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The impact of spelling regularity on handwriting production: A coupled fMRI and kinematics study

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ABSTRACT

Current models of writing assume that the orthographic processes involved in spelling retrieval and the motor processes involved in the control of the hand are independent. This view has been challenged by behavioral studies, which showed that the linguistic features of words impact motor execution during handwriting. We designed an experiment coupling functional magnetic resonance imaging and kinematic recordings during a writing to dictation task. Participants wrote orthographically regular and irregular words. The presence of an irregularity impacts both the initiation of the movement and its fine motor execution. At the brain level, the left inferior frontal and fusiform gyri, two regions belonging to the core of the written language system, were found to be sensitive to the presence of an irregularity and to its position in the word during writing execution. Moreover, the left superior parietal lobule, the left superior frontal gyrus and the right cerebellum, three motor-related regions, displayed a stronger response to irregular than regular words. These results constitute direct evidence that orthographic and motor processes occur in a continuous and interactive fashion during writing.

Introduction

While orthographic processing and its neural correlates have been widely studied in reading tasks, the motor production of written words remains poorly understood. To write a word, we retrieve its spelling to know which letters we have to produce. These letters are traced by the execution of hand movements with a pen. Neuropsychological studies reported patients presenting impairments of the linguistic processes involved in orthographic retrieval (central agraphia). Other patients had difficulties with movement control and resulted in unreadable writing (apraxic agraphia or pure agraphia). Finally, some patients have normal spelling skills and readable handwriting, but are specifically impaired in the selection of the motor pattern corresponding to the activated letter (Rapp & Caramazza, 1997). The clinical independence of orthographic and motor impairments led researchers to consider the apraxic and central agraphias separately (Baxter & Warrington, 1986; Ogle, 1867; Roeltgen, 2003). This dissociation influenced writing studies and the elaboration of cognitive models (Rapp, 2002). They assumed that writing relies on so-called “central” orthographic processes common to all spelling modalities (handwriting, oral spelling, typing, etc…) and “peripheral” motor processes specific to handwriting.

Neuropsychological and neuroimaging studies have shown that these processes have distinct neural substrates. Spelling is mostly supported by the left fusiform gyrus (FuG) and the left inferior frontal gyrus (Planton, Jucla, Roux, & Démonet, 2013; Purcell, Turkeltaub, Eden, & Rapp, 2011). The key role of the left FuG in accessing or storing the orthographic forms of words (orthographic long-term memory) is well acknowledged (Nakamura et al., 2000; Purcell et al., 2011; Rapp, Purcell, Hillis, Capasso, & Miceli, 2016; Ueki et al., 2006). This is consistent with the sensitivity of this region to lexical frequency in spelling tasks (Rapp & Dufor, 2011; Rapp et al., 2016). The left IFG, in the pars opercularis, is also reliably activated during tasks where spelling has to be retrieved (Planton et al., 2013; Purcell et al., 2011), but the exact functional role of this activation remains unclear. Left IFG damage can lead to impairments in phono-graphemic conversion (Henry, Beeson, Stark, & Rapcsak, 2007), but some data are also consistent with a role in the access or storage in orthographic long-term memory (Rapp & Dufor, 2011) or in lexical selection (Purcell et al., 2011). On the motor side, the control of handwriting movements is supported mainly by the left superior frontal gyrus (SFG) extending to the precentral gyrus, the left superior parietal lobule (SPL), and the right cerebellum (Ce). These regions display functional specificity for writing, as they respond more strongly to writing than to matched movements (Planton et al., 2013), and because their lesion can lead to apraxic agraphia (Anderson, Damasio, & Damasio, 1990; De Smet, Engelborghs, Paquier, De Deyn, & Mariën, 2011; Hodges, 1991; Magrassi, Bongetta, Bianchini, Berardesca, & Arienta, 2010; Sakurai et al., 2007). The left SFG, often associated to the so-called Exner’s area (Exner, 1881; Roux et al., 2009), seems to be crucial for the instantiation of motor commands for producing letters (Longcamp, Anton, Roth, & Velay, 2003; Longcamp et al., 2014; Rapp & Dufor, 2011; Roux et al., 2009; Sugihara, Kaminaga, & Sugishita, 2006). Some authors have given this region the label Graphemic Motor Frontal Area (GMFA) to emphasize its role of an interface between graphemic representations and motor programs specific to handwriting (Roux et al., 2009). The left SPL is involved in the representation of graphomotor trajectories (Menon & Desmond, 2001; Seitz et al., 1997). Meta-analyses showed that those regions form a network that is consistently activated in handwriting tasks (Planton, Jucla, Roux, & Démonet, 2013; Purcell, Turkeltaub, Eden, & Rapp, 2011).

While the dissociation of orthographic and motor processes and their neural substrates is an established fact, the nature of the relationship between the two is debated. According to a first general perspective in language production research, motor processes can be initiated only when linguistic processes are completed (Levelt, Roelofs, & Meyer, 1999; McClelland, 1979). In handwriting, an (often-implicit) assumption is that spelling must be completed before the information is sent to the motor level, which then operates independently. Orthographic and motor processes are thus conceived as discrete and independent. According to a more recent perspective, the processing flow between the orthographic and motor levels is continuous. Motor representations of letters are activated before spelling retrieval is fully completed. Variations in the activation of linguistic information impact the processing at the motor level. This idea is supported by a series of behavioral studies revealing that specific orthographic features may affect the way movement production is executed (Delattre, Bonin, & Barry, 2006; Kandel & Perret, 2015; Planton, Jucla, Démonet, & Soum-Favaro, 2017; Planton, Jucla, Roux, & Démonet, 2013). However, such evidence for interactive and continuous processing is not always found (Damian & Stadthagen-Gonzalez, 2009; Scaltritti, Pinet, Longcamp, & Alario, 2017) (Damian & Stadthagen-Gonzalez, 2009)and there is currently no consensus.

Here the aim of the present study was to contrast these two ways of approaching the relationship between orthographic and motor processes in handwriting with an fMRI experiment. We used a writing to dictation task with single words inspired by Roux et al. (2013). Words were either regular (**REG**) or irregular; with an orthographic irregularity at the beginning of the word (**IRB**) or in the final position (**IRF**). Orthographic regularity refers to sound-to-letter conversion consistency. For example, in French CHAPITRE (/ʃapitʁ/, chapter) is orthographically regular because unambiguously /ʃ/ = CH, /a/ = A, /p/ = P, /i/= I, /t/= T, /ʁ/ = R and silent E in final position appears by rule. Instead, CHARISME (/kaʁism/, charisma) is irregular because, according to sound-letter conversion rules /k/ should be written C and not CH. When a word has to be spelled out, the irregularity induces a mismatch between the outputs of a procedure (the "sublexical route") that maps phonemes into their associated graphemes, and a procedure (the "direct or lexical route") that relies on an orthographic long-term memory (Beauvois & Dérouesné, 1981; Ellis, 1988; Rapp, Epstein, & Tainturier, 2002; Shallice, 1981). This mismatch leads to competition between orthographic representations and to an increase in writing latencies (Bonin, Chalard, Méot, & Fayol, 2002; Bonin, Peereman, & Fayol, 2001; Houghton & Zorzi, 2003). Its resolution can be impaired in the case of brain lesions, leading to massive spelling errors in irregular words (Beauvois & Dérouesné, 1981; Rapp et al., 2002). We used a ROI approach to define the orthographic and motor components of the handwriting network individually based on an independent localizer and tested whether those components were sensitive to the presence and position of an irregularity. In order to target possible differences between the three types of words during writing, we recorded the kinematics of the writing movements with an MRI-compatible digitizing tablet during fMRI scanning. We constrained the individual statistical models of the BOLD signal to account for the duration of each trial and to discriminate the variations of the hemodynamic response related to the writing of the beginning vs the end of the words. We examined whether the kinematic and neural data supported one of the two accounts of the relationships between orthographic and motor processes in handwriting.

Operationally, the two accounts lead to different predictions:

If orthographic and motor processes operate in a discrete and independent fashion, we should observe an effect of orthographic regularity on reaction times. The effect of orthographic regularity should also be detected in orthographic regions at the beginning of the writing response, due to the spreading of the BOLD signal changes occurring during the latency, but not at the end of the writing response, where only the motor processes are assumed to be active. This effect should not differ as a function of the position of the irregularity because the competition between orthographic representations should only be a function of the presence/absence of the irregularity. Furthermore, the movement kinematics should be similar in the 3 conditions and the response of the motor regions should be independent of the orthographic features of the words.

If orthographic and motor processes operate in a continuous and interactive fashion, we should observe an effect of orthographic regularity on latencies and in the linguistic regions (FuG and IFG) at the beginning of the writing response. However, only the continuous account predicts that the BOLD signal measured at the end of writing will remain stronger for the words with an irregularity in final position, for which the orthographic conflict is still present, than for the words with an irregularity in initial position, for which the conflict is no longer present and for regular words. Furthermore, if orthographic and motor processes interact, we should observe that both writing kinematics and the response of the motor regions are affected by the presence of an orthographic irregularity.

Materials and Methods

Participants

Twenty-five native French speakers (ages 19 to 37, mean 24) participated in the experiment. They reported that they had never been followed by a therapist for linguistic or motor difficulties. They were all right-handed (ratios between 80 and 100, mean 90), had normal audition and normal or corrected-to-normal vision. Participants signed a written consent after the procedure was fully explained. The study received the approval of the Ethics Committee (N_ RCB 2010-A00155-34).

Procedure

The participants were instructed to write isolated words under dictation, as quickly and correctly as possible in a limited time. They wrote on an MRI-compatible digitizing tablet, while being scanned. As in Roux et al. (2013), the participants were instructed to write in upper-case letters and to lift the pen between letters. The goal of this instruction was to facilitate letter segmentation.

The fMRI recordings started with a session of localizer during which the participants alternated 5 writing blocks of 24.2s where they wrote the words in uppercase letters under dictation with visual feedback, and 5 blocks of rest of 26.6s where they had to hold the pen and rest their hand on the left edge of the tablet. In the writing blocks, the trials lasted 5s. Trials began with a 100ms beep followed by the auditory word presentation 200ms later. The participants were instructed to start to write as soon as they recognized the word and to move back to their initial resting position when they had completed the writing of the word. In each block of writing, the participants wrote the same four words presented sequentially in a random order (“renard” (*fox*), “brevet” (*patent*), “camion” (*truck*) and “cabane” (*hut*)). The four words shared several linguistic characteristics (grammatical class, lexical frequency, consistency value at the beginning and at the end of the word, number of letters, number of homographs, number of homophones) and are representative of the stimuli chosen for the experiment. The written traces were displayed via a mirror positioned in front of the participant's eyes (see ‘material’).

After the localizer, the participants performed four sessions of word writing without visual feedback. The absence of feedback was intended to avoid effects related to reading the produced graphic trace. The blocks were composed of 48 words (16 of each condition) constructed as an event-related design semi-randomized to counterbalance an eventual effect of word length and consistency. A fixation cross was displayed in the middle of the screen throughout the whole trial. Each trial began with a 100ms beep followed by the auditory stimulus 200ms later. The participants were instructed to start writing once they recognized the word, and to return to their initial position (left edge of the tablet) once they had completed the word. The digitizer started recording at stimulus onset, during 8400ms. After this period, 3 # replaced the fixation cross for 1.5s to signal the end of the trial. If the word was not completed yet, the participants had to stop and return to their initial position. The delay between the trials was randomly set to either 133ms or 333.3ms. We choose two different inter-trial intervals to decorrelate the beginning of the TRs from the course of the events in the trials. A variable temporal jitter between successive trials was automatically induced by the variable duration of writing execution (see below, statistical model and Fig.1 a).

