

Functionally localising letter-specific responses in time, space and current polarity using magnetoencephalography.

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RUNNING TITLE:

FUNCTIONALLY LOCALISING LETTER-SPECIFIC RESPONSES

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31

Abstract

32 Recent neurophysiological evidence suggests that a hierarchical neural network of
33 low-to-high level processing subserves written language comprehension. While a
34 considerable amount of research has identified distinct regions and stages of
35 processing, the relations between them and to this hierarchical model remain
36 unclear. Magnetoencephalography (MEG) is a technique frequently employed in
37 such investigations; however, no studies have sought to test whether the
38 conventional method of reconstructing currents at the source of the magnetic field is
39 best suited for these across-subject designs. The present study details the results of
40 three MEG experiments addressing these issues. Neuronal populations supporting
41 responses to low-level orthographic properties were housed posteriorly near the
42 primary visual cortex. More anterior regions along the fusiform gyrus encoded
43 higher-level processes and became active ~80ms later. A functional localiser of
44 these early letter-specific activations was developed for the production of functional
45 regions of interest in future studies. Previously established response components
46 were successfully grouped based on proximity to the localiser, which characterised
47 location, latency and functional sensitivity. Unconventional anatomically constrained
48 signed source estimates of MEG data were most sensitive to the primary
49 experimental manipulation, suggesting that the conventional unsigned unconstrained
50 method is sub-optimal for studying written word processing.

51

52 Keywords: *fROI; LCD Model; source estimation; VWFA; visual word processing*

53
54

1. Introduction

55

56 1.1 *Primary responses to written words*

57

58 Tarkiainen *et al.* (1999) was one of the first studies to successfully disassociate the
59 neural dynamics of visual feature analysis and letter-specific recognition, in terms of
60 both neuronal location and response timing. Employing magnetoencephalography
61 (MEG), the authors identified two primary neural responses to written words,
62 interpreted as an early linguistically insensitive response (Type I), and a later letter-
63 specific response (Type II). They interpret these responses as reflecting the role of
64 the left inferior occipital-temporal cortex in supporting the processing of letter strings
65 during visual word processing, and propose that the Type II signals may act as the
66 first port of call when filtering valid letter strings for further lexical processing.

67

68 A wealth of research utilising a wide range of methodologies has since been
69 conducted on the neural processes underlying written language comprehension.
70 Much of this research has focused on identifying distinct regions and stages of
71 processing that are specifically responsive to linguistic content. Table 1 below
72 outlines a number of such response components, which overlap to different extents
73 in latency, spatial location and lexical sensitivity.

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76

Response / Region	Latency	Location(s)	Sensitivity	Method(s)	Representative Studies
Type I	~100 ms	V1; occipital cortex	Luminosity, visual complexity; non-linguistic properties	MEG	Tarkiainen et al., 1999; Helenius et al., 1999
Type II	~140 ms	Temporal-occipital junction	Symbol strings vs. Letter strings, legibility of letter strings	MEG	Tarkiainen et al., 1999; Helenius et al., 1999
M130	~130 ms	Occipital lobe	Orthographic/surface properties (e.g., bigram freq., orthographic affix freq.)	MEG	Solomyak and Marantz, 2009; 2010; Lewis et al., 2011
M170	~170 ms	Occipital-temporal cortex and fusiform gyrus	Morphological properties (e.g., lemma freq., morphological affix freq., transition probability)	MEG	Solomyak and Marantz, 2009; 2010; Lewis et al., 2011; Zweig and Pylykkänen, 2009; Fruchter et al., 2013
VWFA	~180 ms	Fusiform gyrus; Talairach co-ordinates ($x = -43$, $y = -54$, $z = -12$)	High level features such letter shapes; Real words vs. Consonant strings	EEG & fMRI	Cohen et al., 2000; 2002; Dehaene et al., 2001; 2002
LFA	~160 ms	Occipital-temporal cortex; MNI co-ordinates (-40, -78, -18)	Consonants vs. False fonts	ECoG, MEG & fMRI	Thesen et al., 2012
WFA	~225 ms	Posterior fusiform gyrus; MNI co-ordinates (-46, -52, -20)	Real words vs. Consonants	ECoG, MEG & fMRI	Thesen et al., 2012

77

78

79 **Table 1.** Summary of response components and regions specifically associated with early written
80 word processing. VWFA = “Visual Word Form Area”; LFA = “Letter Form Area”; WFA = “Word Form
81 Area”; EEG = “Electroencephalography”; fMRI = “Functional Magnetic Resonance Imaging”; ECoG =
82 “Electrocorticography”.

83

84 Recent investigation has suggested that rather than a single “lexically-sensitive
85 region” of the brain, there exists a collection of hierarchical networks set along the
86 occipital-temporal lobe and fusiform gyrus. The Local Combination Detector (LCD)
87 model (Dehaene et al., 2005), for example, proposes graded sensitivity along the
88 entire occipital-temporal cortex to high-level visual stimuli (i.e., written word forms)
89 coded in a posterior-to-anterior progression. Under this account, posterior regions
90 closest to the primary visual cortex are less selective and become active with less
91 proximity to real words, while the most anterior portion of the fusiform overlapping
92 with the Visual Word Form Area (VWFA) has greatest selectivity for high-level visual
93 features.

94

95 Initial neuropsychological support for the LCD model was gathered from hierarchical
96 neural detectors in macaque monkeys (Booth and Rolls, 1998; Rolls, 2000), finding
97 neurons located anteriorly to support more abstract processing than populations
98 located posteriorly. The generalisation of these results to humans was directly tested
99 later by Vinckier *et al.* (2007). Using Functional Magnetic Resonance Imaging (fMRI),
100 they compared responses along the occipitotemporal cortex to visually presented
101 items differing systematically in their similarity to valid words: 1) false fonts; 2) strings
102 of infrequent letters; 3) infrequent bigrams; 4) infrequent quadrigrams; 5) frequent
103 quadrigrams; 6) real words. Consistent with the LCD model, they found gradient
104 sensitivity to real words in a posterior-to-anterior progression. The authors
105 characterised the specialisation of responses along the “visual word form system” as
106 supporting evidence for a graded sensitivity anterior from the occipital lobe towards
107 the defined location of the VWFA.

108

109 Recent work by Lewis *et al.* (2011) examined the influence of linguistic variables of
110 varying “abstractness” on a MEG component (putatively overlapping with the VWFA)
111 associated with morphological detection (the MEG M170; Solomyak and Marantz,
112 2009, 2010). Restricted ROI analyses of posterior and anterior portions of the M170
113 yielded distinct sensitivities to linguistic variables; the anterior ROI showed an effect
114 of transition probability from stem to suffix of apparently morphologically complex
115 words, whereas the posterior portion was only sensitive to surface (high-level n-
116 gram) frequency. Transition probability effects were associated with activation of
117 abstract morphemic representations, and surface frequency effects with activation of
118 concrete n-gram representations. The sources set more anterior upon the fusiform
119 gyrus therefore appeared to code more abstract representations. This finding is in

120 corroboration to the LCD model as well as Vinckier *et al.*'s (2007) results, and
121 suggests that even within a single evoked response component, defined by the
122 timing of a peak response over MEG or Electroencephalography (EEG) sensors, not
123 all sources may display the same sensitivity.

124

125 Later work by Thesen *et al.* (2012) employed fMRI and time-sensitive methodologies
126 including MEG and intracranial EEG recordings to identify distinct temporal and
127 spatial attributes of a “letter-form area” (LFA) and a “word-form area”. Findings
128 included letter-selective responses peaking 160 ms post-stimulus onset, around 60
129 ms earlier than activation of the VWFA (Cohen *et al.*, 2000; 2002). The authors
130 propose a feed-forward structure of responses, whereby the system assesses
131 information for word-likeness at different stages of processing, and subsequently
132 carries it forward through the system. This implies that access to the visual word
133 form (VWF: Warrington and Shallice, 1980) is first fed by identification of valid letters,
134 and then valid word-shapes, suggesting that the first stage of visual word recognition
135 is not VWF access but rather identification of valid letters in posterior regions.

