

Short Communication

Spectro-temporal correlates of lexical access during auditory lexical decision

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ABSTRACT

Lexical access during speech comprehension comprises numerous computations, including activation, competition, and selection. The spatio-temporal profile of these processes involves neural activity in peri-auditory cortices at least as early as 200 ms after stimulation. Their oscillatory dynamics are less well understood, although reports link alpha band de-synchronization with lexical processing. We used magnetoencephalography (MEG) to examine whether these alpha-related oscillations reflect the speed of lexical access, as would be predicted if they index lexical activation. In an auditory semantic priming protocol, monosyllabic nouns were presented while participants performed a lexical decision task. Spatially-localizing beamforming was used to examine spectro-temporal effects in left and right auditory cortex time-locked to target word onset. Alpha and beta de-synchronization (10–20 Hz ERD) was attenuated for words following a related prime compared to an unrelated prime beginning about 270 ms after stimulus onset. This timing is consistent with how information about word identity unfolds incrementally in speech, quantified in information-theoretic terms. These findings suggest that alpha de-synchronization during auditory word processing is associated with early stages of lexical access.

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1. Introduction

Lexical access during speech comprehension comprises numerous computations, including lexical activation, competition, and selection (e.g. Marslen-Wilson, 1987; McClelland & Elman, 1986; Norris, 1994). Activation describes the stochastic retrieval from memory of lexical representations cued by a spoken or written stimulus; competition and selection describe down-stream stages whereby one representation is chosen from a set of activated possibilities for subsequent processing. While a substantial body of literature has focused on the spatial and temporal profile of the neural substrates of these computations (see e.g. Friederici, 2012; Hickok & Poeppel, 2007 for reviews), there is growing interest in the oscillatory dynamics, i.e. spectro-temporal properties, of the underlying neural generators (e.g. Bastiaansen & Hagoort, 2006). One reason for this shift is the advent of neurophysiological models of speech perception processes that posit a central role for oscillatory mechanisms (e.g. Giraud & Poeppel, 2012). Another is that pathological oscillatory patterns in disorders such as autism

(Coben, Clarke, Hudspeth, & Barry, 2008; Cornew, Roberts, Blaskey, & Edgar, 2012; Edgar et al., 2013; Gandal et al., 2010; Uhlhaas & Singer, 2007) and schizophrenia (Edgar et al., 2008; Gandal, Edgar, Klook, & Siegel, 2011) have raised interest in characterizing the role of such activity in both non-pathological and pathological language processing.

Recent work studying time-locked spectral changes during auditory speech processing with magnetoencephalography (MEG) has found that decreases in power relative to baseline, or event related de-synchronization (ERD; Pfurtscheller & Lopes da Silva, 1999), in left auditory cortex between roughly 6 and 14 Hz (alpha band, extending into theta and beta bands) are sensitive to various lexical factors, including lexicality, word frequency, and word repetition within 200–600 ms of word onset (Tavabi, Embick, & Roberts, 2011a; Tavabi, Embick, & Roberts, 2011b). Words that are semantically incongruent in a sentential context also show a left-lateralized decrease in alpha- and beta-power (i.e. increased ERD) relative to congruent words (Wang et al., 2012). These results accord well with electroencephalography (EEG) findings showing left-lateralized alpha- and beta-band ERD effects of word-class (Bastiaansen, van der Linden, ter Keurs, Dijkstra, & Hagoort, 2005), a finding also observed in a population of older adults (Mellem, Bastiaansen, Pilgrim, Medvedev, & Friedman, 2012). Thus,

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converging evidence from MEG and EEG implicates ERD spanning theta, alpha, and beta frequency bands in lexical processing. However, it remains to be seen how this ERD relates to the different subcomponents of lexical access identified in cognitive models of that process.

The majority of prior studies have manipulated lexical processing by presenting different classes of words (e.g. high or low frequency, open or closed class, congruent vs. incongruent). Such manipulations alter numerous factors simultaneously: for example, word frequency effects co-vary with word neighborhood effects, leading to confounding influences on lexical activation and competition (Vitevitch, Luce, Pisoni, & Auer, 1999). Tavabi et al. (2011b) partially address this concern by holding target words constant while varying whether or not words are repeated, but repetition may facilitate multiple stages of speech perception, from phoneme decoding through lexical activation, selection, or task-specific decision processing. Thus, it is difficult to draw strong conclusions about the precise stage(s) of processing indexed by associated neural activity from the finding that theta-alpha ERD is affected by repetition priming alone.

If ERD centered in the alpha-band is associated with lexical activation, then it should be attenuated when lexical activation is facilitated. Semantic priming is a familiar mechanism for facilitating lexical activation (Meyer & Schvaneveldt, 1976), whether via automatic spreading activation or controlled executive processes (Neely, 1991). Changes at the activation stage, however, can also have down-stream consequences by reducing competition and speeding selection and these effects can be challenging to tease apart (but cf. Pylkkänen, Stringfellow, & Marantz, 2002; Vitevitch et al., 1999). Thus, it is important to consider carefully the temporal characteristics of any responses in order to distinguish early activation from later competition and selection effects.

No studies to date have examined local synchrony via spectro-temporal power in an auditory semantic priming protocol, though at least two have examined power or coherence during priming with visual stimulation. Mellem, Friedman, and Medvedev (2013) report that priming during visual word recognition with a letter recognition task leads to decreased gamma ERS in right-posterior electrodes for related targets beginning around 150 ms after stimulus onset. This priming effect is complemented by a later (300–800 ms) increase in gamma ERS in mid-line posterior electrodes as well as a late (600–1000 ms) reduction in alpha ERD in left frontal sites. Kujala, Vartiainen, Laaksonen, and Salmelin (2012) report results from an MEG study in which participants read a list of words that were either semantically or phonologically related. They find an increase in long-range coherence in the theta band between left and right temporal sites associated with semantic relatedness. While both results point towards a role for low frequency (theta/alpha) activity, Mellem et al. also find evidence for a relatively early role of gamma oscillations in lexical processing.

Earlier studies using event-related potentials demonstrated that semantic priming attenuates the evoked N400 response component beginning approximately 200–300 ms after stimulus onset for both visual (Kutas & Hillyard, 1984) and auditory (Holcomb & Neville, 1990) presentation. Converging evidence from MEG has found that semantic priming leads to a sustained reduction in left superior temporal activation during visual and auditory word processing (Vartiainen, Parviainen, & Salmelin, 2009). Left posterior-temporal activation around 300–400 ms after word onset (i.e. the visual M350) has been found to correlate with lexical activation, but not competition or selection (Pylkkänen et al., 2002). Imaging studies using fMRI localize auditory semantic priming effects to left hemisphere superior temporal gyrus near Heschl's gyrus, middle frontal gyrus bilaterally, and precentral gyrus (Rissman, Eliassen, & Blumstein, 2003). While the latter effects are consistent with response differences during lexical

decision for target words for related and unrelated word pairs, the observed superior temporal activation is consistent with effects of facilitated lexical activation.

