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Multi-center N400 ERP consistency using a primed and unprimed word paradigm [1]

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Abstract

A word priming paradigm involving primed, unprimed, and non-word experimental conditions was used to elicit event-related potentials (ERPs) in normal, young adult males in identically equipped electrophysiology laboratories located in 6 different cities in the USA. Analyses of the average amplitude of a specified latency window containing the N400, the N400 peak amplitude, or the latency of the N400 peak amplitude found no differences among laboratory locations. The shape of the N400 ERP wave form was also found to be highly correlated across laboratory sites for each experimental condition. Comparison of the data with analogous word priming paradigms revealed similar patterns for the N400 components and response times in both the primed and unprimed experimental conditions. These findings suggest that the data from all 6 laboratory locations are consistent with each other and are congruous with those found in other N400 studies and will permit pooling of subject data for future research.

Keywords: Event-related potentials; N400; Word priming; Response time

1. Introduction

During the last 15 years, experiments to elicit event-related potentials (ERPs) have explored possible neurophysiologic activity in semantic processing. In one of the more typical paradigms, brain electrical activity is recorded during the presentation of a sequence of contextually related words in which one of the words is semantically deviant. A late negative peak, the N400, occurs approximately 400 msec after the onset of the deviant word and is maximal in the centro-parietal area (Kutas and Hillyard 1980; Holcomb 1988; Kutas and Van Petten 1988; Van Petten and Kutas 1990; Kounios and Holcomb 1992; Bentin et al. 1993). This pattern is observed whether the stimulus is presented in an auditory or visual modality (McCallum et al. 1984; Kutas et al. 1987; Connolly et al. 1990).

Assessment of neurophysiologic activity through semantic processing of single words uses a different paradigm and typically involves paired stimuli. The first stimulus (S1) is generally a word and is used as a prime to a second stimulus (S2); S2 may be a semantically related word, a semantically non-related word, or a non-word. The N400 is observed approximately 400 msec after the onset of S2

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[1] Collaborative Study on the Genetics of Alcoholism (H. Begleiter, SUNY HSCB, Principal Investigator, T. Reich, Washington University, Co-Principal Investigator) includes 6 different centers where data collection takes place. The 6 locations and Principal Investigators and Co-Investigators are: Indiana University (J. Nurnberger, P.M. Conneally); University of Iowa (R. Crowe, S. Kuperman); University of California at San Diego and The Scripps Research Institute (M. Schuckit, F. Bloom); University of Connecticut (V. Hesselbrock); State University of New York Health Sciences Center at Brooklyn (H. Begleiter, B. Porjesz); and Washington University in St. Louis (T. Reich, C.R. Cloninger). This national collaborative study is supported by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) by USPHS Grants NIAAA U10AA08401, U10AA08402, and U10AA08403.

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when S2 is a non-word or a word that is not semantically related to S1 and is absent or significantly reduced when the S2 is preceded by a semantically related word (Bentin et al. 1985; Kutas and Van Petten 1988; Holcomb and Neville 1990; Koyama et al. 1991; Holcomb 1993). The N400 elicited using a word priming paradigm is smaller than that produced using a sequence of meaningful words and is believed to result from the fact that the former has lower contextual constraints than does the latter (Kutas 1985).

The N400 may be a useful tool for study of a possible genetic predisposition for alcoholism. The rationale for this is based on epidemiological, neuropsychological, and neurophysiological investigations of alcoholics and their offspring. Family history studies (Goodwin 1985; Cloninger et al. 1988) have demonstrated a significantly increased risk for alcoholism in sons who come from families with a positive history of alcoholism (FHP) compared to sons who come from families with a negative history of alcoholism (FHN). Neuropsychological evaluations of FHP sons, who were themselves not alcoholic, revealed poorer performance on cognitive and linguistic measures in comparison to non-alcoholic FHN sons (Gabrielli and Mednick 1983; Drejer et al. 1985; Whipple et al. 1988; Peterson et al. 1992). A significant proportion of neurophysiological investigations of the P300, an ERP component associated with attentional and memory mechanisms (Pritchard 1981; Donchin et al. 1986), have demonstrated a lower P300 amplitude in non-alcoholic FHP sons (particularly when there are other first and second degree relatives with alcoholism) in comparison to non-alcoholic FHN sons (Begleiter et al. 1984, 1987; O'Connor et al. 1986, 1987; Parsons et al. 1990; Porjesz and Begleiter 1990; Hill and Steinhauer 1993; Polich et al. 1994). Finally, a decreased N400 amplitude was observed in a small study that utilized a rhyming letter priming task in non-alcoholic FHP sons compared to non-alcoholic FHN sons (Schmidt and Neville 1985). Together, these findings suggest a likely genetic predisposition to alcoholism and that this predisposition may be related to deficits in cognitive, linguistic, and neurophysiological functioning.