136

137 Taken together, these findings strongly suggest that the visual system is composed
138 of neuronal populations that support graded low-to-high level processing in a
139 posterior-to-anterior arrangement. As such, established response components and
140 regions can be placed along this graded visual processing system, both to index the
141 complexity of processing they support and to assess their similarity to other
142 response components.

143

144 *1.2 Methods of source estimation*

145

146 As illustrated, investigation into the neurophysiological underpinnings of visual word
147 processing has focused on categorising stages of processing based on information
148 such as timing, location, and sensitivity of particular neural responses. An additional
149 dimension that has been used in methodologies that measure electrical current
150 directly, either from the cortical surface (Electrocorticography: ECoG) or through the
151 skull (EEG), is the polarity of the electrical current (in this case, relative to the
152 reference electrode). For example, the N400 component is defined by negative
153 current potential, and the P600 by a positive current potential. Although polarity
154 relative to a reference electrode is arbitrary, activity with opposing polarities reflect
155 distinct response components. Directionality is therefore an important dimension in
156 characterising responses in these methodologies.

157

158 MEG does not measure the electrical current in the brain directly, but rather the
159 magnetic field generated around the brain from which location, amplitude and
160 direction of neuronal currents can be estimated. In many methods of source
161 localisation, including the MNE software used in this paper, source estimation is
162 achieved by placing a current dipole at each source to be estimated, spread across
163 the brain's volume or across the cortical surface. Length of a fitted dipole indexes
164 strength of activation, and the direction of the current is reconstructed relative to
165 either the MRI co-ordinate space ("free orientation") or perpendicular to the cortical
166 surface ("fixed orientation"). Directionality is then interpreted from the sign of the data
167 relative to the orientation constraint. In "free orientation", positive indicates up
168 towards the top of the head and negative towards the bottom of the head. In "fixed
169 orientation", positive indicates that the current dipole is directed out of the cortical

170 mass, and negative into the cortical mass. The vast majority of MEG studies have
171 adopted the convention of using free orientation in source reconstruction and
172 removing the directional information during statistical data analysis, only taking the
173 absolute strength of activity (indexed by the magnitude of the dipole vector
174 regardless of orientation) – a method termed “unsigned free orientation”.

175

176 Cortically-constrained, signed estimates model the physiology of the cortical mass,
177 thus making it the most anatomically motivated method given the hypothesised
178 source of the MEG signal in pyramidal cells of the cortex, which are oriented
179 perpendicular to the cortical surface (Hämäläinen *et al.*, 1993). Furthermore, current
180 flowing from the base of a pyramidal cell to the pial surface is likely to support
181 distinct processes from neuronal populations whose current flows from the surface
182 into the cortical mass; however, the exact differences between polarities of the
183 current are poorly understood (da Silva, 2010). Assuming that switches in polarity
184 mirror distinct responses, unsigned free orientation loses one dimension of
185 discrimination. As a consequence, neuronal populations whose current shifts from
186 one polarity to another may be incorrectly characterised as displaying just one rather
187 than two separate responses. Furthermore, the timing of distinguished response
188 peaks may be misidentified due to erroneous averaging (see Fruchter and Marantz,
189 2015).

190

191 One complication of using fixed orientation, where sources are fitted perpendicular to
192 the surface, is caused by the convolution of the cortex. Fixed orientation results in
193 the localisation of the reconstructed current as outgoing activity on one side of a
194 sulcus and ingoing on the other side. One of the localisations and directionalities

195 represents the “true” source of activity, while the other represents a reconstruction
196 “bleed”. Averaging positive and negative sources together would lead to a shallower
197 estimate of source amplitude, and thus reduce sensitivity to experimental
198 manipulations. Care must therefore be taken not to cancel out activity by selecting
199 both positive and negative sources when averaging over a ROI; for example,
200 anatomical regions often encapsulate sources from both sides of a cortical fold, and
201 may be unsuitable for analysis utilising a cortically constrained method.

202

203 Despite extensive investigation into the different methods of generating source
204 estimates of EEG and MEG data, there is little study into the consequences of using
205 signed versus unsigned estimates in terms of sensitivity to experimental
206 manipulations across subjects. Comparisons have instead focused on the spatial
207 accuracy of locating a source in data simulations when using free, fixed and loose
208 dipole constraining parameters, often in a single subject. Such work has advocated
209 the advantages of incorporating anatomical constraints on source orientations to
210 avoid over-estimating the spatial extent of activity (Chang *et al.*, 2013; Dale, *et al.*,
211 2000; Hauk, 2004; Lin *et al.*, 2006; Lui *et al.*, 1998; 2002). To our knowledge, only
212 one study has considered the implications of activity polarity relative to experimental
213 sensitivity (Fruchter & Marantz, 2015, Appendix B), although comparing the
214 functional differences between methods was not the main purpose of the
215 experiment. The current study therefore focused on the difference between three
216 methods of source reconstruction (free unsigned, free signed, fixed signed) relative
217 to experimental sensitivity rather than spatial accuracy. Based on these comparisons
218 we determined whether the sign of MEG data is a useful dimension to retain, and
219 characterised the directionality of Type II responses relative to the cortical surface.

220

221 *1.3 Letter-specific functional ROI*

222

223 The use of functionally defined regions of interest (fROIs) is frequent with
224 methodologies such as fMRI, but is not common practice with MEG. This technique
225 involves a localiser experimental task known to robustly evoke a functionally specific
226 region of the brain, and subsequent analysis of the same region for a critical
227 manipulation of interest in a separate experiment (see Poldrack, 2007 for a
228 discussion of fROIs in fMRI). This “localiser”, which is typically run on the same
229 sample of participants during the same experimental session, allows for a motivated
230 method of selecting a particular region of the brain to analyse.

231

232 Importantly for the present purposes, using a fROI for a MEG experiment avoids the
233 complication of polarity striping that comes along with using fixed orientation. This is
234 because the fROI will consist of a uni-directional set of sources, which will match the
235 response of interest *if* the processes underlying the localiser and the critical
236 experiment are the same. Furthermore, it has advantages over anatomically defined
237 regions in avoiding analysing larger areas than necessary (a problem when
238 correcting for multiple comparisons across space, and when averaging activity within
239 a given ROI), and is not constrained by borders between parcellations. Thus, if the
240 localiser truly identifies the same underlying response, statistical power should be
241 increased, and the analysis will be less susceptible to Type I errors.

242

243 Given the statistical and theoretical advantages of utilising a localiser of functionally
244 specific activity, we assessed whether fROIs of early letter-specific responses could

245 be created by results of a reduced version of the Tarkiainen paradigm. To achieve
246 this, we replicated a study known to evoke both lower- and higher-level lexical
247 processing - Solomyak and Marantz (2010: henceforth "S&M") involving a visual
248 lexical decision task of mono-morphemic and bi-morphemic words. The original
249 study's main finding was that activity around 170 ms in the fusiform gyrus (M170)
250 was modulated by transition probability from stem to suffix of the morphologically
251 complex words, as well as by morphological but not orthographic affix frequency.
252 The M170 response component appeared to index high-level processes sensitive to
253 sub-lexical (*i.e.*, morphological) structure. Earlier and more posterior processing at
254 the M130 was sensitive only to surface properties of the stimulus, whereby activity
255 was modulated by orthographic affix frequency.

256

257 Testing the utility of Tarkiainen *et al.*'s paradigm as a localiser importantly allows us
258 to assess whether fROIs can overcome the issue of activity cancellation of positive
259 and negative sources when using cortically constrained estimates. Further, if lexical
260 variables from the S&M replication modulate activation of the region(s) shown to
261 display Type II responses in the abridged Tarkiainen design, it would suggest that
262 the Type II response can be used to localise the lower and higher level lexical
263 processing as identified in S&M. For the present purposes, this would enable a
264 functional comparison between neuronal populations underlying the Type II
265 component and other established responses and regions in the literature.

