Observational Study

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The functional significance of the P600

Some linguistic P600's do localize to language areas

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Abstract

A recent paper in the journal Neuroreport suggested that, upon source localization, the semantic P600 localizes to executive function areas, that is, outside language. But is this true for all types of linguistic P600? We report a cross-sectional source localization study of a classical (agreement) syntactic paradigm.

The results show a clear localization to the temporal lobe, in classical language areas.

The P600 is probably not a unitary phenomenon in term of source localization, and the question whether it localizes within or outside the language system depends on the type of P600.

Abbreviations: ANOVA = analysis of variance, BA = Brodmann area, EEG = electroencephalogram, EOG = electrooculogram, ERP = event related potential, fMRI = functional magnetic resonance imaging, LAN = left anterior negativity, MEG = magnetoencephalogram, sLORETA = standardized low-resolution brain electromagnetic tomography, SnPM = statistical nonparametric mapping, SNR = signal-to-noise ratio.

Keywords: P600, standardized low-resolution brain electromagnetic tomography, source localization

1. Introduction

Any respectable textbook on language processing would mention the N400, P600, and Left Anterior Negativity (LAN) as the staple of event related potentials (ERPs) of language. But their functional significance is still a matter of hot debate. In fact, until a few years ago, the classification of the 3 main language ERP waves (LAN, N400, P600) in terms of timing and elicitation conditions was so asymmetric as to suggest little hope of a general description of the general landscape: the LAN was elicited early and under syntactic conditions, the N400 was elicited early and by semantic conditions, and the P600 was elicited late, and by syntactic conditions as well.[1] A ground-breaking paper by Tanner and Van Hell[2] made the quest for a functional significance much easier by showing that the LAN is just an epiphenomenon: when inter-individual differences are taken into account, the LAN is just an overlap of a biphasic bilateral N400 and the early part of a right-lateralized P600 (these results were replicated in Grey et al[3] and Tanner[4]). In the new landscape, there is no LAN at all, while the N400 is elicited early and by both syntactic and semantic conditions, and the P600 is elicited late and by syntactic conditions. Looking back, this development dovetailed nicely with another rearrangement of the language ERP landscape, namely the semantic P600 literature, which found P600-looking late positivities under semantic conditions (e.g., Kim and Osterhout[5]). Incorporating these findings, there is now no LAN, the N400 is elicited early, by both syntactic and semantic conditions, and the P600 is elicited late, by both syntactic and semantic conditions as well. Nevertheless, the functional significance of both the N400 and the P600, in terms of the underlying cognitive processes, is still a topic of hot debate (e.g., Shen et al[6] and Ito et al[7]). In this context,[6] have shown, that a semantic P600 paradigm source localized to executive rather than classical language areas, thus supporting an extra-linguistic rather than an intra-linguistic interpretation of the P600. But would that be true for all types of P600?

In this study, we tested the source localization of a classical (subject agreement violation) syntactic P600 paradigm. We hypothesized, that unlike the semantic P600 paradigm in,[6] this linguistics P600 would localize within rather than outside the language system, supporting an intra-linguistic rather than an extra-linguistic interpretation.

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2. Methods

2.1. Participants

Twenty healthy volunteers (9 men) participated in the study, which is a usual size for a source localization study. Participants were right-handed, native speakers of English, recruited from the Be'er Sheva English speaking community via the Overseas Student Program in Ben Gurion University, billboards, mailing lists and social media, recruited and tested during the academic years of 2013 to 2014. Their mean age was 27.9, with a range of 23 to 63 years. All participants had normal or corrected to normal vision, and no known learning or language disabilities. Following approval by the Local Ethics Committee of the University Psychology Department, the participants gave written consent before participating in the experiment. The participants received modest payment for their participation. Two participants were excluded from data analysis, one due to a recording artifact, and the other due to excessive blinking.

2.2. Stimuli

Stimuli were a subset of the stimuli used in,[8] which compared the time parameters of the scalp ERP response for several ungrammatical conditions, successfully obtaining a classical scalp P600 to all of them. The ungrammatical condition chosen for the current work is a representative for the paradigmatic P600 "agreement violation" condition, assumed to elicit a syntactic P600. Sentences were past tense sentences constructed around a critical verb. In the control condition, the critical verb appeared with a past tense suffix, and in the ungrammatical condition the critical verb appeared as an uninflected root form (e.g., "show") that failed to exhibit the expected past tense. Table 1 contains a sample set of stimuli items.