The present N400 study is based on the data being collected by the Collaborative Study on the Genetics of Alcoholism (COGA). COGA, composed of 6 centers located in California, Connecticut, Iowa, Indiana, Missouri, and New York, has as its objective the ongoing study of the relationships of various behavioral, biochemical, neuropsychological, genetic, and neurophysiologic phenomena and to determine how these phenomena are related to the expression of alcohol abuse/alcoholism.

To enable the pooling of N400 data from each of the 6 COGA sites, preliminary analyses of the data need to be done to ensure the following goals: (1) the data from each of the 6 COGA locations contain N400 ERP components (i.e., average N400 amplitude, N400 peak amplitude, and latency of the N400 peak amplitude) that are not significantly different from each other; (2) the overall shapes of the N400 wave forms from each of the COGA locations are similar to each other; and (3) the designed paradigm produces N400 components and behavioral responses that are similar to those seen in other investigations using word priming paradigms.

2. Methods

Subjects

IRB approval was obtained for this study with subjects providing informed consent. Using identically structured interviews, each of the COGA laboratory locations screened 15 male subjects, aged 18–29 years, to determine their handedness and to ensure that they had no neurologic, psychiatric, or medical problems. Just prior to their ERP collection, all subjects were required to have a negative breath alcohol test.

Experimental procedure

All laboratory locations used a Sensorium model EPA-2 AC-coupled EEG amplifier, a Concurrent model 5550 mini-computer, and identical software to record the electrophysiologic activity from subjects seated in a dimly lit, electrically insulated, and acoustically isolated chamber. A total of 19 electrodes were placed on the scalp in the standard 10–20 international pattern using the ECI Electrode-cap: Fp1/2, F3/4, F7/8, Fz, T3/4, C3/4, Cz, T5/6, P3/4, Pz, and O1/2. A forehead electrode served as ground while a nose reference was utilized to maximize the ability to detect hemisphere asymmetry (Katznelson 1981). Electrode impedance was maintained at 5 kΩ or less. Both vertical and horizontal electro-ocular (EOG) activities were monitored using electrodes placed above the bridge of the nose and at the outer canthus of the left eye respectively.

The EEG amplifiers were calibrated before each subject was tested. The gain was 10,000 with the high- and low-pass filters set at 0.02 and 50 Hz, respectively. The EEG activity was sampled at a rate of 256 Hz with sampling beginning 187 msec prior to and continuing for 1413 msec after the stimulus onset. Inter-stimulus interval was 1600 msec. On-line monitoring of the EEG and EOG was used to automatically reject trials when voltages exceeded ± 73.3 μV.

Stimuli consisted of a pseudo-randomized list of words followed by either their antonyms (primed condition), other non-semantically related words (unprimed condition), or sequences of randomized letters (non-word condition). The stimuli were displayed on a computer monitor located within the isolation chamber. All subjects were presented with an equal number of words (150) and non-words (150). Word length was the same for primed and unprimed conditions and averaged 4.5 letters. Non-word length also averaged 4.5 letters and consisted of pronounceable combi-

nations of letters. Word familiarity, using the scale of Toglia et al. (1978), for both the primed and unprimed words, averaged 6.3 on a scale of 1 (unfamiliar) to 7 (very familiar). A standardized spelling list (Forbes 1968) placed the average grade level of the primed and unprimed words in the 3rd grade and ranged from 2nd to 7th grade.

The subjects performed a lexical decision task and were instructed to press a button with an index finger if the presented stimulus was a word and to press another button with the index finger of the opposite hand if the stimulus was a non-word. Half of the subjects used their right index finger to indicate primed or unprimed word stimuli and half used their left index finger for this task. The subjects were instructed to respond as quickly and as accurately as possible. Trials in which response time exceeded 1000 msec were excluded from all analyses. Accepted trials were stored and averaged on-line for each of the 3 conditions using the same computer that generated the stimuli.

3. Results

Data analysis

The behavioral data were assessed with 2-factor repeated measures analyses of variance (ANOVA), with laboratory location as a between-subject factor (consisting of the 6 COGA centers) and experimental condition as a within-subject factor (composed of the primed, non-word, and unprimed conditions). When appropriate, Geisser-Greenhouse correction procedures were used to adjust the degrees of freedom for violations of the sphericity assumption intrinsic to repeated measures ANOVA designs.

ERP wave forms for each of the 3 experimental conditions were first digitally filtered using an inverse FFT 8 Hz low pass filter. A computer algorithm was used to calculate the average ERP amplitude occurring in a window 300–500 msec after the onset of the stimulus. This window was chosen due to the similar nature of this paradigm to other investigations of the N400 (Holcomb and Neville 1990; Holcomb 1993).

ERP data were assessed by 3-factor repeated measures analyses of variance (ANOVA), with 1 between-subject factor (laboratory location) and 2 within-subject factors (experimental condition and electrode site). The data from all 19 electrode sites were used in the analyses to demonstrate no significant N400 component differences among the 6 COGA laboratory locations. All F values have been reported whether significant or not. Greenhouse-Geisser correction procedures were again used to adjust the degrees of freedom for violations of the sphericity assumption intrinsic to repeated measures ANOVA designs.