266

267 *1.4 Aims*

268

269 The principle aim was to establish the location, timing, and functionality of the Type II
270 response relative to associated regions (e.g., VWFA, letter-form area, word-form
271 area) and responses (e.g., M130, M170) defined in the literature, as well as the
272 posterior-to-anterior progression of higher-level processes more broadly. The original
273 Tarkiainen *et al.* study employed multiple dipole modelling analysis, which does not
274 provide information regarding the spatial coverage of response-specific activation in
275 a region. To fully ascertain the spatio-temporal extent of Type II activity, we ran an
276 English-adaptation of Tarkiainen *et al.*'s (1999) study while recording neural
277 responses with MEG. We then conducted a distributed source analysis to locate
278 brain regions most sensitive to our critical manipulations.

279

280 The second aim was to develop a localiser of early letter-specific activity for use as a
281 fROI in future experiments. To do so, we identified a manageable abridgement of the
282 Tarkiainen paradigm to be administered in the same recording session as a
283 replication of the S&M study – consisting of a visual lexical decision task of mono-
284 morphemic and bi-morphemic words. We examined the influence of the lexical
285 variables from S&M on activity in the regions identified by the localiser to determine
286 whether the Type II response taps into the same neuronal populations as the M130
287 or M170 components. Determining the functional sensitivity of these regions would
288 allow us to: 1) make stronger connections with other MEG responses, following aim
289 one above; 2) position the regions supporting the Type II response relative to the
290 hierarchical LCD model; and 3) determine whether underlying neural populations are
291 shared between components, allowing the Type II responses to be used as a
292 localiser of letter-specific activity more broadly construed.

293

294 In aiming to characterise the Type II response, the final goal of this study was to
295 ascertain the direction of the neural current at the source of the recorded magnetic
296 field with respect to the cortical surface. This purpose is built upon the assumption
297 that a shift in polarity indexes a distinct neural response, and that retaining the sign
298 of activation avoids loss of evoked responses due to averaging. Ultimately, we
299 assess whether using signed estimates allows for greater ease in discriminating
300 neural responses in comparison to unsigned source estimates.

301

302 To address these questions, we conducted three MEG experiments: 1) A full
303 Tarkiainen *et al.* (1999) replication, 2) An abridged localiser, and 3) A S&M
304 replication.

305

306 **2. Method**

307

308 *2.1 Participants*

309

310 Participants in all three experiments were right-handed native English speakers with
311 normal or corrected-to-normal vision and were recruited from the NYU Abu Dhabi
312 community. Written informed consent was provided by all participants prior to data
313 collection. The Tarkiainen replication experiment included 16 participants (6 females,
314 mean age = 23.8, $SD = 4.5$). The abridged localiser and S&M replication experiment
315 included 24 participants (17 females, mean age = 21.9, $SD = 6.18$)

316

317 *2.2 Materials*

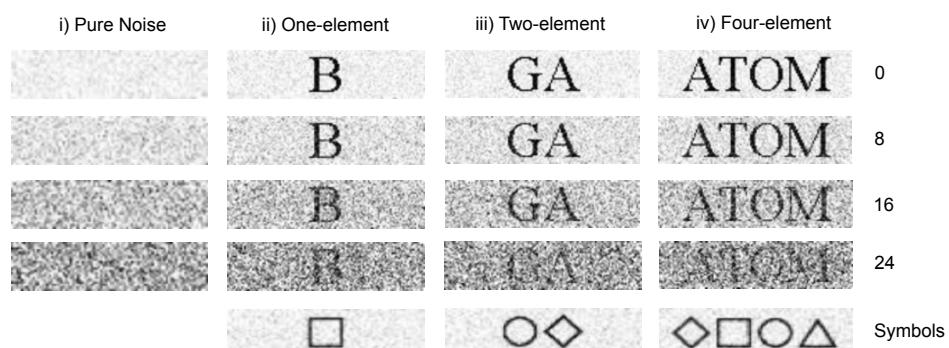
318

319 *2.2.1 Tarkiainen Replication*

320

321 Stimuli were an English adaptation of materials originally developed by Tarkiainen *et*
322 *al.* (1999). There were 950 items in total, consisting of four different categories of
323 stimulus: i) pure Gaussian noise; ii) single element: one letter (total of 25 letters,
324 without the letter "O") or one geometrical symbol (a triangle, diamond or square); iii)
325 two-element: two-letter English syllables (25 different syllables) or two-element
326 symbol strings (four possible combinations of a triangle, diamond, square or circle);
327 and iv) four-element: four-letter English words (50 different words) or four-element
328 symbol strings (four combinations of triangle, diamond, square or circle). All four-
329 letter words two-syllable common English nouns (e.g., SODA, PONY, ATOM).
330 Letters, syllables and words were embedded in four different levels of Gaussian
331 noise, increasing from 0, 8, 16 to 24. Symbols of all lengths were always presented
332 in the lowest noise, and served as controls for the low-noise letters, syllables and
333 words. Items in noise levels 0 and 8 were clearly visible, whereas noise level 16
334 made identification more difficult, and items at noise level 24 were extremely difficult
335 to identify. Figure 1 shows examples of these stimuli.

336



337

338

339 **Fig. 1.** Full set of stimuli used in the experiment. All are English adaptations of those used by
340 Tarkiainen *et al.* (1999).

341

342 *2.2.2 Abridged Localiser*

343

344 A subset of the original stimuli was used for the localiser: the four-element (four letter
345 words and length-matched symbols) and one-element items (single letter and single
346 symbol), in the lowest and highest noise levels. This resulted in a subset of 300 trials
347 (50 trials x 6 conditions).

348

349 *2.2.3 S&M Replication*

350

351 The S&M replication experiment employed a lexical decision task of 530 stimuli. Half
352 of the stimuli were valid English words, and half were non-words. The word stimuli
353 were split into a series of five conditions, with 53 items per condition: 1) *Truly*
354 *Complex Free*, “leakage”: +free stem, +congruent suffix; 2) *Truly Complex Bound*,
355 “sociable”: +bound stem, +congruent suffix; 3) *Pseudo-Complex*, “trolley”: +stem, -
356 congruent suffix; 4) *Unique* stems, “excursion”: -[productive] stem, +congruent
357 suffix); 5) *Pseudo-Unique* stems, “sausage”: -[productive] stem, -congruent suffix.
358 Unique items were defined as “congruent” because their form and meaning matched
359 that of productively formed words with the same suffix, which was not the case for
360 “incongruent” Pseudo-Unique items. The collection of items varied in their values on
361 a range of lexical variables known to modulate early letter-specific activity, presented
362 in Table 2 below.

363

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368

Condition	Bigram LM		Affix OLF		Affix MLF		Surf. LF.		Lem. LF.		Log TP	
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
Free Stem, Congruent <i>Mileage</i>	3.63	0.14	5.51	0.59	4.68	0.39	1.8	0.55	3.08	0.56	1.28	0.7
Bound Stem, Congruent <i>Sociable</i>	3.53	0.13	5.07	0.4	4.45	0.37	1.75	0.55	2.49	0.72	0.75	0.66
Free Stem, Incongruent <i>Trolley</i>	3.54	0.12	5.16	0.56	4.1	0.83	1.65	0.63	2.78	0.97	1.29	0.71
No Stem, Congruent <i>Excursion</i>	3.59	0.15	5.16	0.46	4.13	0.65	1.69	0.72	NA	NA	NA	NA
No Stem, Incongruent <i>Winter</i>	2.54	0.15	5.31	0.57	4.22	0.84	1.61	0.58	NA	NA	NA	NA

373 **Table 2.** Lexical statistics of S&M replication experiment. LM = Log of the Mean; OLF = Orthographic
 374 Log Frequency; MLF = Morphological Log Frequency; Surf. = Surface, LF. = Log Frequency, TP =
 375 Transition Probability.

377 **2.3 Procedure**

379 All participants' head shapes were digitised using a hand-held FastSCAN laser
 380 scanner (Polhemus, VT, USA) to allow for co-registration during data preprocessing.
 381 Five points on each participant's head were also digitised: the nasion, just anterior of
 382 the left and right auditory canal, and three points on the forehead. Marker coils were
 383 later placed at the same five positions to localise each participant's skull relative to
 384 the sensors. These marker measurements were recorded just before and after the
 385 experiment in order to track the degree of movement during the recording.

387 At the beginning of each of the three experiments, participants completed a practice
 388 session outside of the machine to ensure full understanding of the task prior to
 389 entering the magnetically shielded room. The Tarkiainen replication was recorded in
 390 one session, while the S&M replication and localiser were recorded together in a
 391 separate session.