These data, in combination with the spectro-temporal lexical effects above, offer constrained hypotheses concerning the temporal (200–400 ms) and spatial (superior temporal gyrus) properties of lexical activation during auditory speech perception. They also implicate both low-frequency ERD spanning theta, alpha, and low-beta bands and high-frequency gamma ERS (e.g. Mellem et al., 2013; Tavabi et al., 2011a; Tavabi et al., 2011b). These studies further suggest that lexical facilitation manifests as an attenuation of event-related power (ERD or ERS; see also Wang et al., 2012). Notably, while Tavabi et al. do not report high frequency gamma activity in their auditory studies, both Tavabi et al. and Mellem et al. report theta-alpha ERD. Given the differences in task, modality, and methodology, these results need not be at odds, but they leave open the question of whether we expect an early reduction in low-frequency ERD and/or an early reduction of gamma ERS associated with auditory semantic priming.

In the present study we tested whether both alpha-band ERD and gamma-band ERS signals in left and right auditory cortex are sensitive to semantic priming, as would be expected if the oscillatory pattern in this region were associated with lexical activation. We used an auditory semantic priming protocol in MEG with 83 target words that were related (REL) or unrelated (UNREL) to a preceding prime word; pronounceable non-words (NON) could also appear as targets, and subjects performed a lexical decision on the target word. Target words used in UNREL and REL conditions were matched in bottom-up characteristics, which included word frequency and cohort entropy, a measure that quantifies the uncertainty surrounding the recognition of a word based on the existence of other words that begin with the same phonemes. We also explored whether cohort entropy, which reflects the amount of competition during lexical activation, provided insight regarding how incremental information about lexical identity modulated the target neural signals. MEG data were analyzed using Synthetic Aperture Magnetometry (SAM) to identify the spectro-temporal profile of lexical priming effects in the auditory cortex bilaterally.

2. Results

2.1. Behavioral results

Lexical decision times for correct responses from fifteen subjects showed that REL targets ($M = 950$ ms) were identified faster than UNREL ($M = 984$) and NON ($M = 1090$) targets; the mean priming effect (UNREL-REL) was 34 ms ($SE = 10$). Reaction times for each condition are shown in Fig. 1. Analysis using linear mixed-effects models of log-transformed RTs for correct-response trials confirmed that the effect of condition was significant as assessed by a Chi-squared log-likelihood ratio test, $\beta_{REL} = -.057$, $SE_{REL} = .016$; $\beta_{NON} = .16$, $SE_{NON} = .031$, $\chi^2(2) = 21.0$, $p < .001$. There was also a significant effect of target item cohort entropy as computed after the first phoneme of the target on reaction time. Higher cohort entropy targets—words whose identity is more difficult to predict from partial input—elicited a slower response, $\beta_{ENT} = .017$, $SE_{ENT} = .0062$, $\chi^2(1) = 7.8$, $p < .01$. For an intercept-level trial (955 ms), the model predicts a priming effect of 38 ms and a difference in RT latency of 81 ms between the lowest and highest cohort entropy targets. Post hoc pairwise comparisons using Tukey's HSD test showed that all comparisons between conditions were statistically reliable, $p_{NON-UNREL} < .001$; $p_{NON-REL} < .001$; $p_{REL-UNREL} < .001$.

Accuracy for REL targets ($M = 99\%$) was higher than for UNREL ($M = 98\%$) and NON ($M = 92\%$) targets. The effect of condition on

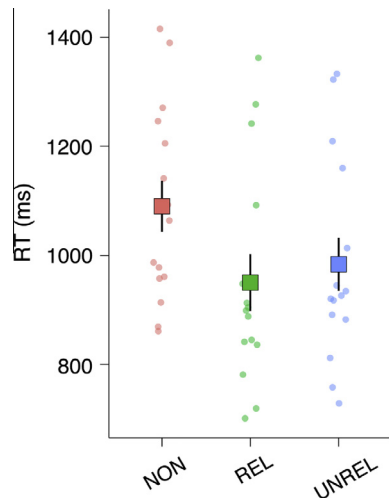


Fig. 1. Mean lexical decision reaction times. Circles indicate individual subject averages; large squares indicate the grand-average per condition and error bars indicate ± 1 SEM.

accuracy was statistically significant, $\beta_{REL} = .97$, $SE_{UNREL} = .63$; $\beta_{NON} = -1.63$, $SE_{NON} = .53$; $\chi^2(2) = 19.1$, $p < .001$. Post hoc pairwise comparisons using Tukey's HSD test showed that the difference between the NON condition and each of the UNREL and REL conditions was statistically reliable ($p_{NON-UNREL} < .01$, $p_{NON-REL} < .001$), while the difference between REL and UNREL was not ($p_{REL-UNREL} = .27$).

2.2. MEG results

Grand-averaged MEG sensor data for an epoch spanning from -2.1 to 1.3 s from the target word onset are shown in Fig. 2A. Auditory M50, M100, M200, and later sustained components are clearly visible relative to both prime and target word onsets.

M100 dipole fits to the auditory functional localizer (1 kHz tones) for two example subjects are shown in Fig. 2B. One subject out of fifteen did not show a robust auditory M100 (goodness of fit $< 80\%$) and was excluded from subsequent MEG analysis. Left and right auditory cortex (LAC, RAC) dipole locations were used to define virtual sensors using Synthetic Aperture Magnetometry (SAM).

Time–frequency plots from LAC virtual sensors, time-locked to the target word onset for REL, UNREL, and NON conditions, are shown in Fig. 2C. All plots show a transient power increase (event-related synchronization; ERS) around 100 ms, primarily in delta and theta bands, consistent in time and duration with the auditory M100 response (Roberts, Ferrari, Stufflebeam, & Poeppel, 2000). The low frequency ERS is followed by a sustained decrease in power in alpha and beta-band activity, primarily between 10 and 20 Hz, beginning about 250 ms after word onset and extending approximately 800 ms. This event-related de-synchronization (ERD) is notably attenuated in REL.

A cluster-based permutation test comparing power between 0 and 1.1 s after target onset was conducted within two bands based on our hypotheses: from 5 to 35 Hz, and from 30–50 Hz. Between 5 and 35 Hz, we found a single significant cluster of reduced de-synchronization (ERD) for REL ($M = -2.42\%$) compared to UNREL ($M = -7.26\%$), cluster sum = 4068, $p_{montecarlo} < .05$. The cluster of ERD attenuation spanned 10–20 Hz, with an onset at about 270 ms and extended until approximately 900 ms after target onset. No effect for NON ($M = -6.52\%$) compared to UNREL was observed. The mean ERD within this significant cluster is plotted

for each condition in Fig. 2D. No significant effects in the gamma band, from 30 to 50 Hz, were found.