All the words in the control and ungrammatical sentences except for the main verb were preserved, resulting in at least 5 identical words preceding and following the main verb. Ninety main verbs were used in the experiment, and 2 sets of sentences were constructed for each verb.

2.3. Procedure

The procedure was similar to Gouvea et al.[8] Ninety sentences, 45 for each condition, were introduced to each subject. Each subject saw each main verb once, chosen in a random fashion from 1 of the 2 sets. The sentences were interspersed with 180 filler sentences of comparable length and complexity. Sentence and filler order was randomized prior to the experiment. A yes/no question (1:1 ratio between "yes" and "no" as correct answers) followed each sentence. Participants were instructed to answer as quickly and accurately as possible. The session consisted of 5 blocks of 54 sentences, each lasting approximately 15 minutes and followed by a short break. Participants were comfortably seated in an adjustable chair, in front of a computer screen at a distance of about 70 cm. Each trial began with a fixation cross in the middle of the screen. The cross stayed on the screen until the participant pressed a button to ensure readiness.

Sentences were then presented in a word by word manner at the center of the screen, using black letters over white background, paced by the computer (300 ms per word + 200 ms average of white screen between words, with ±25 ms of jitter). The trial ended in a yes/no question, to which the participants responded using a respond box placed on a desk in front of them. The comprehension question was presented as a whole and stayed on the screen until the participant responded. Feedback on accuracy was given on all trials. Participants were asked to restrain from blinking during the presentation of the sentences, restricting them to the time of either the question or the fixation cross. The test session was preceded by a short practice session to familiarize the participants with the task and the blinking restriction. The practice session contained sentences that were not introduced again later on.

2.4. Data acquisition

A continuous electroencephalogram (EEG) was recorded from 64 scalp electrodes placed according to the International 10–20 System.[9] Additional electrodes were placed below the left eye to measure vertical electrooculogram (EOG) activity, and at the outer canthi of the right and left eyes in order to measure horizontal EOGs. All of the channels were referenced offline to the mastoid channels. Data were recorded using a 0.01- to 100-Hz band pass filter. Signals were at digitized at 512 Hz with a 24-bit A/D converter. During the recordings, noisy channels and channels that had a distinct voltage drift were noted as faulty channels for data analysis.

2.5. Data analysis

2.5.1. Comprehension accuracy. Accuracy in each experimental condition was compared using repeated measures analysis of variance (ANOVAs). Only sentences that had a correct response to the yes/no answer were included in the EEG analysis.

2.5.2. Calculation of ERPs. The EEG data were processed using EEGLAB[10] and ERPLAB. The raw data were re-referenced to the average of the mastoid electrodes, subjected to a 30 Hz low pass filter, and faulty channels were interpolated. The output EEG was then segmented between 200 ms before the event of the critical word onset, and 1300 ms post-event. A few stages of automatic artifact rejection followed: segments that contained blinking and eye movement artifacts were rejected using a threshold of 50 μV on the horizontal and vertical EOG channels, and large fluctuations were rejected by a general filter, with a threshold of 100 μV. The EEG was further averaged for each experimental condition (control, ungrammatical) locked to the event of the critical verb presentation, and baseline-corrected to 200 ms prestimulus onset, producing an ERP for each subject. A grand average ERP was calculated from the subjects' individual ERPs and was subject to the statistical scalp analysis.

2.5.3. Scalp ERP analysis. Following,[8] statistical analyses were performed on 18 electrodes, which were distributed among 6 regions of interest. The regions of interest were left anterior (FT7, F3, FC3), midline anterior (FZ, FCZ, CZ), right anterior (F4, FC4, FT8), left posterior (TP7, P3, CP3), midline posterior (PZ, CPZ, OZ), and right posterior (P4, CP4, TP8), creating 2 topographical factors, laterality (right, middle, left), and anteriority (anterior, posterior). Statistical analyses were performed on the mean amplitude relative to baseline within 7 time windows: 0 to 300 ms, 300 to 500 ms, 500 to 700 ms, 600 to 800 ms, 700 to 900 ms, 900 to 1100 ms, 1100 to 1300 ms, post stimulus onset. For each time window a repeated measures

Table 1

Sample set of stimuli items.

Control	The student answered the man while the woman with the black skirt recommended the book during the conference.
Ungrammatical	The student answered the man while the woman with the black skirt recommend the book during the conference.

ANOVA was preformed, using the Grammaticality factor (control, ungrammatical) in addition to the topographical factors Anteriority (anterior, posterior) and Laterality (right, middle, left). The source of main effects or interactions was further sought using follow up repeated measures ANOVA analyses. The time frames and electrode groupings were maintained for the follow up analysis.