392 MEG data were recorded continuously using a 208 channel axial gradiometer
393 system (Kanazawa Institute of Technology, Kanazawa, Japan), with a sampling rate
394 of 1000 Hz and applying an online low-pass filter of 200 Hz.

395

396 Stimuli in all three experiments were displayed using Presentation software. Stimuli
397 were projected onto a screen 85 cm away from the individual's face.

398

399 *2.3.1 Tarkiainen Replication*

400

401 Stimuli were organised into four blocks, so that all of the items within a single block
402 contained the same stimuli type; i.e., all of the single-element items were within a
403 single block, and all of the four-element items were displayed in a separate block.

404 There were 8 possible block orders, and two participants were allocated to each
405 block-order. The order of stimulus presentation was randomised within
406 conditions/blocks but was the same for all subjects. It was ensured that the same
407 word did not appear within 10 trials of presentation to avoid repetition effects.

408

409 Each item was presented in a centrally placed rectangular patch (~5 X 2), and was
410 displayed on the screen for 60 ms with a 2 second inter-stimulus interval.

411 Participants were instructed to focus on the images and to verbally report the item if
412 a question mark appeared. The prevalence of these question-mark trials was 5% (40
413 out of 950 trials) and served to aid concentration. There were no question-mark trials
414 during the pure noise block. As this block was 20% shorter, it was easier to maintain
415 concentration. The whole experiment lasted around 40 minutes.

416

417 2.3.2 *Abridged Localiser*

418

419 Stimuli were presented using the same parameters as the full paradigm. Unlike the
420 full Tarkiainen replication, stimulus order was fully randomised within and between
421 six blocks of presentation so that each block contained a mixture of the six types of
422 stimuli; this was done in order to make the task more engaging. Each block lasted
423 around 60 seconds, and participants were asked not to blink during stimulus
424 presentation. No overt task was employed due to the brevity of the paradigm;
425 participants were simply asked to pay attention to the items as they appeared on-
426 screen. The localiser took around 6 minutes.

427

428 2.3.3 *S&M Replication*

429

430 Each trial began with a fixation cross (“+”) for 400 ms, followed by the critical item for
431 2 seconds. Participants were asked to indicate whether the item was a word or not
432 by pressing one of two buttons with their left hand. No feedback was provided. Order
433 of stimulus presentation was fully randomised, and each participant received a
434 unique randomisation. The experiment was split into 4 blocks and lasted around 20
435 minutes.

436

437 2.4 *Analysis*

438

439 Data from all three experiments underwent the same preprocessing steps. The
440 continuous MEG data were first noise reduced by utilising eight magnetometer
441 reference channels located away from the participant’s head, using the Continuously

442 Adjusted Least Squares Method (CALM; Adachi, Shimogawara, Higuchi, Haruta, &
443 Ochiai, 2001), with MEG160 software (Yokohawa Electric Corporation and Eagle
444 Technology Corporation, Tokyo, Japan). The noise-reduced MEG data was imported
445 into MNE-Python (see Gramfort *et al.*, 2014), low pass filtered at 40 Hz, and
446 epoched from 200 ms pre-stimulus onset to 800 ms post-stimulus onset. In order to
447 clean the data, we automatically rejected all trials whose amplitude exceeded a 2e-
448 12 femtotesla threshold; additional artifact rejection was performed through manual
449 inspection of the data, removing noisy trials that were contaminated with movement
450 artifacts or extraneous noise. These clean epochs were averaged across conditions
451 to produce an evoked signal at each MEG sensor.

452

453 To reconstruct the location of MEG sensors relative to the individuals' heads, the
454 neuromagnetic data were co-registered with the FreeSurfer average brain (CorTechs
455 Labs Inc., Lajolla, CA). This involved scaling the average brain to the participant's
456 head-shape by importing the digitised scan and aligning the digital fiducial points to
457 the coil markers' position. Next, an ico-4 source space was created, consisting of
458 2562 potential electrical sources per hemisphere. At each source, activity was
459 computed for the forward solution with the Boundary Element Model (BEM) method,
460 which provides an estimate of each MEG sensor's magnetic field. For each subject,
461 the inverse solution was computed from the forward solution and the grand average
462 activity across all trials.

463

464 For the Tarkiainen replication, two different orientation parameters were employed in
465 the inverse solution and applied to the data: 1) fixed orientation, which defines the
466 direction of the current normal to the cortex by locking the fitted dipoles

467 perpendicular to the cortical surface; 2) free orientation, which allows the fitted dipole
468 at each potential electrical source to orient in any direction. Free orientation sources
469 were then further processed as either unsigned or signed: The free signed estimates
470 were calculated by projecting the tip of the dipole vector onto the z axis of the MRI
471 co-ordinate system, which establishes activity up (positive) or down (negative) with
472 respect to the head; unsigned estimates were calculated from the magnitude
473 (absolute length) of the current dipole fitted at the source. Fixed signed estimates are
474 calculated as the magnitude of the current dipole normal to the cortex. The inverse
475 solution was applied to each condition average employing an SNR value of 3, which
476 produced a conversion into noise-normalised Dynamic Statistical Parameter Map
477 (dSPM) units (see Dale *et al.*, 2000). For the localiser and S&M replication datasets,
478 only fixed signed orientation was applied.

479

480 **3. Results**

481

482 In order to localise the Type I and Type II responses in our data, we ran spatio-
483 temporal permutation cluster tests over the time-windows and regions reported in
484 Tarkiainen *et al.*'s (1999) results using the *eelbrain* module in Python
485 (<https://pythonhosted.org/eelbrain/>). This established the location of sources
486 sensitive to the experimental manipulation, and when these sensitivities arose. All
487 cluster-based permutation tests reported here followed the procedures detailed in
488 Maris in Oostenveld (2007): First, each of the source estimates within a selected
489 region were used in turn as the dependent measure of the statistical test (in this
490 case, ANOVA) and assigned a *t*-value for each millisecond of the selected time
491 window. All sources that had a *t*-value exceeding a $p < .05$ threshold were clustered

492 based on spatio-temporal adjacency. If a cluster consisted of a minimum of 10
493 sources and lasted for at least 20 ms, the *t*-values within this cluster were summed,
494 resulting in a cluster-level statistic for comparison with test statistics of 10,000
495 random permutations of the data. If the critical test statistic fell at or beyond the
496 97.5th percentile of the distribution of the permuted values, the cluster was
497 considered significant at a corrected level of $p < .05$. All results reported here are
498 based on cortically constrained (fixed orientation) source estimates.

499

500 *3.1 Type I response: Source localisation*

501

502 Tarkiainen *et al.* (1999) localised the Type I response bilaterally in the occipital lobe,
503 with peak latency of dipole activity between 95-115 ms post stimulus onset. All
504 stimulus items displayed a correlation of activity with noise, whereby more noise
505 elicited higher amplitude of activity, and there was crucially no fall-off in activation
506 between level 8 noise and level 24 noise. Activity also positively correlated with
507 stimulus length, whereby longer items elicited more activation.

508

509 To capture this response, we ran a 4 x 4 ANOVA with the factor of Stimulus (Blank x
510 Letter x Syllable x Word) and Noise Level (0 x 8 x 16 x 24) over the 50 ms time-
511 window of 80-130 ms, restricting the sources to the left and right hemisphere of the
512 primary visual cortex (BA's 17, 18 & 19).

513

514 The results suggest that a large portion of the left and right visual cortex analysed
515 was sensitive to the experimental manipulation in this 50 ms time-window. Figure 2
516 shows all significant clusters as averaged over time. In total, the analysis yielded four

517 significant clusters: The lateral occipital lobe displayed a main effect of Noise ($p <$
518 $.001$) and Stimulus-Type ($p < .001$) bilaterally, and clusters in the lingual gyrus of the
519 right hemisphere were also significant for a main effect of Noise ($p < .001$) and
520 Stimulus-Type ($p < .001$). All clusters remained significant for the entire duration of
521 our time-window.