Turning to the RAC virtual sensor time–frequency representations, there were no significant main effects of condition in either the 5–35 Hz band, or the 30–50 Hz between 0 and 1.3 s after target onset (see Supplementary materials). To further test for hemispheric lateralization of the ERD attenuation, we averaged power in a window spanning 250–500 ms and 10–20 Hz and entered the result into a 2 (hemisphere) \times 3 (condition) ANOVA. This test showed a significant main effect of condition, $F(2,26) = 3.52$, $p < .05$, driven by reduced ERD in the REL condition, but no significant interaction between hemisphere and condition. Accordingly, while the effect of condition is statistically more reliable in the left hemisphere, our results are consistent with a non-lateralized priming effect.

2.3. Cohort entropy analysis

Cohort entropy offers an estimate of the information that the initial sounds of a word provide about word identity, quantified in terms of the expected number of bits required to encode the information contained in the distribution of words consistent with the input at a given moment in time. Entropy was estimated for each of our target words phoneme-by-phoneme to test how partial information about lexical identity unfolds in time.

Cohort entropy, which reflects bottom-up information only, is plotted per condition in Fig. 3. Importantly, no differences between UNREL and REL target words emerge during the target interval, indicating strong experimental control of bottom-up information. Further, the time-courses show that entropy reductions, indicating increased information about lexical identity, begin no earlier than 80–100 ms after stimulus onset for UNREL and REL items. We estimate a 100–120 ms lag between the auditory periphery and auditory cortex, following from the observation that the M100 response reflects complex spectral characteristics of an acoustic stimulus (Roberts et al., 2000). Further, evidence suggests that the incremental speech percept is quantized on the order of 40–60 ms (Giraud & Poeppel 2012). Summed together, the latency of entropy change, the ear–brain lag, and speech quantization provide an estimate of when this change in entropy might be reflected in auditory processing: 220–280 ms after word onset. This value accords well with the onset of the statistically reliable 10–20 Hz ERD effect at 270 ms.

A strong test of this explanation for the timing of the ERD effect would be to correlate entropy over the first approximately 100 ms of auditory input with the ERD effect. However, first-phoneme entropy did not correlate with 10–20 Hz power, averaged within 50 ms windows spanning the target time-window. This post hoc analysis has several limitations, discussed below, that stand in the way of a clear interpretation of a null result.

3. Discussion

This study aimed to test whether alpha ERD and/or gamma ERS in left and right auditory cortex are associated with the speed of lexical activation during auditory stimulation. Previous work has linked left hemisphere ERD across theta, alpha, and low beta bands with lexical differences between items (Bastiaansen & Hagoort, 2006; Bastiaansen et al., 2005; Mellem et al., 2012; Tavabi et al., 2011a; Tavabi et al., 2011b; Wang et al., 2012), or with lexical repetition (Tavabi et al., 2011b), but no previous studies focused on lexical activation. In addition, results from visual semantic priming have linked facilitated lexical access with reduced gamma-band ERS (Mellem et al., 2013). While semantic priming effects may be mediated by automatic or controlled mechanisms, they uniformly

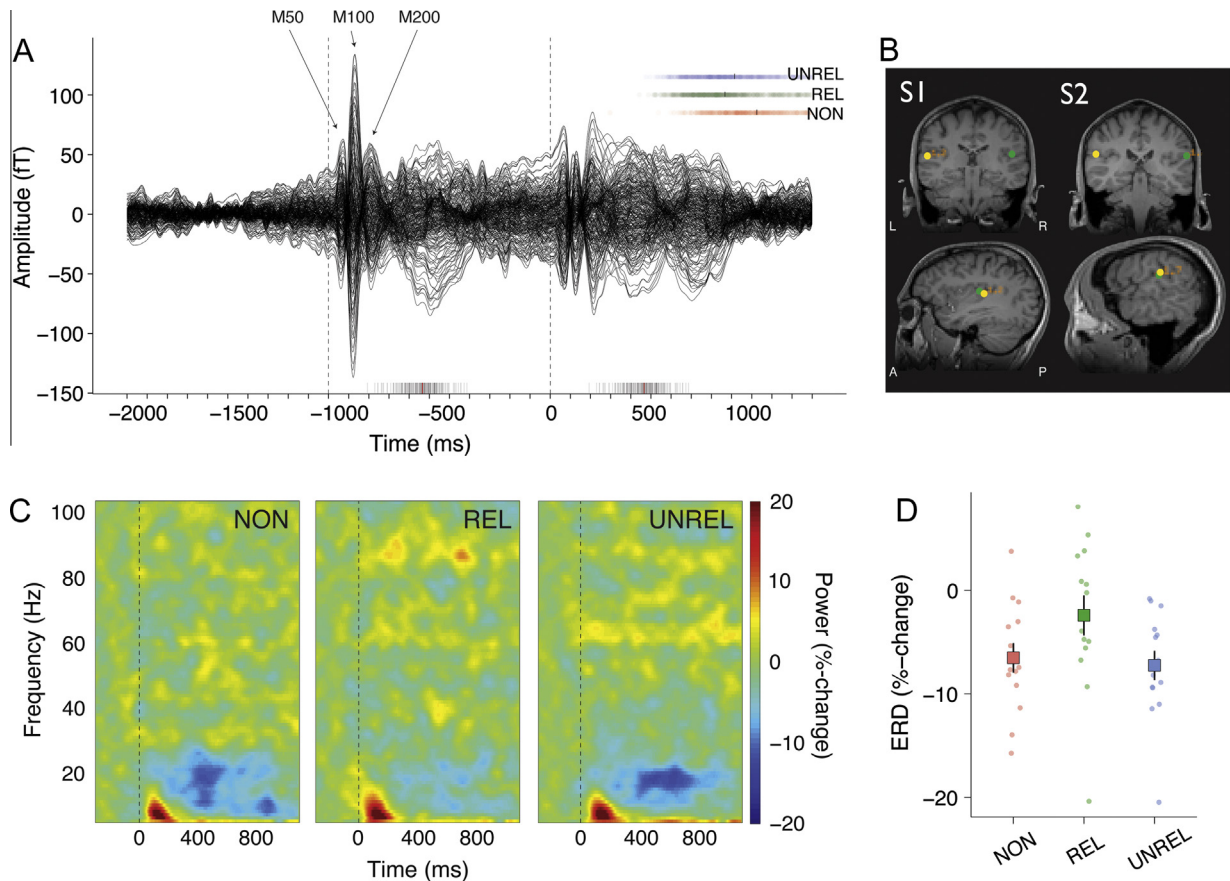


Fig. 2. (A) Sensor waveforms grand-averaged across subjects and conditions, time-locked to target onset. Prime onset is indicated at -1100 ms; distributions in the top right show individual trial RTs and grand-median (black lines) for REL (green), UNREL (blue) and NON (red) conditions. Distributions shown along the x -axis indicate median (red) and individual stimulus (black) offsets. (B) Left (yellow) and right (green) auditory cortex dipole fits to auditory functional localizer for two representative subjects shown on individual subject MRIs. (C) Spectro-temporal plots in each condition for the left auditory cortex virtual sensor, time-locked to target onset. (D) Mean ERD within a spectro-temporal cluster showing reliable attenuation in REL compared to UNREL (see Section 5). The cluster spans approximately 270–900 ms between 10 and 20 Hz. Circles indicate individual subject averages; large squares indicate the grand-average per condition and error bars indicate ± 1 SEM.

