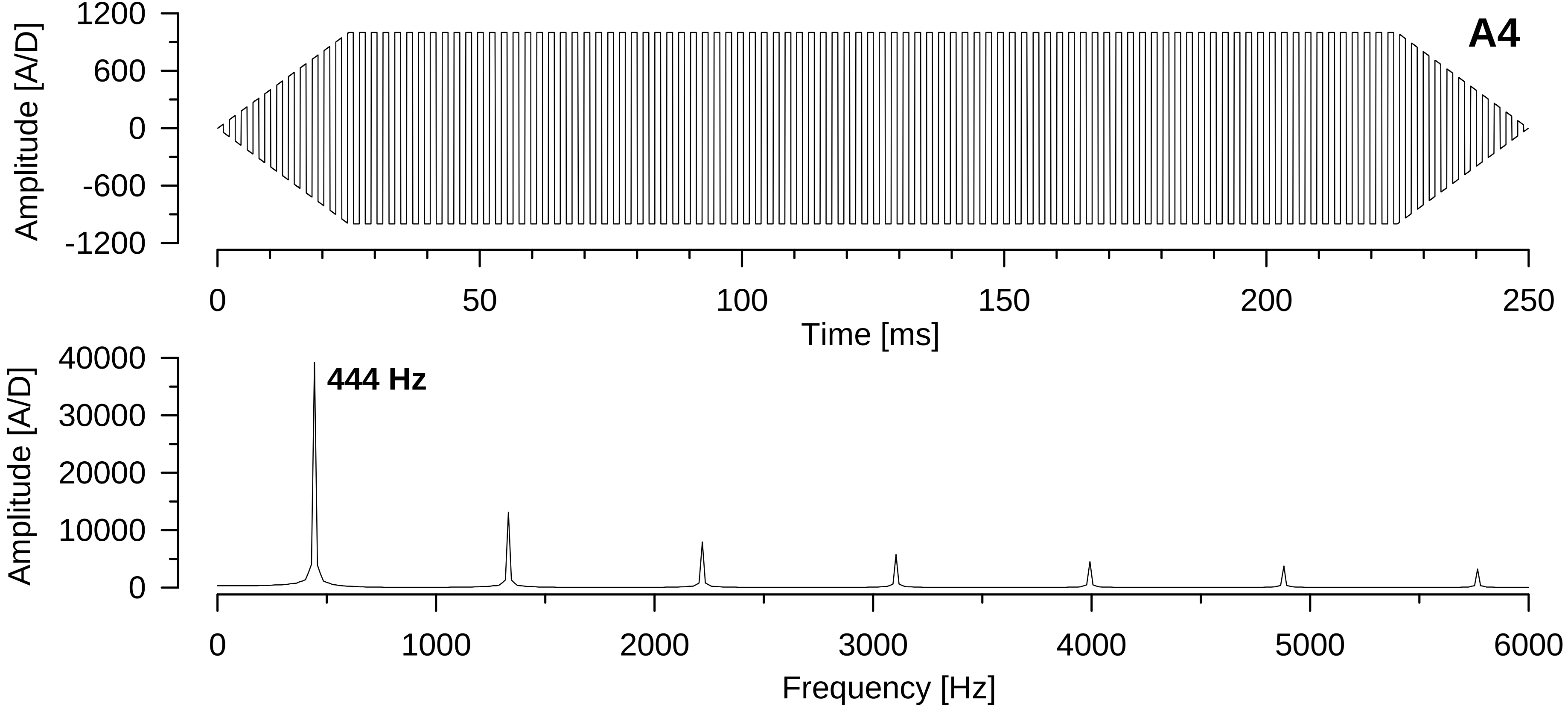
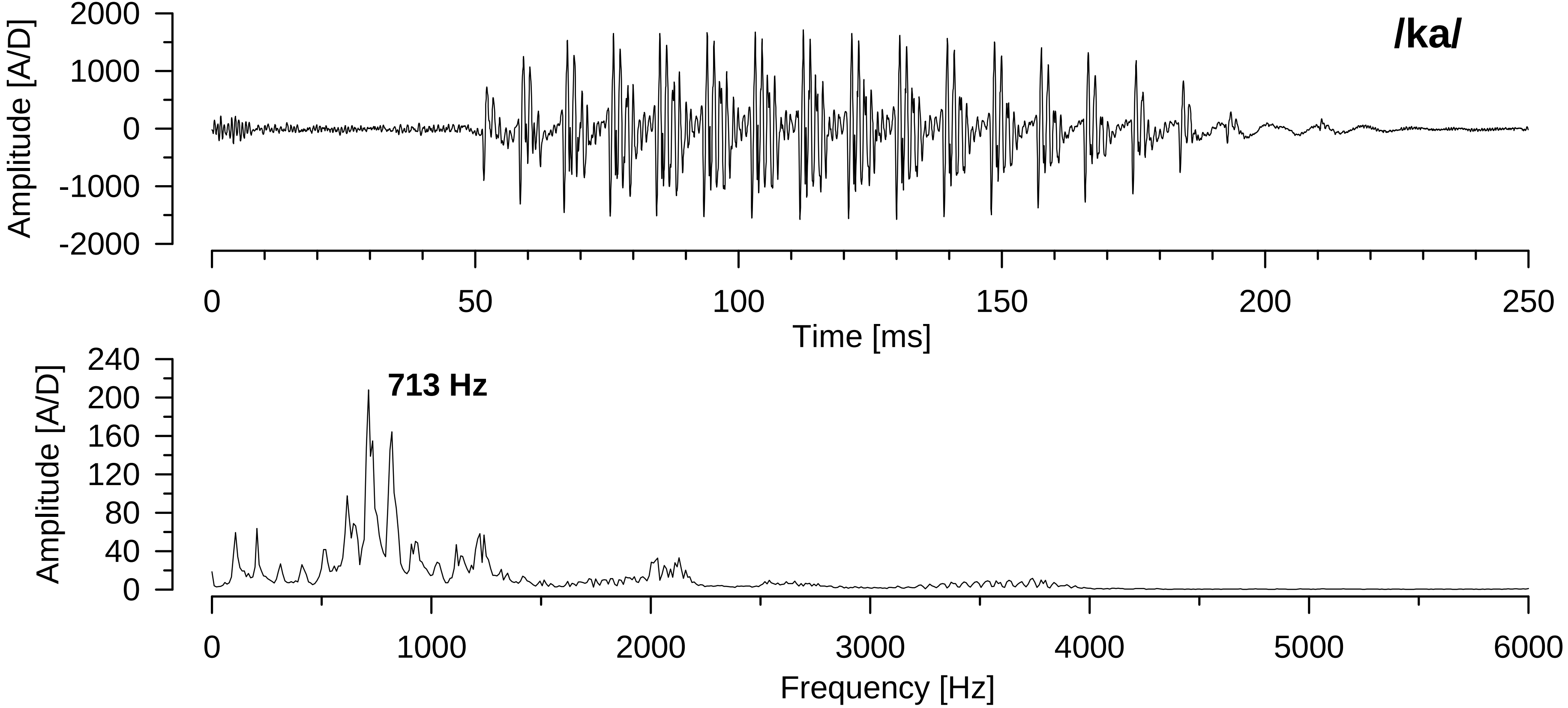

A4
Amplitude [A/D]
1200
600
0
-600
-1200
0
50
100
150
200
250
Time [ms]
444 Hz
Amplitude [A/D]
40000
30000
20000
10000
0
0
1000
2000
3000
4000
5000
6000
Frequency [Hz]



/ka/
Amplitude [A/D]
2000
1000
0
-1000