Stimuli

We used a set of 96 French words that differed in phono-orthographic consistency. There were 32 regular words (**REG**; e.g., NATURE/natyʁ/, nature) that had a high phono-orthographic consistency (POC). The rest of the words was irregular because they had a low phono-orthographic consistency. There were 32 words that presented the orthographic irregularity at the beginning of the word (**IRB**; e.g., PHARMACIE /faʁmasi/, pharmacy; the orthographic irregularity is underlined) or at the end (**IRF**, e.g. MANUSCRIT, /manuskʁi/, manuscript) (Table S1). The words were matched across the 3 conditions on several linguistic variables. To quantify the degree of irregularity of the first and last phoneme of each word we took their phono-orthographic consistency (POC). POC is a quantitative index based on the measured frequencies of the phoneme-to-grapheme correspondences that compose a given word (Bonin, Collay, & Fayol, 2008; Soum, 1997). Regular words present very high phono-orthographic consistency because each phoneme is represented by specific letters unambiguously. The POC calculation was based on the work of Soum (1997) and Planton (2014) (Planton, 2014; Soum, 1997) and was made using the Lexique 3 database (New, Pallier, Brysbaert, & Ferrand, 2004; New, Pallier, Ferrand, & Matos, 2001) (New et al., 2004, 2001) composed of more than 142000 spelling forms (of 1 to 25 letters); words composed of only one phoneme have been excluded. POC values were computed by dividing the number of occurrences of the phoneme with a particular spelling by the total number of occurrences of the phoneme. We used the POC value by token; i.e., weighted by the lexical frequency of words. POC can reach a value between 0.01 and 1, with POC = 0.01 (very infrequent association) and POC = 1 (one possible association). This method of calculation was applied by phoneme and took into account the position (initial or final) of the correspondence within the word. It allowed us to select bi- and tri-syllabic words. This procedure allowed us to select words of variable length, ranging between 6 and 9 letters. This is important because the only available French lexical database providing consistency information is restricted to monosyllabic words (New et al., 2001; Peereman & Content, 1999).

The words were also matched across the 3 conditions on their number of phonemes, syllables, homographs and homophones, number of phonological neighbors, phonological uniqueness point, their frequency of occurrence and the frequency of occurrence of their lemma, and the mean frequency of bigrams and trigrams ((New et al., 2001; Peereman & Content, 1999). To make the motor complexity of the words comparable across the three conditions we also matched the lists as a function of the mean number of letter strokes on the entire word, the first two and the last two positions (Spinelli, Kandel, Guerassimovitch, & Ferrand, 2012).

The auditory stimuli were recorded by a French male speaker in an anechoic room. The item's acoustic durations were matched across conditions. The duration varied from 507ms to 946ms (mean = 720ms).

For most of the matches, the pairwise t-tests between conditions were non-significant (all p-values > 0.01). The only exceptions are small differences in the number of orthographic neighbors between IRB and IRF and of initial consistency between IRF and REG, that were impossible to match completely. The difference of initial consistency between IRF and REG remains very small compared to the difference between IRB and the other two conditions. The complete list of the words used in each of the 3 conditions, with their associated parameters and the t-values, is provided as supplementary materials (supplementary Table S2).

Material

We recorded the kinematic parameters of the writing movements using an fMRI compatible digitizer and a PVC pen developed in our lab (Longcamp et al., 2014). The device was composed of a touchscreen whose force range was set between 0.1 and 0.8N (Apex Material Technology Corp.) and an USB controller board, that allowed a 100Hz sampling rate (TSHARC- 10 from Hampshire Company). The touchscreen had a resolution of 1280 x 1024 pixels with a spatial accuracy of 0.3mm and the (x,y) coordinates were recorded as a function of time. To protect the device, the screen was inserted in a PVC case and the USB controller in a shielded box. The synchronization between stimulus presentation and kinematic recording was done by a software developed using the National Instruments LabVIEW environment. The digitizer was placed on the participants' abdomen. It was slightly elevated and inclined with a cushion. The participant could adjust its position to be able to write comfortably throughout the experiment. The auditory stimuli were presented via MRI-compatible pneumatic earphones; Flat Response Over 100Hz - 8 kHz Bandwidth (SENSIMETRICS S14). A mirror system in front of the participant's eyes, together with a projection screen at the back and a video projector, allowed the participants to follow online the trajectory of their writing movements during the localizer scans (Longcamp et al., 2014) and to view the visual stimuli (fixation cross and #) during the dictation task.

Kinematic data analysis

The variations in x and y positions of the pen tip were converted from pixels to millimeters (Fig.1 b). Then, they were analyzed using a custom-made software that allows to concatenate the segments into letters (one segment is defined as a contact between the pen and the digitizer occurring between two pen lifts). Following this step, the trials containing errors were discarded from the statistical analyses. There were several kinds of errors: misspelled words, incomplete words, trials with no pen-lift between letters, unreadable or unrelated response or with no response at all. In a few cases (0.6% of the trials), the digitizer did not record the data correctly.

After discarding the errors, there were in average 36 trials out of 48 per participant per session.

For the correct trials we analyzed writing latencies, total writing duration, and stroke duration, which is a normalized measure of letter duration (Fig.1 b).

- Latency: time between the onset of the auditory stimulus and the first contact of the pen with the tablet.
- Total writing duration: time elapsing between the first contact with the tablet and the last pen lift.
- Stroke duration: normalized measure of letter duration. This decreases the impact of the graphic complexity of the letters. It refers to the time taken to write a given letter divided by a theoretical standard number of strokes (Spinelli et al., 2012). The stroke number for one given letter corresponds to the average number of tangential velocity minima in the velocity profile when the letter is written in uppercase by a proficient writer. (i.e. "A" has 3 strokes, "R" has 5 strokes).

The effect of orthographic regularity on these variables was tested by participants with a one-way repeated measures ANOVA and by items with a one-way independent measures ANOVA.

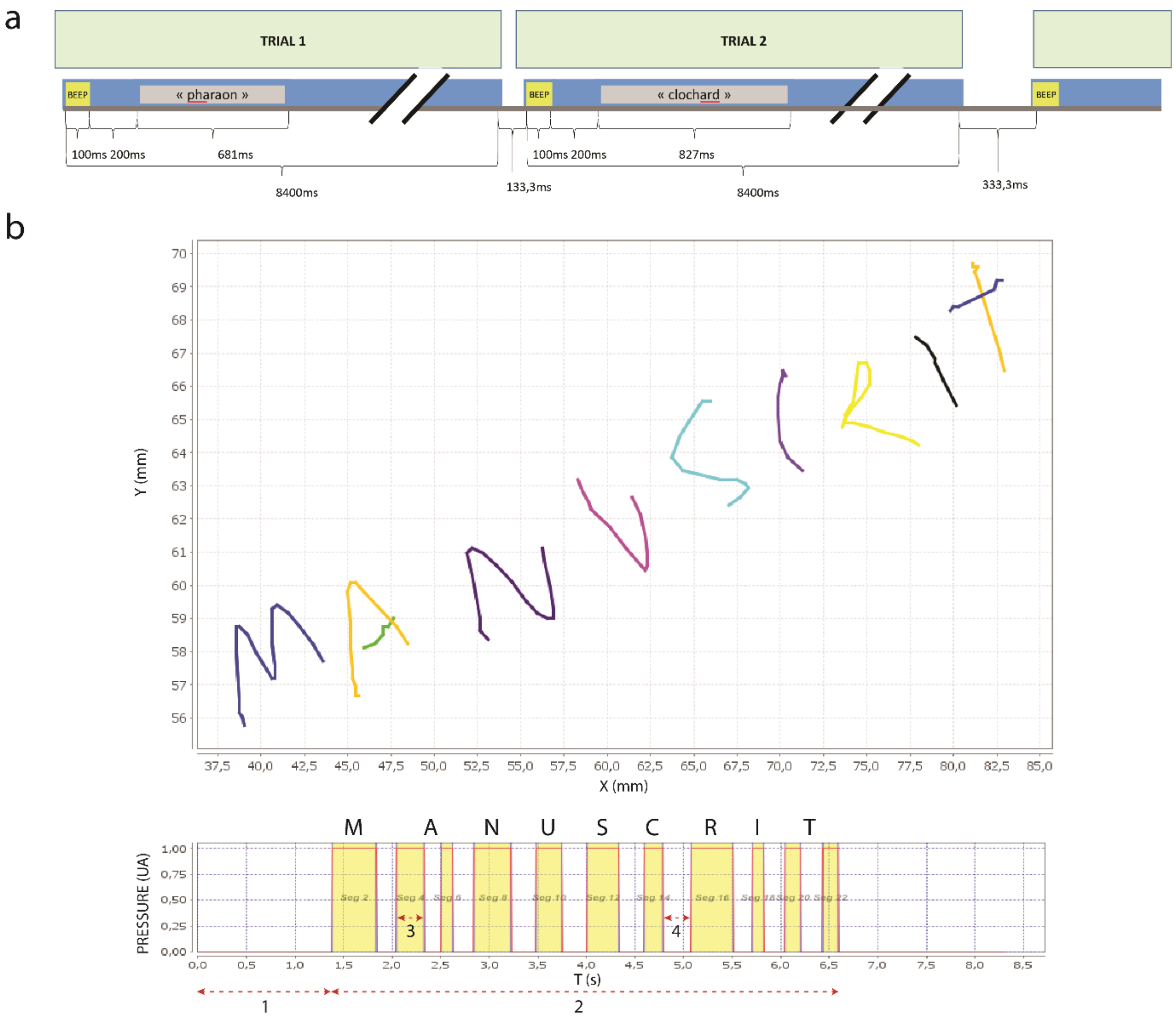

Figure 1. Experimental design and example of kinematic recording for one trial. (a) Example of the temporal structure of two consecutive trials. (b) Example of a trial recorded on the digitizing tablet for the word MANUSCRIT. Pressure on the tablet = 0 when the pen is in the air and 1 when it is in contact with the tablet. 1: latency, 2: total writing duration, 3 one segment duration, 4: duration of the interval between segments.

fMRI acquisition and preprocessing

Structural and functional MRI data was collected on a 3-T Brucker scanner (3-T MEDSPEC 30/80 AVANCE whole-body imager; Brucker, Ettlingen, Germany). For each participant, a high resolution structural T1-weighted image was acquired first. The functional images were acquired using a T2*-weighted FID-echo planar sequence. The whole brain was covered with 36 interleaved slices of 3mm thick spaced from 1mm in the AC-PC plane (TE= 30 ms, TR= 2400 ms, flip angle =82°, voxel resolution 3x3x4 mm). 110 volumes were acquired for the localizer, and 208 volumes were acquired in each of the four experimental sessions. To correct possible geometric distortions, we created a field map using a 3D gradient echo sequence with two different echo times [3.7 and 8.252 ms].

Spatial processing and data analysis were performed using the SPM12 software, according to the General Linear Model. We discarded 4 dummy scans at the beginning of each session, to allow the magnetization to stabilize. Slice acquisition time and head motion were corrected on the remaining scans. A co-registration of each participants' anatomical scan to the mean functional image was made and anatomical scans were segmented in 6 different types of tissue. The results of the segmentation allowed for the normalization of structural and functional images to the MNI template. Finally, the images were spatially smoothed with a 5 mm FWHM Gaussian Kernel.

fMRI analysis

Localizer

Writing and rest periods were modeled respectively as blocks of constant 24.2 s and 26.6 s duration convolved with the HRF. The 6 parameters of head movement were modeled as regressors of no interest. The difference between writing and rest was evaluated by means of a one sample t-test.