facilitate lexical activation via pre-activation of primed items (Neely, 1991). The facilitatory effect of auditory semantic priming has been localized with fMRI to the superior temporal gyrus and Heschl's gyrus (Rissman et al., 2003), and MEG studies have shown superior temporal sensitivity to lexical activation, but not competition, between 300–400 ms after word presentation (Pylkkänen et al., 2002). Consistent with predictions based on auditory manipulations, we found that semantic priming leads to an attenuation of ERD in left auditory cortex beginning about 270 ms after target word onset. In contrast to results from semantic priming in the visual domain (Mellem et al., 2013), we did not find any reliable effects in the gamma band. However, in addition to the stimulus domain, several methodological differences preclude direct comparison of these results.

The average word length for the monosyllabic target items was 459 ms. Thus, priming effects were observed at a point about half-way through the average stimulus item. The effect onset follows even the shortest of target stimuli by only 76 ms. The average point at which an item reached its minimum entropy, representing the point at which a hearer is most confident about which word is being recognized, was 377 ms, suggesting that the effect we observed shows that lexical access begins prior to word uniqueness, in a manner consistent with dominant models of incremental lexical activation (Marslen-Wilson 1987; McClelland & Elman 1986).

Given that changes in cohort entropy begin on average 80–100 ms after stimulus onset, and incorporating reasonable

estimates about the lag between stimulus presentation at the ear and cortical processing of complex speech sounds (Roberts et al., 2000; Giraud & Poeppel, 2012), we hypothesize that the change in ERD beginning at 270 ms reflects or follows only shortly after the earliest stages at which bottom-up speech information about lexical identity is merged with top-down expectations reflected in the priming manipulation.

Facilitated activation may have down-stream consequences for competition, selection, and post-lexical decision processes. While the present semantic priming manipulation does not provide the cognitive resolution to distinguish these different stages, the temporal lag between changes in cohort entropy and the onset of the ERD effect provide strong indirect support for linking this neural signal with early stages of access. Furthermore, Pylkkänen et al. (2002), in a visual lexical decision experiment, identified an evoked MEG component peaking at 350 ms that was sensitive to phonotactic probability but not to neighborhood density; while the former modulates lexical activation, the latter has been linked with competition (Vitevitch et al., 1999). The ERD onset latency of 270 ms thus appears to be earlier than the emergence of competition effects.

Interestingly, as shown in Fig. 2C, the ERD effect persists until between 800 and 900 ms after stimulus onset (about 400 ms after median stimulus offset). While our hypotheses make concrete predictions about the cognitive state that must be reached for a neural effect to register, they do not carry predictions about the state that must be reached for the effect to cease. We might nonetheless

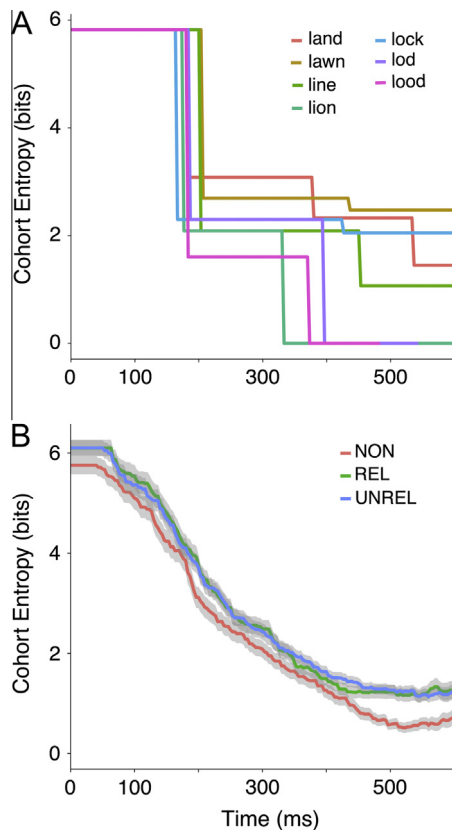


Fig. 3. (A) Example single-word cohort entropy estimates for seven target items beginning with/l/. (B) Average cohort entropy estimates for NON (red), REL (green) and UNREL (blue); gray intervals indicate standard error of the mean. Note that REL and UNREL are closely matched throughout the time interval.

speculate that the ERD effect spans subsequent competition and selection stages. At the very least, the duration of the ERD effect suggests that subsequent studies can examine the effects of theta–alpha ERD of cognitive manipulations that affect competition and selection.

A post hoc correlation between initial-phoneme cohort entropy and 10–20 Hz ERD did not reveal a significant relationship. This null result may reflect a higher order relationship between continuous changes in entropy and lexical processing, or may reflect limits due to our stimuli or entropy estimates. It may be difficult to detect entropy effects using monosyllabic items as monosyllabic items exhibit relatively low variation in entropy and estimates of their entropy are particularly sensitive to the inclusion of morphologically related items in the word list used for estimation. Using a set of items explicitly selected for high variance in entropy, Ettinger et al. (in press) found a correlation between cohort entropy and evoked activity in left auditory cortex at a latency of 335–377 ms after stimulus onset. Interestingly, the correlated brain signal was lagged 200 ms from the speech signal in that study, a time shift of similar magnitude to the onset latency of ERD we observed relative to the onset of entropy reduction. Further work is necessary to test the relationship between cohort entropy and the processes indexed by alpha-related ERD in auditory-cortex.

The onset of the priming effect accords well with evoked data from both EEG and MEG. The N400 EEG effect, which is sensitive to semantic priming (Holcomb & Neville 1990; Kutas & Hillyard 1984), shows an onset in auditory presentation between 150 and 250 ms after target onset. Semantic priming in MEG has been associated with the M350 component during visual presentation (Pykkänen, Llinás, & Murphy, 2006; Vartiainen et al., 2009;

Table 1
Example stimuli for each condition.

