PAPER

WILEY

The handwriting brain in middle childhood

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Funding information
Agence Nationale de la Recherche, Grant/Award Number: ANR-11-LABX-0036, ANR-16-CONV-0002 and ANR-14-CE30-0013

Abstract

While the brain network supporting handwriting has previously been defined in adults, its organization in children has never been investigated. We compared the handwriting network of 23 adults and 42 children (8- to 11-year-old). Participants were instructed to write the alphabet, the days of the week, and to draw loops while being scanned. The handwriting network previously described in adults (five key regions: left dorsal premotor cortex, superior parietal lobule (SPL), fusiform and inferior frontal gyri, and right cerebellum) was also strongly activated in children. The right precentral gyrus and the right anterior cerebellum were more strongly activated in adults than in children, while the left fusiform gyrus (FuG) was more strongly activated in children than in adults. Finally, we found that, contrary to adults, children recruited prefrontal regions to complete the writing task. This constitutes the first comparative investigation of the neural correlates of writing in children and adults. Our results suggest that the network supporting handwriting is already established in middle childhood. They also highlight the major role of prefrontal regions in learning this complex skill and the importance of right precentral regions and cerebellum in the performance of automated handwriting.

KEYWORDS
children, development, expertise, handwriting, motor learning

1 | INTRODUCTION

Handwriting is a very complex skill that requires years of practice to be mastered. The acquisition of handwriting is a factor contributing to academic and professional success and to social integration. The behavioral evolution of handwriting during learning has already been described (Palmis et al., 2017 for review) but currently the organization of the brain network sustaining handwriting in children is poorly understood.

In skilled adults, the main network is composed of five regions which display functional specificity for writing: the left inferior frontal gyrus (IFG), the left fusiform gyrus (FuG), the left superior parietal lobule (SPL), the left superior frontal gyrus or dorsal premotor cortex (SFG/PMd), and the right cerebellum (Ce) (for meta-analyses see Planton et al., 2013; Purcell, Napoliello, et al., 2011; Purcell,

Turkeltaub, et al., 2011). These five regions display preferential involvement in either linguistic or motor processing during writing.

The left IFG pars opercularis and the left FuG are consistently activated in tasks requiring orthographic recall (Planton et al., 2013; Purcell, Napoliello, et al., 2011). The left FuG has an acknowledged role in access to or storage in orthographic long-term memory (Purcell, Napoliello, et al., 2011; Purcell, Turkeltaub, et al., 2011; Rapp & Dufor, 2011; Rapp et al., 2016). In addition, a part of the left FuG has been shown to respond specifically to visually presented letters (Joseph et al., 2006; Polk et al., 2002; Rothlein & Rapp, 2014). The FuG is also consistently activated during the written production of letters (James & Gauthier, 2006; Longcamp et al., 2003). Rothlein and Rapp (2014) have proposed that the left FuG computes an abstract representation of letters that could, therefore, be accessed both when the letters are read and are written.

The left SPL, SFG, and the right cerebellum are consistently mobilized in relation to the motor control of handwriting. Both the SPL and the SFG have been assigned a role in the manual motor representation of letters (Exner, 1881; Kadmon Harpaz et al., 2014; Magrassi et al., 2010; Roux et al., 2009; Seitz et al., 1997; Vinci-Booher et al., 2016). The consistent involvement of the right Ce in writing tasks may be related to its known importance in the coordination of fine movements and in the retention of acquired motor skills in the form of internal models (Doyon et al., 2003; Hardwick et al., 2013; Manto et al., 2012; Marien et al., 2007).

Whether the organization of this network is similar in children is currently an open question. The aim of the present study is therefore to define the handwriting network of typical middle-childhood aged writers, and to understand how it differs from that of adults. To date, one single fMRI study has directly measured the brain correlates of writing in children (Richards et al., 2011). The aim was to compare the brain activation patterns of good and poor 11-year-old writers during the written production of graphic shapes. The results of Richards et al. indicated that the elements of the adult handwriting network are activated in children who produce single characters. Poor writers displayed extra activations in regions that do not belong to the core of the handwriting network. Interestingly, the activation of the left FuG was stronger in good writers, and it correlated with standard measures of writing proficiency and orthographic coding.

Other studies have provided more indirect but valuable insights into the neural correlates of writing in children. The rationale is to relate the anatomical or functional features of the brain in non-writing tasks to either measures of writing proficiency recorded outside the scanner (Gimenez et al., 2014; Richards et al., 2009), or to the children's previous experience with handwriting (James, 2010; James & Engelhardt, 2012; James et al., 2016).