Demographic and behavioral data

Of the total of 90 subjects, left-handed subjects (n = 3) and subjects with less than 20 accepted trials for each of the 3 experimental conditions (n = 10) were excluded from the analyses performed in this study. Table 1 presents the distribution of the remaining 77 (85%) subjects as well as their demographic and behavioral data broken down by laboratory location. The mean age of the subjects (22.4 ± 2.4) was not significantly different across the laboratory locations.

The average numbers of accepted trials for the primed, unprimed, and non-word conditions were 37.3 ± 7.2, 37.4 ± 7.3, and 112.2 ± 20.7, respectively. A 2-factor repeated measures ANOVA was performed on the number of accepted trials for the various experimental conditions across laboratory location. Of importance, neither laboratory location nor the interaction of experimental condition × laboratory location was significant; this indicated that the number of accepted trials by experimental condition was not different among the 6 COGA laboratories.

The same analysis was performed on response times for the various experimental conditions. Experimental condi-

Table 1
Demographic and behavioral data by COGA laboratory location

Laboratory location (N)	Age years		No. of primed word trials		No. of non-word trials		No. of unprimed word trials		Reaction time for primed word trials (msec)		Reaction time for non-word trials (msec)		Reaction time for unprimed word trials (msec)	
	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)
CA (13)	23.0	(2.9)	37.0	(6.9)	111.5	(24.4)	36.0	(5.5)	538.9	(67.7)	664.5	(86.8)	595.7	(71.9)
CT (14)	21.0	(2.3)	38.1	(6.3)	116.4	(18.8)	38.4	(6.0)	523.9	(96.1)	604.4	(80.0)	584.3	(101.6)
IA (14)	22.8	(1.6)	35.7	(6.6)	103.2	(18.5)	32.8	(8.1)	487.3	(86.5)	563.8	(74.4)	544.2	(72.6)
IN (14)	23.0	(2.3)	40.3	(6.5)	117.1	(18.4)	40.8	(5.1)	510.6	(69.0)	626.4	(88.2)	562.8	(66.8)
MO (11)	22.4	(2.3)	33.8	(9.1)	109.3	(25.0)	36.5	(9.9)	526.2	(56.6)	609.4	(68.2)	577.0	(45.9)
NY (11)	22.0	(2.3)	38.2	(8.1)	109.1	(19.3)	40.4	(6.8)	538.9	(69.5)	649.7	(64.7)	589.6	(55.2)
Total	22.4	(2.4)	37.3	(7.2)	111.2	(20.7)	37.4	(7.3)	519.8	(76.1)	618.4	(82.7)	574.8	(72.4)

tion was highly significant (F (2, 142) = 125.5, $P <$ 0.0001), but similar to the number of accepted trials, neither laboratory location nor the interaction of experimental condition × laboratory location was significantly different.

ERP differences

Fig. 1 illustrates the grand mean ERP wave forms for the primed, unprimed, and non-word conditions for all 77 subjects. The N400 peak appears at approximately 345 msec and is clearly more negative for the unprimed and non-word conditions than for the primed condition. Table 2 presents these same data in numeric form; the mean for the average N400 amplitude, N400 peak amplitude, and latency of the N400 peak amplitude is presented for all 77 subjects by experimental condition and electrode site.

Fig. 2 depicts the same ERP wave form for electrode site Cz for each of the 6 laboratory locations. Though variability exists, the wave forms for each of the laboratory locations produce a similar pattern for the primed, unprimed, and non-word conditions; the N400 peak is the least negative for the primed condition and approximately equally negative for the unprimed and the non-word conditions.

The ERP data for the average amplitude of the N400 within the 300–500 msec window were analyzed in a similar fashion but used the 3-factor repeated measures design described previously. Since one of the goals of this study was to demonstrate that the various experimental conditions produced different results and that these results were not different among the various laboratory locations, particular attention was given to the factors of experimental condition and laboratory location (as well as any interaction term containing laboratory location).

The within-subject factors of experimental condition, electrode site, and the interactive term of experimental condition × electrode site were highly significant (F (2, 142) = 76.45, $P < 0.0001$, F (18, 1278) = 44.40, $P <$ 0.0001, and F (36, 2556) = 16.83, $P < 0.0001$, respectively), and indicated that overall, both experimental condition and electrode site influenced average amplitude. The between-subject factor of laboratory location and the interactive terms of experimental condition × laboratory location, electrode site × laboratory location, and experimental condition × electrode site × laboratory location were all non-significant, and indicated that laboratory location produced neither a significant main effect, a significant effect on experimental condition, a significant effect on electrode average amplitude, nor a significant effect on the average amplitude of the N400 by experimental condition for the individual 19 electrode sites. (Though these results are non-significant, the F values for the laboratory location factor and interactive terms are shown in Table 3 section A to demonstrate the magnitude of their effects.)