-2000
0
50
100
150
200
250
Time [ms]
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Amplitude [A/D]
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200
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120
80
40
0
0
1000
2000
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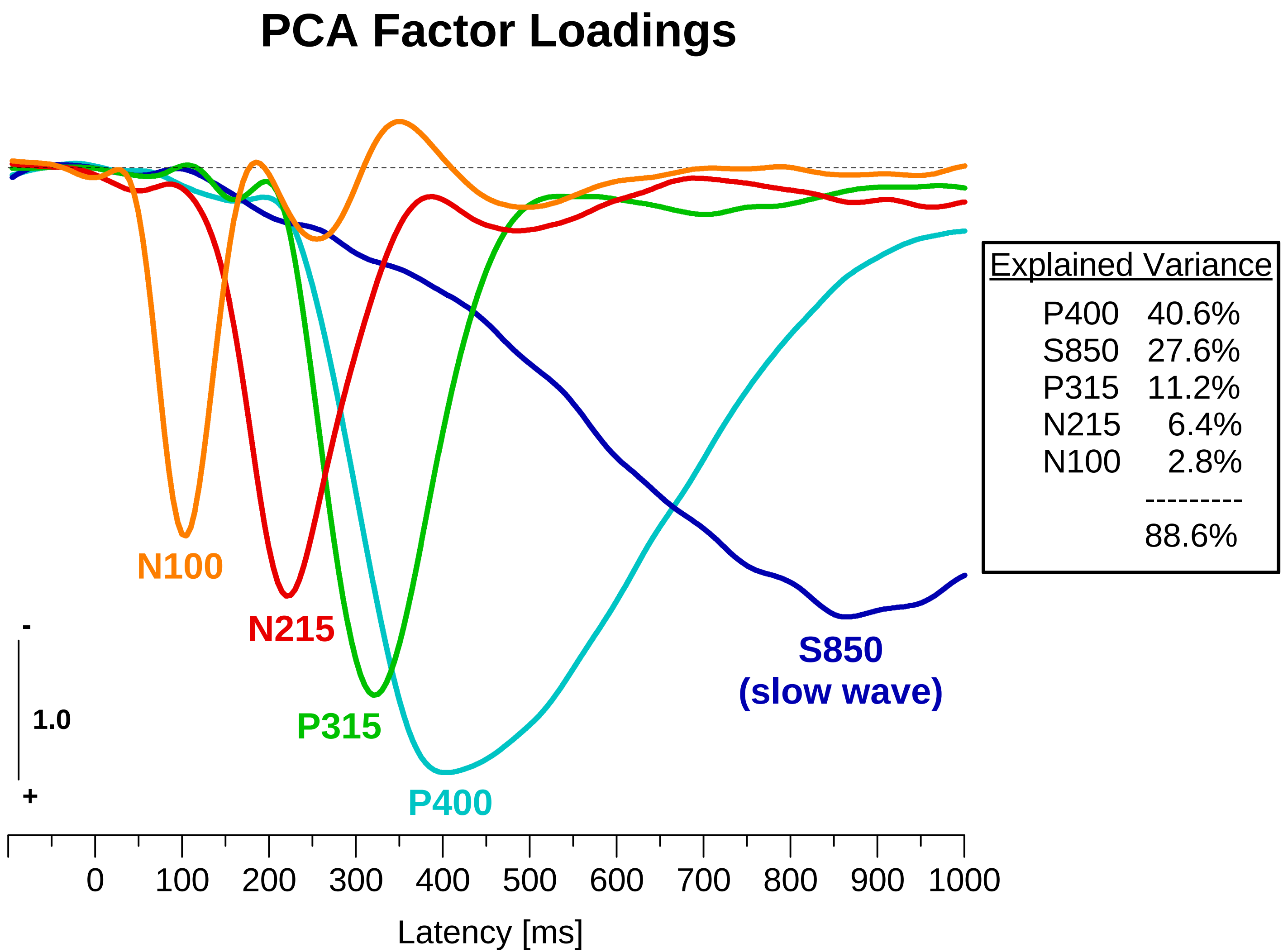
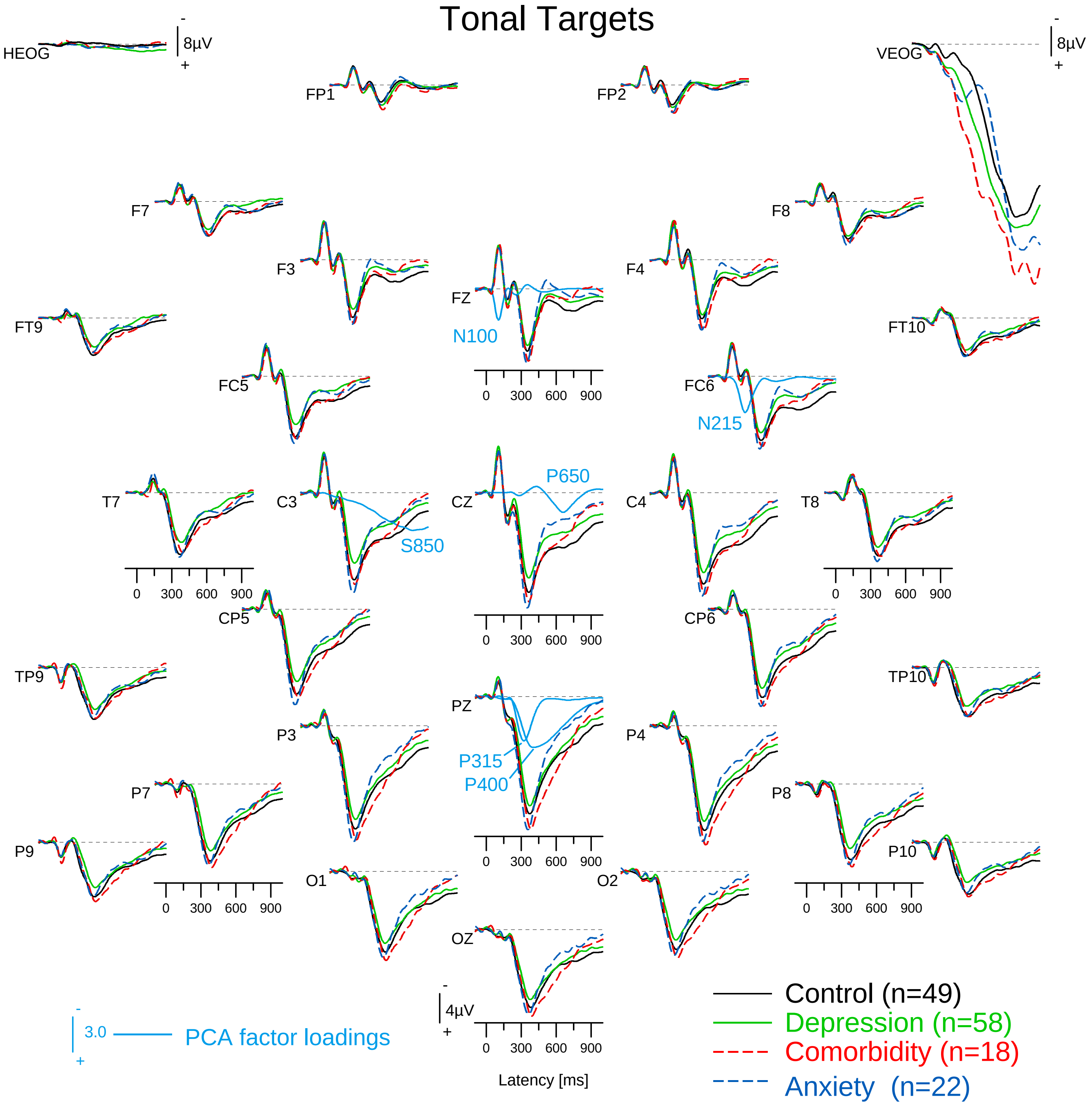
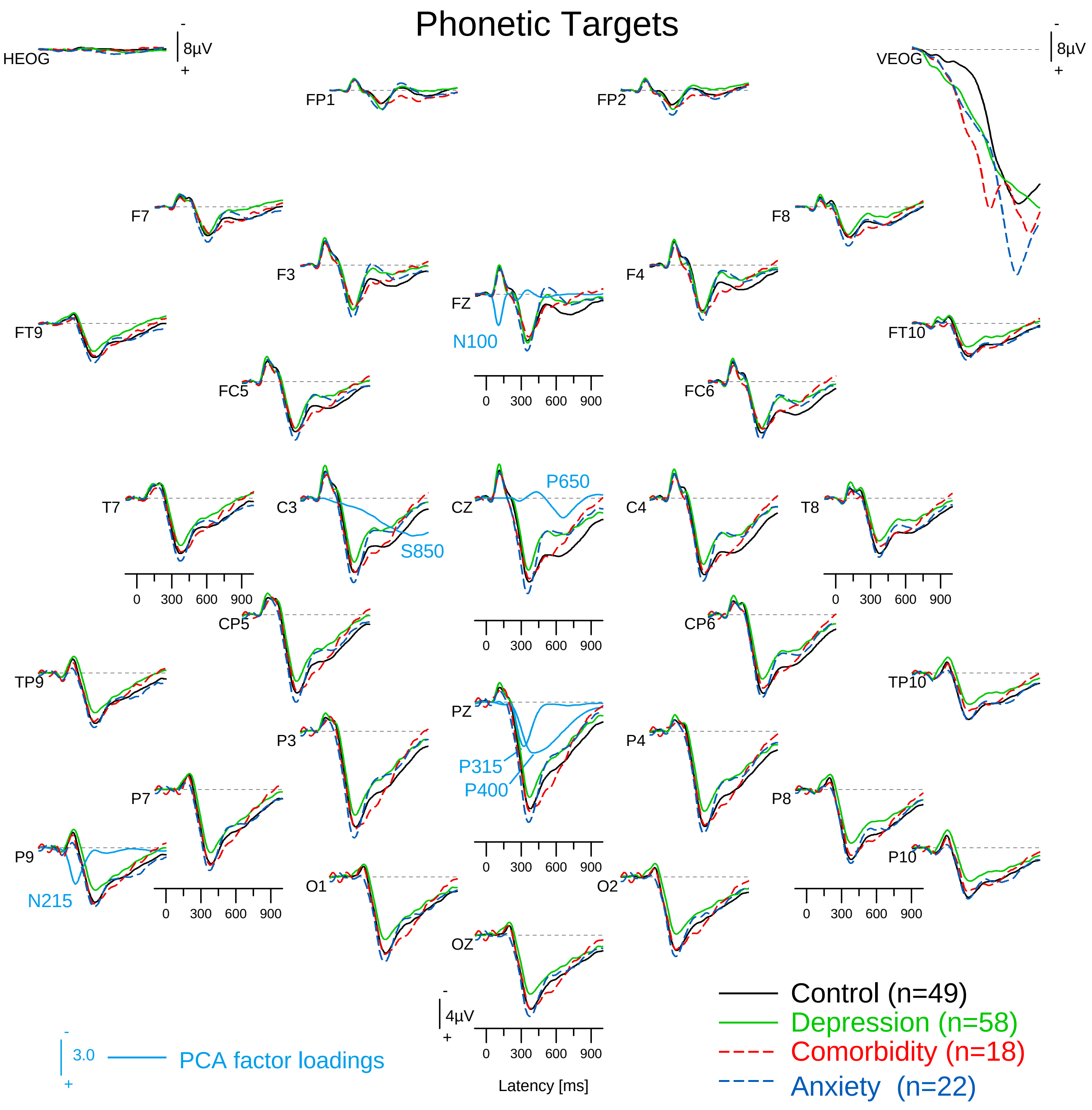
4000
5000
6000
Frequency [Hz]


PCA Factor Loadings
N100
N215
P315
P400
S850
(slow wave)
-
1.0
+
Explained Variance
P400 40.6%
S850 27.6%
P315 11.2%
N215 6.4%