For instance, Richards et al. (2009) showed that the activation patterns of good and poor 11-year-old writers in a finger sequencing task differ in a series of regions involved in motor control (pre- and postcentral cortices, superior parietal cortex, and cerebellum), but also in the fusiform and cingulate gyri. Moreover, the individual amount of activation within these regions correlated with the children's handwriting automaticity and/or with their spelling skills. In a group of preschoolers, Gimenez et al. (2014) found that the activation in the right IFG during a phonological task correlated negatively with a measure of handwriting quality. The amount of gray matter in this same region correlated positively with handwriting quality. These findings were interpreted as evidence for the importance of neural efficiency in phonological processing for handwriting development. Changes also occur in the visual system: in preschoolers, letters trained through handwriting elicit stronger responses in the FuG than letters trained by other means (tracing, typing, and visual analysis), when they are subsequently presented visually (James, 2010; James & Engelhardt, 2012). In fact, writing knowledge not only enhances the fusiform response, but also increases the response of precentral and inferior frontal regions (James & Engelhardt, 2012), and promotes the setup of functional connections between fusiform and precentral regions (Vinci-Booher et al., 2016). Overall, this body

Research Highlights

- We used fMRI to uncover the brain correlates of writing acquisition and demonstrate that the network previously described in adults is also strongly activated in children.
- However, group effects in the right cerebellum and left fusiform gyrus indicate that the network continues to mature between middle childhood and adulthood.
- We also found group differences in prefrontal and precentral regions, which likely underpin changes in the control of writing with the acquisition of expertise.
- These results fill a considerable gap in the field of writing acquisition.

of data indicate that the functional systems associated with letter processing can be shaped by handwriting experience even in young children, and that the efficiency of processing in motor and phonological networks underpins writing proficiency during development.

All the studies cited above have focused on variability among children. In addition, the study of Richards et al. (2011), where children actually wrote in the scanner, was performed on a relatively small sample (11 good and 9 poor writers). In the present study, we measured the brain activations generated by writing tasks in a large group of typical middle-childhood aged writers and in a group of adults. We performed contrasts that are typically used to define the handwriting network in adults (writing letters or words vs. a control graphomotor task; see Planton et al., 2013, for examples of such contrasts). This allowed us to describe how the elements of this network are mobilized in children, and whether children recruit brain regions that do not belong to this network to perform the tasks. More importantly, we focused on the comparison between the two groups. This approach allowed us to document the brain changes that likely underpin the shift between developing writing and writing expertise.

In addition to the possible maturation of the handwriting network, differences between the groups may also result from more general motor learning mechanisms (Palmis et al., 2017). For instance, plastic changes in the primary motor cortex are an important feature of the stabilization of a motor skill in memory (Galea et al., 2011; Hardwick et al., 2013; Karni et al., 1995; Pascual-Leone et al., 1995). Another typical feature of motor learning at the brain level is the variable involvement of the cortico-striatal and cortico-cerebellar loops in the different phases of the acquisition (Doyon & Benali, 2005; Doyon et al., 2003; Manto et al., 2012). It can thus be assumed that children and adults will differ in the involvement of the primary motor cortex and cortico-subcortical loops.

Finally, we expect to observe differences between children and adults in the lateralization of activations. Hemispheric lateralization during language and visuospatial tasks has been shown to evolve with age and to reflect the maturation of the underlying brain

networks (Everts et al., 2009). In the context of graphomotor control, Planton et al. (2017) have shown that adults display stronger left lateralization during writing than during drawing tasks. According to these authors, this difference could be related to learning how to write. Writing may develop from networks that are initially bilaterally distributed, as they are for drawing, and "lateralization could arise through frequent interactions with the areas of the left hemisphere that support language processing when learning to write, at least in right-handed individuals." Left lateralization should thus be less prominent in children than in adults.

Middle childhood is an ideal period to study the acquisition of handwriting. In terms of writing kinematics, middle-age children are undergoing a massive transition between a previous strategy based on sensory control of the trajectory and a strategy based on a proactive mode of control where motor programs have been integrated (Palmis et al., 2017). In terms of spelling, 8- to 11-year-old children are able to make use of both a lexical stock and sublexical knowledge (phonographic conversions) (Treiman, 2017), but their lexical stock is less rich and accessed less efficiently than that of adults (Zesiger, 1995).

2 | MATERIAL AND METHODS

2.1 | Participants

Seventy-four native French speakers took part in the experiment; data from nine participants (seven children and two adults) were discarded because of MRI acquisition problems (one participant), problems with data quality (two participants, see below), benign brain malformation (one participant), and technical problems with the auditory stimulation (five participants). The final group statistics were carried out on 65 participants: 23 adults (11 males and 12 females aged 19–40, mean 24.91) and 42 children (20 males and 22 females, aged 8–11, mean 8.88). All participants were right-handed (Edinburgh laterality test mean 81.49), had normal audition, and normal or corrected-to-normal-vision. Their reading, graphomotor, and spelling skills were in the normal range, as assessed by standardized tests. The detail of the tests used and the scores of the two groups for each subtest are given in Supplementary Materials in section "pretest."

Informed consent was signed by the adult participants and by the children's parents after the experimental procedure was fully explained. The study received the approval of the Ethics committee 2017-A01789-44.

2.2 | Procedure

The task was organized into 16 blocks, where participants wrote in a lying position on an MRI compatible digitizing tablet while being scanned. Three conditions were tested: the writing of the letters of the alphabet, of the days of the week, and the tracing of loops.

The participants were instructed to write in cursive at their usual writing speed. In the French educational system, children are taught how write in cursive. Cursive remains the dominant writing style, although adults tend to mix it with script. This task allowed each participant to write at their own pace, the imposed factor being the time spent writing (block duration). Participants wrote without visual feedback.