ROIs definition

The ROI approach aimed at analyzing the dynamic response of the handwriting network to the irregularity. To this end we used the MarsBar SPM toolbox (Brett, Anton, Valbregue, & Poline, 2002) to define individual regions of interest at the vicinity of the localizations highlighted in the two meta-analysis of writing for their particular involvement in orthographic or motor stages of processing (Planton et al., 2013; Purcell et al., 2011): the left fusiform gyrus (FuG), inferior frontal gyrus (IFG), superior parietal lobule (SPL)[1], superior frontal sulcus (SFG), and the right cerebellum (Ce)[2] (Fig.2). We also created a control ROI located in the primary motor cortex (M1). This control ROI is involved in hand movement execution but is not specific to handwriting. The position of the ROIs is displayed in Fig 2.

The procedure for defining the individual ROIs was the following:

- Definition of the search volumes: We first created six search volumes at the group level (Fig.2) by taking, in the group localizer contrast ‘writing – rest’, the coordinates of the local maximum nearest to the coordinates reported in the meta-analyses. We then defined 10 mm radius spheres centered on those local maxima coordinates. [Meta-analysis coordinates];[our coordinates]: Left Fusiform Gyrus [-46, -62, -12]; [-48, -63, -6], left superior parietal lobule [-32, -38, 56], [-33, -39, 55], left inferior frontal gyrus [-46, 16, 18], [-42, 3, 21], left superior frontal gyrus (SFG) [-22, -8, 54], [-18, -6, 60], right cerebellum [4, -66, -16], [6, -63, -15] and primary motor cortex [-34, -24, 60], [-30, -27, 54].
- Definition of the individual ROIs: For each participant and each search volume, we selected the cluster of activation included in the search volume, whose peak coordinates were the closest to the center of the search volume as a ROI. The size of the ROI was limited by combining the individual cluster with the search volume, so that only the part of the individual cluster that fell in the search volume was selected as the ROI.
- The threshold used to localize the clusters and transform them into ROIs was set at $p < .001$, uncorrected for multiple comparisons. However, for some participants, the activations were

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[1] It should be noted that the coordinates previously labeled as SPL in meta-analyses and in the literature correspond here to actual clusters extending to the postcentral gyrus (Segal & Petrides, 2012)

[2] The Ce ROI was called “posterior cerebellum” in the meta-analysis but was rather located on the anterior cerebellum.

very extended spatially and the clusters extended in neighboring areas. Therefore, if the targeted cluster had a size higher than 80 voxels, the significance level was set to $p < 0.05$ (FWE-corrected; overall, 65 ROIs out of 150). Furthermore, if the participants presented no significant cluster or a cluster of less than 10 voxels, a ROI of 6mm radius centered on the group coordinate was created (overall, 30 ROIs out of 150). This last procedure was applied for all the ROIs of participant 1, whose localizer data was artifacted.

The relevant information about the ROIs (individual coordinates and volumes, mean coordinates) is listed in Table S3.

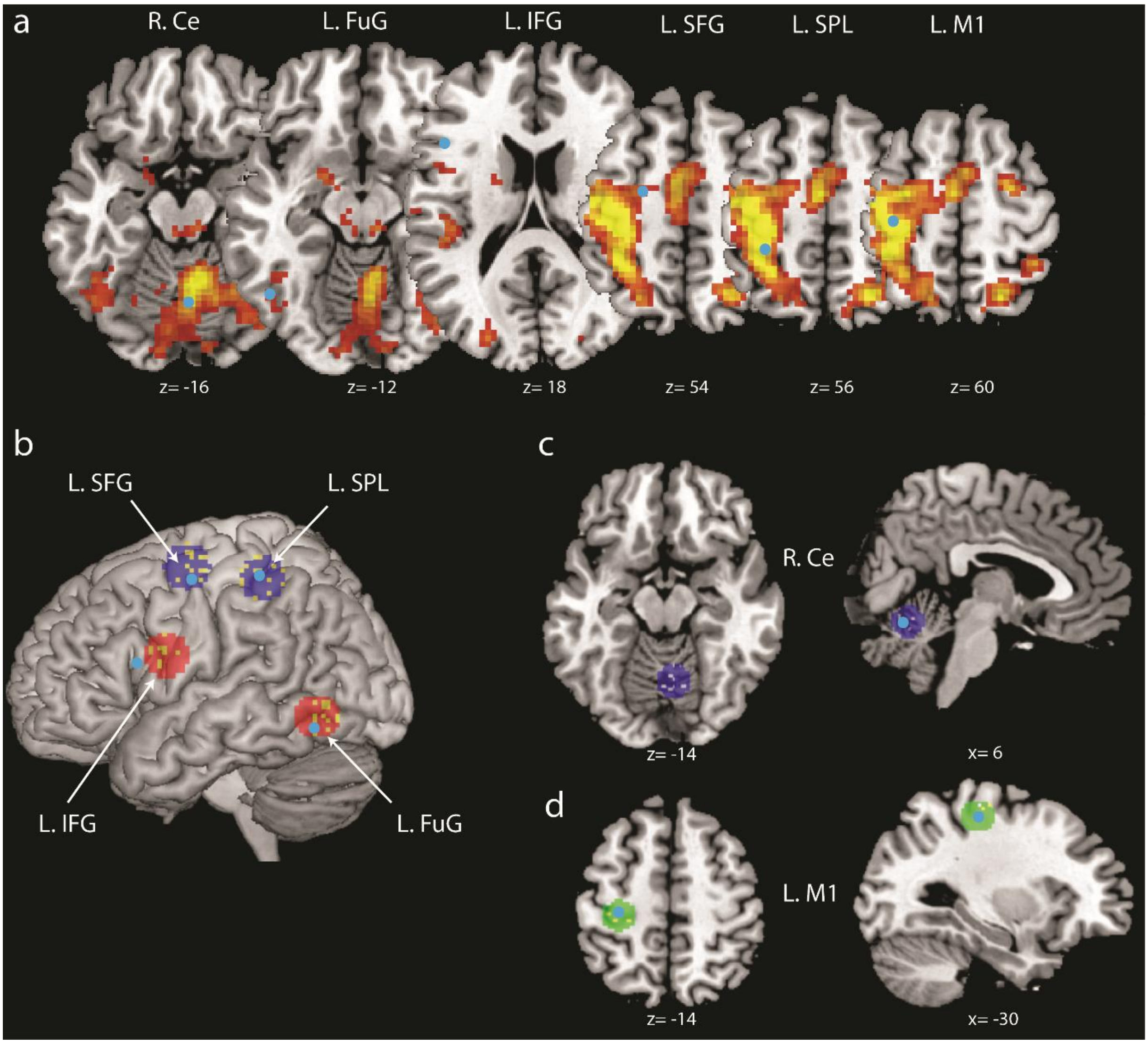


Figure 2. ROI definition: position of the search volumes and of the individual ROIs. a- Red/yellow scale: group activation in the localizer contrast 'writing-rest'. Cyan dots: coordinates of the regions of the handwriting network from the meta-analyses of Planton et al., 2013 and Purcell et al., 2011 that were used to define the search volumes (see methods, ROI definition); b-d: Position of the search volumes (blue, red and green spheres) and of the centers of the individual ROIs (yellow points). b- left SPL, SFG, FuG and IFG; c- right Ce; d- left M1). Blue spheres: search volumes for the motor ROIs; Red spheres: search volumes for the orthographic ROIs; Green sphere: search volume for the control ROI search group. Cyan dots: coordinates of the regions of the handwriting network from the meta-analyses of Planton et al., 2013 and Purcell et al., 2011.

fMRI statistical analysis

ROI analysis:

An important feature of the individual statistical analysis of the BOLD signal in the experimental task is that the regressors representing each writing trial were built using the actual individual kinematic parameters: writing duration, writing latency, and the position in time of the production of the first and last letters.

Both the independent and the interactive accounts predict differences between regular and irregular words in relation to the beginning of the writing response. Only the interactive account predicts that differences would occur in relation to the writing of the last letters.

The statistical model was designed to target the beginning vs. the end of each writing trial, because those phases included the moments where the participants were writing the first and last letters of the word. We identified for each trial the times when the first letter and the last two letters were written. For each type of word (IRB, IRF and REG), we therefore created separate regressors of zero duration to model the first letter (condition beginning (b)) and the last two letters (condition end (e)). The temporal resolution of fMRI is limited and we acknowledge that the regressors could capture more than the signal variations triggered by the processing of the first and last letters. However, it remains fully possible to contrast the beginning and the end of the trial for at least two reasons. First, the writing of each word lasted several seconds. Second, there was a large variability in the duration of the responses that induced a time-jitter between the writing of the first and last letters of the different words (mean time between the onset of the first and last letters = 3.72s; SD between participants = 0.83; mean SD within participant = 0.74; min-max = 1.61 - 6.38s). This leads to 6 regressors of interest (IRBb, IRBe, IRFb, IRFe, REGb and REGe) where writing was modeled as events of zero duration convolved with the HRF. This procedure allows to test whether the effects of the presence and position of the irregularity vary between the beginning and the end of writing execution. The rest of the writing trials were modeled as regressors of no interest: auditory stimulation (with onset = onset of the auditory stimuli and duration = 0s) and writing execution (with onset = onset of the auditory stimulus + latency value, and duration = writing duration of each trial), both undifferentiated for the 3 conditions. Errors and movement parameters were also modelled as regressors of no interest. The error regressors included all types of errors (mean ratio of errors: 0.19). The trials where the kinematic data were not recorded accurately by the digitizer (ratio: 0.006) were included in the pool of the correct trials, with onsets and duration estimated from the average of the participant.

To carry on ROI group statistics, we extracted the signal from the ROIs using the rfxplot SPM12 toolbox (extraction of the mean beta parameter values per condition and per participant). The values were entered in repeated measures ANOVA using JASP (jasp-stats.org) to test for the main effect of orthographic regularity (IRB, IRF and REG), and the interaction between irregularity and writing location (beginning or end of writing). Pairwise contrasts were tested with paired t-test and Bonferroni-corrected for multiple comparisons (6 ROIs). Both corrected and non-corrected t-tests are reported at the ROI level.

Whole-brain analysis:

In addition to the ROI analysis, we also carried out a whole-brain analysis, using an ANOVA model in SPM12 with F-contrasts to test for the main effect of orthographic regularity in relation to either the processing of the auditory stimulus, or to the execution of the response (Fig. S1), and with pairwise t-tests between conditions in the clusters where the F-contrast was significant. We therefore created two distinct first-level statistical models per participant (Fig. 3).

The first statistical model ("Effect of orthographic regularity in relation to the auditory stimulus") was designed to discriminate between conditions right after the onset of the stimulus. For each trial we identified the onset of the stimulus, and the onset of writing and its duration based on the digitizer recordings. We created a regressor of interest for each condition of irregularity time-locked to the onset of the stimulus (modeled as events of zero duration convolved with the HRF). Regressors of no interest included writing execution (modeled as events whose duration corresponded to the actual writing duration, undifferentiated for the 3 conditions), errors and the corresponding stimuli, and movement parameters (6 regressors).

The second statistical model ("Effect of orthographic regularity in relation to the processing of the writing response") was designed to differentiate the conditions in the course of writing execution. We created a regressor of interest for each condition of irregularity time-locked to the onset of the writing response (trials were modeled as events whose duration corresponded to the actual writing duration convolved with the HRF). Regressors of no interest included stimulus (modeled as events of zero duration convolved with the HRF, undifferentiated for the 3 conditions), errors and the corresponding stimuli, and movement parameters (6 regressors).