Condition	Prime	Target
Related (REL)	Bag	Purse
Unrelated (UNREL)	Bag	Neck
Non-word (NON)	Bag	Vun

Zipse, Kearns, Nicholas, & Marantz, 2011), a component that shows sensitivity to numerous factors that affect lexical activation, including word frequency (Embick, Hackl, Schaeffer, Kelepir, & Marantz, 2001; Solomyak and Marantz, 2010) and phonotactic probability (Pykkänen et al., 2002) but not to factors affecting lexical competition such as neighborhood density (Pykkänen et al., 2002). Pre-lexical effects of orthography have been found at the earlier M170 component, peaking between 150 and 250 ms post visual word presentation. Such effects include lexicality (Tarkiainen et al., 1999), orthographic frequency (Solomyak & Marantz, 2009), and transition probability (Lewis, Solomyak, & Marantz, 2011). These data provide lower and upper limits on the timing of lexical activation in visual word recognition and are consistent with the onset of our auditory effect.

The timing estimates for lexical activation discussed above contrast with some studies of auditory lexical processing showing extremely early effects of lexicality in lexical decision (MacGregor, Pulvermüller, van Casteren, & Shtyrov, 2012) and odd-ball (Pulvermüller et al., 2003) protocols. Our study differs from these in that only top-down information was modulated. Analysis of the cohort entropy of our target items confirmed that REL and UNREL targets conveyed equal amounts of information within the first 500 ms. Our results are most consistent with auditory EEG studies of semantic priming and visual lexical recognition in MEG above.

The timing and spectral profile of our priming effect shows both similarities and differences to that observed to visual priming by Mellem et al. (2013). That study showed a late beta ERD effect, overlapping in time and frequency with the extended effect we observe, as well as early gamma ERS about 150 ms after stimulus onset. Several differences between that study and the present one make it difficult to pinpoint the factor(s) responsible for the absence of gamma ERS and the relatively early onset of the ERD. In addition to differing in modality of stimulation, Mellem et al. employed a letter-search task, not lexical decision. Differences may also reflect the differential sensitivity of MEG and EEG to cortical activation. It is worth noting, however, that the timing of effects between the two studies may be in closer accord than first appears. Assuming that the ERD effect in our study reflects a sensitivity to information encoded in the first 80–100 ms or so of speech stimulus, the effect's onset has a lag between approximately 170 ms and 190 ms; this estimate is not far from the 150 ms latency of the gamma ERS effect reported by Mellem et al.

We did not observe a difference between pronounceable non-words and words in the spatial and spectro-temporal window we probed. This result differs from that of Tavabi et al. (2011a). We note that non-words in that study were created by acoustic vocoding with white-noise, yielding totally unintelligible stimuli. This contrasts sharply with the pronounceable non-words (i.e. pseudo-words) used in the present study. The word-like status of our non-words may have led to strong activation at initial stages of lexical activation. The average point at which a non-word item reached its minimum cohort entropy was 389 ms, suggesting that a large portion of the stimulus needed to be heard before a decision regarding its status could be made.

4. Conclusion

The spatial and temporal properties of the neural mechanisms subserving lexical activation have been characterized with

increasing precision by previous studies. The current study adds spectro-temporal detail, building on previous work that found sensitivity to lexical properties in alpha-band de-synchronization. We used a semantic priming protocol to facilitate lexical activation while keeping bottom-up input matched across conditions. Quantifying how lexical information unfolds incrementally using cohort entropy provides further perspective on the timing of the observed neural signatures. The results demonstrate that alpha and low beta de-synchronization generated in left auditory cortex is attenuated when lexical activation is facilitated, suggesting that this spectro-temporal pattern is linked with early stages of lexical access.

5. Methods

5.1. Participants

15 subjects participated in this experiment (7 females) with ages ranging from 25 to 54 (median = 27). Participants were right-handed and reported no history of neurological disorder. All procedures complied with institutional review regulations at the Children's Hospital of Philadelphia.

5.2. Stimuli

Related prime and target words (REL) were selected using the following criteria designed to generate a set of stimuli optimized for future studies with multiple populations, including children. We identified monosyllabic concrete nouns with a forward association greater than .23 (corpus median from the University of Florida Free Association norms; Nelson, McEvoy, & Schreiber, 1998), log spoken frequency greater than 2.75 (corpus median from the SUBTLEXus corpus; the English Lexicon Project, Balota et al., 2007), concreteness greater than 4.5 (corpus median from the MRC Psycholinguistic Database, Wilson 1988) and age of acquisition less than six years (MRC Psycholinguistic Database and Bristol Norms; Gilhooly & Logie, 1980). We then manually trimmed this set of 490 word pairs, removing instances where two raters (J.B., D.E.) judged the association too mature, too abstract, or where the pair formed a potential word compound (e.g. CHURCH-BELL). Finally, pairs sharing a prime or target word were selectively removed so that each target had a unique prime, and each prime had a unique target. These steps yielded a final set of 83 related prime–target pairs.

Unrelated (UNREL) prime–target pairs were formed by pseudo-randomly shuffling the primes to create pairs judged to have no association. This judgment was confirmed using Latent Semantic Analysis (Landauer, Foltz, & Laham 1998) to estimate the pairwise relationship in related ($M_{REL} = .33$; $SD_{REL} = .19$) and unrelated ($M_{UNREL} = .08$; $SD_{UNREL} = .07$ pairs), $t(82) = 10.9$, $p < .001$. Due to experimenter error, stimulus items were removed from the set according to the criteria noted above after this shuffle step, leading about 40% of target words to differ between REL and UNREL conditions. Using norms from the English Lexicon Project (Balota et al., 2007), we confirmed that REL and UNREL target words were matched in number of phonemes ($M_{REL} = 3.37$, $M_{UNREL} = 3.43$; $t(164) = -0.65$, $p > .1$), number of phonological neighbors ($M_{REL} = 18.98$, $M_{UNREL} = 17.32$; $t(164) = 1.14$, $p > .1$), mean bigram frequency ($M_{REL} = 1602$, $M_{UNREL} = 1536$; $t(164) = -0.26$, $p > .1$), orthographic length ($M_{REL} = 4.36$, $M_{UNREL} = 4.37$; $t(164) = -0.09$, $p > .1$), mean lexical decision reaction time ($M_{REL} = 586$, $M_{UNREL} = 590$; $t(164) = -0.66$, $p > .1$). There was a marginally significant difference in log spoken frequency (SUBTLEXus corpus; $M_{REL} = 3.43$, $M_{UNREL} = 3.31$; $t(164) = 1.91$, $p = .06$). However, statistical analysis of reaction times for real target words (REL and UNREL) showed that the effect of frequency did not approach significance,

$\beta_{FREQ} = -.001$, $SE_{FREQ} = .006$, $\chi^2(1) = 3.2$ $p = .88$, suggesting that differences in frequency between REL and UNREL targets did not contribute to the size of priming effect observed.

Pronounceable non-word targets (NON) were formed by changing one, or in a few cases two, phonemes in related target words and were randomly paired with a prime item.