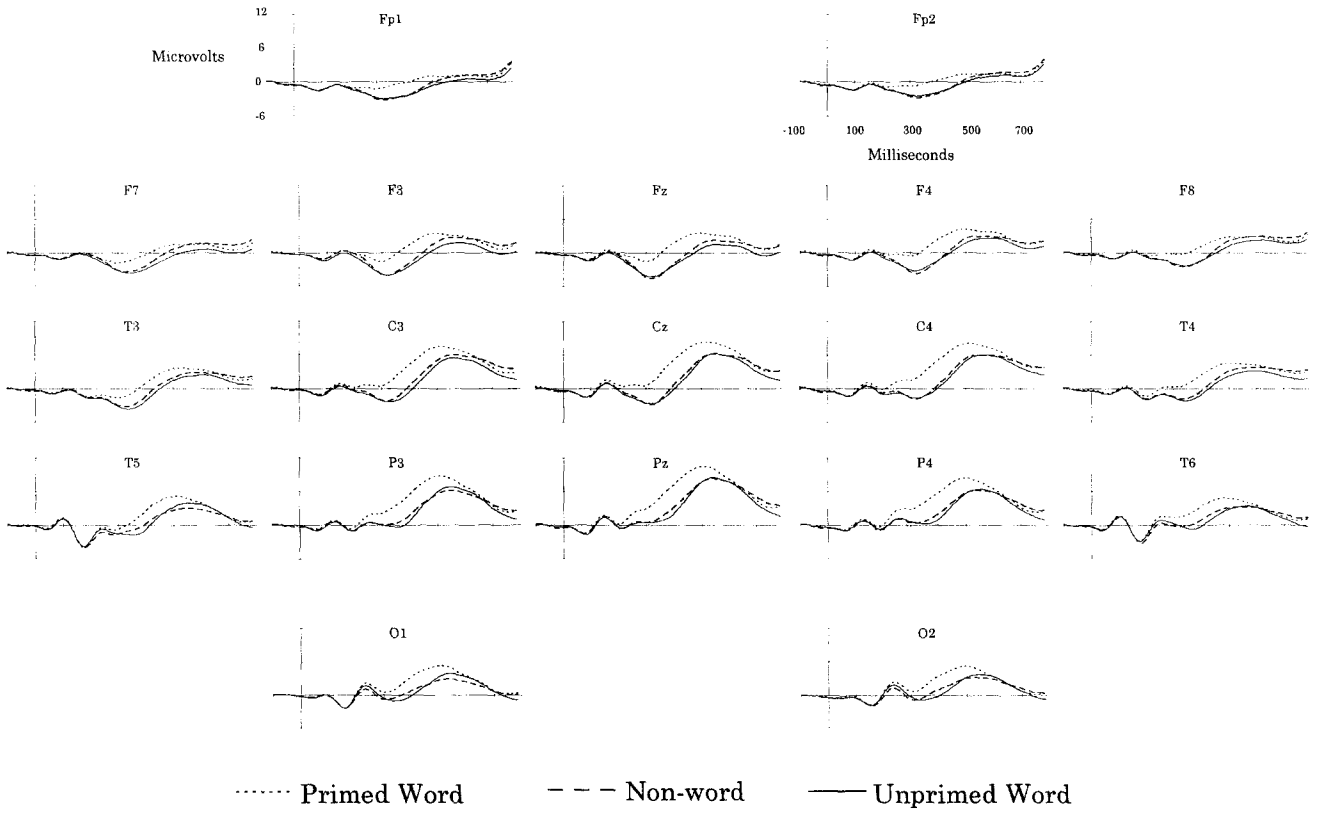

Fig. 1. Grand mean event-related potential wave forms for the primed, non-word, and unprimed experimental conditions at each of the electrode sites (N = 77).

Table 2
Mean and standard deviation data for the average amplitude of the N400 in the latency window of 300–500 msec, N400 peak amplitude, and the latency of the N400 peak amplitude