2.5.4. Source localization. The source localization for the difference between the ungrammatical and the grammatical conditions was performed using the standardized low resolution brain electromagnetic tomography (sLORETA) software. This method computes images of electric neuronal activity from EEG and magnetoencephalography (MEG).[11] sLORETA calculates the standardized current source density at each voxel of 6239 voxels, at a spatial resolution of 5 mm in the gray matter and the hippocampus, under the assumption that neighboring voxels should have maximally similar electrical activity. The transformation matrix was calculated with a regularization parameter (smoothness) corresponding to a signal-to-noise ratio (SNR) of 100, as is usual for averaged ERPs. In all statistical tests, a subject-wise normalization was used with no baseline correction. Baseline correction was not necessary since the repeated measurements of the same participants avoided significant baseline differences between the different conditions. The differences were evaluated with a paired group t test, using the average value for the statistical measure of log of ratio of averages (log of F-ratio) in each time interval. A randomization test based on statistical nonparametric mapping (SnPM, number of randomizations: 5000, described in Holmes et al[12]) was used to correct for multiple comparisons. The significance level applied to the data was set at $P<.05$ for the one-tailed test UG > Ctrl.

3. Results

3.1. Comprehension accuracy

Overall accuracy in answering the comprehension questions was 86% for all experimental conditions combined. Mean accuracy was 86% (standard deviation [SD] 11%) in the control condition, and 85% (SD 10%) in the ungrammatical condition. These scores showed no difference between conditions ($P>.2$). The overall accuracy (average = 0.88, SD = 0.013) did not differ between blocks within the session ($F<1$), thus excluding a general fatigue effect.

3.2. Event related potentials

Trials with eye movements or other artifacts were rejected, affecting 10.9% of the trials. Figure 1 shows a comparison of grand average ERPs (control vs ungrammatical) averaged across the electrodes in each of the 6 topographic regions. Grand average waveforms were treated using a 10 Hz low-pass filter for visualization purposes, but all analyses were conducted on unfiltered data.

Looking at scalp distribution, a positive shift for the ungrammatical condition seemed apparent at the 500 to 700 ms interval, gaining prominence at 600 to 800 ms, and maintained, though slightly reduced, until the 1100 to 1300 ms interval. There seemed to be no negative shift in the data.

3.3. Scalp ERP analysis

A full list of the statistically significant results of the ANOVA can be obtained upon request. Here we discuss those time intervals that are likely to exhibit a P600 effect, and that showed a grammaticality effect or an interaction between grammaticality and anteriority. Looking at the interval 600 to 800 ms after critical stimulus onset: a main effect for Grammaticality was obtained ($F[1,17]=7.08$, $P=.016$, Eta squared = 0.29), stemming from a larger amplitude for the ungrammatical compared with the grammatical condition. Following,[8] we treat this positive shift as a syntactic P600. A significant Laterality main effect was also obtained ($F[34,2]=3.3$, $P=.048$, Eta squared = 0.16). None of the pairwise comparisons were significant. A laterality–anteriority interaction was also present, stemming from a laterality effect in the anterior, but not posterior, regions. Post

