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Steady-state visual evoked responses reflect reading efficiency in visual word recognition

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## Abstract

Steady-state visual evoked potentials (SSVEPs) have become a popular method for studying a variety of cognitive functions. Here, we tested the possibility to use SSVEPs as a tool to investigate the core mechanisms in visual word recognition. The present approach was based on the assumption that SSVEP power provides a measure of the underlying network organization with higher power corresponding to better organized neural activity (i.e. more structured representations). The aim of the study was to assess the extent to which written words and pseudowords would elicit SSVEPs in a classic naming task. In particular, we investigated three benchmark effects of reading aloud: lexicality (words vs. pseudowords), frequency (high-frequency vs. low-frequency words), and orthographic familiarity ('familiar' versus 'unfamiliar' pseudowords). We found that words and pseudowords elicited robust SSVEPs. Words showed larger SSVEPs than pseudowords and high frequency words showed larger SSVEPs than low frequency words. SSVEPs were not sensitive to orthographic familiarity. We further localized the neural generators of the SSVEP effects. For the lexicality effect, we found higher activation for words in bilateral occipital sites and in the right cerebellum, while a left parieto-temporo-frontal area and a posterior area of the right temporal gyrus were more active for pseudowords than for words. For the frequency effect, the left temporal pole was activated more by high frequency words than by low frequency words, while low frequency words showed higher activation in the right parietal lobe. Together, the results suggest that SSVEP provide a promising tool to investigate the network dynamics underlying visual word recognition.

*Keywords:* SSVEP, visual word recognition, lexical effect, frequency effect, neuroimaging

Steady-state visual evoked responses reflect reading efficiency in visual word recognition

## 1. Introduction

The steady state visual evoked potentials (SSVEPs) are the electrophysiological response of the cortex to flickering visual stimuli (Regan, 1989; for recent reviews, see Norcia, Appelbaum, Ales, Cottreau, & Rossion, 2015, and Vialatte, Maurice, Dauwels, & Cichocki, 2010). Although the exact mechanisms behind SSVEP generation are still debated (e.g. Capilla, Pazo-Alvarez, Darriba, Campo, & Gross, 2011; Klimesch, Sauseng, Hanslmayr, Gruber, & Freunberger, 2007; Nikulin et al., 2007; Moratti, Clementz, Gao, Ortiz, & Keil, 2007; Srinivasan, Bibi, & Nunez, 2006), SSVEPs are generally interpreted as the consequence of the reorganization of spontaneous brain oscillations in response to a stimulus (Vialatte et al., 2010). SSVEPs have been successfully applied to study a variety of cognitive functions from lower level visual processes, such as, contrast sensitivity (e.g. Norcia, Tyler, Hamer, & Wesemann, 1989) or texture segmentation (e.g. Appelbaum et al., 2012), to higher level functions, such as attention (see e.g. Norcia et al., 2015 for review), working memory (e.g. Perlstein et al., 2003; Peterson et al., 2014), or face processing (see Rossion, 2014 for reviews). SSVEPs have also been applied in clinical neuroscience (e.g. Kim et al., 2006; Macpherson, Pipingas, & Silberstein, 2009; Marx et al., 1986; Moratti et al., 2008; and others) and Brain-Computer Interface (BCI) systems (see for reviews Ferraina et al., 2016; Vialatte et al., 2010; Zhu, Bieger, Garcia Molina, & Aarts, 2010).

Although the SSVEP response modulation could arise from different processes (Bergholz, Lehmann, Fritz, & Ruther, 2008; Rossion, & Boremanse, 2011), it is generally assumed that larger SSVEP responses are caused by more efficient network dynamics (Zhang, Guo, Cheng, Yao, & Xu, 2015). For example, in a visual search task, SSVEP amplitude in the feature-conjunction condition reflected increased salience and rapid localization of feature-conjunction targets (Andersen, Hillyard, & Müller, 2008). In an orientation discrimination task, SSVEP activity produced a tuned response that peaked at the angle of the stimulus (Garcia, Srinivasan, & Serences, 2013). In a visual working

memory task, SSVEP amplitudes were larger for stimuli that were later remembered than for items that were subsequently forgotten (Peterson et al., 2014, see also Perlstein et al., 2003). Finally, it is well established that attention modulates SSVEP amplitude with attended items systematically exhibiting greater amplitudes compared to unattended items (e.g. Cosmelli et al., 2004; Joon Kim, Grabowecky, Paller, Muthu, & Suzuki, 2007; Kelly, Lalor, Reilly, & Foxe, 2006; Malinowski, Fuchs, & Müller, 2007; Muller, Malinowski, Gruber, & Hillyard, 2003; Müller, Teder-Sälejärvi, & Hillyard, 1998; Wang, Clementz, & Keil, 2007; and others). The effects of attention on SSVEP amplitudes probably result from a response gain effect (Di Russo, Spinelli, & Morrone, 2001), possibly mediated by enhanced neural synchronization (Joon Kim et al., 2007).

The aim of the present study was to test the possibility to use SSVEPs to study visual word recognition. To our knowledge, only a few studies have applied SSVEP paradigms to written language processing (Lochy, Van Belle, & Rossion, 2015; Lochy, Van Reybroeck, & Rossion, 2016; Yeatman & Norcia, 2016). Lochy and coll. (Lochy et al., 2015) adopted a periodic oddball paradigm (e.g. Heinrich, Mell, & Bach, 2009; Liu-Shuang, Norcia, & Rossion, 2014), in which they presented words interspersed at regular intervals in sequences of either pseudowords, nonwords, or false fonts. They found significant SSVEP activity at the presentation frequency of words in all conditions, demonstrating that words generate a clear SSVEP response in the oddball paradigm. Remarkably, SSVEPs to words were obtained in the absence of an explicit task, which was taken to suggest that SSVEPs can index automatic lexical access. Recently, Lochy and coll. (Lochy et al., 2016) used the same paradigm with preschoolers to demonstrate that SSVEP responses to letter strings correlated with letter knowledge. In both studies, the oddball response was dominant over the left occipito-temporal region, consistent with left hemispheric specialization for word processing (e.g. Dehaene et al., 2010; Price, 2012). A different study compared SSVEP responses between images of words and faces (Yeatman & Norcia, 2016). Interestingly, the authors found that temporal acuity, peak response frequency, and delay of the SSVEP differed between words and faces, with temporal acuity for faces being substantially higher than for words.

SSVEP paradigms with flickering words have previously been used to study the processing of

emotional content of words. In a study by Trauer et al. (2015) using a lexical decision task, neither emotional content nor lexicality modulated SSVEPs generated by flickering words at 12.14 Hz. In contrast, in a study by Koban et al. (2010), emotional content modulated the SSVEPs but in the opposite direction than the one that was expected, with pleasant word showing reduced power compared to neutral words.