Participants were trained to the task in a mock scanner, immediately before the actual scanning. After being familiarized to the scanner environment and the horizontal writing posture, they had to produce the blocks of the three conditions with and without visual feedback in two separate sub-sessions. The visual feedback was provided by a mirror system in front of the participant's eyes, showing them a projection screen located at the back of the mock scanner and a video projector. It consisted of a black line unfolding on the screen as a function of the progression of the xy position of the stylus on the tablet. The order (with vs. without feedback) was counterbalanced between participants. The aim was to measure the effect of removing visual feedback on the performance (see Supplementary Materials, Figure S1). We found that the performance was not disturbed by the absence of visual feedback compared to when the feedback was provided on the screen. This was true for both the adult and child participants. In fact, most participants wrote faster and more accurately without visual feedback.

The fMRI data were recorded in one session lasting 7 min and 30 s where eight blocks of each of the three conditions were semi-randomly alternated. At the beginning of each block, participants were instructed to hold the pen and to rest their hand in the left edge of the tablet. Each block began with an auditory instruction stimulus indicating the condition: "Jours" (Days), "Lettres" (Letters), and "Boucles" (Loops). Participants had to start to write as soon as they recognized the instruction. A fixation cross was displayed in the middle of the screen throughout the block, and at the end, the cross was replaced by three #, indicating that the participants should stop writing and move their hand back to the initial hand position (Figure 1).

2.3 | Stimuli

The three auditory stimuli, used as auditory instructions for the three conditions, were recorded in an anechoic room by a French female speaker without regional accent. Stimuli were matched for their acoustic duration and pitch.

2.4 | Material

Writing kinematics were recorded using an MRI compatible digitizing tablet and a PVC pen developed in our lab (Longcamp et al., 2014). The tablet is composed of a touchscreen whose force range was set between 0.1 and 0.8 N, and an USB controller board that allowed a 100 Hz sampling rate. The tablet was placed on the
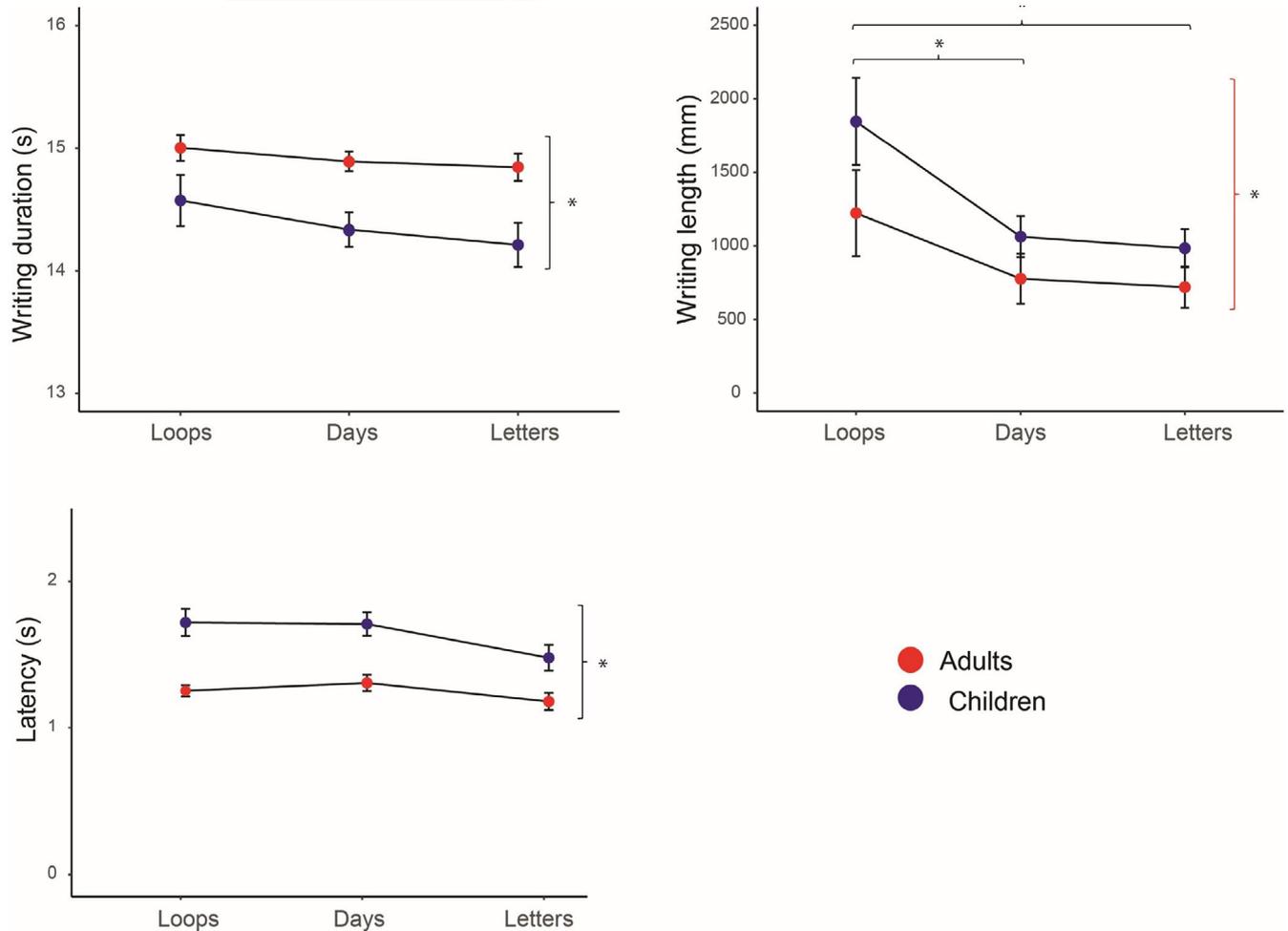
FIGURE 1 Behavioral results, as a function of the condition and to the group. Upper left panel: writing duration (second); Upper right panel: writing length (millimeter); Lower left panel: writing latency; for the three conditions: Loops, Words, and Letters and for the two groups, Adults (red dots) and Children (blue dots). Red braces indicate a significant interaction between group and condition.