We quantified how information about word identity unfolded incrementally using cohort entropy. This measure reflects the amount of competition in a cohort—the words consistent with a given phonological prefix—in terms of the expected number of bits required to represent a probability distribution over those words (Shannon, 1948), with the probability of each word defined as its lowercase-form frequency in SUBTLEXus corpus. Cohort entropy was calculated phoneme-by-phoneme for each word using the 40,481-word lexicon of the English Lexicon Project (Balota et al., 2007). For example, for the item *lion* the cohort entropy measured after the first phoneme is 5.8 bits, computed over a cohort of all words starting with *l*. After the syllable nucleus it is 2.1 bits, computed over a cohort including *lie*, *lye*, *live*, etc. and showing a large decrease in entropy as the uncertainty about the completion of the word is reduced. Examples of single-item cohort entropy estimates are shown in Fig. 3A. The use of word frequency in the cohort entropy measure allows for a strong test of whether target words differed in bottom-up characteristics between conditions.

To analyze the impact of cohort entropy, we selected a single per-item measure of entropy that best predicted the variance in reaction times not explained by other predictors included in the model. To do so, we fit a baseline linear mixed-effects model that included all predictors other than entropy, accounting for variance due from the semantic priming effect and subject identity, and correlated the residuals of that model with a set of predictors that provided a summary measure of cohort entropy for each item: the mean and maximum cohort entropy computed after each phoneme in each word, cohort entropy after the first phoneme, after the syllable onset (leading consonants), and after the syllable nucleus. The strength of this correlation represented the ability of that predictor to contribute additional information beyond that expressed by the baseline predictors. The entropy computed after the first phoneme was the best predictor of residual reaction times under this approach ($\rho = .097$).

The item selection procedure returned 83 triples of matched REL, UNREL, and NON word pairs. Importantly, the target words in both REL and UNREL conditions were matched in bottom-up characteristics between conditions. Non-words and words appeared in a 1:2 ratio which may lead to a bias towards “word” responses in the lexical decision task. This ratio was chosen to encourage lexical processing while minimizing the length of the experiment. Example stimuli are shown in Table 1. The full stimulus set is given in Supplementary material.

All words were recorded by a female speaker in a sound-attenuated booth spoken within a carrier phrase (“Say ___ again”), and digitized at 44,100 Hz. Stimuli were re-sampled to 22,050 Hz, trimmed to ensure that onsets were precisely aligned across stimuli, and normalized to 70 dB in Praat software (Boersma, 2001). Stimuli ranged in duration from 193 to 687 ms ($M = 459$). There were no duration differences between target stimuli in any of the three conditions, REL–UNREL $t(164) = -.18$, $p > .5$; REL–NON $t(164) = -0.57$, $p > .5$; UNREL–NON $t(164) = -.39$, $p > .5$.

The stimuli were organized into three lists such that no two items from the same triplet occurred in the same list.

5.3. Procedure and MEG acquisition

Participants were seated in a dimly lit magnetically shielded room for MEG recording while auditory stimuli were delivered binaurally via insert-earphones (Etymotic Inc.) Trials consisted of a

prime word followed by a target. Stimulus onset asynchrony between prime and target was 1.1 s, and the inter-trial interval ranged from 1.9 to 2.1 s; trials were terminated by a lexical decision button press to the target word or after four seconds following target word offset. Prior to recording, each participant's hearing threshold was assessed using 1 kHz tones (300 ms duration). Experimental stimuli were presented at 45 dB above threshold. An auditory functional localizer using 120 1 kHz tones (0.95–1.05 s ISI) was also administered.

Participants were fitted with three fiducial coils, two placed anterior to the left and right tragus of the ear, and one placed on the nasion. These were used to continuously monitor head position during recording and for subsequent co-registration between the MEG data and anatomical images. Electrodes were also placed above and below the left eye to monitor eye-blinks and on the left and right clavicle to monitor the heart beat. MEG was recorded using 275 CTF axial gradiometers (VSM MedTech, Coquitlam, BC) with third-order synthetic gradiometer noise correction at 1200 Hz with no on-line filters.

Participants were presented with each of the three stimulus lists, ordered by a latin-square across participants, and they took a short break between lists. Stimulus order was fully randomized within lists. Participants were instructed to indicate if the second word in each pair was a real word or not using the index (“word”) and middle (“non-word”) fingers of their left hand. The experiment, including the functional localizer, lasted between 20 and 30 min.

Structural MRIs were recorded from each participant with a 3T Siemens Verio scanner using a 32 channel receiver only head RF coil. We recorded a T1-weighted image for each participant with a magnetization-prepared radio-frequency pulse (MPRAGE) sequence (126 slices, $1 \times 1 \times 1$ mm voxels, field of view 256, matrix 256×256 , echo time 2.87 ms, repetition Time 1900 ms, flip angle 9° , inversion time 1050 ms).

5.4. Behavioral data analysis

Lexical decision data were cleaned by removing all trials with RTs below the duration of the target stimulus or above 2000 ms as outliers, which constituted 1.1% of correct-response trials. In addition, duplicated items were removed from one subject who heard the same stimulus list twice due to a technical error. Statistical analysis of correct-response log base two-transformed RTs was conducted using linear mixed-effects modeling (Baayen, Davidson, & Bates, 2008; Pinheiro & Bates, 2000) with the lme4 package (Bates, Maechler, Bolker, & Walker, 2013) in R with fixed effects of condition, and speaker gender, random intercepts for speakers and items, and a per-subject random slope for condition. Accuracy was analyzed using generalized linear mixed effects modeling with a logit link function (Jaeger, 2008) with the same model structure except for the removal of the word frequency predictor as both words and non-words were modeled. A second model of reaction time discussed above for the purpose of examining word frequency effects added an additional fixed effect and per-subject random slope for log word frequency as given in SUBTLEX, with Laplace smoothing applied to the counts. Statistical significance was assessed using Chi-squared log-likelihood ratio tests. For both reaction time and accuracy models, the UNREL condition was coded as model intercept.

5.5. MRI data processing

MRI data were aligned with the MEG datasets based on the fiducial points and a multi-sphere head-model, created with CTF analysis tools based on each subject's outer skull shape, was used for subsequent source modeling.

5.6. MEG data processing and analysis

MEG data were low-pass filtered off-line at 150 Hz, resampled to 300 Hz, and a notch filter at 60 Hz and 120 Hz was applied to attenuate power line artifacts. Data were then epoched from -2.1 to 1.3 s relative to target word onset. This interval begins one second prior to the onset of the prime stimulus (See Fig. 1A). Epochs with excessive noise were marked for exclusion based on visual inspection, and epochs with behavioral errors or duplicated presentation were also excluded from further analysis.