The first aim of our study was to assess whether different types of words and pseudowords elicit reliable SSVEPs in a classic delayed naming task. Contrary to the oddball paradigm, SSVEPs were elicited for each word or pseudoword by flickering the stimulus at a selected frequency (i.e. 18.75 Hz). SSVEP activity synchronized to the stimulus flicker was extracted using Fourier transformation. We investigated SSVEP responses to different lexical and nonlexical letter strings. First, we compared words against pseudowords. Real words are typically processed faster than pseudowords (i.e., lexicality effect). Then, we compared high-frequency against low-frequency words. Readers are typically faster in processing high-frequency than low-frequency words (i.e., frequency effect). Finally, we compared nonwords with orthographically familiar letter patterns against nonwords with unfamiliar letter patterns. Nonwords with familiar letter patterns (high bigram frequency or many orthographic neighbors) are typically read faster than nonwords with unfamiliar letter patterns. Both lexicality and frequency effects have been extensively investigated with standard event-related brain potentials (ERPs) in studies that focused on the time course of visual word recognition (e.g., Barber & Kutas, 2007; Grainger & Holcomb, 2009). The earliest word-nonword differences were found between 100 to 200 ms and frequency effects typically show up at multiple time points (see Barber & Kutas, 2007 for review). The pattern of ERP effects related to orthographic familiarity suggests that pseudowords with many word neighbors generate higher levels of lexical activity than less familiar pseudowords (Holcomb et al., 2002; Proverbio et al., 2008).

In our study, we expected larger SSVEP responses to words than to pseudoword (i.e. lexicality effect) because the neural representation of words should be more structured and more efficient than that of pseudowords. In addition, word representations should be further supported by a more extended network that includes the associated semantic concepts. Similarly, larger SSVEP

amplitudes were expected for high-frequency words than for low-frequency words (i.e. frequency effect) because neural representations of high-frequency should benefit from stronger connections, more efficient network dynamics, and higher resting levels. Finally, if SSVEP amplitudes reflect processing difficulty, the SSVEP power amplitudes of familiar pseudowords should be higher than those of unfamiliar pseudowords (i.e. orthographic familiarity effect). In contrast, if SSVEP taps lexical processing dynamics, we expect small or no SSVEP modulations for familiar versus unfamiliar pseudowords.

With respect to the neural basis of reading, there are still many open issues even if there are rather convergent patterns across studies (see Schlaggar & Mccandliss, 2007; Price, 2012; Taylor, Rastle, Davis, & Holloway, 2012; Wandell, 2011, for reviews). For example, the role of the ventral occipitotemporal cortex in reading and the specific functional significance of the VWFA is still debated (e.g., Carreiras, Armstrong, Perea, & Frost, 2014; Price, 2012). Some argue that it is a prelexical hub (Cohen et al., 2002) while others suggest that it contains lexical representations (Bruno, Zumberge, Manis, Lu, & Goldman, 2008; Glezer, Jiang, & Riesenhuber, 2009; Kronbichler et al., 2004, 2007). In general, it is not clear how the circuitry devoted to reading segregates from other neural populations (e.g., Dehaene et al., 2010; Price, 2012; Price & Devlin, 2003; Vogel et al., 2013; Yeatman & Norcia, 2016). Even the overlap and dissociation of pathways linked to lexical or phonological reading is not completely clear (Church, Balota, Petersen, & Schlaggar, 2011; Mechelli, Gorno-Tempini, & Price, 2003). In that context, we were interested in localizing the neural generators of SSVEPs generated by written words. In order to further consolidate our approach, we compared our results with those of previous studies that have attempted to dissociate the neural pathways of the reading network.

## **2. Material and Methods**

### **2.1 Participants**

Sixteen proficient readers, naive to the purpose of the experiment, participated in the experiment as paid volunteers (age 17-24 years, mean = 20.25). All participants were native French

speakers, they had normal or corrected-to-normal vision and they had no history of developmental disorders. Before participating, participants gave informed written consent.

## 2.2 Apparatus and stimuli

Participants were seated 56 cm from the monitor in a dimly-lit, electrically isolated room. Stimuli were generated using OpenSesame 3.0 (Mathôt, Schreij, & Theeuwes, 2012) and PsychoPy (Peirce, 2007) and they were presented on a 17-in. cathode ray tube monitor (resolution: 800 x 600 pixels, refresh rate: 75 Hz). Strings were presented in black against a white background, at the center of the screen, using Selectric font, and they flickered on and off at 18.75 Hz (4 monitor refresh cycles per period: 1 on- and 3 off-cycles). 240 strings (between five and eight letters long) were used as stimuli. 60 high frequency words (HFW, mean printed frequency greater than 100 occurrences per million) and 60 low frequency words (LFW, mean printed frequency less than 10 occurrences per million) were selected from a large lexical corpus of written French (*Lexique*, New, Pallier, Brysbaert, & Ferrand, 2004). Sixty orthographically familiar pseudowords (FWP) and 60 orthographically unfamiliar pseudowords (UPW) were selected from the *French Lexicon Project* (*FLP*, Ferrand et al., 2010). FWPs had on average more lexical neighbors than UPWs (4.10 vs. 0.35,  $p < .0001$ ) and FWPs contained on average more frequent bigrams than UPWs (type: 146 vs. 100,  $p < .0001$ ; token 1210 vs. 790,  $p < .0001$ ). Corpus analyses using *FLP* confirmed that reaction times (RTs) of FWPs were significantly different from RTs of UPWs ( $p < .0001$ ).

## 2.3 Procedure

Each trial started with a fixation point (black cross on a white screen) displayed at the center of the screen for 500 ms. After an empty screen lasting 200 ms, the flickering string was presented for 2000 ms. Then, a screen prompted participants to name the string aloud ('Répétez à haute voix': name aloud). The next trial started after 4000 ms. Vocal responses were assessed online by the experimenter in order to be sure the participant was engaged in the task. Due to the long presentation time, accuracy was 100%. Session consisted of three blocks of 80 trials each with a brief pause



between each block. The block sequence was counterbalanced between participants while the target string sequence in each block was randomized for each subject.