participants' stomachs, and its position could be adjusted with a foam cushion to facilitate writing. The tablet and the right arm were elevated with cushions to ensure that participants were as comfortable as possible, and to prevent head movements. The auditory stimuli were presented via MRI compatible pneumatic earphones; Flat Response Over 100 Hz to 8 kHz Bandwidth (SENSIMETRICS S14). The size of the earphones was adapted to participant's ear size particularly for children. A mirror system in front of the participant's eyes, together with a projection screen located at the back of the scanner and a video projector, allowed the participants to view the visual stimuli (fixation cross and #) during the task.

2.5 | Behavioral data analysis

The xy position of the pen was tracked for each block and then converted from pixels to millimeters. The resulting writing traces were analyzed using custom-made software. Trials with unreadable or un-related responses or with no response at all were discarded from the

statistical analyses. In a few cases (0.25% of the trials), the digitizer did not record the data correctly.

For each correct trial, we analyzed the latency, the total writing duration (in seconds), time lapse between the first and the last contact with the tablet, and the total trajectory length between the first and the last contact with the tablet (in millimeters). The length measure accounted for the trajectory when the pen was touching the tablet. The latency measures were log-transformed prior to the statistical analysis.

The kinematic differences between groups and between conditions on these three variables were tested using linear mixed effect models (LmerTest library (calls on the Lme4 library), function Lmer, (Kuznetsova et al., 2017)) implemented on R software. This model allowed missing values to be accounted for, as two participants did not have any kinematic measures for certain conditions. This was the case for two 8-year-old children who did not apply sufficient pressure when writing, making the written trace unreadable and unanalyzable. For each of the three variables analysis, two fixed effects (group and condition) and one random effect (subject) were included. We used the following three equations: Latency: lmer(mean

latency~group*condition + (1|subject),data=mean latency); Duration: lmer(mean duration~group*condition + (1|subject), data=mean duration); Length: lmer(mean length~group*condition + (1|subject), data=mean length). P-values were accessed by doing REML *t*-tests using Satterthwaite's method, obtained with the summary function on the model.

A certain amount of trials was discarded from the analysis, according to several criteria.

- Empty trials due to recording issues were removed as were trials that did not have enough pressure segments (not allowing confirmation that the participant has performed the correct condition).
- Trials where writing or tracing duration was inferior to 2.5 standard deviation were discarded. Standard deviations were calculated separately for adults and children for the three conditions combined: adult's inferior writing duration limit = 13.33 s and children's inferior writing duration limit = 10.24 s. The discarded trials corresponded to abnormally short trials due to a lack of pressure on the tablet either at the beginning or at the end of the trace (23 trials for children with an average time spent without writing of 8.053 s; 9 trials for adults with an average time spent without writing of 4.40 s, out of a trial duration of 16.23 s). This sorting method based on group performance did not impact slower/younger participants because of the time limitation of trial duration with the fMRI blocks duration.
- The last step was to discard outlier trials when considering the writing length even if the performed condition was identifiable.

After the sorting process, a total of 1,100 trials from an initial 1,170 trials (94%) were kept for the final behavioral analysis. For adults, 13 trials (3% of the total amount) were removed. For children, 57 trials (8% of the total amount) were removed. Since most of those trials were removed because of recording issues, they were kept for the fMRI analysis.

2.6 | fMRI acquisition and preprocessing

Structural and functional MRI data were acquired on a 3-Tesla MRI Scanner (Magnetom-Prisma, Siemens, Erlangen, Germany). For each participant, we acquired a high-resolution T1 volume, a fieldmap, and BOLD images.

BOLD images were acquired using a gradient-echo EPI sequence with TR = 957 ms, TE = 30 ms, voxel size = 2.5 mm^3, multiband factor = 4, slices = 56, FOV = 210 × 210 mm^2, and 335 volumes in a single session. Anatomical images: voxel size: 1 mm^3.

The quality of the individual T1 images was checked visually to identify possible movement artifacts. For the EPI images, we used the MRIqc toolbox (Esteban et al., 2017) to generate group descriptive statistics of image quality metrics (SNR, temporal SNR, Mean Framewise Displacement, and DVARS) to identify possible outliers. With this procedure, the data from two participants were found to deviate by 2 SDs from the rest of the group and were discarded

from the analysis (one child with a low SNR, and one child with several abnormal image quality metrics due to large head movements). The quality metrics of the groups included in the final analyses are reported in Table S1. Images were preprocessed using the SPM12 software. Head movements were corrected, images were co-registered to the mean image, and T1 image was segmented. Structural and functional images were normalized using DARTEL. The DARTEL toolbox allows the optimal alignment of the cortex masks of all participants of both groups.