Electrode site	Average amplitude in window						N400 peak amplitude						Latency of the N400 peak					
	Primed word		Non-word		Unprimed word		Primed word		Non-word		Unprimed word		Primed word		Non-word		Unprimed word	
	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)
FP1	−0.18	(3.0)	−2.23	(2.7)	−2.32	(3.0)	−2.05	(2.7)	−3.87	(2.6)	−4.14	(3.1)	346.82	(58.0)	344.44	(44.2)	361.58	(57.1)
FP2	0.26	(3.1)	−1.79	(2.7)	−1.67	(3.1)	−1.69	(2.9)	−3.55	(2.6)	−3.57	(3.0)	355.75	(67.3)	350.98	(49.5)	357.88	(58.9)
F7	−0.28	(2.7)	−2.03	(2.4)	−2.66	(2.5)	−2.45	(2.7)	−4.03	(2.5)	−4.67	(2.4)	333.94	(44.4)	343.02	(36.4)	353.21	(47.2)
F8	1.15	(2.8)	−0.93	(2.3)	−1.13	(2.8)	−0.94	(2.6)	−3.12	(2.1)	−3.27	(2.4)	343.52	(50.7)	347.18	(35.3)	358.89	(47.8)
F3	1.22	(3.3)	−1.69	(2.9)	−2.20	(2.9)	−2.22	(3.3)	−4.82	(3.0)	−5.24	(3.1)	332.06	(48.9)	330.39	(33.7)	347.23	(47.4)
F4	2.15	(3.7)	−1.20	(2.8)	−1.25	(3.3)	−1.30	(3.5)	−4.41	(2.9)	−4.40	(3.1)	337.13	(56.4)	332.87	(32.9)	344.89	(48.4)
T3	0.87	(3.0)	−1.18	(2.6)	−1.84	(2.4)	−2.24	(3.0)	−3.74	(2.5)	−4.47	(2.5)	325.21	(32.4)	335.31	(27.6)	344.44	(36.1)
T4	2.41	(2.7)	−0.01	(2.2)	−0.62	(2.4)	−0.40	(2.6)	−2.47	(2.1)	−3.08	(2.5)	331.65	(37.2)	340.48	(31.6)	360.47	(46.2)
C3	4.19	(4.1)	0.71	(3.2)	−0.09	(3.2)	−0.18	(4.1)	−2.99	(3.0)	−3.78	(3.5)	322.73	(36.4)	330.44	(30.8)	342.97	(43.3)
C4	5.01	(4.3)	1.00	(3.0)	0.63	(3.5)	0.90	(4.1)	−2.72	(2.9)	−3.04	(3.3)	328.46	(45.4)	334.19	(35.7)	351.79	(49.8)
T5	2.41	(4.6)	0.42	(4.3)	−0.08	(4.2)	−1.58	(5.0)	−2.37	(4.8)	−3.32	(4.5)	331.81	(44.7)	346.36	(56.0)	351.08	(44.4)
T6	3.26	(4.1)	1.12	(3.7)	0.52	(3.4)	0.03	(4.3)	−1.61	(4.1)	−2.22	(3.7)	342.97	(51.4)	358.79	(56.7)	369.29	(50.0)
P3	5.60	(4.9)	2.20	(4.0)	1.67	(4.2)	1.47	(4.9)	−0.88	(4.1)	−1.88	(4.2)	324.81	(37.0)	343.12	(43.6)	352.35	(44.2)
P4	5.87	(4.7)	2.44	(3.8)	1.92	(4.0)	2.14	(4.6)	−0.76	(3.8)	−1.44	(4.0)	332.62	(45.6)	342.87	(44.3)	360.67	(45.7)
O1	3.11	(5.0)	0.84	(4.8)	0.39	(4.6)	−0.66	(5.4)	−1.88	(5.1)	−2.68	(4.7)	337.49	(49.9)	352.71	(56.5)	356.97	(48.6)
O2	3.24	(4.7)	1.02	(4.3)	0.51	(4.2)	−0.38	(5.0)	−1.82	(4.8)	−2.39	(4.3)	343.47	(55.9)	346.36	(56.4)	355.39	(44.0)
Fz	1.41	(3.7)	−1.97	(3.1)	−2.23	(3.3)	−2.31	(3.7)	−5.44	(3.2)	−5.57	(3.5)	331.86	(49.2)	333.18	(36.9)	341.9	(47.8)
Cz	4.85	(4.7)	0.68	(3.4)	0.20	(3.6)	−0.13	(4.6)	−3.79	(3.3)	−4.23	(3.8)	325.57	(42.2)	331.30	(35.6)	343.27	(48.0)
Pz	7.21	(5.2)	3.53	(4.1)	2.93	(4.2)	2.41	(4.9)	−0.32	(3.9)	−1.15	(4.1)	319.07	(30.3)	332.77	(37.7)	348.80	(46.9)

The values represent a total of 77 subjects and are presented for all 3 experimental conditions.

Because the average amplitude within a latency window method might mask COGA laboratory differences, a finer grain approach was also initiated. This consisted of obtaining the amplitude of the point in the ERP wave form that represented the most negative point in the specified window of 300–500 msec as well as the actual latency of this point. These data were obtained for the 3 experimental conditions and for each of the 19 electrode sites. The previously described 3-factor repeated measures ANOVA was used to analyze both the N400 peak amplitude and the latency of the N400 peak amplitude and revealed identical patterns to that observed for the average amplitude. Analysis of the peak amplitude indicated that the within-subject factors of experimental condition and electrode site as well as the interactive term of experimental condition × electrode site were all highly significant (F (2, 142) = 48.05, $P < 0.0001$, F (18, 1278) = 22.57, $P < 0.0001$, and F (36, 2556) = 12.59, $P < 0.0001$, respectively); and the between-subject factor of laboratory location and any interactive term containing "laboratory location" were similarly all non-significant (the F values for these factors are shown in Table 3 section B). Analysis of the latency of the peak amplitude indicated that the within-subject factors of experimental condition (F (2, 142) = 13.48, $P <$ 0.0001), electrode site (F (18, 1278) = 6.39, $P < 0.000$), and the interactive term of experimental condition × electrode site (F (36, 2556) = 1.96, $P < 0.03$) were again all highly significant while the between-subject factor of laboratory location and all interactive terms containing this factor also were non-significant (the F values for these factors are shown in Table 3 section C).