## **2.4 EEG recording and analysis**

EEG activity was acquired at 512 Hz using a Biosemi Active Two system provided with 64 Ag/AgCl sintered active electrodes. Electrodes were mounted on an elastic cap (Electro-Cap, Inc. Eaton, OH) that was positioned according to the 10-20 International system (American Clinical Neurophysiology Society, 2006). Two additional electrodes (CMS/DRL) were used as on-line reference (see [www.biosemi.com](http://www.biosemi.com)). Three extra electrodes were used to monitor eye movements and blinks (two placed at the outer canthi of the eyes, one placed below the left eye). Other two extra electrodes were used for an online re-referencing (placed behind ears on mastoid bone). For the EEG analysis, we used EEGLAB (Delorme & Makeig, 2004), Erplab (Lopez-Calderon & Luck, 2014) and Fieltrip (Oostenveld et al., 2011) toolboxes for Matlab and Matlab customized functions (Matlab 2014, The Mathworks). Data were re-referenced off-line to the average of left and right mastoid electrodes, bandpass filtered from 5 to 100 Hz and then segmented to include 200 ms before and 2000 ms after stimulus onset. Epoched data were normalized based on a prestimulus period of 200 ms, and then evaluated according to a sample-by-sample procedure to remove noisy sensors that were replaced using spherical splines. Additionally, EEG epochs that contained data samples exceeding threshold (100  $\mu$ V) were excluded on a sensor-by-sensor basis, including horizontal and vertical eye channels. On average, 6.54 % of the data were interpolated and 4.71 % of the data rejected. Slow drifts were removed in order to reduce “sawtooth” artifacts in the Fourier spectrum (Bach & Meigen, 1999). EEG data were then segmented again, discarding the first 533 ms in order to remove the initial transient response, and the last 400 ms to have epochs containing integer number of flicker periods. The resulting 1092 ms lasting epoch corresponds to 20 complete cycles within stimulation.

## **3. Results**

### **3.1 SSVEP power**

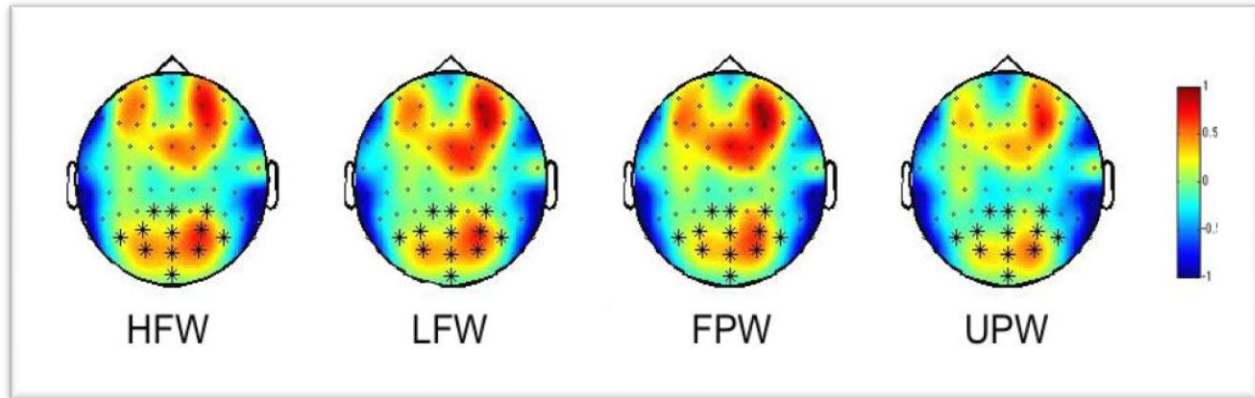


Figure 1. Topographic distribution of SSVEPs power (z scores) at the stimulation frequency (18.75 Hz) for the four types of string. HFW = high frequency word, LFW = low frequency word, FPW = familiar pseudoword, UPW = unfamiliar pseudoword. “\*” symbols indicate electrodes included in the regression models.

To extract SSVEP activity synchronized to the stimulus flicker, the EEG signal of each epoch was decomposed using Fast-Fourier Transform (FFT, frequency resolution 0.94 Hz). First, in order to verify that words and pseudowords elicited reliable SSVEPs, we calculated a statistic specifically conceived to detect and quantify steady-state responses,  $T_{circ2}$  (Victor & Mast, 1991). We calculated  $T_{circ2}$  for each subject and electrode. Significant SSVEP responses were obtained for all participants. Then, following the logic of Chicherov and Herzog (2015), we averaged across subjects and conditions to select the channels with the strongest SSVEP entrainment for further analysis. We selected the first 12 electrodes (Iz, Oz, O2, O1, PO8, POz, PO4, PO3, PO7, P1, P4, Pz) that were grouped in three electrode locations: left (O1, PO3, PO7, P1), centre (Iz, Oz, POz, Pz) and right (O2, PO8, PO4, P4). Figure 1 shows the topographic distribution of SSVEP power for the four types of strings along with the selected electrodes. Because the absolute amplitude of the EEG signal varies widely across participants, we standardized data calculating z-scores of SSVEP power from each electrode, condition and participant based on the participant’s overall average and standard deviation of SSVEP power across all scalp electrodes and across all of the conditions. Statistical analyses of SSVEP power were performed using lme4 package (Bates, Maechler, Bolker, & Walker, 2014) and lmerTest package (Kuznetsova, Bruun Brockhoff, & Haubo Bojesen Christensen, 2015)

in the R environment (R Core Team, 2014). The SSVEP power (z scores) was subjected to three separated mixed-effect multiple regression models (Baayen, Davidson, & Bates, 2008; type III test, Satterthwaite approximations to degrees of freedom) to inspect the effects of lexicality, frequency and orthographic familiarity (see below). Each model included two fixed effects and their interaction. The first effect was either *lexicality* (two levels: word vs. pseudoword), *frequency* (two levels: high frequency word vs. low frequency word) or *orthographic familiarity* (two levels: familiar pseudoword vs. unfamiliar pseudoword). The second fixed effect was *electrode location* (three levels: left, centre, right). By-subject and by-electrode random intercepts were included in all models.

**3.1.1 Lexicality effect.** The SSVEP power for words and pseudowords are shown in the left panel of Figure 2. The main effect of lexicality was significant,  $F(1, 43878) = 28.16, p < 0.001$ , reflecting the fact that the SSVEP power was higher for words compared to pseudowords. The main effects of electrode location was not significant  $F(2, 9) = 0.1, p = 0.901$ , indicating that the SSVEP power was equally distributed across the three different locations (left, centre, right). The lexicality by electrode location interaction was not significant  $F(2, 43878) = 1.36, p = 0.256$ .

**3.1.2 Frequency effect.** SSVEP power for low- and high-frequency words is shown in the middle panel of Figure 2. The main effect of frequency was significant  $F(1, 21894) = 14.61, p < 0.001$ , indicating that the SSVEP power was higher for HFW compared to LFW. The main effect of electrode location was not significant,  $F(2, 9) = 0.15, p = 0.865$ , indicating that the SSVEP power was equally distributed across the three different locations (left, centre, right). The lexicality by electrode location interaction was not significant  $F(2, 21894) = 0.11, p = 0.895$ , indicating that the effect of frequency was equal across locations.

**3.1.3 Orthographic familiarity effect.** Neither the effect of orthographic familiarity nor the effect of electrode location nor their interaction were significant ( $F(1, 21954) = 1.79, p = 0.181$ ;  $F(2, 9) = 0.14, p = 0.869$ ;  $F(2, 21954) = 0.07, p = 0.937$ , respectively). Right panel of Figure 2 shows the effect of orthographic familiarity.