MEG data analysis was conducted using a combination of CTF analysis tools and custom scripts written in MATLAB. Primary auditory cortex was identified in each subject using the auditory M100 response elicited by the 1 kHz tones functional localizer (Fig. 1B). Localizer data were band-pass filtered from 1–20 Hz, and two equivalent current dipoles were fit to a 10 ms window showing the most pronounced bilateral topography. All fitted dipoles were in close proximity to Heschl's gyrus; goodness of fit for 14 of 15 subjects was $>80\%$ ($M = 90.1\%$, $SD = 4.9\%$). Goodness of fit for one subject was $<80\%$ and this subject was excluded from subsequent analysis.

Synthetic Aperture Magnetometry (SAM; Robinson, Vrba, et al., 1999) was used to create a virtual sensor at the left auditory cortex (LAC) and right auditory cortex (RAC) coordinates identified by the dipole models for each of 14 subjects. SAM analysis was conducted over the entire epoch with a covariance band from 1.5 to 80 Hz. This scalar beamformer acts as a spatial filter, passing signal originating from the target coordinate while attenuating signals originating from other locations, including artifacts such as muscle movement and eye-blinks.

The virtual sensor time-courses for each epoch was converted to a time-frequency representation using the Hilbert transform from 1 to 100 Hz in 1 Hz increments with a width of 8 Hz (e.g. Muthukumaraswamy, Singh, Swettenham, & Jones, 2010). Percent change in power was calculated per frequency bin relative to a baseline of -300 to -100 ms prior to target onset (Fig. 1C).

Statistical analyses were conducted on the time-frequency representations for each subject, from each of three conditions between a time window from 0 to 1100 ms after target onset, in two frequency bands, one from 5 to 35 Hz which includes theta, alpha, beta, and low gamma bands, and a second from 30 to 50 Hz. A non-parametric cluster-based monte carlo permutation test with 10,000 iterations was used to test for statistically reliable spatio-temporal differences between conditions (Maris & Oostenveld 2007). Hemispheric effects were tested by averaging power in a window spanning 250–500 ms and 10–20 Hz. These averaged were entered into a 2 (hemisphere) \times 3 (condition) repeated measures ANOVA. There is some flexibility in exactly how the time-window for the hemisphere analysis might have been defined, but identical statistical results were obtained across a range of windows ($\{10\text{--}20$ Hz, $10\text{--}25$ Hz} in frequency, and $\{250\text{--}500$, $250\text{--}800$ ms} in time).

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.bandl.2014.03.006>.