Thus, analyses of the N400 average amplitude, peak amplitude, and latency of the peak amplitude indicate no significant "mean" differences among the various COGA laboratory locations in regard to data obtained in the latency range (300 –500 msec) commonly believed to contain the N400 peak (Holcomb and Neville 1990; Holcomb 1993).

ERP data similarities

Though these analyses attested to no significant laboratory location differences, the actual similarity of the data from the various laboratory locations still needed further investigation. Using the grand mean wave form for each of the laboratory locations, similarity was assessed by computing Pearson product-moment correlation coefficients for the data points contained within the latency window used for the previous analyses (N = 52 points) for each of the 3 experimental conditions. This resulted in each experimental condition having a total of 15 correlations for each electrode site. The mean of the 15 correlation coefficients for each electrode site was then calculated to obtain a general measure of agreement among laboratory locations. The means and standard deviations for all 3 conditions

Table 3

Factor or interactive term	F value	P value
(A) Average N400 amplitude for the latency window of 300 – 500 msec		
Experimental condition [a]	F (2, 142) = 76.45	< 0.0001
Electrode site [b]	F (18, 1278) = 44.4	< 0.0001
Laboratory location [c]	F (5, 71) = 1.49	< 0.25
Experimental condition × electrode site	F (36, 2556) = 16.83	< 0.0001
Experimental condition × laboratory location	F (10, 142) = 1.53	< 0.20
Electrode site × laboratory location	F (90, 1278) = 1.04	< 0.45
Experimental condition × electrode site × laboratory location	F (180, 2556) = 0.99	< 0.50
(B) N400 peak amplitude		
Experimental condition	F (2, 142) = 48.05	< 0.0001
Electrode site	F (18, 1278) = 22.57	< 0.0001
Laboratory location	F (5, 71) = 1.26	< 0.30
Experimental condition × electrode site	F (36, 2556) = 12.59	< 0.0001
Experimental condition × laboratory location	F (10, 142) = 0.91	< 0.60
Electrode site × laboratory location	F (90, 1278) = 0.81	< 0.70
Experimental condition × electrode site × laboratory location	F (180, 2556) = 0.96	< 0.60
(C) Latency of the N400 peak amplitude		
Experimental condition	F (2, 142) = 13.48	< 0.0001
Electrode site	F (18, 1278) = 6.39	< 0.0001
Laboratory location	F (5, 71) = 1.56	< 0.30
Experimental condition × electrode site	F (36, 2556) = 1.96	< 0.03
Experimental condition × laboratory location	F (10, 142) = 0.83	< 0.65
Electrode site × laboratory location	F (90, 1278) = 1.21	< 0.25
Experimental condition × electrode site × laboratory location	F (180, 2556) = 1.06	< 0.40

[a] Experimental condition: primed word, non-word, unprimed word.
[b] Laboratory location: CA, CT, IA, IN, MO, NY.
[c] Electrode site: the 19 electrodes specified in Table 2.

were similar and ranged from 0.80 to 0.99 and 0.01 to 0.21, respectively. All of the individual correlations for each of the 3 experimental conditions and for each of the electrode sites were highly significant ($P < 0.01$ to $P < 0.0001$). Thus, these analyses indicated that inter-laboratory similarity of the N400 wave form was robust among the laboratory locations.

Experimental paradigm

The last goal of this study was to determine whether the experimental paradigm used produced data similar to those found in other experiments involving word priming tasks. Analyses to test this goal were limited to the experimental conditions of primed and unprimed words since the paradigm used in this study was conceptualized as using the non-word condition as a "filler" to challenge subjects to respond with the appropriate button press to the occurrence of a word stimulus.

Response time and the size of the N400 peak are the two measures that appear to be consistently influenced by N400 paradigms and were the measures analyzed to determine whether the present study produced an effect similar to that found in other studies.