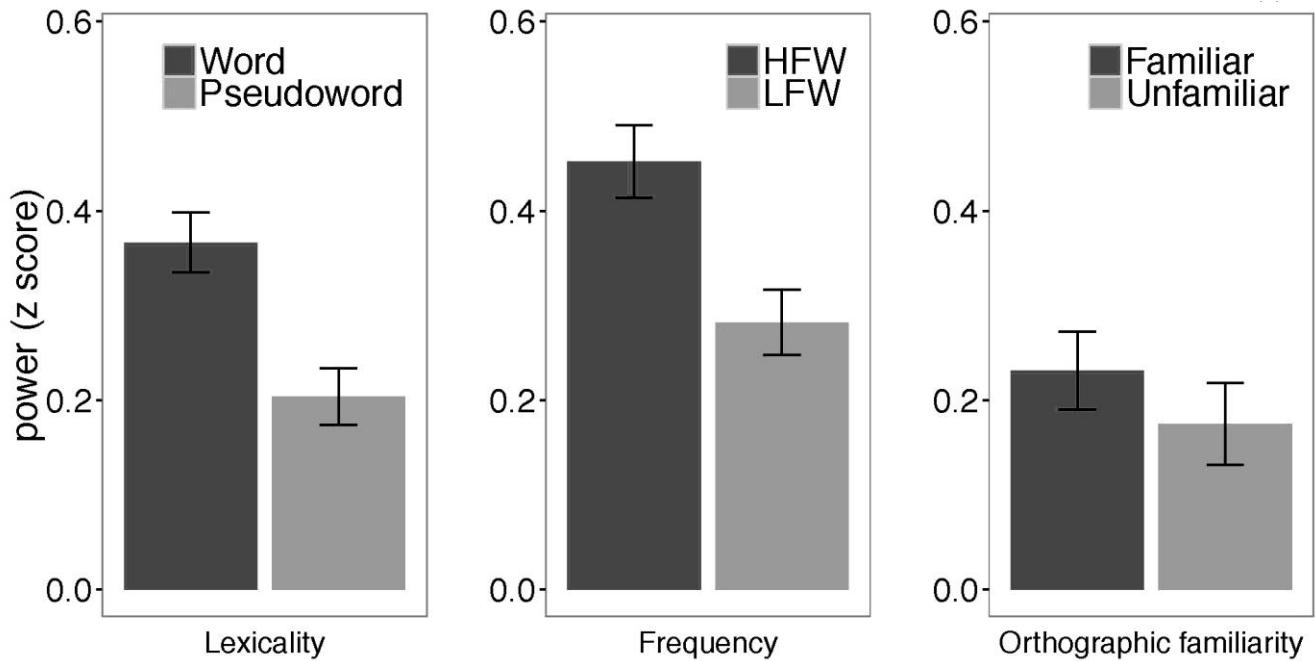


Figure 2. SSVEP power (z scores) for the three effects: lexicality effect (word vs. pseudoword), frequency effect (high-frequency word vs. low-frequency word), orthographic familiarity effect (orthographically familiar pseudoword vs. orthographically unfamiliar pseudoword). HFW = high frequency word, LFW=low frequency word. Error bars represent standard error of the means (SEMs) adjusted to correctly reflect the variance in the within-subject design (Morey, 2008)

### 3.2 SSVEP in source space

EEG cortical source analysis was performed with the source reconstruction method eLORETA (exact Low-Resolution Electromagnetic Tomography), which models 3D distributions of EEG cortical sources (Pascual-Marqui, 2007, for a review, see Grech et al., 2008) in the frequency domain. Power spectral analyses were first performed using a single-taper hanning method implemented in the Fieldtrip toolbox (<http://www.ru.nl/donders/fieldtrip>) using the frequency and time window of interest (frequency: 18.75 Hz; time window between 533 and 1600 ms) as well as a 8Hz smoothing box. Sources were modeled as equivalent current dipoles (ECDs, i.e. point sources or dipoles with a location and orientation), which are restricted to the volume conduction model of the head. We used a standard Boundary Element Method (BEM) volume conduction model in which the head geometry is realistic and based on the ‘Colin27’ template (see Fuchs, Kastner, Wagner, Hawes, & Ebersole, 2002). The standard BEM model is expressed in the Montreal Neurological Institute coordinate system (in mm) and it can be associated with a standard file of electrode positions defined

in the same coordinate system. The template file of the 10-20 system for electrode placement was adapted (64 among 97 electrodes were selected) to model the position of the electrodes compatible with the current EEG acquisition system. A three-dimensional grid with 5 mm spacing dipoles was defined in the inner skull volume, resulting in 54180 dipoles. Specific contrasts were performed in order to study the effects of interest (with the exclusion of the orthographic familiarity effect that did not significantly modulate the SSVEP power at the scalp level). To identify the neural sources of the lexicality effect, we contrasted the activation for words (collapsing HFW and LFW in one group) with the activation for pseudowords (collapsing FPW and UPW in the other group). To identify neural sources of the frequency effect, we contrasted the activation for HFW with the activation for LFW. Cortical activation was analyzed with nonparametric statistical tests based on Montecarlo permutation (Maris & Oostenveld, 2007). *P*-values were corrected for multiple comparison using False Discovering Rate (e.g. Genovese, Lazar, & Nichols, 2002).

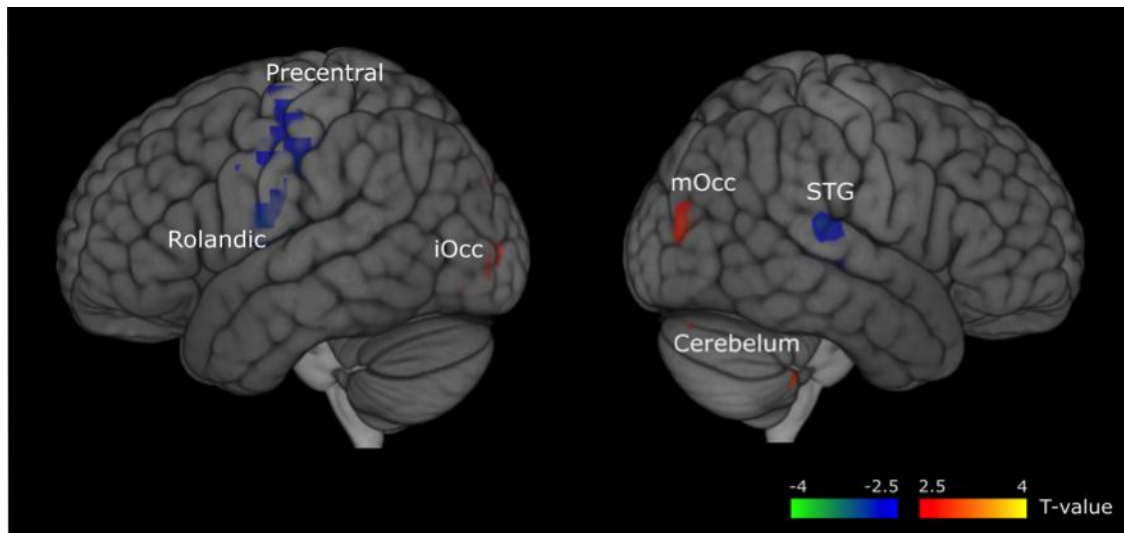


Figure 3. Regions whose source signal activity differed between words and pseudowords (positive and negative significant activations are shown in red and blue, respectively). Statistical threshold =  $p < .05$ , corrected for multiple comparison using FDR. [on the left side of cerebral hemisphere: Rolandic for Rolandic Operculum and iOcc for inferior Occipital; on the right side: mOcc for middle Occipital and STG for superior Temporal Gyrus].