The normalization stage creates a common template that takes into account the two groups' specific anatomies. Because the head size of a middle-age child is on average similar to that of an adult, all the participants were merged into a single template (Burgund et al., 2002; Hoeft et al., 2007). The results of this normalization procedure were checked participant by participant, in order to ensure that no deformation was induced in the child group. Finally, data were spatially smoothed (FWHM 5 mm).

2.7 | fMRI Statistical analyses

2.7.1 | First- and second-level statistical models

The first-level statistical models were computed using the general linear model implemented on the SPM12 software. The models included one regressor for each of the three conditions. The blocks of each condition were modeled as boxcars with onset at the time of the auditory stimulus of the block, and duration of 16.44 s convolved with the HRF. Regressors of no interest were also included to account for head movement and for variations related to physiological activity (see below). The contrasts between the two writing conditions ("Words" and "Letters") and the graphomotor condition ("loops") were calculated for each participant and entered in the second-level analysis.

As younger participants could be more prone to head movement and physiological noise, we followed a specific procedure to account for possible motion and physiological artifacts within the first-level statistical models through extra regressors of non-interest (Caballero-Gaudes & Reynolds, 2017). First, we included 24 motion regressors. Those regressors were generated from the six classical motion parameters which were then squared, derived, and both squared and derived to constitute the 18 other parameters (Friston, 1996). Second, the toolbox ART (https://www.nitrc.org/projects/artifact_detect/) allowed us to pick up the scans where head movements exceeded a 3 mm absolute motion threshold and to put them in an extra nuisance regressor. With this procedure, scans were detected and modeled as outliers for 15 children and one adult. The number of outliers varied between 2 and 16 functional images out of 335. Finally, the "TAPAS - PhysIO" toolbox was used to account for physiological noise (Kasper et al., 2017). This toolbox allows data-driven estimation of the physiological noise components for model-based noise correction. Physiological noise is estimated by computing a principal components analysis on the white matter and

cerebrospinal fluid, enabling the explanation of the signal variability present in these two ROIs and thus unrelated to actual BOLD variations. Twenty-six principal components were used as nuisance regressors in the GLM (12 components per ROI, and two regressors modeling the average of the principal components of each ROI, aCompCor method; Behzadi et al., 2007).

The second-level statistical analyses were performed using the GLM flex fast 4 (http://mrtools.mgh.harvard.edu/) method to assess the whole brain activations for each group separately and the main effect of group (differences between adults and children), condition (differences between writing words and letters), and interaction between group and condition. Whole brain T contrasts for adults and children were performed in order to visualize the two groups' handwriting networks separately. These contrasts correspond to the conjunction of the two contrasts, "Words versus Loops" and "Letters versus Loops." Activations were displayed and figures were created using the bspmview toolbox (http://www.bobspunt.com/bspmview/). Activations were considered significant when they reached a threshold of $p < .001$, uncorrected for multiple comparisons at the voxel-level, and $p < .05$, FWE-corrected for multiple comparisons at the cluster-level.

In order to check whether the results were influenced by possible behavioral confounds (different writing behavior of the two groups within the scanner) or by the procedure used to correct for head movements, we ran two complementary first-level models per participant. In the first complementary model, we added an extra regressor that represented the writing duration of each block, modeled as a parametric modulation of the task blocks convolved with the HRF. It allowed checking whether the group effects were influenced by the actual writing duration of each block. In the second complementary model, we used a more stringent threshold for scrubbing scans subject to head movements (FD < 0.9; Siegel et al., 2014). The group effect for these two complementary analyses is reported in Figure S2 and Tables S2 and S3. The descriptive statistics for the amount of scans scrubbed in the second model are reported in Table S1. The pattern of distribution of the activations in the main group that contrasts with the two complementary models is very similar to that of the main analysis reported below. The group statistics remain very similar, with only minor changes in the *t*-values or in the clusters' extent or position, suggesting that the results at the group-level were not confounded by the individual behavior or by head movements.

2.7.2 | Laterality analysis

The lateralization of the activations was evaluated for the whole hemispheres using the LI toolbox (Wilke & Lidzba, 2007) and a mask combining all the lobe images provided by the toolbox. We used an additional mask that excluded the signal at the midline +5 mm. We calculated a laterality index (LI) using the method described in Wilke and Schmithorst (2006) and the corresponding MATLAB tools provided by Marko Wilke. The images used were the individual t-contrast images (Words vs. Loops and Letters vs. Loops), so that for each subject, we obtained one LI for Words and one LI for Letters.