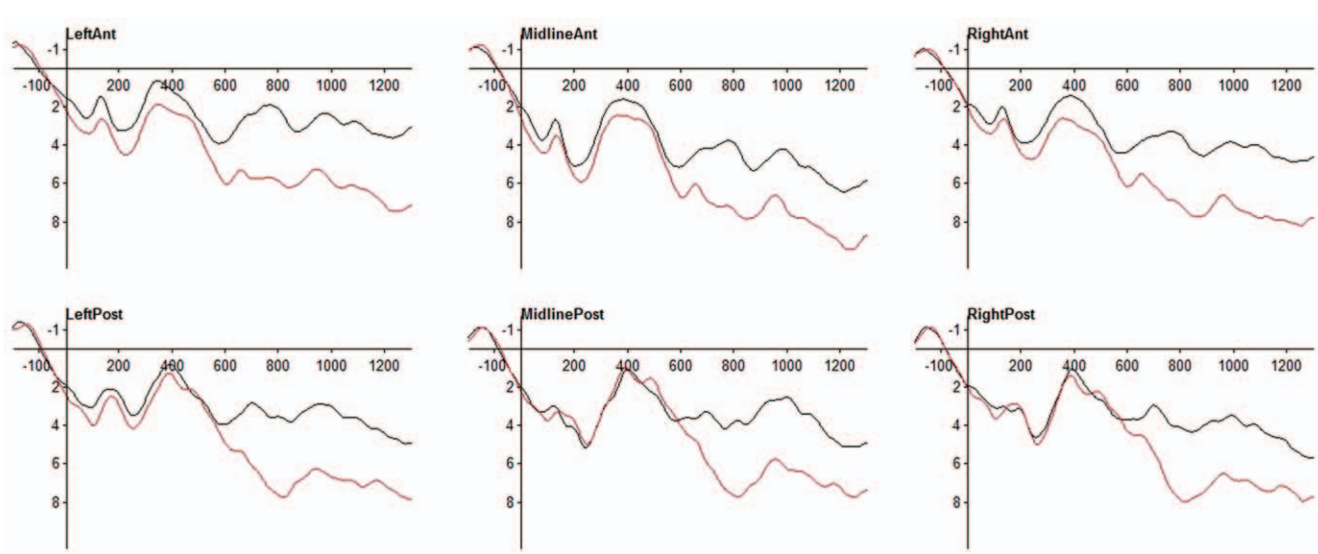

Figure 1. Grand average ERPs at 6 groups of topographically arranged electrode sites for the control and ungrammatical conditions (examples of the stimuli can be found in Table 1).

hoc comparisons showed a greater negativity in the right anterior region compared with other anterior regions ($F[1,17]=8$, $P=.01$, Eta squared = 0.28). This laterality effect and laterality–anteriority interaction were each present at 6 out of 7 analyzed intervals. A similar pattern of results, though slightly attenuated, appeared at the 500 to 700 ms time window. The first 200 ms time window where grammaticality was significant, was the interval 580 to 780 ms post stimulus onset ($F[1,17]=6.17$, $P=.024$, Eta squared = 0.27). The neural source of this P600 effect was then further examined using sLORETA.

3.4. Source localization

We compared the current density values obtained for each voxel in the 2 experimental conditions (control, ungrammatical), corrected for multiple comparisons. A full list of the statistically significant results can be obtained upon request. For the 600 to 800 ms time window, overall results are depicted in Fig. 2(A, B). The voxels attesting a significant higher activation in the ungrammatical condition are localized at the left middle and superior temporal cortex, BA38 and BA21, in red in Fig. 2C.

A similar pattern was obtained for the 500 to 700 ms time window, but with more significant voxels in the left BA38 and BA21.

4. Discussion

In the present study we tested a classical (subject agreement violation) syntactic P600. Using standardized low resolution brain electromagnetic tomography, we localized the P600 in the temporal lobe (BA38 and BA21), within language areas. Limitations include an acceptable but small sample size, as well as the use of just one, however classical, paradigm.

These results serve to fill a gap in the P600 ERP literature on the interpretation of grammatical anomalies or incongruities. While one of the most important language related ERPs (N400, P600), the linguistic P600 does not seem to be a unitary phenomenon. Previous studies reported that the P600 was located in language related areas such as the left Inferior Frontal Gyrus—BA 44/45/47[13] the middle temporal gyrus and the posterior part of the temporal lobe.[14,15] Furthermore it was assumed that the P600 component reflects the integration of syntactic and semantic information in the temporo-parietal Junction.[16] In contrast to these findings, Shen et al.[6] found a semantic P600 localized outside of the language system, in executive function areas (anterior cingulate cortex) questioning the P600 function in language comprehension. Furthermore, there is additional evidence that the P600 component is not only limited to syntactic processes,[17] and that patients with basal ganglia lesions show dissociation of P600 components.[18]