**3.2.1 Lexicality effect.** Figures 3 and 4 show the activation map for the lexicality effect for corrected and uncorrected contrasts, respectively. There were three narrow peaks in the map showing positive significant activation, the cerebellum [40 -40 -50], the right middle occipital lobe [45 -80 14], the left inferior occipital lobe [-40-76 -6], in which there was greater activation for words than for pseudowords ( $t(16) = 3.61, p < .05$ ;  $t(16) = 2.83, p < .05$ ;  $t(16) = 2.1, p < .05$  respectively). While, a negative significant effect was located in a large left region including parts of the rolandic operculum, the insula and the pre- and post-central gyri [-35 -25 20], and in a peak located in the right temporal superior gyrus [55 -26 3], in which there was greater activation for pseudowords compared to words ( $t(16) = -3.61, p < .05$ ;  $t(16) = -2.9, p < .05$ ).

**3.2.2 Frequency effect.** Figure 5 shows the activation map for the frequency effect. The positive contrast (i.e., greater activation for HFW than for LFW) was located in the left temporal superior and middle pole [-45, 20, -30]. This effect was significant ( $t(16) = 3.04, p < .05$ ). The negative contrast (greater activation for LFW than for HFW) was located in a right region encompassing parts of the postcentral gyrus, the parietal superior and inferior lobule and the supramarginal gyrus [40, -35, 60]. This effect was significant ( $t(16) = 3.9, p < .05$ ).

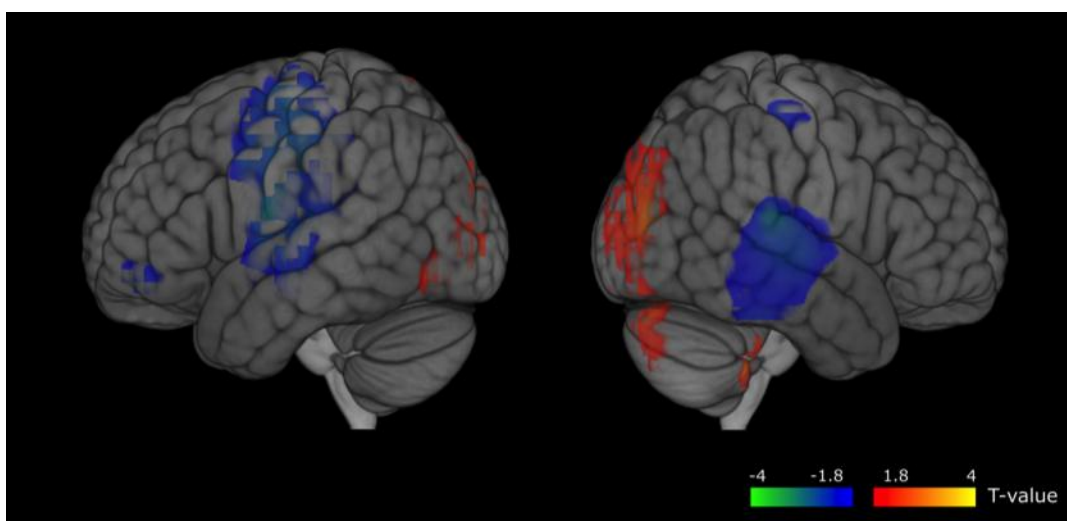


Figure 4. Regions whose source signal activity differed between word and pseudoword. Statistical threshold =  $p < .05$ , not corrected

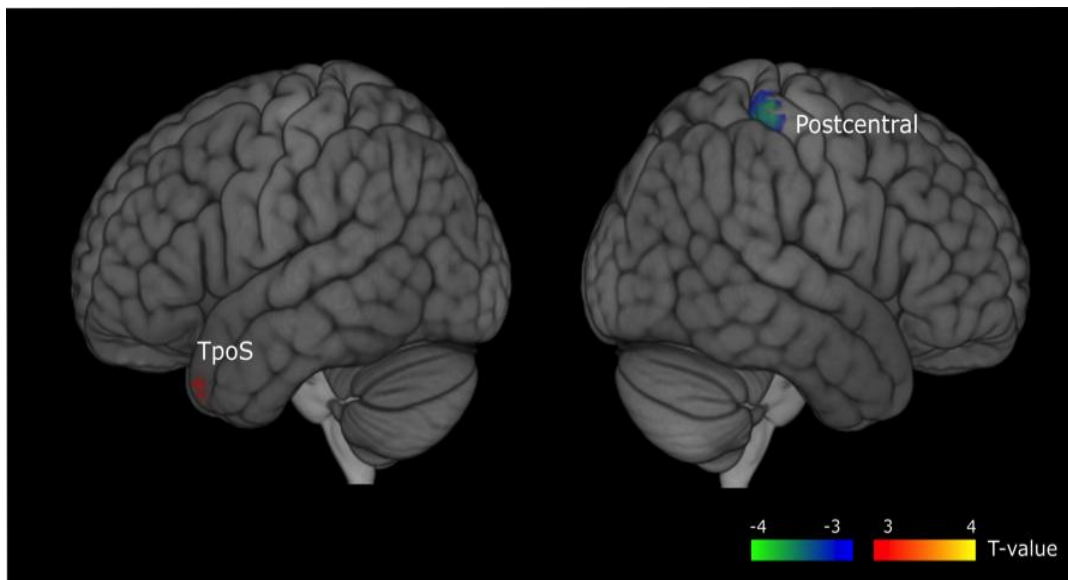


Figure 5. Regions whose source signal activity differed between HFW and LFW (positive and negative significant activations respectively red and blue). Statistical threshold=  $p < .05$ , corrected for multiple comparison using FDR.[on the left side of cerebral hemisphere: TpoS for Temporal Pole Superior and on the right side: Postcentral for a large region encompassing parts of postcentral gyrus, superior and inferior parietal lobule and supramarginal gyrus].