Figure 3 shows that when the auditory stimulus is modeled, the regressor correctly accounts for the variance in the bilateral auditory cortices while when motor execution is modeled, the regressor correctly accounts for the variance in left fronto-parietal regions including the primary motor cortex, and in the basal ganglia.

Significant activations were localized using a brain atlas (Duvernoy, 1999) combined to the wfu_pickatlas spm12 toolbox (Tzourio-Mazoyer et al., 2002). When a main effect of orthographic

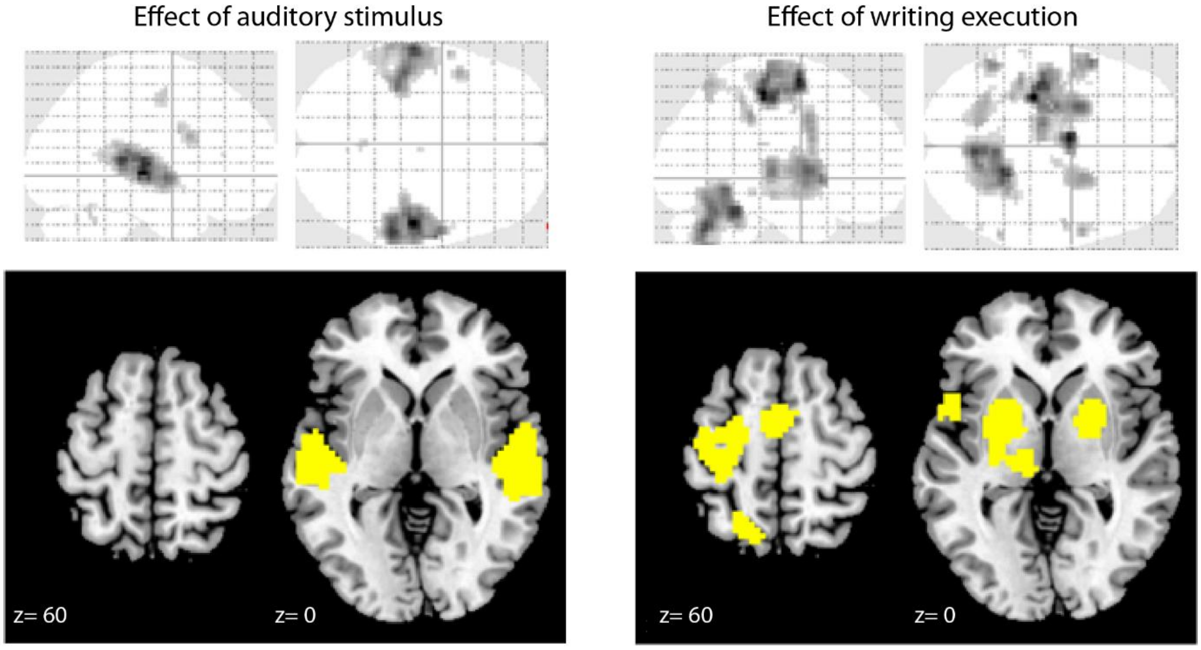


Figure 3. Displays of one-sample t-test contrasts of task vs rest for the two whole-brain statistical models. Left panel: Model where the regressors of interest are defined as events of zero duration time-locked to the onset of the auditory word. Right Panel: Model where the regressors of interest are defined as blocks whose duration

corresponds to the writing duration, time-locked to the onset of the writing movements. The contrasts are displayed at a threshold of p<.05, FWE-corrected for multiple comparisons.

Results

Kinematic data

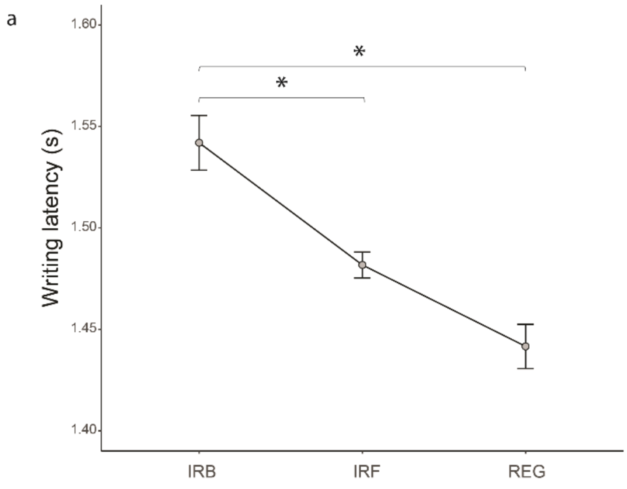
Only significant main effects both by participants (F1) and items (F2) will be presented.

Latency

Orthographic regularity significantly impacted latency (F1(2, 48)= 22,4, p<0.001; F2(2, 93) = 7.4, p<0.001). IRB words yielded higher latencies (mean RT= 1.54 s) than IRF words (mean RT= 1.48 s; t1(24)= 4.1, p<0.001; t2(31)= 2.4, p< 0.05) and, in turn, than REG words (mean RT= 1.44 s, t1(24)=-5.2, p<0.001; t2(31)= -4.1, p<0.001). There were no significant differences between IRF and REG (t1(2,48)= 4.2, p<0.001; t2(31)=1.4, p=0.2) (Fig.4 a).

Stroke Duration

Orthographic regularity significantly impacted stroke duration for the first letter (F1(2, 48)= 77.6, p<0.001; F2(2, 93)= 3.8, p<0.05) and last letter (F1(2, 48)= 58.63, p<0.001; F2(2, 93)= 8.9, p<0.001). The writing duration of the first letter was longer for irregular than regular words (F1(2, 48)= 77.6, p<0.001; F2(2, 93)= 3.8, p<0.05). These differences were particularly important between the IRB (mean= 0.22 s) and REG conditions (mean= 0.17 s, t1(24)= -10, p<0.001 and t2(31)= -2.4, p<0.05). For the last letter, stroke duration was higher for IRF (mean= 0.157s) than IRB (mean= 0.128s, t1(24)= 7.8, p<0.001; t2(31)= 7.4, p<0.01) and for REG (mean= 0.127s, t1(24)= 8.2, p<0.001; t2(31)= 8.2, p<0.01) (Fig. 4 b).



Total writing duration

No significant differences in terms of overall writing duration between IRB, IRF, and REG were found (F < 1). However, it is noteworthy that numerically, irregular words (mean duration IRB= 4.48 s; mean duration IRF= 4.55 s) yielded longer writing durations than regular words (mean duration REG= 4.46 s). The differences reached significance in the by-participants analysis (F1(2, 48)= 3.7, p<0.05; F2(2, 93)= 0.3, p= 0.72).

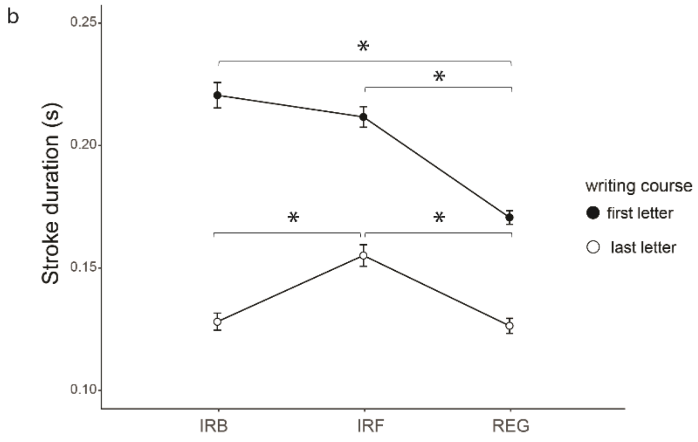


Figure 4. Kinematic Results. (a) Writing latency for the three conditions (from the onset of the auditory stimulus until the onset of writing). (b) Mean stroke duration of first letter (black dots) and last letter (white dots) in each condition.

Errors

The participants produced 14.5% of spelling errors and there were recording errors in 4.3% of the trials. There were significantly more errors for irregular than for regular words (mean error IRD= 0.05; mean error IRF= 0.06; mean error REG= 0.03; main effect of orthographic regularity, F(2, 48)= 19.2, $p<0.001$; IRF vs REG t(24)= 6.6, $p<0.001$; IRB vs REG t(24)= 3.9, $p<0.001$; IRF vs IRB t(24)= 2.1, $p< 0.05$).

fMRI data

ROIs Analysis

The values of all the pairwise contrasts between conditions are available in Table 2.

In this statistical model, the effects tested were the main effect of orthographic regularity that indicates that the level of activation differs between the three types of words in the ROIs, the interaction between writing course and regularity that indicates that the effect of orthographic regularity changes between the writing of the beginning and the end of the word, and the main effect of writing course, which indicates that the level of activation of the ROIs changes during writing. Those effects are reported in Table 2.

The left FuG, IFG, Ce and SPL displayed a main effect of orthographic regularity, with a greater activation for irregular than regular words. The left FuG and IFG displayed a significant interaction between irregularity and writing course (Fig.5, Table 1). The activation profile of those 2 regions was similar, with greater activation for IRB and IRF than REG words during the beginning of writing, and greater activation for IRF than for IRB and REG during the end of writing. The difference between IRB and IRF therefore emerged only at the end of the writing course. This effect is in agreement with the effects observed on writing kinematics, for letters durations. The M1 control ROI, the SFG, SPL and the Ce, displayed no such interaction.

The left FuG, IFG, SFG and Ce, but not the SPL displayed a main effect of writing course, with activation decreasing strongly between the beginning and the end of writing.

ROI	irregularity	writing course	interaction
Left fusiform gyrus	F(2,48)= 7.4, p<0,01	F(1,24)= 4.8, p<0,05	F(2,48)= 4.5, p<0,05
Left superior parietal lobule	F(2,48)= 5.2, p<0,01	N.S	N.S
Left inferior frontal gyrus	F(2,48)= 12.9, p<0,001	F(1,24)= 31.2, p<0,001	F(2,48)= 4, p<0,05
Left superior frontal gyrus	F(2,48)= 3.8, p<0,05	F(1,24)= 5.1, p<0,05	N.S
Right cerebellum	F(2,48)= 5.4, p<0,01	F(1,24)= 4.3, p<0,05	N.S
Left primary motor cortex	N.S	N.S	N.S

Table 1. Results of ROIs analysis, for the main effect of the presence and position of an irregularity (IRB, IRF, REG), the main effect of the writing course (beginning, end) and the interaction between the two factors.