N100 2.8%

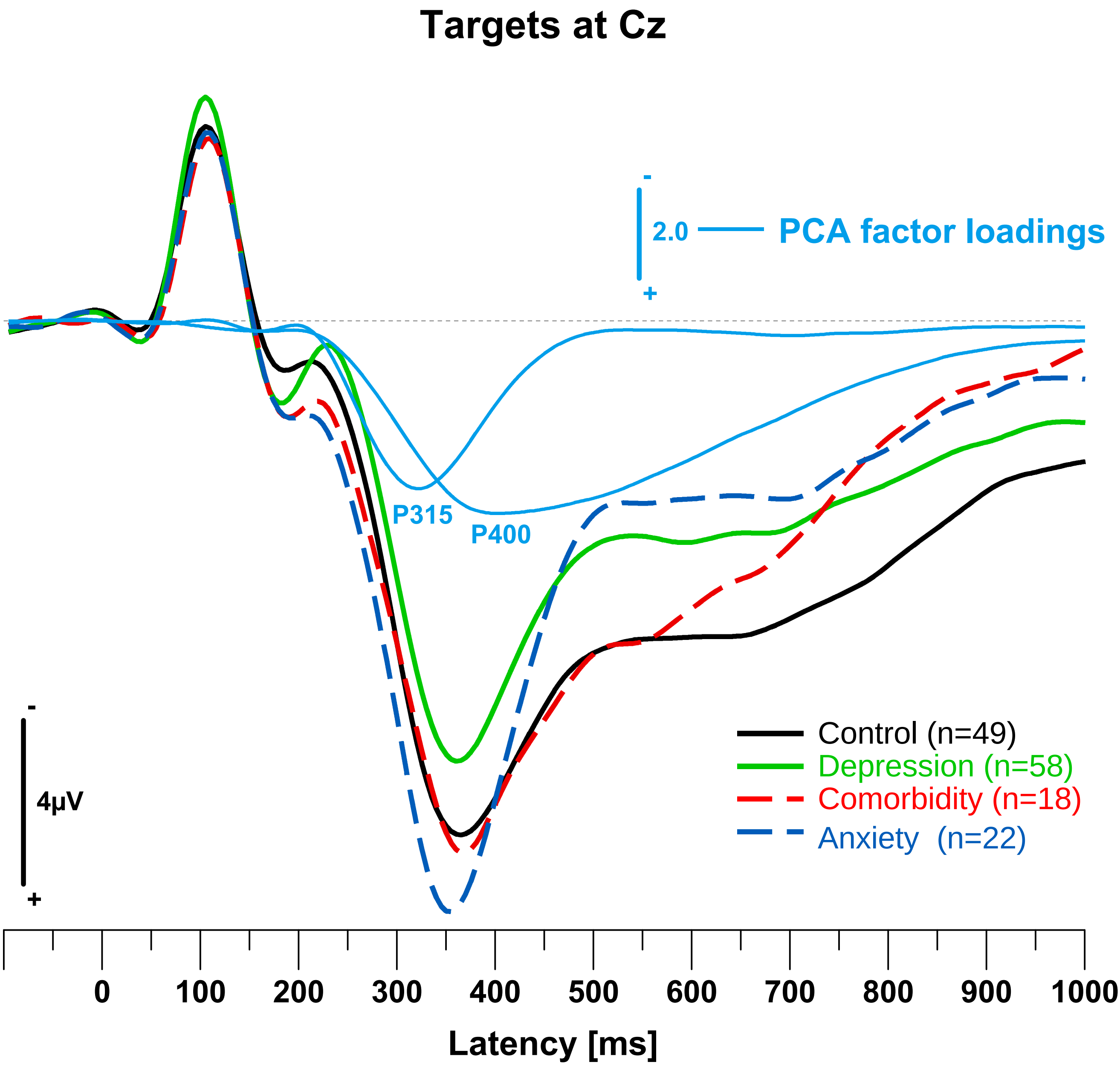
88.6%
0
100
200
300
400
500
600
700
800
900
1000
Latency [ms]



Tonal Targets
HEOG
8µV
VEOG
FP1
FP2
F7
F8
F3
FZ
F4
FT9
FT10
FC5
FC6
T7
C3
CZ
C4
T8
CP5
CP6
TP9
TP10
P3
PZ
P4
P7
P8
P9
P10
O1
OZ
O2
N100
N215
P650
S850
P315
P400
0
300
600
900
4µV
Latency [ms]
3.0
PCA factor loadings
Control (n=49)
Depression (n=58)
Comorbidity (n=18)
Anxiety (n=22)



Phonetic Targets
HEOG
VEOG
8µV
FP1
FP2
F7
F8
F3
FZ
F4
FT9
FT10
FC5
FC6
T7
C3
CZ
C4
T8
CP5
CP6
TP9
TP10
PZ
P3
P4
P7
P8
P9
P10
O1
OZ
O2
N100
P650
S850
P315
P400
N215
0
300
600
900
4µV
3.0
PCA factor loadings
Latency [ms]
Control (n=49)
Depression (n=58)
Comorbidity (n=18)
Anxiety (n=22)


Targets at Cz
-
2.0
PCA factor loadings
+
P315
P400
-
4µV
+
Control (n=49)
Depression (n=58)
Comorbidity (n=18)
Anxiety (n=22)
0
100
200
300
400
500
600
700
800
900
1000
Latency [ms]