#### 4. Discussion

We evaluated whether words and pseudowords could elicit reliable SSVEPs in a naming task using a paradigm in which words and pseudowords were presented in isolation and flickered at 18.75 Hz. In order to test the presence of significant SSVEP activity, we calculated a statistic specifically designed for the analysis of Fourier components (Victor & Mast, 1991). Significant SSVEP activity was detected especially in the parieto-occipital area (see Figure 1), and more importantly, the SSVEP power showed a clear modulation in the expected direction with stronger SSVEP power for words over pseudowords (i.e., lexicality) and for high- over low-frequency words (i.e., frequency). No modulation of SSVEP power was obtained for the orthographic familiarity effect (familiar versus unfamiliar pseudowords), which suggests that SSVEP taps lexical rather than sublexical mechanisms.

Overall, our results are compatible with the hypothesis that the SSVEP power reflects the underlying network efficiency (Zhang et al., 2015) because words benefit from more efficient lexical network dynamics than pseudowords, which also results in shorter reaction times and higher accuracy in standard naming tasks. Similarly, high-frequency words also benefit from more efficient lexical networks because they tend to have stronger network connections or resting levels, which typically results in faster RTs and higher accuracy for high-frequency over low-frequency words. In current computational models of reading (Perry et al., 2007, 2010), reading high-frequency words relies on the fast and efficient lexical route that allows to retrieving the overlearned representation of the word from the orthographic lexicon. On the contrary, pseudowords are decoded by the way of the sublexical route that requires the sequential parsing of the string into the constituent orthographic units and then the assembling of the phonology from the sublexical parts. Similarly, LFW reading, compared to HFW reading, would rely to a greater extent onto the less efficient sublexical route.

Neural synchrony is crucial for object representation (e.g. temporal binding theory). In that view, information is stored in flexible cell assemblies, transiently synchronized by dynamic connections (see e.g., Buzsáki, 2010, 2004; Engel, Fries, & Singer, 2001; Fries, 2005; Varela, Lachaux, Rodriguez, & Martinerie, 2001 for reviews). Two mechanisms, not mutually exclusive, can explain how the build-up of such connections may be reflected by the SSVEP. A network characterized by an internally more coherent activity could be more easily entrained by the external periodic stimulation, possibly by the way of phase alignment (e.g. Kashiwase, Matsumiya, Kuriki, & Shioiri, 2012; Moratti et al., 2007), eventually showing larger steady-state activity. Alternatively, a larger number of cell assemblies showing synchronized activity produce larger SSVEPs.

The proposed interpretation is also consistent with the finding that attended stimuli generate higher SSVEPs than unattended items. Indeed, there is some evidence that attentional effects are mediated by selective synchronization (e.g., Bosman et al., 2012) and this seems to be the case for SSVEP as well (Joon Kim et al., 2007). It is important to note that we are not claiming that lexical processing involves more attentional resources than sublexical processing. Computational models (e.g. Perry et al., 2007) and behavioral evidence (e.g. Montani, Facoetti, & Zorzi, 2014, see Besner



et al., 2016 for review) suggest exactly the opposite. In our paradigm, there is no attentional manipulation and we are not explicitly measuring the allocation of attention on the stimulus. Rather, we suggest that SSVEP power reflects the level of coherence of the network underlying the processing of the different type of strings. Because, for example, word processing should be sustained by a larger coherent activity, SSVEP power for this type of stimuli is higher than for pseudoword processing. Whereas in paradigms in which attention is manipulated, attended items show higher power because attention selectively increases the synchronization of the population of cells that are involved in the processing of the attended stimulus.

Two previous studies presenting flickering words reported inconsistent results. Koban et al., 2010 found that SSVEP power for positive emotional words was reduced compared to power for neutral words, contrary to previous results obtained when presenting emotional pictures. The unexpected finding could be explained on the basis of some methodological issues, as suggested by the authors. First, words were presented for 8 sec, that is, far longer than the standard time necessary to process written words. During this long time, processes of different nature could have taken place. Then, words were flickered at 7.5 Hz. Steady-state responses in different frequency bands showed different sensitivities to physical stimulus parameters (Regan, 1989) suggesting that at least to some extent, different flicker frequencies can entrain functionally distinct cortical networks (Srinivasan et al., 2006). For example, Kaspar, Hassler, Martens, Trujillo-Barreto, & Gruber, 2010 found that familiar objects elicited higher SSVEP amplitudes compared to unfamiliar objects at 12 and 15 Hz but the effect reversed at 7.5 Hz. Ding and coll. (Ding, Sperling, & Srinivasan, 2005) found a reversed effect of attention on SSVEP amplitude at frequencies in the lower alpha band. However, in a recent study, SSVEP amplitude was completely unaffected by emotional word content, and more importantly for the present discussion, by the lexical status of the string (Trauer et al., 2015). While the presentation time and stimulation frequency used by Trauer and coll. were more similar to the parameters used here, unlike that in our study, in which we adopted a naming task, in their study participants were engaged in a lexical decision task. It has been proposed that lexical decision task entails partially different computational processes than standard reading task (e.g. Chen, Davis,

Pulvermüller, & Hauk, 2013; Montani, Facoetti, & Zorzi, 2015), which might explain the different findings. In addition, and also with reference to the lack of effect for the emotional content, authors concluded that affective words may not capture early visual processing resources. Indeed, both studies reported results relative to few occipital electrodes that reflect activity in early visual cortex only. On the contrary, the effect of emotional words should start at later lexico-semantic stages (Trauer et al., 2015).

At the level of cortical source, in order to dissociate sublexical and lexical reading routes, and localize the source of the lexical effect, we contrasted the activation for word with the activation for pseudoword. The generators of the lexical effect were located posteriorly and bilaterally in occipital areas, and in the right cerebellum (see Figure 3). More specifically, we found three peaks that showed higher activation for word located respectively in the left inferior occipital cortex, in the right middle occipital cortex and in the right inferior cerebellum. The map of significant activations with no correction for multiple comparisons reported in Figure 4, may further clarify the results.

The peak in the left inferior occipital cortex was located slightly posteriorly to the VWFA, and before correcting for multiple comparisons, the area included also portions of the fusiform and the lingual gyri (Figure 4). Overall, the finding is in line with the substantial evidence that the ventral occipitotemporal (vOT) cortex is involved in skilled reading (Cohen et al., 2002; Dehaene & Cohen, 2011; Price, 2012) and with previous studies that reported that the vOT is sensitive to word vs. pseudoword contrasts (for a review, see Price & Mechelli, 2005). Remarkably, the presence of the lexical effect in an area associated with early visual processing, from visual feature extraction to letter processing, suggests feedback effects from higher level areas and supports the interactive account of word reading (Carreiras et al., 2014; Price & Devlin, 2011). It is noteworthy that the most common finding in previous studies was a greater activation for words in more anterior portions of the vOT (Price & Mechelli, 2005), while we detected a rather posterior effect (but for a similar result, see Fiebach, Friederici, Müller, & von Cramon, 2002). A possible explanation is the long stimulus presentation of our paradigm that could have supported more prolonged and extended feedback effects. The peak in the right hemisphere was almost symmetrical to the peak on the left side and

likely reflects early stages of processing as well, supporting again a relevant role of feedback connections. Alternatively, the findings could be explained supposing that the occipital cortex bilaterally contains neurons tuned to complex orthographic features such as morphemes or words (Schurz et al., 2014).