References

- Baayen, R. H., Davidson, D. J., & Bates, D. M. (2008). Mixed-effects modeling with crossed random effects for subjects and items. *Journal of Memory and Language*, 59(4), 390–412.
- Balota, D. A., Yap, M. J., Cortese, M. J., Hutchinson, K. I., Kessler, B., Loftis, B., et al. (2007). The English lexicon project. *Behavior Research Methods*, 39, 445–459.
- Bastiaansen, M., & Hagoort, P. (2006). Oscillatory neuronal dynamics during language comprehension. *Progress in Brain Research*, 159, 179–196.
- Bastiaansen, M. C. M., van der Linden, M., Ter Keurs, M., Dijkstra, T., & Hagoort, P. (2005). Theta responses are involved in lexical-semantic retrieval during language processing. *Journal of Cognitive Neuroscience*, 17(3), 530–541.
- Bates, D. M., Maechler, M., Bolker, B., Walker, S. (2013). lme4: Linear mixed-effects models using Eigen and S4 (Version 1.0-5). <<http://CRAN.R-project.org/package=lme4>>.
- Boersma, P. (2001). Praat, a system for doing phonetics by computer. *Glott International*, 5(9/10), 341–345.
- Coben, R., Clarke, A. R., Hudspeth, W., & Barry, R. J. (2008). Eeg power and coherence in autistic spectrum disorder. *Clinical Neurophysiology*, 119(5), 1002–1009.
- Cornew, L., Roberts, T. P. L., Blaskey, L., & Edgar, J. C. (2012). Resting-state oscillatory activity in autism spectrum disorders. *Journal of Autism and Developmental Disorders*, 42(9), 1884–1894.
- Edgar, J. C., Hanlon, F. M., Huang, M.-X., Weisend, M. P., Thoma, R. J., Carpenter, B., Hoehstetter, K., Cañive, J. M., & Miller, G. A. (2008). Superior temporal gyrus spectral abnormalities in schizophrenia. *Psychophysiology*, 45(5), 812–824.
- Edgar, J. C., Khan, S. Y., Blaskey, L., Chow, V. Y., Rey, M., Gaetz, W., et al. (2013). Neuromagnetic oscillations predict evoked-response latency delays and core language deficits in autism spectrum disorders. *Journal of Autism and Developmental Disorders*.
- Embick, D., Hackl, M., Schaeffer, J., Kelepir, M., & Marantz, A. (2001). A magnetoencephalographic component whose latency reflects lexical frequency. *Brain Research. Cognitive Brain Research*, 10, 345–348.
- Ettinger, A., Linzen, T., Marantz, A. (in press). The role of morphology in phoneme prediction: Evidence from MEG. *Brain and Language*.
- Friederici, A. D. (2012). The cortical language circuit: From auditory perception to sentence comprehension. *Trends in Cognitive Sciences*, 16(5), 262–268.
- Gandal, M. J., Edgar, J. C., Ehrlichman, R. S., Mehta, M., Roberts, T. P. L., & Siegel, S. J. (2010). Validating gamma oscillations and delayed auditory responses as translational biomarkers of autism. *Biological Psychiatry*, 68(12), 1100–1106.
- Gandal, M. J., Edgar, J. C., Klook, K., & Siegel, S. J. (2011). Gamma synchrony: Towards a translational biomarker for the treatment-resistant symptoms of schizophrenia. *Neuropharmacology*, 63(3), 1504–1518.
- Gilhooly, K. J., & Logie, R. H. (1980). Age-of-acquisition, imagery, concreteness, familiarity, and ambiguity measures for 1944 words. *Behavior Research Methods & Instrumentation*, 12(4), 395–427.
- Giraud, A.-L., & Poeppel, D. (2012). Cortical oscillations and speech processing: Emerging computational principles and operations. *Nature Neuroscience*, 15(4), 511–517.
- Hickok, G., & Poeppel, D. (2007). The cortical organization of speech processing. *Nature Reviews Neuroscience*, 8(5), 393–402.
- Holcomb, P. J., & Neville, H. J. (1990). Auditory and visual semantic priming in lexical decision: A comparison using event-related brain potentials. *Language and Cognitive Processes*, 5(4), 281–312.
- Jaeger, T. F. (2008). Categorical data analysis: Away from ANOVAs (transformation or not) and towards logit mixed models. *Journal of Memory and Language*, 59(4), 434–446.
- Kujala, J., Vartiainen, J., Laaksonen, H., & Salmelin, R. (2012). Neural interactions at the core of phonological and semantic priming of written words. *Cerebral Cortex*, 22(10), 2305–2312.
- Kutas, M., & Hillyard, S. A. (1984). Brain potentials during reading reflect word expectancy and semantic association. *Nature*, 307(5947), 161–162.
- Landauer, T. K., Foltz, P. W., & Laham, D. (1998). Introduction to latent semantic analysis. *Discourse Processes*, 25, 259–284.
- Lewis, G., Solomyak, O., & Marantz, A. (2011). The neural basis of obligatory decomposition of suffixed words. *Brain and Language*, 118(3), 118–127.
- MacGregor, L. J., Pulvermüller, F., van Casteren, M., & Shtyrov, Y. (2012). Ultra-rapid access to words in the brain. *Nature Communications*, 3, 711.
- Maris, E., & Oostenveld, R. (2007). Nonparametric statistical testing of EEG- and MEG-data. *Journal of Neuroscience Methods*, 164(1), 177–190.
- Marslen-Wilson, W. (1987). Functional parallelism in spoken word-recognition. *Cognition*, 25(1), 71–102.
- McClelland, J. L., & Elman, J. L. (1986). The TRACE model of speech perception. *Cognitive Psychology*, 18(1), 1–86.
- Mellem, M. S., Bastiaansen, M. C. M., Pilgrim, L. K., Medvedev, A. V., & Friedman, R. B. (2012). Word class and context affect alpha-band oscillatory dynamics in an older population. *Frontiers in Psychology*, 3, 97.
- Mellem, M. S., Friedman, R. B., & Medvedev, A. V. (2013). Gamma- and theta-band synchronization during semantic priming reflect local and long-range lexical-semantic networks. *Brain and Language*, 127(3), 440–451.
- Meyer, D. E., & Schvaneveldt, R. W. (1976). Meaning, memory structure, and mental processes. *Science*, 192(4234), 27–33.
- Muthukumaraswamy, S. D., Singh, K. D., Swettenham, J. B., & Jones, D. K. (2010). Visual gamma oscillations and evoked responses: Variability, repeatability and structural MRI correlates. *NeuroImage*, 49(4), 3349–3357.
- Neely, J. (1991). Semantic priming effects in visual word recognition: A selective review of current findings and theories. *Basic processes in reading: Visual word recognition*, 11.
- Nelson, D. L., McEvoy, C. L., & Schreiber, T. A. (1998). *The University of South Florida word association, rhyme, and word fragment norms*. <<http://www.usf.edu/FreeAssociation/>>.
- Norris, D. (1994). Shortlist: A connectionist model of continuous speech recognition. *Cognition*, 52(3), 189–234.
- Pfurtscheller, G., & Lopes da Silva, F. H. (1999). Event-related EEG/MEG synchronization and desynchronization: Basic principles. *Clinical Neurophysiology*, 110(11), 1842–1857.
- Pinheiro, J. C., & Bates, D. M. (2000). *Mixed-effects models in S and S-PLUS*. New York: Springer.
- Pylkkänen, L., Llinás, R., & Murphy, G. L. (2006). The representation of polysemy: MEG evidence. *Journal of Cognitive Neuroscience*, 18(1), 97–109.
- Pulvermüller, F., Shtyrov, Y., & Ilmoniemi, R. (2003). Spatiotemporal dynamics of neural language processing: an meg study using minimum-norm current estimates. *NeuroImage*, 20(2), 1020–1025.
- Pylkkänen, L., Stringfellow, A., & Marantz, A. (2002). Neuromagnetic evidence for the timing of lexical activation: An MEG component sensitive to phonotactic probability but not to neighborhood density. *Brain and Language*, 81(1–3), 666–678.
- Rissman, J., Eliassen, J. C., & Blumstein, S. E. (2003). An event-related fMRI investigation of implicit semantic priming. *Journal of Cognitive Neuroscience*, 15(8), 1160–1175.
- Roberts, T. P. L., Ferrari, P., Stufflebeam, S. M., & Poeppel, D. (2000). Latency of the auditory evoked neuromagnetic field components: Stimulus dependence and insights toward perception. *Journal of Clinical Neurophysiology*, 17(2), 114–129.
- Robinson, S., Vrba, J., et al. (1999). Functional neuroimaging by synthetic aperture magnetometry (SAM). *Recent Advances in Biomagnetism*, 302–305.
- Shannon, C. E. (1948). A mathematical theory of communication. *Bell System Technical Journal*, 27(3), 379–423.
- Solomyak, O., & Marantz, A. (2009). Lexical access in early stages of visual word processing: A single-trial correlational MEG study of heteronym recognition. *Brain and Language*, 108(3), 191–196.
- Solomyak, O., & Marantz, A. (2010). Evidence for early morphological decomposition in visual word recognition. *Journal of Cognitive Neuroscience*, 22(9), 2042–2057.
- Tarkiainen, A., Helenius, P., Hansen, P. C., Cornelissen, P. L., & Salmelin, R. (1999). Dynamics of letter string perception in the human occipitotemporal cortex. *Brain*, 122(11), 2119–2132.
- Tavabi, K., Embick, D., & Roberts, T. (2011a). Word repetition priming-induced oscillations in auditory cortex: A magnetoencephalography study. *NeuroReport*, 22(17), 887–891.
- Tavabi, K., Embick, D., & Roberts, T. P. L. (2011b). Spectral-temporal analysis of cortical oscillations during lexical processing. *NeuroReport*, 22(10), 474–478.
- Uhlhaas, P. J., & Singer, W. (2007). What do disturbances in neural synchrony tell us about autism? *Biological Psychiatry*, 62(3), 190–191.
- Vartiainen, J., Parviainen, T., & Salmelin, R. (2009). Spatiotemporal convergence of semantic processing in reading and speech perception. *Journal of Neuroscience*, 29(29), 9271–9280.
- Vitevitch, M. S., Luce, P. A., Pisoni, D. B., & Auer, E. T. (1999). Phonotactics, neighborhood activation, and lexical access for spoken words. *Brain and Language*, 68, 306–311.
- Wang, L., Jensen, O., van den Brink, D., Weder, N., Schoffelen, J.-M., Magyari, L., et al. (2012). Beta oscillations relate to the N400m during language comprehension. *Human Brain Mapping*, 33(12), 2898–2912.
- Wilson, M. D. (1988). The MRC psycholinguistic database: Machine readable dictionary, version 2. *Behavior Research Methods, Instruments, & Computers*, 20, 6–11.
- Zipse, L., Kearns, K., Nicholas, M., & Marantz, A. (2011). A MEG investigation of single-word auditory comprehension in Aphasia. *Journal of Speech, Language, and Hearing Research*, 54, 1577–1596.