522

523 *3.2 Type II response: Source localisation*

524

525 The Type II response reported by Tarkiainen *et al.* was characterised by a fall-off in
526 activity in the highest noise level (24) eliciting greater activity for the lower noise
527 letter strings than the strings with the highest level of noise. It was also reported that
528 greater activity was observed for letter strings over length-matched symbol strings.
529 The peak latency of the fitted dipoles was between 140-170 ms post stimulus onset,
530 and was localised to the left-hemisphere occipital-temporal junction.

531

532 Type II sources were identified with two spatio-temporal cluster tests. The first was a
533 2 x 3 ANOVA using Noise (8 x 24) and Stimulus-Type (Letter x Syllable x Word). We
534 restricted time-points to a 50 ms window between 130-180 ms, and sources to the
535 lateral-occipital cortex, fusiform gyrus, and temporal gyrus, extracted from the
536 FreeSurfer annot parcellation (available for download at
537 <http://surfer.nmr.mgh.harvard.edu>).

538

539 Three clusters of activity displayed a main effect of Noise (8 > 24): In the lateral-
540 occipital cortex, 32 sources from 130-180 ms (Fig 3A: $p < .001$) as well as 20
541 sources from 133-171 ms ($p < .003$); In the fusiform gyrus, 14 sources from 130-176

542 ms (Fig 3B: $p < .002$). No clusters were formed for a main effect of Stimulus-Type or
543 an interaction between the two factors. All clusters displaying this main effect of
544 Noise displayed negative current with respect to the cortex.

545

546 The second cluster test was a 2×3 ANOVA with String-Type (Letter Strings x
547 Symbol Strings) and Stimulus-Type (Letter x Syllable x Word) as factors. Spatial and
548 temporal restrictions were the same as the first Type II analysis above. Results
549 showed one cluster to display a significant main effect of String-Type, consisting of
550 24 sources in the fusiform gyrus, anterior to the Noise sensitive sources, from 135-
551 180ms (Fig 3C; $p < .001$). This cluster displayed a positive current with respect to the
552 cortex. Again, there were no clusters formed for a main effect of Stimulus-Type or an
553 interaction between the two factors.

554

555 *3.3 Functional localiser*

556

557 3.3.1 Designing the abridged paradigm

558

559 We next ran an exploratory analysis to identify stimuli from the Tarkiainen replication
560 that would yield significant effects of the Type II response. These stimuli would be
561 used in the abridged Tarkiainen adaptation for the purpose of informing a fROI for
562 use in future studies. We found that using just the four-element (four letter words and
563 length-matched symbols) and one-element items (single letter and single symbol), in
564 the lowest and highest noise levels achieved this goal. This resulted in a subset of
565 300 trials (50 trials x 6 conditions), which would take a participant around 6 minutes
566 to complete.

567

568 In order to maximise statistical power for the abridged paradigm, we coded
569 conditions as binary variables for a regression analysis. We next identified the
570 posterior Type II Noise response based on responses to the one and four element
571 letter string items (recall that the noise-level for all symbol strings was 0). A
572 regression on Noise Level created a beta value for each source and each
573 millisecond from stimulus onset to 500 ms after onset. Threshold-based spatio-
574 temporal cluster tests were performed from 130-180 ms on beta values in the
575 fusiform gyrus, lateral-occipital lobe, and inferior temporal lobe merged into one
576 region. This resulted in one significant cluster of 64 sources in the lateral-occipital
577 lobe for the entirety of our time-window of interest ($p < .001$). An identical regression
578 was run over the same time-window and spatial extent on the String Type variable,
579 comparing low-noise letter strings to low-noise symbol strings. This identified the
580 anterior Type II String-Type response: one significant cluster of 19 sources in the
581 inferior temporal lobe from 145-180 ms ($p < .001$).

582

583 3.3.2 Results of localiser

584

585 To assess the suitability of the reduced stimulus set as a localiser of early lexical
586 processing, we ran the abridged Tarkiainen paradigm during the same recording
587 session as the replication of the S&M visual lexical decision task. The S&M stimuli
588 included nonwords and an equal number of mono-morphemic and bi-morphemic
589 words falling along continua of linguistic variables tested in the original S&M study,
590 including transition probability from stem to suffix, and orthographic and
591 morphological affix frequency. Also included were bigram frequency and lemma

592 frequency, which were found to be significant determiners of M130 and M170 activity
593 in later studies (Lewis *et al.*, 2011; Simon *et al.* 2012). We later tested the
594 modulation of activity in localised regions as a function of these continuous lexical
595 variables.

596

597 Data analysis procedures were identical to those used for the full dataset: Type II
598 sources were identified by running spatio-temporal cluster tests on a 130-180 ms
599 time-window in the fusiform gyrus, lateral-occipital lobe and inferior temporal lobe;
600 conditions were coded as continuous variables for use in a regression model rather
601 than a categorical analysis. Tests revealed clusters located very close to those found
602 in the full dataset, with an effect of Noise ($p = .01$), and of String Type 200 - 250ms
603 ($p = .009$). The next step was to extract regions found to be sensitive to the
604 Tarkiainen localiser experiment, and to test the same regions' sensitivity to lexical
605 variables in the lexical decision task. To do this, we ran temporal cluster tests on the
606 S&M data from 80-180 ms (chosen to encompass potential M130 and M170 effects)
607 in each Tarkiainen-identified region, assessing the significance of the five continuous
608 variables. The regression included all items with meaningful values on a given
609 variable (*i.e.*, not listed as “NA” in Table 2).

610

611 Activity in the posterior Noise-Level region significantly correlated with orthographic
612 affix frequency ($p = 0.008$) from 80-100 ms; morphological affix frequency ($p = 0.03$)
613 from 80-100 ms and log transform of mean bigram frequency ($p = 0.01$) from 100-
614 130 ms. No clusters surpassed the threshold for either of the other two variables.
615 The anterior String-Type region correlated with lemma frequency from 135 – 170 ms

616 ($p = .001$) and log transition probability from 130 – 170 ms ($p = .008$). No other
617 variables surpassed the cluster-forming threshold.

618

619 **4. Discussion**

620

621 The primary goal of the present study was to compare the localisation and timing of
622 the letter-specific Type II response (Tarkiainen *et al.*, 1999) with other established
623 MEG responses (e.g., M130, M170). We achieved this by conducting a replication
624 study of Tarkiainen *et al.*'s original MEG experiment with distributed source analysis
625 and spatio-temporal cluster tests. The second goal was to assess the functionality of
626 these responses. For this purpose, we designed an abridged version of the
627 Tarkiainen experiment that may be used to localise letter-specific responses in future
628 studies. We assessed sensitivity of these fROIs by testing the influence of
629 continuous variables from the S&M replication on neural activation; in doing so, we
630 further linked the sensitivity to other reported components in the literature. Our final
631 goal was to spell out differences between cortically constrained source estimates
632 and head-constrained and unconstrained methods of MEG source reconstruction
633 and to characterise the Type II responses in terms of current polarity.

634

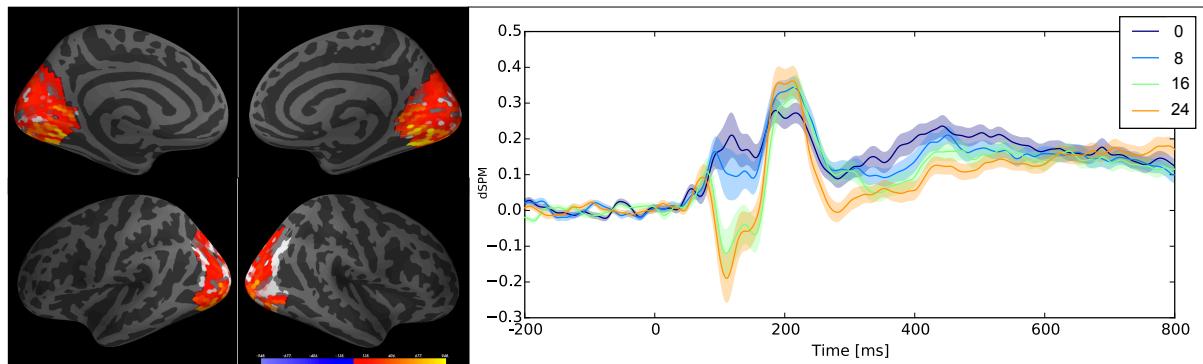
635 *4.1 Type I*

636

637 The Type I response was localised bi-laterally in the occipital lobe between 80-130
638 ms post stimulus onset, beginning in V1 / BA 17 and extending up to V3 / BA 19: see
639 Figure 2. This response temporally coincides with the M100, and encapsulates the
640 primary visual evoked response at around 100 ms. Consistent with Tarkiainen *et al.*,

641 signal amplitude of the Type I response increased systematically as a function of
642 noise (greater Gaussian noise correlated with greater amplitude of activity), and
643 increasing stimulus length, suggesting that the neural populations underlying this
644 response are sensitive to the visual complexity of the given stimulus.