Interestingly, before correcting for multiple comparisons, a bilateral region including the cuneus, the precuneus and the posterior cingulum showed the same effect. Recently, Taylor and coll. (Taylor et al., 2012) in their metaanalysis identified some clusters showing larger activity of word compared to pseudoword that include also that region. Crucially, they found an extensive overlap between their activation maps in these regions and activation maps identified in the meta-analysis of neuroimaging studies of semantic processing of Binder et al. (Binder, Desai, Graves, & Conant, 2009). Therefore, the positive effect we detected in this medial region suggests that the difference between words and pseudowords is possibly sustained by lexico-semantic processes (Braun, Jacobs, et al., 2015; Gold, Balota, Kirchhoff, & Buckner, 2005; Graves, Desai, Humphries, Seidenberg, & Binder, 2010). Previous findings indeed suggest that this region is sensitive to semantic variables such as imageability (Hauk, Davis, Kherif, & Pulvermüller, 2008a; Wise et al., 2000). Furthermore, the precuneus showed decrease of activation for low versus high frequency words in (Carreiras, Riba, Vergara, Heldmann, & Münte, 2009), which provides further support for a semantic account. Full activation of the semantic representations associated with word could have been promoted by the long presentation of our stimuli.

Finally, we also found positive activation in the posterior lobe of the right cerebellum, at the level of the lobules VII and VIII, and, in Crus 1 and 2 (Fig. 3 and 4) although these latter effects did not “survive” correction for multiple comparisons. The cerebellar posterior lobe is strongly coupled to the somatomotor cortex, it contains motor maps (Buckner, 2013) and has been also associated with articulation (Ackermann, Vogel, Petersen, & Poremba, 1992; Chen & Desmond, 2005). Therefore, a possible explanation of our finding is that words exhibited a more coordinate articulatory planning activity compared to pseudowords. However, the involvement of the cerebellum in higher cognition, beyond the motor domain, is widely recognized (Annabel Chen, Ringo Ho, & Desmond, 2012;

Buckner, 2013). There is evidence that the cerebellum, in particular the right posterolateral region (Crus 1), is involved in language (Stoodley & Schmahmann, 2008, 2009), and even specific patterns of activations or cerebellum structural properties have been associated to reading disorder (Feng et al., 2016; Laycock et al., 2008; Linkersdörfer et al., 2012; Nicolson, Fawcett, & Dean, 2001). In fact, the cerebellum is connected to the cerebrum mainly by contralateral projections, with the right cerebellum hemisphere connected to the left cerebral cortex (Buckner, 2013). Its precise role in reading or language processing is not clear but a promising hypothesis is the extension to the language domain of a theory originally developed to explain the role of cerebellum in motor processing (Ito, 2008; Ramnani, 2006). The cerebellum is thought to have a coordinative role encoding internal models, neural representations of context-specific properties of objects that can be used to predict action consequences or more generally, generate related expectancies. Applied to linguistic domain, the theory holds that the cerebellum may support predictive language processing (Lesage, Morgan, Olson, Meyer, & Miall, 2012; Moberget, Gullesen, Andersson, Ivry, & Endestad, 2014). Thus, a possible alternative explanation of our finding is that the greater activation for words reflected the activation of the context associated with words, while pseudowords have no such internal models.

Concurrently, we found higher activation for the pseudowords in left sensorimotor areas, in left perisylvian regions classically associated to the language system and in the right temporal superior gyrus. Pre- and post-central regions are usually activated to control orofacial muscles during production of speech sounds, while the right temporal superior gyrus is commonly activated during acoustic and auditory processing (Price, 2012). However, we detected this pattern of activation during the presentation of the stimulus, a moment in which participants were engaged in passive viewing only. We can speculate that the activation was due to articulatory planning activity in preparation of naming and that this preparatory activity involved the sensorimotor areas as well as areas involved in speech processing. The perisylvian region included the rolandic operculum, the insula and the supramarginal gyrus, areas that have been consistently found more activated for reading pseudowords than words (Jobard, Crivello, & Tzourio-Mazoyer, 2003; Price & Mechelli,

2005; Taylor et al., 2012), and for which a specific role in spelling-to sound conversion has been hypothesized (e.g. Bitan et al., 2007; Braun, Hutzler, et al., 2015; Braun, Hutzler, Ziegler, Dambacher, & Jacobs, 2009). In addition, damage in those areas has been associated to deficits in phonological decoding (Fiez & Petersen, 1998; Roeltgen, Sevush, & Heilman, 1983). Therefore, the most plausible explanation of our finding is that because pseudowords place increased demands on the sublexical conversion of orthography to phonology, the involved areas are recruited to a greater extent for pseudowords than for words.

With respect to the frequency effect, the contrast between HFW and LFW showed a composite pattern (see Figure 5). Firstly, we found higher activation for HFW compared to LFW in a left region including the superior and middle parts of the temporal pole. The most consistent finding across previous studies that compared words of high and low frequency has been greater activation for low relative to high frequency words in the left pre/SMA region, and in the left inferior frontal cortex (Fiebach et al., 2002; Fiez, Balota, Raichle, & Petersen, 1999; Carreiras et al., 2009; Carreiras, Mechelli, & Price, 2006; Chee, Hon, Caplan, Lee, & Goh, 2002; 2003; Hauk, Davis, Kherif, & Pulvermüller, 2008b; Joubert et al., 2004) and it has been interpreted in terms of differential recruitment of lexico-phonological processes. Consistently with the above mentioned studies, we found greater activation for HFW compared to LFW in a left region around the orbital part of the inferior frontal cortex but again that activation was no longer significant after correction for multiple comparisons. Regarding the higher activation in the temporal pole, the anterior temporal lobe (ATL), of which the temporal pole is the anterior end, is crucial for semantic processing (see Patterson, Nestor, & Rogers, 2007 for review). It has been proposed that object representations in the ANTs are abstracted away from perceptual properties to support conceptual object knowledge (Peelen & Caramazza, 2012) and that there is a posterior-to-anterior gradient in the specificity of semantic processing in the ATL, with more fine-grained semantic information relying more on anterior regions (Tyler et al., 2004). The left ATL is extensively connected to the left dominant language centers (Friederici, 2009; 2011) and consistently showed to be more engaged in tasks that include a strong verbal component (see ; Price, 2012; Wong & Gallate, 2012 for reviews). A possible explanation of

our finding, therefore, is the presence of more pronounced semantic associations for high frequency words (Devlin, Matthews, & Rushworth, 2003; Carreiras et al., 2009; Prabhakaran, Blumstein, Myers, Hutchison, & Britton, 2006). Accordingly, semantic retrieval for HFW should be facilitated compared to LFW, showing higher activation in areas subserving semantic processing. Remarkably, activation for high-frequency words in brain areas that support semantic processing has been difficult to be uncovered despite it is predicted above all by neuropsychological data (Graves, et al., 2010; Taylor et al., 2012). As we have previously mentioned to explain the word vs. pseudoword contrast, the long presentation time compared to standard naming task could have had peculiar effects, such as in this case, to facilitate the detection of selective recruitment of areas associated with semantic processing.