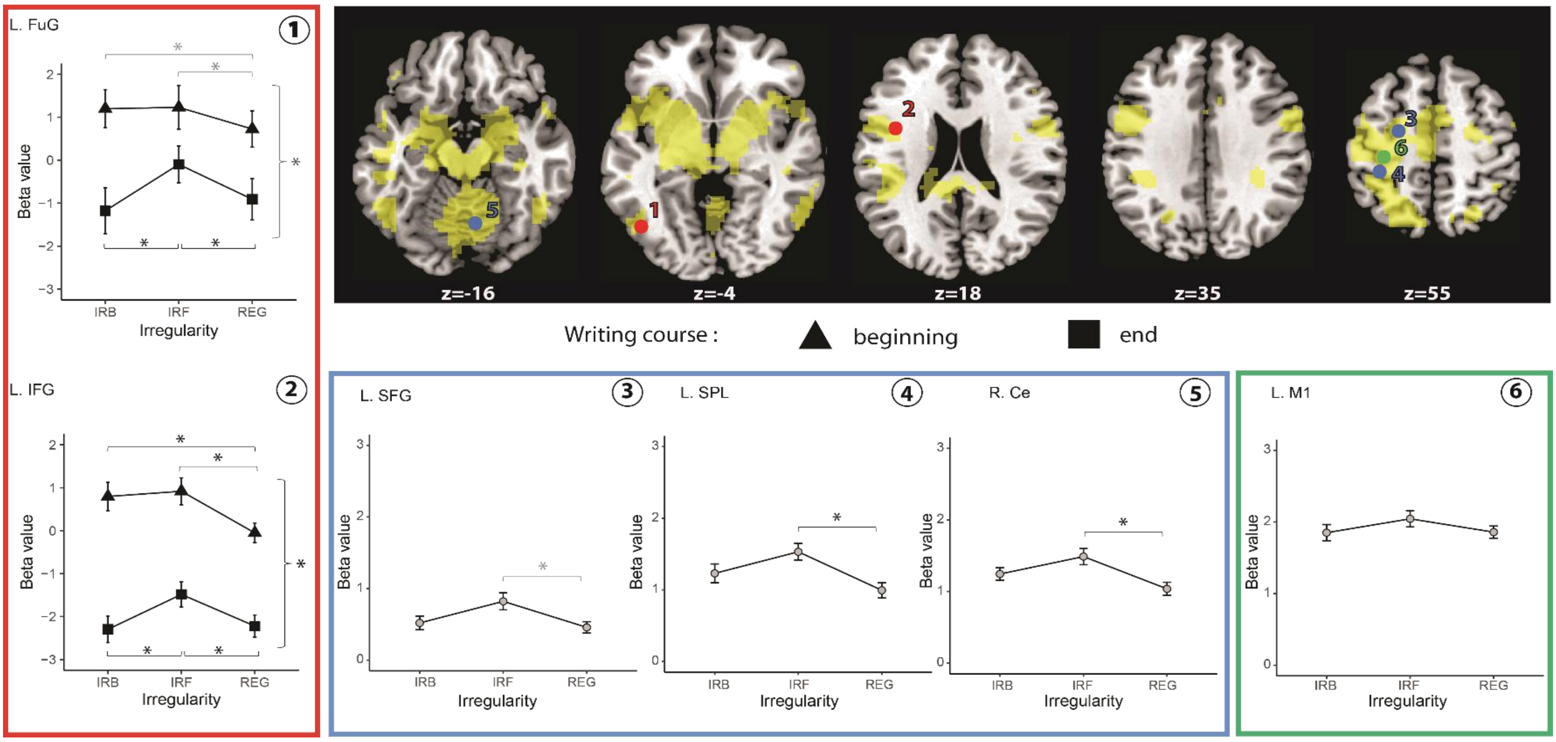


Figure 5. Results of ROIs analysis. Top-row: network of regions activated in response to writing execution (yellow), and mean position of the ROIs (Red dots: orthographic ROIs: left FuG and IFG; Blue dot: motor ROIs: left SFG, left SPL and right Ce; Green dot: control ROI: left M1). Red frame: ROIs activations (mean beta values) corresponding to the writing of the first letters (▲) and writing of the last two letters (■), for each type of word (IRB, IRF, REG) in the 2 orthographic ROIs. Blue and green frames: ROIs activations (mean beta values) corresponding to the writing of the three types of words (IRB, IRF and REG) in the 3 motor ROIs (blue) and the control ROI (green). The error bars represent the within-subject SEM (Morey, 2008). Black asterisks: pairwise contrasts (t-tests) significant with Bonferroni-correction for multiple comparisons; Grey asterisks: pairwise contrasts (t-tests) significant without correction for multiple comparisons.

ROIs	**Contrast Pairwise t-test**					
Differencial effect of regularity during the writing course (beginnning (b) vs. end (e))						
Left fusiform gyrus	**IRBb vs. IRFb**	N.S	**IRBe vs. IRFe**	**t(24)=-3.3, p=0.003**	**IRBb vs. IRBe**	t(24)=2.7 p=0.011
	IRBb vs. IRFb	t(24)=2.3, p=0.032	**IRBe vs. REGe**	N.S	**IRFb vs. IRFe**	N.S
	IRFb vs. REGb	t(24)=2.8, p<0.011	**IRFe vs. REGe**	**t(24)=3.1, p=0.005**	**REGb vs. REGe**	N.S
Left inferior frontal gyrus	**IRBb vs. IRFb**	N.S	**IRBe vs. IRFe**	**t(24)=-3, p=0.005**	**IRBb vs. IRBe**	**t(24)=5.6, p<0.001**
	IRBb vs. REGb	**t(24)=3.5, p=0.002**	**IRBe vs. REGe**	N.S	**IRFb vs. IRFe**	**t(24)=4.6, p<0.001**
	IRFb vs. REGb	**t(24)=4.3, p<0.001**	**IRFe vs. REGe**	**t(24)=4, p<0.001**	**REGb vs. REGe**	**t(24)=5.3, p<0.001**

Table 2. Pairwise t-tests between the 3 types of words (IRB, IRF, REG) at the beginning and at the end of writing, in the ROIs where the interaction was significant. The t-values in bold correspond to values significant after Bonferroni-correction for multiple comparisons (6 ROIs).

Whole Brain - Main effect of orthographic regularity

The results of the analysis exploring the effect of orthographic regularity in relation to the processing of the auditory stimulus are displayed in figure S1.

In the analysis exploring the effect of orthographic regularity in relation to the writing response, we observed a network encompassing regions of the temporal, parietal and frontal cortices, mostly lateralized to the left hemisphere. Those regions were sensitive to the presence of an irregularity during writing, with a stronger response to irregular than to regular words (Fig.6, Table 3). The significant activations were located in the left fusiform gyrus, the left superior parietal lobule extending to the inferior parietal cortex and the precuneus, in the left precentral gyrus, the supplementary motor area (SMA), the left insula, and in the right insula extending to the IFG pars orbitalis.

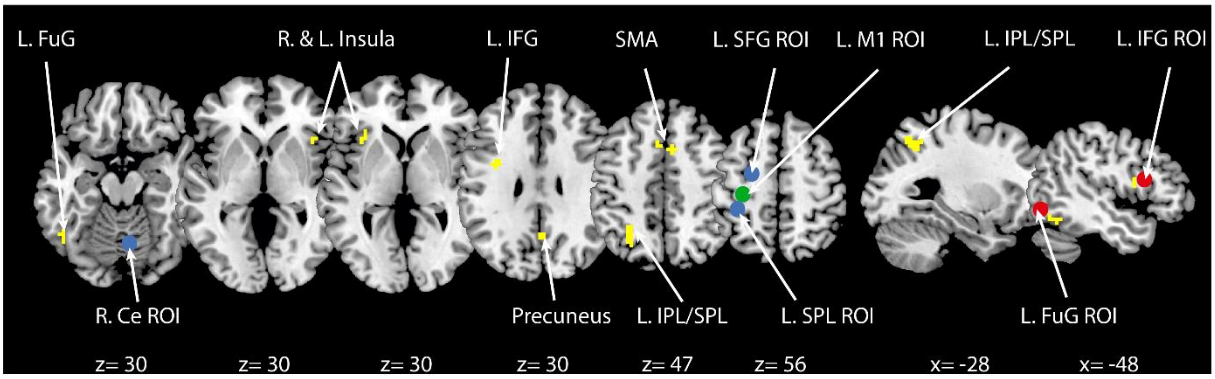


Figure 6. Results of the F contrast for the main effect of orthographic regularity in writing at the whole brain level displayed on axial and sagittal slices. Yellow: network activated in response to writing relative to rest; Red dots: mean positions of orthographic ROIs (left FuG and IFG); Blue dots: mean position of motor ROIs (left SFG, SPL and right Ce); Green dot: mean position of the control ROI (left M1).

Location		Cluster	Z score	MNI Coordinates			Contrast
				x	y	z	
FRONTAL							
Left	Inferior opercularis	245	5.29	-42	6	24	IRF > REG, IRB > REG
	Precentral gyrus		5.03	-36	0	36	IRF > REG, IRB > REG
	Inferior triangularis		4.45	-45	21	30	IRF > REG, IRB > REG
Left	SMA	209	5.20	-3	15	48	IRF > REG, IRB > REG
	SFG		3.45	0	30	36	IRB > REG
Left	Insula	164	4.55	-42	15	0	IRF > REG, IRB > REG
	Inferior triangularis		4.15	-39	27	15	IRF > REG
Rigth	Insula	86	4.93	36	24	3	IRF > REG
	Inferior orbitalis		3.91	33	24	-9	IRF > REG, IRB > REG
PARIETAL							
Left	Superior lobule	182	5.84	-27	-63	48	IRF > REG, IRB > REG
Left/Right	Precuneus	257	4.92	3	-60	30	REG > IRF, REG > IRB
	Precuneus		4.60	0	-60	42	REG > IRF, REG > IRB
TEMPORAL							
Left	Fusiform Gyrus	70	5.35	-48	-57	-18	IRF > REG

Table 3. Results of the effect of orthographic regularity at the whole brain level, MNI space, FWE-corrected for multiple comparisons at the voxel and cluster level. The “Contrast” column shows significant pairwise t-tests between IRB, IRF and REG for voxels located at the local maxima ($p<0.001$ uncorrected for multiple comparisons).

Discussion

The data are in agreement with the predictions of the continuous and interactive account of orthographic and motor processing in word writing. They indicate that orthographic processes are still active when writing movements are executed, and they interact with motor processes.

Our behavioral results replicate those of Roux et al., 2013. These authors found that it took longer to write the letters that produced an orthographic irregularity. Movement time for producing CH in CHARISME (the irregularity is underlined) was longer than in CHAPITRE. The position of the irregularity within the word also modulated writing kinematics. For the words presenting the irregularity at the end (e.g., CLIMAT, /klima/climate) all the letters before the irregularity were longer than in regular words. The presence of an irregularity modulated the initiation of the writing movement as well as its fine motor execution, even in the specific environment of the fMRI scanner and absence of visual feedback. At the brain level, statistical models accounting for the variations of writing kinematics indicate that both orthographic and motor regions were affected by the presence of the irregularity and its position. None of the models yielded significant effects in the control ROI, whose activation is assumed to reflect direct input to the effector muscles for the execution of writing movements. Those results indicate that orthographic and motor processes occur in a continuous fashion during writing. They also suggest that the stability of the activation of a given orthographic representation in the linguistic system influences the selection and implementation of the constituent letters in the motor system.

Evidence for continuous flow of information between the orthographic and motor levels

In both the left IFG and FuG, the response was stronger for irregular than regular words at the beginning of writing. At the end of writing, the response remained stronger for IRF words only. The activation for IRB words dropped at the level of activation of the REG words. These results constitute a strong indication that orthographic processes remain active after the onset of writing execution, until the irregularity is actually computed. This result, combined with the observed pattern of differences in RTs, can be interpreted in the light of an interaction between the elements of the spelling system. Several studies showed that the presence of inconsistent mappings induces a conflict between the lexical and sublexical routes leading to competition between alternative orthographic representations (Bonin et al., 2002; Houghton & Zorzi, 2003), which can explain the increased activation of the orthographic regions at the beginning of writing. This in turn could lead to less robust activation of the letters corresponding to the inconsistent mappings (Buchwald & Falconer, 2014; Jones, Folk, & Rapp, 2009) due to top-down influences of the lexical system on the orthographic short-term memory where the sequence of abstract letter representations resulting from the output of the two routes is held (Sage & Ellis, 2004). In the present results, this view is also supported by the strong effect of regularity observed on the parietal cortex, at the junction between the superior and inferior parietal lobules in the whole-brain analysis. This region is thought to hold an important role in the orthographic working memory (Purcell et al., 2011; Rapp & Dufor, 2011; Rapp et al., 2016). In the literature, there is also evidence that activation from the letters held in orthographic memory can feed back to the lexical level, because the flow of information is bidirectional (McCloskey, Macaruso and Rapp, 2006). The postulated function of this feedback is the strengthening and stabilization of the target word in the lexical system (McCloskey, Macaruso and Rapp, 2006). This feedback mechanism, which may be increased when some letters are not stable in orthographic working memory, may therefore explain why the orthographic regions remain more strongly activated at the end of writing when the irregularity is located at the end of the word than in the other two conditions. It implies that the orthographic representations remain activated while the writing movements are being executed, at least when the irregularity is located at the end of the word. Overall, the results support the idea of a continuous flow of information between the orthographic and motor levels. This had in fact already been proposed by Van Galen's handwriting model (van Galen, 1991), who assumed that cognitive and motor levels of processing operate concurrently in handwriting.