645



646

647

648 **Fig. 2.** Location of Type I sources averaged over the time window of 80-130 ms, and the waveforms
649 of these clusters as a function of noise level.

650

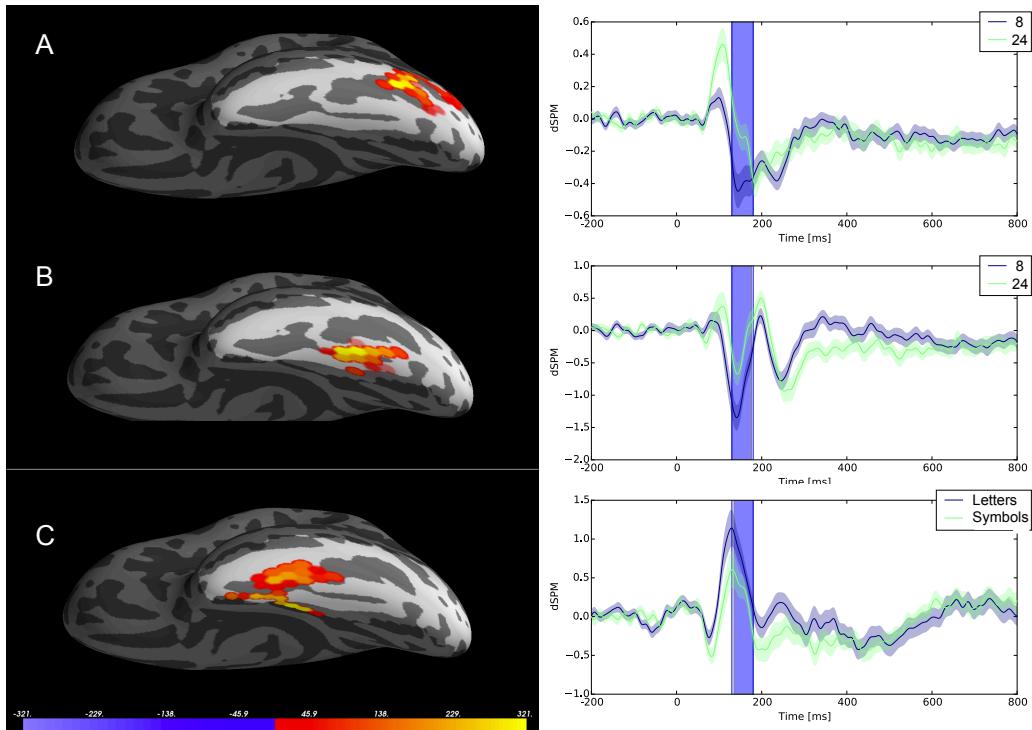
651 4.2 Type II

652

653 The sensitivity to both String-Type (Symbol Strings vs. Letter Strings) and Noise
654 level ($8 > 24$) were originally reported by Tarkiainen *et al.* to originate at the same
655 place and time. However, we found two main effects for the Type II response, each
656 localising to different patches of cortex at different time-points, and realising
657 opposing polarity of the current with fixed orientation (see Figure 3). The main effect
658 of Noise ($8 > 24$) (henceforth the “Type II-Noise” response) was found at the junction
659 between the occipital cortex and temporal lobe, as was the original location reported
660 by Tarkiainen *et al.* The main effect of String-Type (henceforth “Type II-Letter”

661 response), however, was localised at the frontal-most portion of the fusiform gyrus,
662 more anterior than the Type II-Noise response.

663



664

665

666 **Fig. 3.** Location of significant clusters and corresponding waveforms of both Type II main effects: A-B
667 corresponds to the main effect of Noise, and C to the main effect of String-Type.

668

669 Having identified the Type II responses in the full design of our experiment, we
670 established an abridged design that used only a quarter of the stimulus items yet
671 elicited the same robust effects. We recorded neural responses in the same
672 experimental session as a critical experiment of interest – a lexical decision task of
673 visually presented suffixed words, in replication of S&M. Subsequent analysis of the
674 regions sensitive to the localiser manipulation in the critical experiment allowed us to
675 assess to what extent the posterior and anterior Type II regions corresponded to the
676 M130 and M170 responses as originally found by S&M, and whether the Type II

677 regions can be used as a functional localiser of early lexical-specific responses in
678 future studies.

679

680 4.2.1 Functional ROI

681

682 Functionally localised ROIs have a number of advantages over anatomically defined
683 parcellations or ROIs based on peaks in grand-average sensor or source data. In
684 particular, fROIs are not constrained by borders between regions, and do not require
685 analysing larger regions than necessary – a complication when correcting for
686 multiple comparisons in cluster-based analyses. Provided that the localiser and
687 critical experiment tap into the same neural sensitivities, a fROI should yield the least
688 variance between the location of the effect and the region being tested, thus
689 providing the greatest level of statistical power. Functional ROIs also remove the
690 experimenter's role in selecting a region based on visual inspection of the data, and
691 also do not employ arbitrary parameters to localise regions. Further, fROIs are
692 particularly pertinent for cortically constrained source estimates, as the localiser
693 identifies a region of homogenous polarity, and thus fully overcomes the issue of
694 activity cancellation - the principal motivation against using signed source estimates
695 with MEG data.

696

697 In testing just a subset of the experimental materials from Tarkiainen *et al.* (1999),
698 we found a very robust effect for both Type II-Noise and –Letter responses when
699 using just the four-element block (four letter words, noise levels 0 and 24 and length-
700 matched symbols), and one-element block (one letter, noise levels 0 and 24 and one
701 symbol) which takes participants only ~6 minutes to complete. The location and

702 timing of each Type II response corresponded with the full dataset, supporting that
703 the same neural sensitivities can be localised even when using one quarter of the
704 stimulus materials. This set is therefore an ideal candidate for a localiser paradigm.

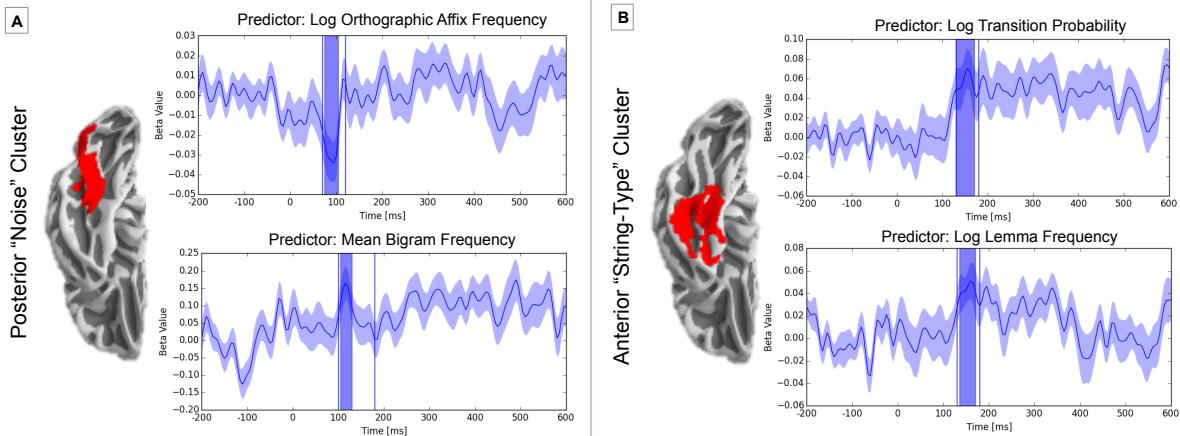
705

706 Tests of the posterior Type II-Noise response revealed significant modulation of
707 activity by orthographic and morphological affix frequency between 80-100ms, and
708 log mean bigram frequency between 100-130 ms. Numerous studies have
709 associated both of these variables with indexing the M130 component (Lewis *et al.*,
710 2011; Simon *et al.*, 2012; Solomyak and Marantz, 2009; 2010), suggesting that the
711 posterior localiser identified spatio-temporal regions associated with lower-level
712 orthographic processing.