Briefly, this method iteratively explores the lateralization at increasing, regularly spaced, thresholds. At each threshold, a bootstrap algorithm is used to compute a large number of LIs based on the surviving voxels using the standard equation:

$$LI = \Sigma\,activation\,left - \Sigma\,activation\,right\,/\,\Sigma\,activation\,left + \Sigma\,activation\,right$$

Only the central 50% of the resulting distribution is then averaged. Finally, the values at the various thresholds are averaged, but the mean is weighted by the threshold value. This method therefore overcomes the problems of sensitivity to outliers, and of threshold dependency encountered in the usual calculation of LIs. Positive values of LIs indicate stronger activations in the left hemisphere, while negative values indicate stronger activations in the right hemisphere. Values above 0.2 and below −0.2 are considered to index significant lateralization of the activations. Values between −0.2 and 0.2 are considered to index bilateral activations (Seghier, 2008).

The distribution of LIs is known to be non-Gaussian (Wilke & Schmithorst, 2006). We therefore used non-parametric tests to assess the differences between groups and conditions.

3 | RESULTS

3.1 | Behavioral data

3.1.1 | Writing duration

The group factor significantly impacted the writing durations (random effects: Subject (SD = 0.33), Residual (SD = 0.35); fixed effects: Child group (estimate = −0.43, SE: 0.12, t(127.61) = −3.44, $p = .0008$)). Durations were higher for adults (mean = 14.91 s) than for children (mean = 14.38 s) due to increased latency for children. No main effect of condition and no interaction between condition and group were found (Figure 1).

3.1.2 | Writing latency

The group factor significantly impacted the latency (random effects: Subject (SD = 0.25), Residual: (SD = 0.26); fixed effects: Child group (estimate = 0.47, SE = 0.095, t(120.95) =5.26, $p = 6.37e$-07)). The latencies were longer for children (mean = 1.62 s) than for adults (mean = 1.24 s). No main effect of condition and no interaction between condition and group were found (Figure 1).

3.1.3 | Trajectory length

The group factor significantly impacted the trajectory length (random effects: Subject (SD = 483.9), Residual (SD = 367.8); fixed effects: Child group (estimate = 623.5, SE = 0.13, t(157.7) =3.95, $p = .0001$)). The

trajectory lengths were higher for children (mean = 1,304.829 mm) than for adults (mean = 906.7748 mm). The condition factor also impacted the trajectory length with longer trajectories for Loops (mean = 1,846.342 mm) than for Words (mean = 1,062.582 mm; fixed effect: Words condition (estimate = −445.7, SE = 108.5, $t(108.5) = −4.11$, $p = 7.24e-05$, Loops vs. Words: $t = 9.2$, $p < .001$, Tukey)) and Letters (mean = 984.5437 mm; fixed effect: Condition Letters (estimate = −502.4, SE = 108.5, $t(121.4) = −4.632$, $p = 9.17e-06$; Loops vs. Letters: $t = 10.305$, $p < .001$, Tukey)). The interaction between group and condition was also significant: fixed Child group x Words condition (estimate = −358.4, SE = 135.4, $t(121.7) = −2.65$, $p = .009$) and Child group x Letters condition (estimate = −395.1, SE = 135.8, $t(121.9) = −2.90$, $p = .0043$). The difference between Loops and the other two conditions was larger for children than for adults (Figure 1).

3.1.4 | Errors

They were only two trials for which participants did not perform the right condition. Instead of being discarded, these two trials were added to the pool of the condition actually produced.

3.2 | fMRI data

We will focus on the main effect of group. Several regions were found to be modulated by the condition. However, the main effect of condition did not differ between the two groups. A single interaction between group and condition was found in the middle occipital area and is reported below. The main effect of condition is therefore reported in Supplementary Material (Figure S3 and Table S4).

3.2.1 | Whole brain analysis

Handwriting network of adults and children
For both groups, the contrast revealed a network composed of regions known to be reliably involved in handwriting and mostly lateralized in the left hemisphere (Figure 2). Significant activations were found in the left FuG, the left IFG pars orbitalis, left inferior parietal lobule extending to the left SPL, left SFG, and at multiple locations on the right and left cerebellum (Table 1). In addition, children displayed significant activations in the left and right insulas and the left and right superior frontal/middle frontal gyri, and their activation of the posterior medial frontal gyrus extended anteriorly towards the anterior cingulate cortex. In general, the child group displayed more clusters of activation in the frontal cortex. Children therefore displayed more activation clusters than adults. The activations found for the two groups are presented in Table 1.

Main effect of group
Adults displayed stronger activations than children in the right precentral gyrus (PrCG), SFG, and in the left and right posterior medial frontal gyrus. Two other significant differences were found in the left lingual/calcarine gyrus and in the right anterior cerebellar lobule IV-V (Figure 3a,b). Conversely, children displayed stronger activations in the left IFG pars orbitalis extending to the insula and in the anterior cingulate lobule (Figure 3a,c) (Figure 3, Table 2).

Interaction
Only the right middle occipital gyrus showed an interaction between group and condition, with a weaker activation only for the Letter condition in children (Figure 4, Table S4 and Figure S3).

LI analysis. A pairwise Wilcoxon rank test indicated that for children, the LIs in the Words condition differed significantly from the LIs in the Letters condition ($W = 195$, $p < .001$). The difference between the two conditions was not significant in adults. A Mann-Whitney rank test indicated that in the Words condition, the lateralization among children was significantly different from that of adults ($U = 633$, $p < .04$). The difference between children and adults was not significant in the Letters condition. Figure 5 indicates that the lateralization of the activations during the writing of words in children was lower than in the other three samples.