In addition, our results extend the scope of the functional properties of the left IFG and FuG in spelling, (Bitan et al., 2005; Planton et al., 2013; Rapp & Lipka, 2011; Rapp et al., 2016). In reading, the left FuG is thought to represent orthographic information on a visual form (Vinckier et al., 2007), but this view remains controversial (Madec et al., 2016; Price & Delvin, 2003; Rapp & Lipka, 2011). In fact, several studies showed that the left FuG is involved in accessing or storing orthographic information during both reading and spelling (Purcell et al., 2011; Rapp & Lipka, 2011; Tsapkini & Rapp, 2010). Here, it was activated in the absence of visual stimuli, and during handwriting. This confirms that the FuG plays another, non-visual role in word representation during spelling (Rapp et al., 2016).

A novel and important finding of the present study is the sensitivity of the FuG and left IFG to the presence of an orthographic irregularity and its position during actual spelling production. Indeed, previous studies have shown that those regions are more active when reading irregular than regular words (Fiez, Balota, Raichle, & Petersen, 1999; Graves, Desai, Humphries, Seidenberg, & Binder, 2010; Peng et al., 2004). But to our knowledge, only two studies have demonstrated an effect of orthographic regularity during spelling, in the left IFG (Bolger, Hornickel, Cone, Burman, & Booth, 2008; Norton, Beach, & Gabrieli, 2015) and left FuG (Bolger et al., 2008). There is also some evidence of effects of irregularity in spelling tasks in brain-damaged patients (Rapcsak & Beeson, 2004). However, the spelling tasks used in those studies did not involve real word writing, but only spelling judgments based on either a visual (Bolger et al., 2008) or an auditory inputs (Norton et al., 2015). Our data are the first to report an effect of orthographic regularity in the course of a handwriting production task and in the absence of visual feedback. Consistent with previous evidence in the reading domain (Fiez et al., 1999; Graves et al., 2010) the presence of an irregularity lead to increases of the BOLD signal. It has been shown that competition between representations in the linguistic system (Zhuang, Tyler, Randall, Stamatakis, & Marslen-Wilson, 2014) and increased duration of certain stages of processing (Coull, Charras, Donadieu, Droit-Volet, & Vidal, 2015) lead to increases of the BOLD signal in the regions where the relevant information is processed. In the left FuG, the increase is probably related to the competition between representations and/or lengthened processing in orthographic long-term memory (Purcell, Jiang, & Eden, 2017; Purcell et al., 2011; Rapp & Dufor, 2011; Rapp et al., 2016). The left IFG showed the most reliable pattern of differences between regular and irregular words in the 3 models tested. This region possibly computes an information related to the presence of low-probability phoneme-to-grapheme correspondences (Henry et al., 2007). This hypothesis is supported by the fact that in reading, the response of the left IFG was found to be strongly modulated by spelling-to-sound consistency (Fiez et al., 1999; Graves et al., 2010). In reading, the influence of spelling-to-sound consistency on the activity of the left IFG has been interpreted either as a role of this region in the conversion between orthographic and phonological information (Fiez et al., 1999), or as a consequence of an increase of the load of semantic information (Binder, Desai, Graves, & Conant, 2009; Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997). In an interesting alternative account in the spelling field, Purcell et al. (2011) suggested that the IFG could generate a signal allowing the coordination of more posterior temporal and/or parietal regions for the selection of competing linguistic information (Bitan et al., 2005). This function would be critical when retrieving the spelling of irregular words because of the conflicting outputs of the lexical and phonological routes (Norton et al., 2015; Rapp et al., 2002).

The overall activation decrease of the two orthographic regions during writing, mostly in the IFG, is noteworthy. This effect is consistent with the observed mean stroke duration, which also strongly decreases between the first and last letters. The fact that this decrease is found even for regular words suggests that this is not explained by the processing of the irregularity but rather by the processing of spelling in general. This pattern argues for a sensitivity of orthographic regions to the load of orthographic information processed and held in memory during writing, despite the fact that they are not known as typically involved in orthographic short-term memory (Cloutman et al., 2009; Rapp et al., 2016).

Evidence for interaction between the orthographic and motor levels

The confirmation of irregularity effects on writing kinematics previously evidenced by Roux et al. (2013) is a strong argument in favor of interactions between orthographic and motor levels of processing in spelling. However, the exact mechanism by which those interactions occur can only be speculated, as the articulation between the two it is never explicitly modelled in current studies of spelling (Houghton, 2018). In a fully interactive system, it could be assumed that degraded activation of the constituent letters of a given orthographic representation in orthographic short-term memory due to the presence of an irregular mapping leads to less efficient selection and activation of the motor programs (Delattre, Bonin, & Barry, 2006; Rapp & Caramazza, 1997). If the motor programs are not optimally activated, it is possible that their actual implementation in the effector muscles is slowed down. Those effects are probably moderate given the independence of orthographic and motor impairments in dysgraphic subjects (Roeltgen 2003), but they could impact fine-grained stroke execution.

Despite this interpretation, some of the behavioral differences between the two conditions of irregularity remain to be clarified: if the irregularity is processed in a continuous and interactive fashion, it is straightforward to explain that both the reaction time and the duration of the first letter, but not the duration of the last letters, are increased for the IRB condition. Indeed, competition among lexical representations should slow down the emergence of the correct orthographic representation and affect the stability of the letters corresponding to the irregular mappings in orthographic short-term memory at the beginning of the sequence (Buchwald & Falconer, 2014; Jones et al., 2009). This would lead to slower activation of the motor representations and slower execution. In contrast, for the IRF condition, the RTs did not significantly differ from the RTs in the REG condition, but both the first and the last letters had increased duration compared to the REG condition. This indicates that the processes affected by the presence of the irregular spelling occur later in this case than in the IRB condition but last longer, until the irregular mappings are actually produced (Roux et al., 2013). If this interpretation holds, it implies that the timing of the interactions between the subcomponents of the spelling system, and between the spelling and motor systems, depends on the position of the irregularity in the words (Bonin, et al., 2001). This requires further investigation.

The pattern of graded effects of irregularity in the motor regions of the handwriting network is also consistent with interactive processing. Statistically, only the difference between REG and IRF words was significant in the motor regions. This indicates that maximal interactions occur when the irregularity is located at the end of the word.

The right Ce and the left SPL displayed a stronger response to irregular than regular words. The implication of these two regions in the programming and control of graphic movements is well acknowledged. The left superior parietal lobule holds an important role in the sensorimotor processes that generate correct motor sequences and trajectories in handwriting (Brownsett & Wise, 2010; Harrington, Farias, Davis, & Buonocore, 2007; Kadmon Harpaz, Flash, & Dinstein, 2014; Segal & Petrides, 2012). The cerebellum is the substrate of internal forward models allowing predictive coding of the trajectories (Wolpert, Miall, & Kawato, 1998). The sensitivity to irregularity indicates that the increase in orthographic processing, which stems from the presence of the low-probability phoneme-to-grapheme correspondence, leads to higher demands on these regions especially when the irregularity is located at the end of the word. The left SFG, corresponding to the so-called Exner's area, presented a marginal effect of irregularity (uncorrected for multiple comparisons). This region, also labeled Graphemic Motor Frontal Area by some authors (Roux et al., 2009) has been conceived as the interface between orthographic representations and motor programs. It would translate abstract letter representations into manual gestures (Planton et al., 2013; Roux et al., 2009). In principle, within the motor network, it should be the locus where the interaction and therefore the differences between the 3 conditions is maximal. It is noteworthy that these effects cannot be explained in terms of low-level global kinematic differences between the three conditions. The total writing duration differed only slightly between the conditions, so the amount of motor activity was equivalent. In addition, although the temporal differences between the conditions at the letter level were clearly reliable, they were too small to impact the estimation of the BOLD signal. Finally, the control ROI in M1, whose activity directly reflects the execution of writing movements (and therefore the massive kinematic variations), was not affected by the experimental manipulations. It could also be argued that what we assume as motor regions could actually be involved exclusively in computing linguistic information. However, this interpretation is unlikely given previous studies showing that these regions are almost silent in spelling tasks that do not require the implementation of manual movements (Planton, Longcamp, Péran, Démonet, & Jucla, 2017; Purcell et al., 2011) whereas they are strongly activated in handwriting and drawing tasks (Planton et al., 2017).

Whole Brain effects

Orthographic regularity affected the whole-brain response mostly during writing execution and mostly in regions of the left hemisphere. Several of the regions activated at the whole-brain scale (ventral Premotor region, insula, SMA) play an important role in language processing, although they are not specific to spelling (Price, 2012). The pattern of response of these regions indicates a graded effect of orthographic regularity. Again, this is evidence against the account of a strict separation between orthographic and motor processing in handwriting, because the orthographic regularity effects occur during writing execution.

The activation of the parietal cortex, at the junction between the superior and inferior parietal lobules, is fully consistent with data pointing towards its important role in spelling processes, most likely in relation to orthographic working memory (Purcell et al., 2011; Rapp & Dufor, 2011; Rapp et al., 2016). This is consistent with data showing that the processing of orthographically irregular words puts a higher demand on orthographic working memory processes (Buchwald & Falconer, 2014; Jones et al., 2009; Sage & Ellis, 2004). The SMA, anterior insula and left ventral premotor cortex have often been reported in neuroimaging (Beeson, Rising, & Volk, 2003; Longcamp et al., 2014; Planton et al., 2013; Purcell et al., 2011) and neuropsychological studies of writing (Kurosaki, Hashimoto, Tatsumi, & Hadano, 2016; Roeltgen & Heilman, 1983; Roeltgen, 2003; Roeltgen & Heilman, 1984) but their contribution was considered non-specific. These regions were well identified in tasks requiring covert or overt articulation (Price, 2012) and they belong to the core of the dorsal route for speech perception and production (Hickok & Poeppel, 2007; Meister, Wilson, Deblieck, Wu, & Iacoboni, 2007). Their involvement in the present study could therefore relate to the increasing demands on phonological processing when irregular words have to be spelled out.

A final perspective for the interpretation of the present results is that of a higher general cognitive demand for irregular words (Duncan & Owen, 2000). In our study, processing irregular words can be assimilated to having to deal with a cognitive conflict, as the output of the two routes converging on orthographic working memory do not match. Accordingly, we found graded error rates between the three conditions, with more errors for IRF, followed by IRB and REG. Conflict detection in turn leads to increased task monitoring, as shown in other domains (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Nozari, Dell, & Schwartz, 2011). Fedorenko et al. 2013 (Fedorenko, Duncan, & Kanwisher, 2013) demonstrated that a so-called multiple-demand network composed of a wide range of parietal and frontal regions is strongly affected by the difficulty of the cognitive task, irrespective of the task domain. We overlaid the main effect of orthographic regularity present during writing execution and the ROIs with the MD network defined by Fedorenko and collaborators on figure 7. Several of the regions affected by the presence of the irregularity either at the ROI or at the whole-brain level (left FuG, IPL, IFG pars orbitalis) were not defined as part of MD system, but belong to the core of the language system in the brain (Fedorenko, Behr, & Kanwisher, 2011). In addition, the motor-related ROIs were defined based on two meta-analyses that demonstrated their functional specificity for writing movements (Planton et al., 2013; Purcell, Turkeltaub, Eden, & Rapp, 2011).