713

714 Analysis of the more anterior Type II-Letter response showed that log lemma
715 frequency and log transition probability significantly modulated activity from 130-170
716 ms (morphological affix frequency was not a significant determiner). Both of these
717 variables have previously been associated with the M170 response (Lewis *et al.*,
718 2011; Simon *et al.*, 2012), suggesting that regions supporting the anterior Type II-
719 Letter response are shared with the M170, which is responsible for more abstract
720 lexical processing. Correlations between activity in the localisers and the continuous
721 variables are presented in Figure 4 below.

722



723

724 **Fig. 4.** Beta values of the regression analysis between (A) the posterior localiser and orthographic
725 affix frequency and mean bigram frequency; (B) the anterior localiser and log transition probability and
726 log lemma frequency.

727

728 This functional disassociation between posterior-anterior responses corresponds to
729 recent results employing cortically constrained MEG data from a lexical decision task
730 (Chen *et al.*, 2015). The authors found that activity in posterior portions of the
731 fusiform correlated with bigram frequency ~100 ms post onset, while anterior regions
732 correlated with word surface frequency ~160 ms, thus strongly corroborating the
733 present results. Lewis *et al.* (2011) also reported similar results using unconstrained
734 signed estimates of MEG data, finding that only posterior portions of the anterior
735 M170 ROI displayed surface frequency effects. This was interpreted as indexing a
736 “high-ngram” effect, and the activation of more concrete representations.

737

738 Our findings therefore support that the abridged Tarkiainen paradigm can be used to
739 successfully localise early posterior orthographic processing, as well as later anterior
740 sub-lexical processing. More specifically, finding activity in these regions to
741 significantly correlate with variables shown to modulate the M130 and M170 is strong

742 functional evidence that the Type II responses may reflect the same response
743 components.

744

745 The stimuli used in the localiser of the present study are available to download,
746 either through github (<https://github.com/LauraGwilliams/TarkiainenLocaliser.git>) or
747 by contacting the first author.

748

749 4.2.2 Graded lexical sensitivity of Type II

750

751 Each linguistic variable included in the localiser analysis is associated with a certain
752 level of processing complexity and has been linked to a specific response
753 component in previous literature. Orthographic affix frequency and bigram frequency
754 are linked to surface orthographic properties entailing relatively low-level processing
755 and access to concrete representations. Both variables modulated activity in the
756 Type II-Noise region, which is in line with the LCD model prediction that posterior
757 cortical regions sub-serve lower level processes. The posterior sensitivities of this
758 region are consistent with the “letter-form” area (Thesen *et al.*, 2012) and the M130
759 component (Solomyak & Marantz, 2010), suggesting that the responses and the
760 localiser share underlying neural mechanisms. Interestingly, previous links have
761 been made between the M130 and the earlier Type I response; however, our results
762 do not support this association.

763

764 Variables such as lemma frequency and transition probability are linked to more
765 abstract processing involving the connection between input and stored word forms.
766 The LCD model accordingly positions neurons tuned to higher-level processes along

767 anterior portions of the fusiform gyrus, in agreement with our results. Finding the
768 Type II-Letter response to be sensitive to these variables, in addition to its anterior
769 location, are consistent with the M170 as identified by S&M, VWFA (Cohen *et al.*,
770 2000) and “word-form” areas (Thesen *et al.*, 2012) that appear to involve higher-level
771 processing.

772

773 The posterior-to-anterior progression of abstract processing is thus supported by our
774 results, whereby lower-level sensitivities such as that to letter frequency arise
775 posteriorly, and higher order variables such as lemma frequency appear to be
776 encoded more anteriorly. Our results are in full corroboration with the LCD model as
777 tested by Vinckier *et al.* (2007), and offer striking similarities in localisation and
778 functionality between the two Type II responses and the “letter-form” and “word-form”
779 regions identified by Thesen *et al.* (2012). Together our findings support the
780 hypothesis that words are first processed through the orthographic properties of
781 letter strings, followed by the processing of word forms and sub-lexical structure.

782

783 *4.3 Comparing source estimate constraints*

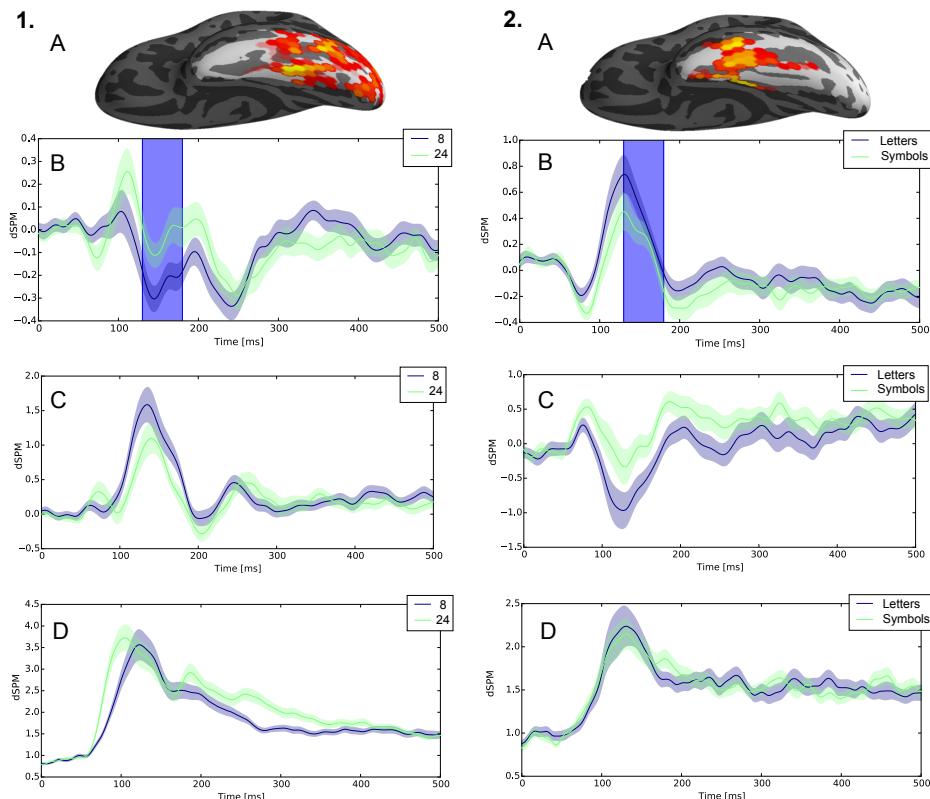
784

785 The final issue to discuss is the implication of applying different methods of source
786 reconstruction. We directly assessed whether, in comparison to signed source
787 estimates, conventional unsigned, directionally unconstrained source estimates of
788 MEG data would reduce the ability to discriminate between spatio-temporally
789 neighbouring responses or “lose” evoked peaks by taking absolute strength of
790 activation.

791

792 Figure 5 presents the two main effects of the Type II response when reconstructing
 793 the source of activity using three methods: 1) signed data fixed normal to the cortical
 794 surface, whereby negative activity corresponds to current flowing into the cortical
 795 mass, and positive to current flowing out of the cortical mass; 2) data signed with
 796 respect to the head co-ordinate system, where negative refers to current flowing
 797 down towards the bottom of the skull, and positive to current flowing towards the top
 798 of the skull; 3) unsigned data, which does not retain the direction of the source and
 799 allows the dipole to freely orient in any direction.

800



801

802

803 **Fig. 5.** Figures in column (1) correspond to sources of the posterior (Type II-Noise) cluster, and
 804 column (2) correspond to the anterior (Type II-Letter) cluster. (A) The location of the significant
 805 sources when using $p < .01$ as a threshold. (B) Waveform when using cortically constrained signed
 806 data. (C) Waveform when using free orientation signed data. (D) Waveforms of free orientation
 807 unsigned data.