One sample Wilcoxon rank tests where the sample was compared to a value of 0.2 indicated that in children, for the Words condition, the LI values differed significantly from 0.2 ($W = 164.5$, $p < .001$). Figure 5 shows that the corresponding median was located below 0.2. The LIs did not significantly differ from 0.2 for the other three samples (adult's letters and words, children's letters; Figure 5, medians located at about 0.2). This suggests that for the children in the words condition, the lateralization values departed from the threshold indicating significant left lateralization. For most children, the values in this condition were indeed either between 0.2 and −0.2 (bilateral activations) or below −0.2 (right lateralized activations).

4 | DISCUSSION

The aim of this study was to describe the handwriting network of typical children and to compare it to that of adults.

Behavioral results are consistent with data of the literature (for review, see Palmis et al. 2017). They show that significant differences remain in the control of the writing movement between middle childhood and adulthood.

The fMRI results showed that the expected handwriting network was activated more strongly for writing Words and Letters than Loops in the adult group. Our results are consistent with previous studies (Planton et al., 2013; Purcell, Napoliello, et al., 2011; Purcell, Turkeltaub, et al., 2011). This same network was also found to be preferentially activated for Words and Letters over Loops in 8- to 11-year-old children. However, the involvement of the left FuG and
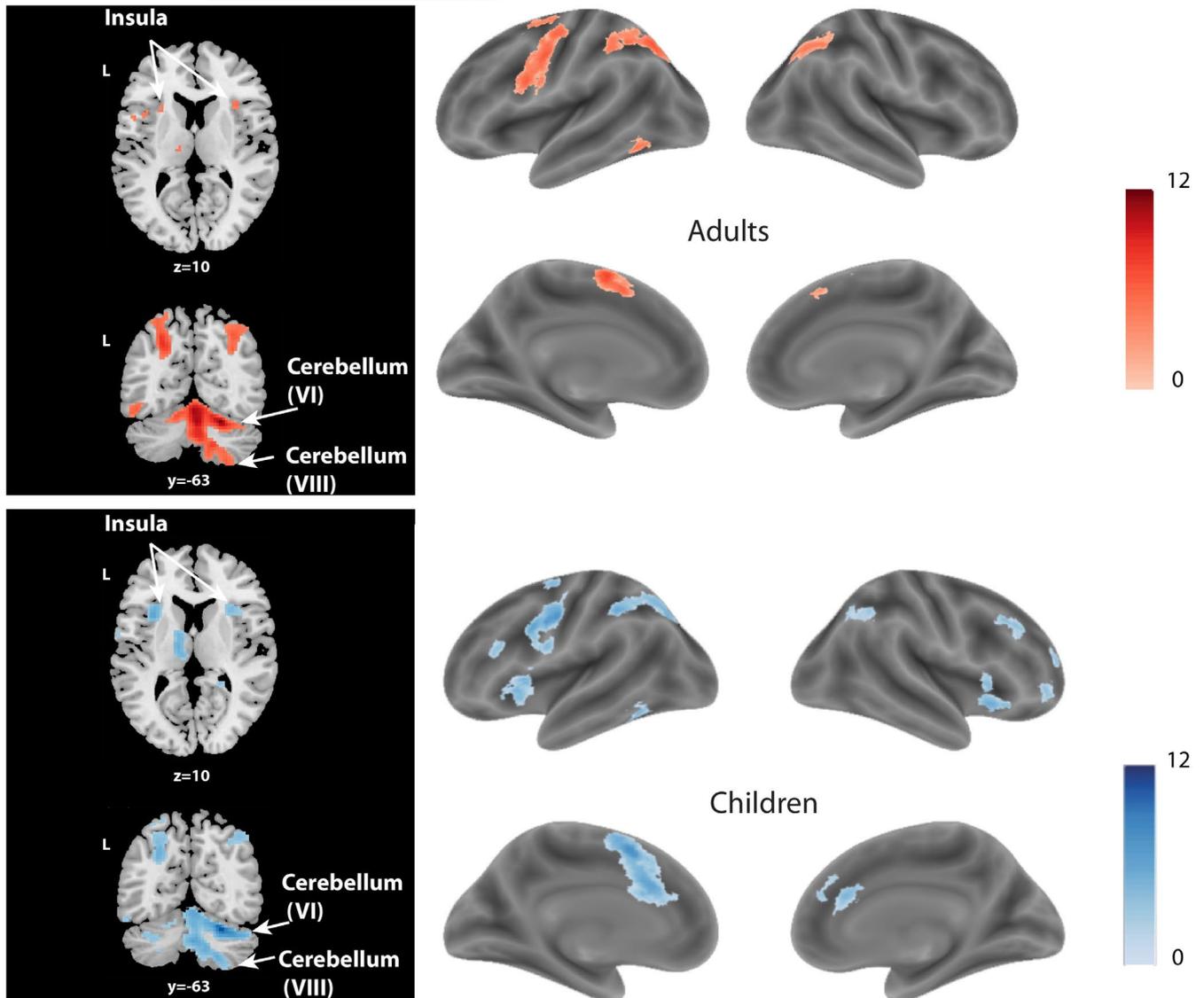
FIGURE 2 Results for the whole brain T contrast representing regions preferentially activated for Words and Letters than for Loops. Upper panel: Adults handwriting network (red); Lower panel: Children handwriting network (blue). Cortical activations were represented on a surface rendering and deep activations (insula and cerebellum) are represented on axial and coronal slices. The contrasts are displayed at a threshold of $p < .001$, uncorrected for multiple comparisons at the voxel-level and $p < .05$, FWE-corrected for multiple comparisons at the cluster-level.

the right Ce differed between the two groups. Group differences were also found in other brain regions with preferential activation of prefrontal regions in children and of the right precentral cortex in adults.