Nevertheless, several brain regions affected by the presence of an irregularity do belong to the MD network. It is likely that the increased monitoring required for processing irregular words impacts both the behavioral indexes as well as the brain activation, even in the absence of an interaction between orthographic and motor processes. For instance, this could impact RTs by slowing down the retrieval of the correct spelling, of the motor programs, and require increased control of the movements corresponding to the irregular phoneme-grapheme mappings (thus explaining increased stroke durations). It is also possible that some of the activations we reported (for instance in the SMA, which is central in the MD network) can be interpreted this way. The effects linked to interactive orthographic and motor processing in the spelling system and the ones resulting from increased task monitoring must be disentangled in future research.

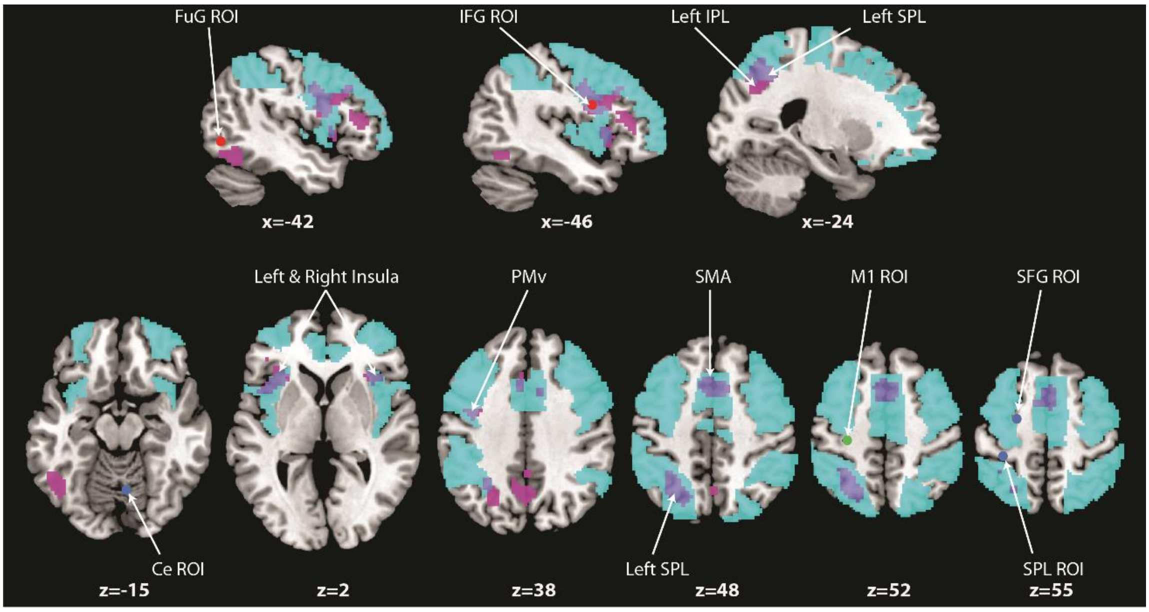


Figure 7. Overlap between the main effect of irregularity at the whole brain level ($p < 0.001$, uncorrected for multiple comparisons), and the multiple demand network (Fedorenko et al, 2013). Red dots: mean position of orthographic ROIs; blue dots: mean position of the motor ROIs; Green dots: mean position of the control ROI. Pink: main effect of irregularity; cyan: multiple demand network (courtesy of Fedorenko); purple: overlap between the main effect of irregularity and the multiple demand network.

Writing skills have remained relatively unchanged in human societies for thousands of years. With the advent of new information technologies, they undergo a massive and extremely fast mutation. The present results help to characterize the cognitive and neural bases of writing. We demonstrated that the left IFG and FuG, two regions belonging to the core of the written language system in the brain, are sensitive to the presence and position of an orthographic irregularity in the word during writing execution. The response of the motor-related regions of the handwriting network also indicates a sensitivity to the irregularity, and in the SFG, to its position. Taken together, these results clearly support the predictions deriving from the account of interacting and parallel orthographic and motor processes in writing. This new empirical evidence could help to better characterize children with developmental disorders such as dysgraphia and dysorthographia, who often display mixed linguistic and motor impairments.

Acknowledgments

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Supplementary Material

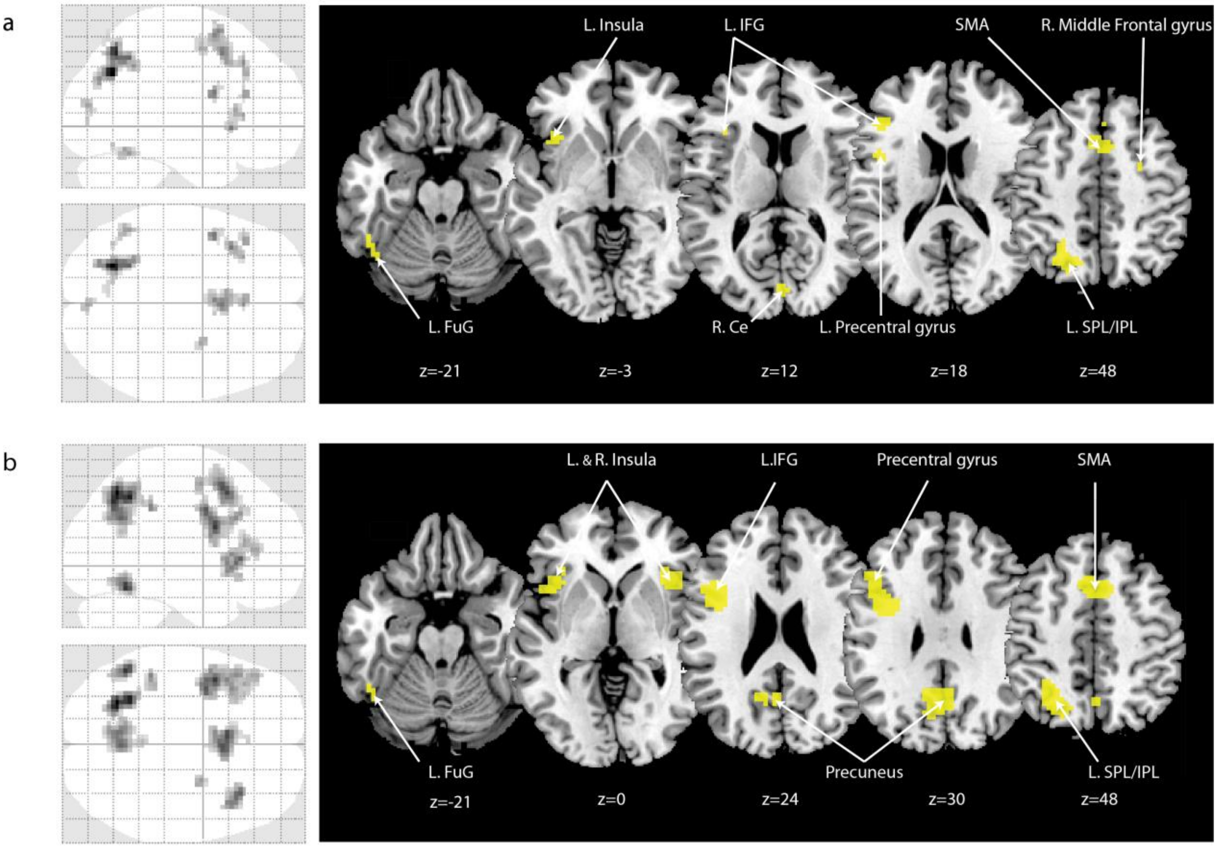
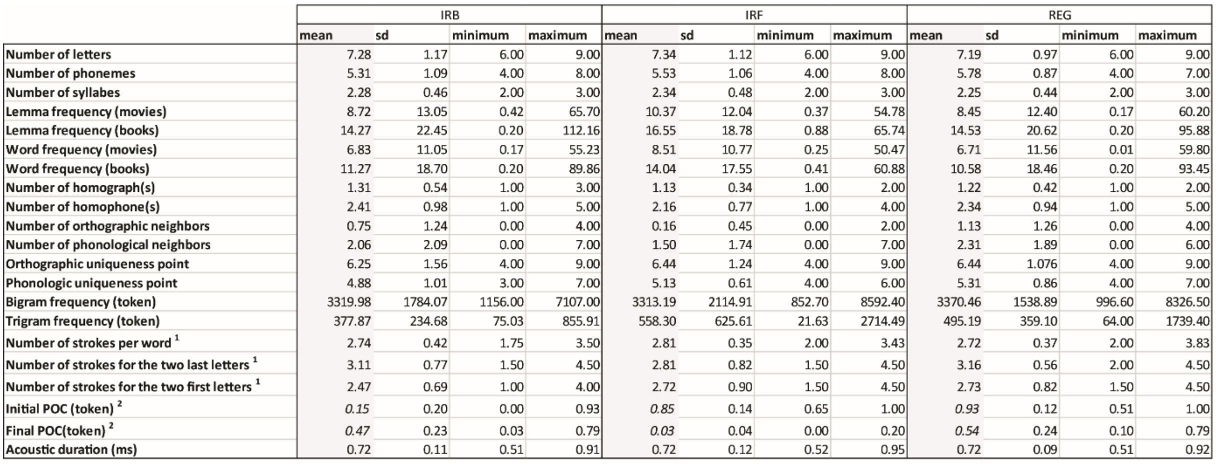


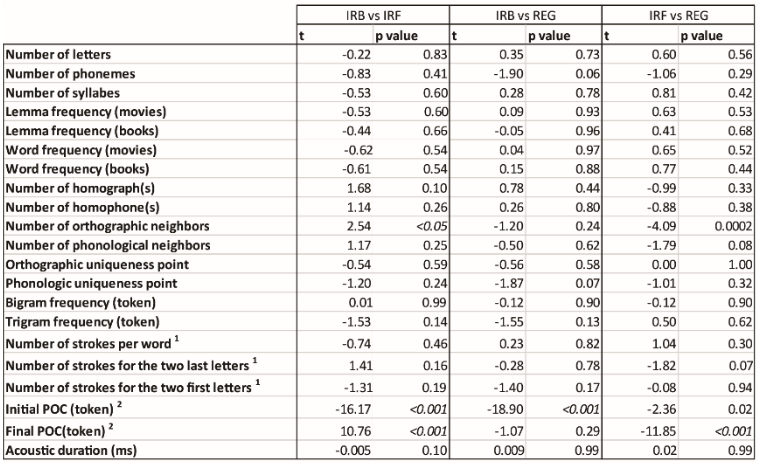
Figure S1. Result of the main effect of irregularity in response to the auditory stimulus (a) and to writing (b) at the whole brain level displayed on glass brain (left panel) one axial slices (right panel. (p<0.05 FWE corrected).