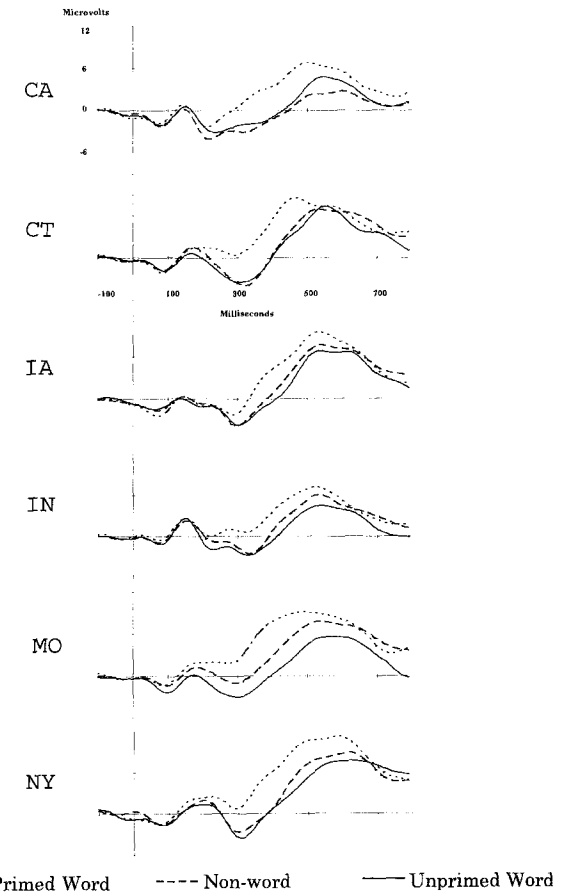

Fig. 2. Cz grand mean event-related potential wave forms for the primed, unprimed, and non-word conditions by COGA laboratory locations (N = 13 for CA, N = 14 for CT, N = 14 for IA, N = 14 for IN, N = 11 for MO, and N = 11 for NY).

A 2-factor ANOVA, with laboratory location as a between-subject factor and experimental condition (confined now to primed and unprimed conditions) as a within-subject factor, revealed that experimental condition (F (1, 71) = 83.65, $P < 0.0001$) significantly affected response time but that neither laboratory location nor the interactive term of laboratory location × experimental condition had any effect on response time. As indicated in Table 1, this difference is accounted for by the faster reaction time associated with the primed (519.8 ± 76.1 msec) versus unprimed word conditions (574.8 ± 72.4 msec).

To visualize what effect experimental condition had on the N400, the grand mean ERP wave form for the primed word was subtracted from the grand mean ERP wave form for the unprimed word. Fig. 3 presents this subtraction wave form and reveals a prominent negative peak at approximately 400 msec after the onset of S2 for all 19 electrode sites. Thus the N400 is a larger negative peak for the unprimed versus the primed word experimental condition.

A 2-factor ANOVA, with laboratory location as a between-subject factor and electrode site as a within-subject factor was performed on this subtraction wave form using the average N400 amplitude. Electrode site demonstrated a significant effect (F (18, 1278) = 21.46, $P < 0.0001$) while laboratory location and the interactive term of electrode site × laboratory location did not have a significant effect on the subtraction wave form.

Two additional analyses were performed to demonstrate similarity between the results of this experimental paradigm and N400 paradigms performed by others. In a similar paradigm, Bentin et al. (1985) demonstrated a midline, antero-posterior effect with the Pz electrode site demonstrating a larger area under the curve (similar to a greater positive average amplitude in the current study) than for either the Cz or Fz sites. Table 2 and Fig. 1 demonstrate similar results for this study; the N400 average amplitude was most positive for the Pz electrode site in comparison to the Cz and Fz sites. A 3-factor ANOVA, with laboratory location as a between-subject factor and within-subject factors of experimental condition (primed versus unprimed) and electrode site (Fz, Cz, and Pz), was performed on the average N400 amplitude. Only the factors of experimental condition, electrode site, and the interactive term of experimental condition × electrode site were significant (F (1, 71) = 128.8, $P < 0.0001$; F (2, 142) = 117.7, $P < 0.0001$; and F (2, 142) = 9.11, $P < 0.002$, respectively). Since the interactive term of experimental condition × electrode site was significant, a 2-factor ANOVA, with laboratory location as a between-subject factor and electrode site (Fz, Cz, and Pz) as a within-subject factor was performed independently for both the primed and unprimed conditions. For the primed condition, only the factor of electrode site was significant (F (2, 10) = 111.8, $P < 0.0001$). Post-hoc testing using the Scheffé's test revealed significant differences ($P < 0.05$) in average ampli-