Concurrently, we found higher activation for LFW compared to HFW in a right region that extended over the postcentral gyrus, the superior and inferior parietal lobule and the supramarginal gyrus. A possible explanation is a greater involvement of the visuo-spatial attentional network in phonological decoding. Visuospatial attention is considered to be primarily controlled by the fronto-parietal attention network (Corbetta & Shulman, 2002), with a prominent role of the right hemisphere (Thiebaut de Schotten et al., 2011). In particular, the role of the superior parietal lobule (Wu et al., 2016) and inferior parietal lobule and supramarginal gyrus (Wang et al., 2016) in attention orientation has been recently confirmed. Consistent behavioral evidence (Auclair & Sieroff, 2002; Givon, Yang, & Gernsbacher, 1990; Montani et al., 2014; Risko, Stolz, & Besner, 2011; Sieroff & Posner, 1988) supports the proposal that phonological decoding is controlled by a top-down mechanism directing the spotlight of attention serially from left to right over the sub-word units (LaBerge & Samuels, 1974). The candidate that most likely subserves this mechanism is the attentional stream located in the parietal lobe (Vidyasagar & Pammer, 2010) and multiple evidence points to a selective involvement of the right parietal lobe when reading is more demanding. Serial reading is required to process unfamiliar format, such as case mixing. Scanning participants using PET during a reading task, Mayall and coll., (Mayall, Humphreys, Mechelli, Olson, & Price, 2001) found that mixed-case words compared to same-case words produced increased activation in the

right parietal cortex. Similarly, the disruption produced by TMS stimulation over the right posterior parietal lobe was more pronounced for mixed-case words (Braet & Humphreys, 2006). Again with an inhibitory TMS protocol, Cazzoli and coll., (Cazzoli, Müri, Kennard, & Rosenthal, 2014), found that TMS application over the right posterior parietal cortex produced an increase in letter migrations errors. Because letter migration is due to an erroneous binding between the letters composing the words and their spatial location, a possible interpretation of that finding is that the transient disruption of the mechanism controlling the precise parsing of the string caused an over reliance on coarse grained orthographic processing (Grainger & Ziegler, 2011). Another example of more demanding reading process from the point of view of visuo-spatial analysis is logographic reading. The square shape of the logograph requires an elaborated analysis of the spatial information and locations of various strokes (Tan et al., 2001). Compared to reading English, a larger involvement of the right hemisphere, including the superior parietal lobule and the supramarginal gyrus, has been demonstrated in Chinese reading (Tan et al., 2001), especially for irregular words (Hai Tan, Ching-Mei Feng, Fox, & Gao, 2001). Finally, visual spatial attention deficits are associated with phonological decoding deficits in developmental dyslexia (Facoetti et al., 2006). Accordingly, in a treatment protocol with dyslexic children, high frequency repetitive TMS stimulation over the right inferior parietal lobule improved non-word reading accuracy (Costanzo, Menghini, Caltagirone, Oliveri, & Vicari, 2013).

However, in our investigation there are some limitations. First, we did not take into account a number of other word properties. For example, our sets of stimuli included strings of different lengths, even if equally distributed in the different groups. The length effect interacts with other factors, for example modulating the lexicality effect. Future studies should explore the length effect as well as the effect of other linguistic properties, such as consistency or imageability (Graves et al., 2010). It is also important to note that few factors limited our source localization analysis. First, spatial resolution of EEG is affected by electrode density. In order to obtain the best possible spatial resolution, it has been estimated that at least 128 electrodes should be applied (Ryynänen, Hyttinen, & Malmivuo, 2006). Next, our precision in localizing neural activity was reduced by the absence of

individual structural MRI for each participant. Lastly, adopting a specific stimulation frequency (in that case, 18.75 Hz), we potentially selected a specific functional network in which natural frequencies match the flicker frequency (Ding et al., 2005). Future investigations should systematically explore the use of different frequencies. Despite the limitations, we found a pattern of activity compatible with the existing literature and with cognitive models of visual word recognition, confirming the validity of our approach.

A great advantage of the approach proposed here is the possibility to use frequency tagging to segregate the signal coming from different portions of the visual arrangement. Often, this method is used with multi-input frequencies as “tags” for different stimuli presented concurrently. Analyzing the frequency bins corresponding to each of the stimulation frequency allows to extract the evoked responses from the population of cells that are selectively entrained by each stimulus (Norcia et al., 2015). Some examples of possible application in reading could be to investigate processing of different strings presented at the same time, or to investigate effects of attentional manipulation on different type of strings. Another interesting application could be using frequency tagging to investigate hierarchical organization of written words. Representation of words is supposed to be based on a hierarchy of “detectors” that are sensitive to increasingly larger fragments of words (Dehaene, Cohen, Sigman, & Vinckier, 2005; Grainger & Ziegler, 2011). Even units of higher levels, such as morpheme or syllables may play a role in recognition of written words (Grainger, 2008; Ziegler & Goswami, 2005). A comprehensive account of how words are processed includes a detailed description of when and how the different units are involved (Carreiras et al., 2014). SSVEPs are a unique tool to investigate role of subunits thanks to the fact that processing of specific subunits can be tagged and distinguished from each other using multiple stimulation frequencies simultaneously.

In conclusion, using a naming task, we demonstrated that SSVEPs generated by written words and pseudowords are sensitive to fundamental effects of reading aloud. In particular, we found that SSVEPs tapped lexical network dynamics. That is, SSVEP amplitudes were modulated by lexical frequency and lexicality but not by sublexical orthographic familiarity. This finding is in favor of the



hypothesis that SSVEPs reflect more structured, organized and efficient neural representation, which result in more synchronized network dynamics. The source localization confirmed that the paradigm is well suited to investigate the cortical generators and neural dynamics of word processing. First, we were able to replicate well-known findings obtained with other neuroimaging techniques, such as activation in vOT in reading. Indeed, the lexicality effect emerged at an early level of processing, supporting the interactive activation account of word reading (Carreiras et al., 2014; Price & Devlin, 2011). Second, we found effects that had been difficult to detect previously, such as frequency effects in areas involved in semantic processing. Third, we found that pseudowords required more activation in areas devoted to speech processing and/or in speech-to-sound conversion. The higher activation for LFW in the right parietal lobe supports a relevant role of attentional processes in the phonological route. We believe that the present approach is well suited to uncover the neural dynamics of written language processing.

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