IRB	IRF	REG
ancien	abdomen	absent
antilope	anorak	adulte
antivol	aplomb	aspirine
ceinture	artichaut	balise
cerise	aspect	boutique
certitude	automne	calepin
chronique	cafard	chapitre
cigare	cassoulet	escapade
cirage	chapelet	fleuriste
citation	climat	garage
citron	clochard	infusion
gencive	cobaye	majeur
guenon	concept	narine
hangar	crapaud	natation
harmonie	escargot	nature
harpon	escroc	notice
havane	faubourg	option
hormone	gadget	pivoine
hospice	inconfort	principe
hostie	instinct	puceron
humeur	internat	reptile
humour	manuscrit	rondeur
hypocrite	mouchard	roulade
kangourou	paquebot	savane
ouistiti	parfum	scrupule
phalange	passeport	tentateur
pharaon	printemps	titane
pharmacie	respect	torchon
phobie	sparadrap	triangle
physique	surnom	ventouse
quartier	suspect	virgule
sciatique	tabouret	vitrine

Table S1. List of stimuli for the three condition IRB, IRF and REG.



	IRB				IRF				REG			
	mean	sd	minimum	maximum	mean	sd	minimum	maximum	mean	sd	minimum	maximum
Number of letters	7.28	1.17	6.00	9.00	7.34	1.12	6.00	9.00	7.19	0.97	6.00	9.00
Number of phonemes	5.31	1.09	4.00	8.00	5.53	1.06	4.00	8.00	5.78	0.87	4.00	7.00
Number of syllabes	2.28	0.46	2.00	3.00	2.34	0.48	2.00	3.00	2.25	0.44	2.00	3.00
Lemma frequency (movies)	8.72	13.05	0.42	65.70	10.37	12.04	0.37	54.78	8.45	12.40	0.17	60.20
Lemma frequency (books)	14.27	22.45	0.20	112.16	16.55	18.78	0.88	65.74	14.53	20.62	0.20	95.88
Word frequency (movies)	6.83	11.05	0.17	55.23	8.51	10.77	0.25	50.47	6.71	11.56	0.01	59.80
Word frequency (books)	11.27	18.70	0.20	89.86	14.04	17.55	0.41	60.88	10.58	18.46	0.20	93.45
Number of homograph(s)	1.31	0.54	1.00	3.00	1.13	0.34	1.00	2.00	1.22	0.42	1.00	2.00
Number of homophone(s)	2.41	0.98	1.00	5.00	2.16	0.77	1.00	4.00	2.34	0.94	1.00	5.00
Number of orthographic neighbors	0.75	1.24	0.00	4.00	0.16	0.45	0.00	2.00	1.13	1.26	0.00	4.00
Number of phonological neighbors	2.06	2.09	0.00	7.00	1.50	1.74	0.00	7.00	2.31	1.89	0.00	6.00
Orthographic uniqueness point	6.25	1.56	4.00	9.00	6.44	1.24	4.00	9.00	6.44	1.076	4.00	9.00
Phonologic uniqueness point	4.88	1.01	3.00	7.00	5.13	0.61	4.00	6.00	5.31	0.86	4.00	7.00
Bigram frequency (token)	3319.98	1784.07	1156.00	7107.00	3313.19	2114.91	852.70	8592.40	3370.46	1538.89	996.60	8326.50
Trigram frequency (token)	377.87	234.68	75.03	855.91	558.30	625.61	21.63	2714.49	495.19	359.10	64.00	1739.40
Number of strokes per word [1]	2.74	0.42	1.75	3.50	2.81	0.35	2.00	3.43	2.72	0.37	2.00	3.83
Number of strokes for the two last letters [1]	3.11	0.77	1.50	4.50	2.81	0.82	1.50	4.50	3.16	0.56	2.00	4.50
Number of strokes for the two first letters [1]	2.47	0.69	1.00	4.00	2.72	0.90	1.50	4.50	2.73	0.82	1.50	4.50
Initial POC (token) [2]	*0.15*	0.20	0.00	0.93	*0.85*	0.14	0.65	1.00	*0.93*	0.12	0.51	1.00
Final POC(token) [2]	*0.47*	0.23	0.03	0.79	*0.03*	0.04	0.00	0.20	*0.54*	0.24	0.10	0.79
Acoustic duration (ms)	0.72	0.11	0.51	0.91	0.72	0.12	0.52	0.95	0.72	0.09	0.51	0.92



	IRB vs IRF		IRB vs REG		IRF vs REG	
	t	p value	t	p value	t	p value
Number of letters	-0.22	0.83	0.35	0.73	0.60	0.56
Number of phonemes	-0.83	0.41	-1.90	0.06	-1.06	0.29
Number of syllabes	-0.53	0.60	0.28	0.78	0.81	0.42
Lemma frequency (movies)	-0.53	0.60	0.09	0.93	0.63	0.53
Lemma frequency (books)	-0.44	0.66	-0.05	0.96	0.41	0.68
Word frequency (movies)	-0.62	0.54	0.04	0.97	0.65	0.52
Word frequency (books)	-0.61	0.54	0.15	0.88	0.77	0.44
Number of homograph(s)	1.68	0.10	0.78	0.44	-0.99	0.33
Number of homophone(s)	1.14	0.26	0.26	0.80	-0.88	0.38
Number of orthographic neighbors	2.54	*<0.05*	-1.20	0.24	-4.09	0.0002
Number of phonological neighbors	1.17	0.25	-0.50	0.62	-1.79	0.08
Orthographic uniqueness point	-0.54	0.59	-0.56	0.58	0.00	1.00
Phonologic uniqueness point	-1.20	0.24	-1.87	0.07	-1.01	0.32
Bigram frequency (token)	0.01	0.99	-0.12	0.90	-0.12	0.90
Trigram frequency (token)	-1.53	0.14	-1.55	0.13	0.50	0.62
Number of strokes per word [1]	-0.74	0.46	0.23	0.82	1.04	0.30
Number of strokes for the two last letters [1]	1.41	0.16	-0.28	0.78	-1.82	0.07
Number of strokes for the two first letters [1]	-1.31	0.19	-1.40	0.17	-0.08	0.94
Initial POC (token) [2]	-16.17	*<0.001*	-18.90	*<0.001*	-2.36	0.02
Final POC(token) [2]	10.76	*<0.001*	-1.07	0.29	-11.85	*<0.001*
Acoustic duration (ms)	-0.005	0.10	0.009	0.99	0.02	0.99

Table S2. Linguistic characteristics matched across the three conditions. a: Linguistic characteristics for IRB, IRF and REG words (New et al., 2004, 2001), b: pairwise t-test between the three types of word for each linguistic parameter. (1- Number of stroke letter (Spinelli, Kandel, Guerassimovitch, & Ferrand, 2012), 2- Phono-Orthographic Consistency (POC) (Planton et al., 2014)

ROI	Left FuG				Left SFG				Left SPL				Left IFG				Right Ce				Left M1			
	x	y	z	size	x	y	z	size	x	y	z	size	x	y	z	size	x	y	z	size	x	y	z	size
Group	-48	-63	-6		-18	-6	60		-33	-39	55		-42	3	21		6	-63	-15		-30	-27	54	
Participant 01	-48	-63	-6	*32	-18	-6	60	*36	-33	-39	55	*40	-42	3	21	*33	6	-63	-15	*33	-30	-27	54	*32
Participant 02	-48	-63	-6	*32	-24	-12	63	**49**	-27	-42	54	**49**	-42	3	21	*33	3	-60	-15	64	-36	-24	60	**78**
Participant 03	-54	-66	-6	16	-18	-6	60	*36	-30	-33	60	**23**	-42	3	21	*33	9	-54	-15	**38**	-36	-21	54	**99**
Participant 04	-48	-63	-6	*32	-24	-9	63	62	-36	-36	63	**21**	-42	3	21	*33	3	-69	-9	**111**	-30	-27	60	**85**
Participant 05	-42	-63	0	10	-18	-6	60	*36	-30	-30	51	**54**	-42	3	21	*33	3	-69	-12	23	-33	-27	51	78
Participant 06	-48	-63	-6	*32	-15	-15	63	26	-33	-30	54	**37**	-42	3	21	*33	0	-66	-15	**64**	-33	-30	54	**53**
Participant 07	-45	-72	-6	22	-21	-9	54	11	-36	-30	51	**19**	-42	3	21	*33	6	-63	-15	*33	-33	-21	51	68
Participant 08	-42	-69	-3	**103**	-24	-9	66	60	-33	-45	60	**37**	-39	6	24	41	3	-69	-12	**32**	-36	-27	54	**24**
Participant 09	-48	-66	0	14	-18	-6	60	*36	-30	-48	51	**30**	-42	3	21	*33	6	-63	-15	*33	-30	-27	54	*32
Participant 10	-39	-69	-9	33	-18	-6	69	32	-36	-48	57	**26**	-48	3	24	34	6	-54	-15	**15**	-33	-27	51	79
Participant 11	-45	-69	-12	**48**	-21	-15	57	19	-36	-36	45	**30**	-42	3	21	*33	3	-63	-21	**14**	-33	-27	60	76
Participant 12	-45	-72	-6	**16**	-24	-9	66	28	-30	-30	54	**12**	-42	3	21	*33	6	-66	-18	55	-30	-27	54	**52**
Participant 13	-45	-63	-15	**48**	-18	-6	60	*36	-33	-30	57	80	-45	9	21	46	12	-66	-15	**40**	-33	-30	57	**55**
Participant 14	-51	-69	-9	45	-24	-6	66	31	-30	-42	48	**25**	-42	3	21	*33	9	-72	-18	**10**	-30	-27	60	**61**
Participant 15	-45	-72	-9	45	-24	-12	57	**41**	-30	-30	57	**73**	-45	6	15	66	6	-63	-15	*33	-30	-27	60	**71**
Participant 16	-45	-72	-9	**41**	-24	-3	54	18	-39	-45	60	**28**	-36	6	24	47	3	-69	-15	**28**	-36	-21	54	**39**
Participant 17	-39	-63	-9	**83**	-21	-6	66	**60**	-39	-36	57	**106**	-45	3	30	**15**	6	-63	-9	**63**	-36	-33	57	**68**
Participant 18	-51	-69	0	**16**	-24	-12	63	42	-33	-45	60	**31**	-45	9	24	57	9	-60	-18	**44**	-24	-27	57	**70**
Participant 19	-45	-66	-3	**49**	-21	-12	54	53	-33	-33	60	65	-42	3	21	*33	0	-66	-12	70	-33	-30	60	44
Participant 20	-45	-72	-6	79	-21	-12	54	15	-36	-36	63	26	-42	3	30	35	6	-66	-15	62	-36	-24	60	**25**
Participant 21	-45	-69	0	49	-24	-9	57	20	-33	-39	63	**32**	-42	3	21	*33	9	-57	-18	**36**	-27	-24	57	**52**
Participant 22	-45	-72	-6	**62**	-24	-9	66	11	-42	-39	57	**34**	-45	6	18	15	9	-69	-18	**60**	-30	-24	57	**56**
Participant 23	-42	-69	0	28	-21	-15	57	33	-33	-30	57	**24**	-42	3	21	*33	9	-63	-9	69	-27	-27	60	**76**
Participant 24	-45	-72	-6	**21**	-27	-6	60	21	-30	-39	57	72	-42	3	21	*33	3	-69	-15	47	-24	-30	54	44
Participant 25	-45	-72	-6	**49**	-18	-6	60	*36	-39	-39	57	26	-36	-3	21	44	12	-69	-18	**67**	-30	-21	60	**44**
Mean	-46	-68	-4		-22	-8	55		-34	-35	56		-42	4	22		6	-64	-15		-32	-26	52	
Standard Deviation	3.5	3.7	5.8		2.8	5.7	25.1		3.6	14.7	4.5		2.6	2.3	3.1		3.3	4.8	3		3.6	3.2	21.7	

Table S3. Individuals ROIs. For each region, the MNI coordinates and size (mm3) of the individual ROIs are given. Size values in BOLD indicate FWE p<.05 thresholded ROIs, and asterisks indicate the cases where 6mm radius spheres centered on the center of the search volume was defined as ROI.