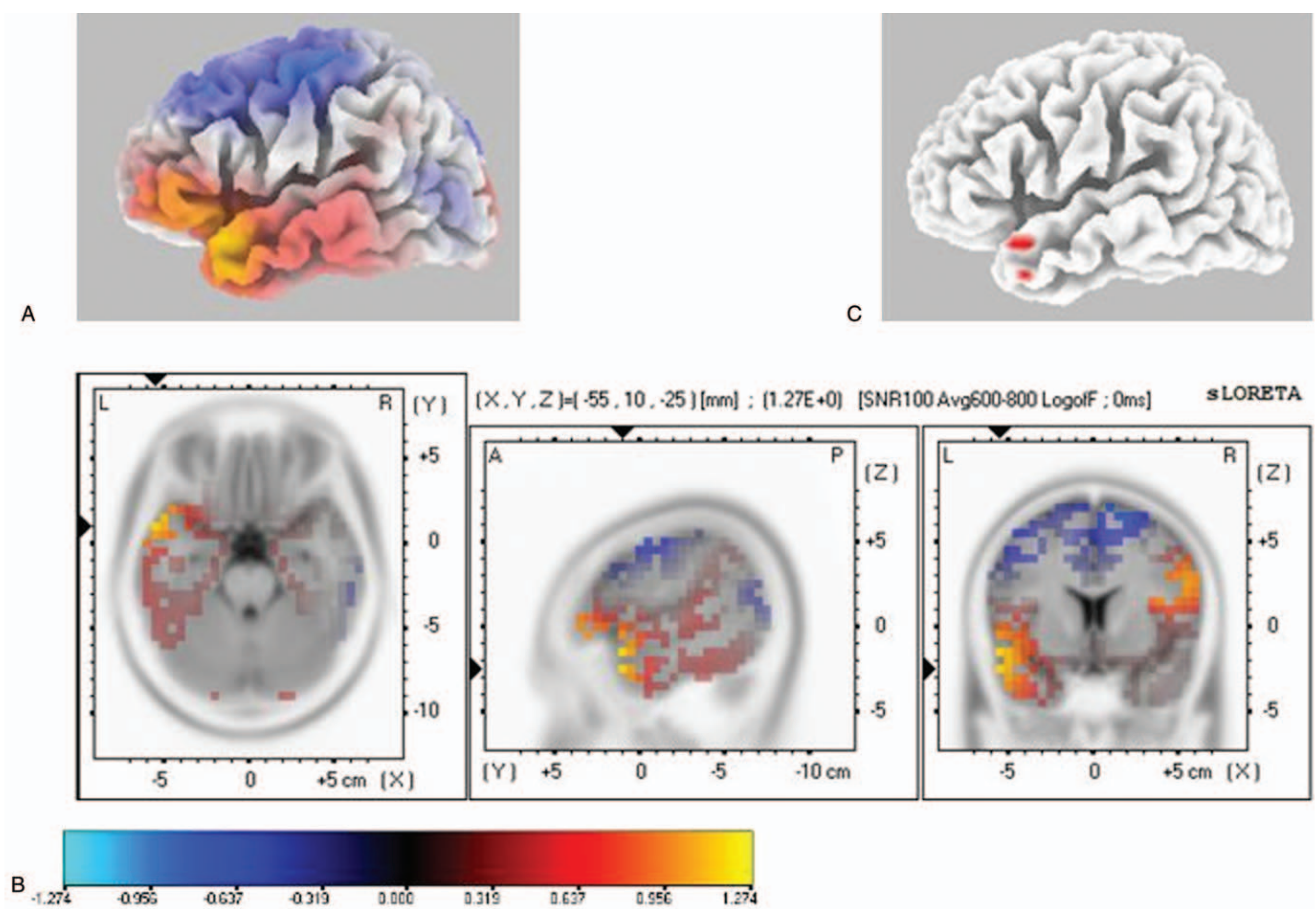

Figure 2. Source localization in the 600 to 800 ms interval. A. Pattern of activation on a 3D model of the cortex. B. Pattern of activation, the slices, and arrows show the place of the most prominent voxel. C. Significant voxels are marked in red.

Putting all these data together, the processes that lie behind the P600 component are still unclear. While Shen et al[6] results suggest that the generation of the semantic P600 reflects executive functions (and specifically cognitive control), our results suggest that some classical syntactic P600 instances involve linguistic computations, as suggested by.[19] One possible option is that the P600 is not a unitary phenomenon, but includes both executive functions and linguistic processes. In accordance, P600 amplitude of syntactic correctness was shown to be affected by attention and mood manipulations.[20] Another possibility is that whether it localizes within or outside the language system depends on the type of P600, maybe as a function on the type of stimuli triggering it. Many different syntactic violations have been reported to trigger the P600 response, including phrase-structure violations,[21] and violations of tense,[22] syntactic gender, and number.[23] However, P600 was also elicited by grammatically correct but temporarily ambiguous garden-path sentences[24] and by unambiguous grammatical items including long-distance dependencies.[25] A recent connectionist simulated model was successful in predicting the syntactic nature of the P600, together with the fact that it can change with experience.[26]

Up to date, several studies have shown different types of stimuli and contextual factors that influence the ERP P600 component, however few studies have attempted to specifically locate the cortical source of such influence. This may be due to the intrinsically poor spatial resolution of EEG. Further studies are needed, focusing both on structural and functional aspects of brain activity, maybe combining EEG and fMRI, to better understand the underlying processes of syntactic and semantic performance.

Author contributions

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