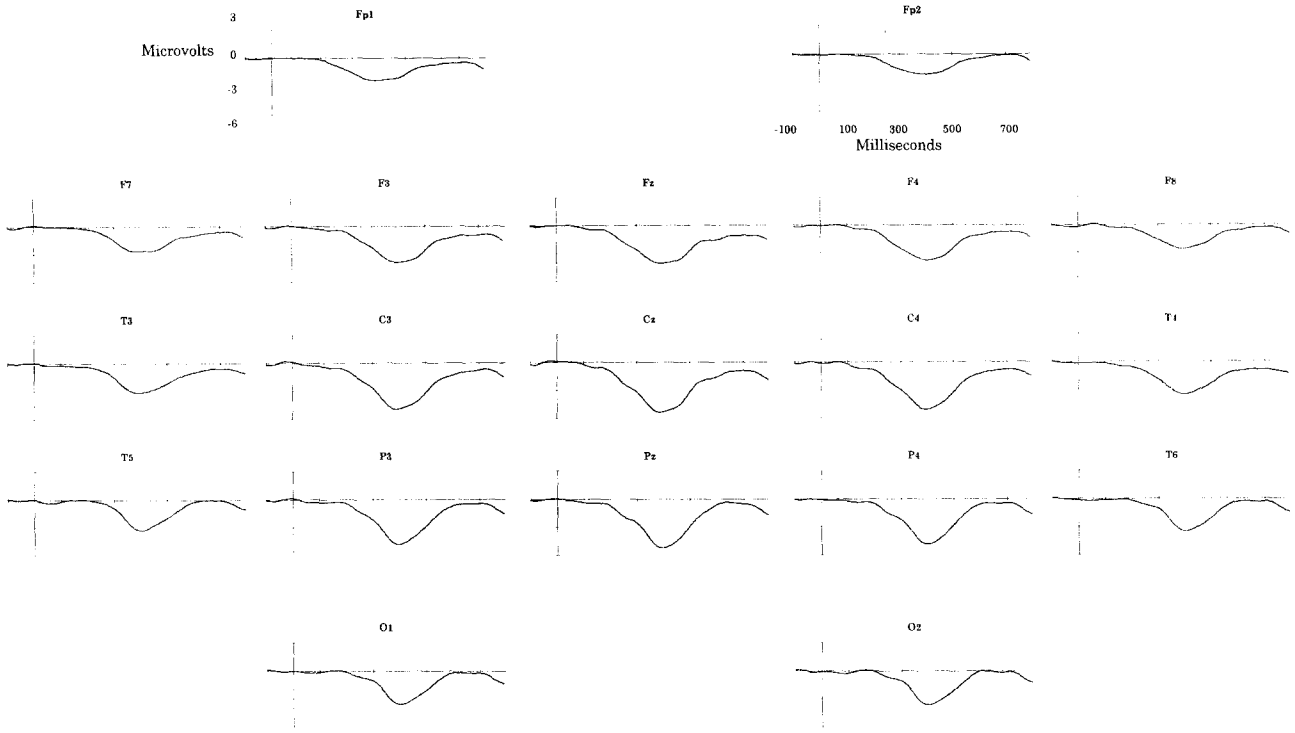

Fig. 3. Grand mean event-related potential wave form obtained by subtracting the primed from the unprimed word conditions for each electrode site (N = 77).

tude of Fz (1.41 ± 3.7) versus both Cz (4.85 ± 4.7) and Pz (7.21 ± 5.2) with no difference between the latter 2 electrode sites. For the unprimed condition, the factor of electrode site was again significant (F (2, 10) = 100.3, $P < 0.0001$), but post-hoc testing using the Scheffé's test revealed significant differences ($P < 0.05$) between all 3 electrode sites.

Using experimental paradigms similar to the present study, researchers have reported N400 ERP components that have right versus left hemisphere asymmetries. Bentin et al. (1985) reported the N400 as having a larger area under the curve for the right versus the left hemisphere. Holcomb (1993), using a similar measurement of average amplitude, also demonstrated a greater average amplitude on the right versus the left hemisphere.

Fig. 1 and Table 2 indicate that this study has similar hemispheric results for the N400 average amplitude. A 3-factor ANOVA, with laboratory location as a between-subject factor and within-subject factors of experimental condition (primed versus unprimed) and hemisphere (left or right) was performed on the average N400 amplitude. Only the factors of experimental condition (F (1, 71) = 99.9, $P < 0.0001$) and hemisphere (F (1, 71) = 29.9, $P < 0.0001$) were significant. The right hemisphere had a greater average amplitude than the left hemisphere for both the primed (2.92 ± 3.1 versus 2.12 ± 3.1) and unprimed conditions (−0.14 ± 2.6 versus −0.89 ± 2.6).

4. Discussion

No significant differences among laboratory locations were obtained in this study. Neither the behavioral measures of the number of accepted trials nor response times for the various experimental conditions differed. Although variability among laboratory centers existed, the average amplitude, the peak amplitude, and the latency of the peak amplitude for the N400 also demonstrated no laboratory location effects. In addition, the N400 ERP wave form was highly correlated across laboratory locations for each of the experimental conditions. Thus the N400 data obtained were not significantly different and, in fact, were similar for each of the laboratory locations.

Analyses of the combined data from all laboratory locations indicated that the experimental paradigm used produced results analogous to those seen in other word priming studies. The pattern of response times observed was comparable to other studies using word priming paradigms and demonstrated faster times for the primed versus the unprimed conditions (Meyer and Schvaneveldt

1971; Neely 1991). The N400 component also demonstrated results that were comparable to those of other N400 word priming paradigms: the N400 peak was larger for the unprimed compared to the primed word conditions; the average N400 amplitude increased in an anterior-to-posterior direction; and the right hemisphere had a more positive average N400 amplitude than the left hemisphere (Bentin et al. 1985; Kutas and Van Petten 1988; Holcomb and Neville 1990; Koyama et al. 1991; Holcomb 1993).

Thus this study demonstrates the validity of obtaining and combining N400 ERP data from multiple locations using identical equipment and paradigms. These data, along with the other behavioral, biochemical, neuropsychological, and genetic data collected by the Collaborative Study on the Genetics of Alcoholism, should help to clarify the relationships between cognitive and linguistic abnormalities, neurophysiological differences, and the apparent increased risk for developing alcoholism in the offspring of alcoholics.

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