808

809 As can be seen in Figure 5, unsigned estimates of the present data do not display
810 distinct peaks of activation as observed in the signed methodologies. This is best
811 noticed in the Type II-Noise cluster (Figure 5.1), whereby two noise 8 > 24 peaks
812 can be seen at ~140 ms and again ~240 ms both in the cortically-signed (1B) and
813 head-signed (1C) reconstruction, but only the earlier peak is observed in the
814 unsigned data (1D). For the Type II-Letter cluster (Figure 5.2), the difference
815 between the peaks of activity observed in the fixed-signed (2B) and free-unsigned
816 (2D) are minimal, perhaps because activity in the anterior cluster does not flip
817 between polarities and largely remains positive though out the time-course of
818 activation.

819

820 Furthermore, both of the free signed (C) estimates of Type II responses reflect
821 positive activity with respect to the head during the latency of the Type II effects, as
822 highlighted in purple (the anterior cluster peaks negative, and then becomes positive
823 later in the time-course). The multiple dipole modelling method employed by
824 Tarkiainen *et al.* orients dipoles relative to the equivalent of the head-coordinate
825 system, which is the same system used to sign data with the free-signed source
826 estimation. Therefore, one possible reason that the original study did not find the
827 distinction between Type II-Noise and -Letter responses that the present study
828 found, is that on a multiple dipole model the two responses may have been
829 accounted for by a single dipole with positive directionality, whereas in a cortically
830 constrained methodology the direction of the effects is distinct.

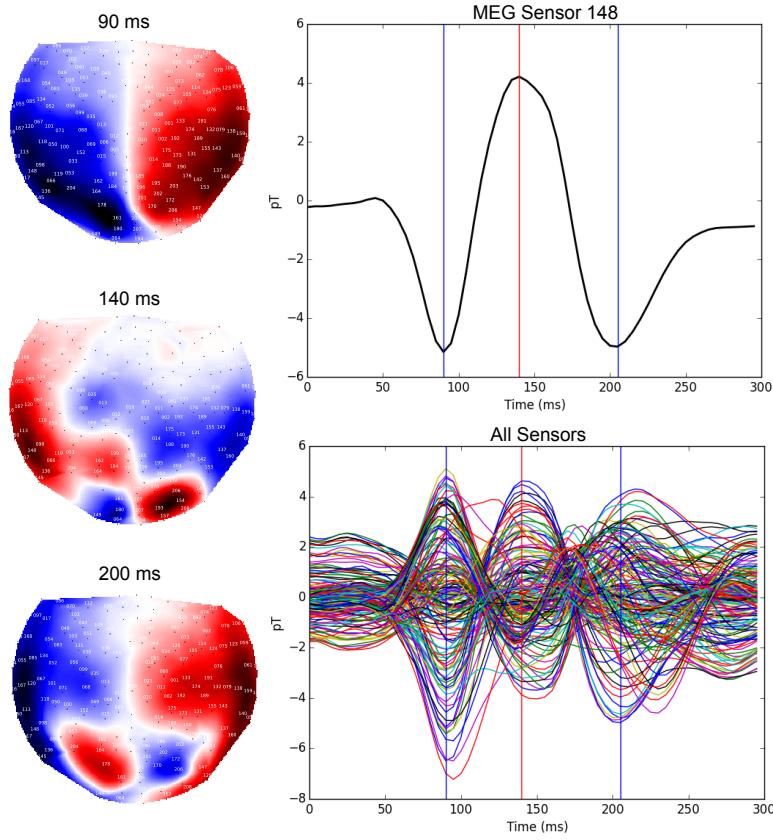
831

832 In the study conducted by Fruchter and Marantz (2015, Appendix B), the authors
833 analysed their data employing the three methods of source reconstruction discussed
834 above. They found that when comparing source estimation methods, the cortical-
835 and head-constrained techniques led to similar interpretations, whereas unsigned
836 data greatly reduced activation peaks. This dampening of evoked responses can
837 also be observed when comparing the unsigned MEG and signed ECoG
838 measurements in Thesen *et al.*'s (2012) study. Figures 4h and 4i from their paper
839 represent the local field potential recorded from the cortical surface directly, and the
840 MEG source reconstruction from the same region. Here we can see very clear
841 polarity shifts in the ECoG data, allowing for discrimination between response
842 components in this dataset; however, in the unsigned free orientation MEG data, it is
843 unclear whether the “bumps” of activity reflect separate responses. One level of
844 discrimination is therefore lost when removing this polarity information, as compared
845 to the method that records the electric potentials generating the MEG signal.

846

847 Such shifts in polarity are not negligible and are clearly observed at the sensor level:
848 A single channel will shift between a positive and negative magnetic field depending
849 upon the orientation of the dipole at the source. Figure 6 below illustrates the
850 strength of the magnetic field at a left lateralised sensor averaged across all subjects
851 and items. In line with the timing we observed for the source analysis of the Type II
852 responses, a field reversal is also apparent, indicating that the current dipole(s) in
853 that region flip direction at different time-points.

854



855

856 **Fig. 6.** Polarity of magnetic field at a single sensor (above) and across all sensors (below) averaged
857 over subjects and items. Topographic plots show the polarity of the magnetic field at each of the three
858 peaks in the sensor data.

859

860 Clearly, this is only a limited investigation into the question of current reconstruction.
861 Further study should aim to ascertain whether all negative response components
862 reflect functionally different computations from all positive components, or if the
863 directionality of the current is an arbitrary dimension of discrimination (similar to
864 polarity in EEG). What the present study illustrates is that polarity of the
865 reconstructed sources is an important element of MEG data, and can be used to
866 disassociate functionally discrete (in this case, Type II) neighbouring responses.
867 Finding evidence, both at the sensor and source level that the neural generators
868 underlying the identified responses are alternating in polarity highlights the
869 importance of current dipole directionality for MEG data.

870

871 **5. Summary**

872

873 Using distributed source analysis of MEG data, we localised the Type II response of
874 Tarkiainen *et al.*'s (1999) study for comparison with other established response
875 components and regions of lexical-specific activity. The Type II response localised to
876 two different regions with different preferences: 1) preference for visible over
877 obscured letter strings in the lateral-occipital lobe with negative activity with respect
878 to the cortical surface; 2) preference for letter over symbol strings in the anterior
879 fusiform gyrus with positive activity. When testing the lexical sensitivities of these
880 regions as part of an abridged paradigm, functional responses were shared between
881 the posterior Type II-Noise response, the M130 and "letter-form" area, and between
882 the Type II-Letter response, the M170 and "word-form" area. These results suggest
883 that each case evokes the same underlying processes, and crucially that a subset of
884 the stimuli materials is sufficient to localise these response components with notable
885 accuracy.

886

887 In order to address the issue of source reconstruction with MEG data, we applied
888 three methods to the current dataset and compared the results to the findings of
889 Tarkiainen *et al.* (1999). In the presence of rapidly alternating polarity, utilising
890 cortically constrained estimates was the most sensitive approach, ensuring the
891 preservation of evoked response components. By contrast, cortically unconstrained
892 unsigned estimates were susceptible to reduction of activation peaks. In this regard,
893 our findings directly indicate that, arbitrary or not, retaining the sign of MEG data can

894 allow for greater sensitivity to experimental manipulations and an additional level of
895 discrimination.

896

897 Bringing our results together, we are able to characterise two localisers of letter-
898 sensitive responses for future studies in time, space and current directionality with
899 respect to the cortical surface. We propose that the posterior Type II sensitivity to
900 visible letter strings can be used to localise orthographic processing, and the anterior
901 Type II sensitivity to letter strings over symbol strings can localise higher-level
902 processing of sub-lexical structure, such as morphological composition. Our results
903 promote the use of cortically constrained signed estimates of MEG data, in unison
904 with functional ROIs when investigating letter-specific neurophysiological responses
905 in future studies.

906

907 **Acknowledgements:**

908 This work was supported by the NYU Abu Dhabi Institute under Grant G1001 (AM)
909 and NSF Grant DGE-1342536 (GL).

910

911
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