4.1 | The handwriting network of adults and children

No major differences between adults and children were observed in the organization of the handwriting network. An important result of the present study is, therefore, that the topography of the handwriting network is already established in typical 8- to 11-year-old writers.

The differences between adults and typical children usually observed on spelling and motor accuracy may therefore not be linked to differences in the organization of the main components of the network. It is possible that most of the organization occurs earlier. In France, children learn to write their first letters and their first word (name, first name...) around the age of 4 or even earlier. Thus, the younger participants of our sample, already have at least 4 years of practice, which is actually enough to implement the neural bases of the handwriting network. Previous work has shown that functional brain changes occur with writing practice even in preschool children (Gimenez et al., 2014; James, 2010; James & Engelhardt, 2012; Vinci-Booher et al., 2016). More generally, the sensorimotor networks are already mature in children aged 6–7 years (Grayson & Fair, 2017; James & Kersey, 2018; Zielinski et al., 2010), and they

TABLE 1 Results of the whole brain analysis for Adults and Children, showing preferential activations for Words and Letters than for Loops, and coordinates are in the MNI space. The contrasts are displayed at a threshold of $p < 0.001$, uncorrected for multiple comparisons at the voxel-level, and $p < .05$, FWE-corrected for multiple comparisons at the cluster-level.

Location		Cluster size	Stats, t-value	MNI Coordinates		
				x	y	z
Adults						
Frontal						
Left/Right	Posterior medial frontal gyrus	1,314	8.8815	−3	0	60
Left	Precentral gyrus		6.5247	−55	−3	45
Left	IFG p. opercularis		6.3387	−45	3	23
Temporal						
Left	Inferior temporal gyrus	75	5.6351	−50	−60	−13
Parietal						
Left	Superior parietal lobule	615	6.8085	−25	−65	45
Left	Inferior parietal lobule		5.9720	−30	−45	43
Right	Inferior parietal lobule	339	5.7783	35	−58	45
Cerebellum						
Right	Cerebellum (VI)	1,991	9.4372	23	−63	−23
Right	Cerebellar lobule vermis 6		9.3419	3	−60	−23
Right	Cerebellum (VIII)		6.1979	28	−55	−53
Sub-lobar						
Left	Midbrain/Thalamus	63	4.8934	−8	−18	−10
Children						
Frontal						
Left	Precentral gyrus	575	10.0246	−50	−5	40
Left	IFG p. opercularis		5.1380	−58	3	23
Left	Posterior medial frontal gyrus	1,006	8.8030	−8	8	50
Left	Anterior cingulum lobule		7.1821	−8	20	28
Right	Anterior Cingulate cortex		4.4394	8	40	23
Left	Insula	344	6.5768	−35	15	13
Left	IFG p. triangularis		3.4915	−53	18	−8
Right	Insula	247	5.9461	30	18	−10
Right	Insula		5.3397	33	18	13
Left	Superior Frontal gyrus	113	5.0702	−23	−10	50
Right	Middle Frontal Gyrus	88	4.9846	35	25	38
Right	Middle Orbital Gyrus	59	4.3018	38	48	0
Temporal						
Left	Inferior temporal gyrus	93	5.4017	−53	−55	−15
Cerebellum						
Right	Cerebellum (VI)	1,927	12.3139	25	−60	−25
Right	Cerebellum (X)		8.2758	30	−43	−35
Right	Cerebellar vermis 8		7.7357	3	−68	−35
Left	Cerebellum Crus 1	202	5.3455	−38	−53	−33
Left	Cerebellum (IX)		4.6707	−15	−58	−38
Parietal						
Left	Inferior parietal lobule/Superior parietal lobule	431	6.2417	−28	−65	40

TABLE 1 (Continued)

Location		Cluster size	Stats, *t*-value	MNI Coordinates		
				x	y	z
Left	Inferior parietal lobule		6.0319	−45	−38	45
Right	Inferior parietal lobule	331	5.4119	48	−50	55
Right	Angular gyrus		4.3849	35	−68	50
Sub-lobar						
Left	Thalamus	265	6.6718	−13	−13	8
Left	Midbrain		3.3939	−5	−20	−20
Left	Pons	86	5.2969	−3	−40	−55

vary little between ages 6 and 10 (Grayson & Fair, 2017; Zielinski et al., 2010).

4.2 | Regional differences between adults and children

Despite this generally similar organization, the two groups differed in the involvement of the right anterior cerebellum and the left FuG. In addition, differences between the two groups were found in other brain regions. Prefrontal regions were more strongly mobilized in children than in adults, whereas the right precentral cortex and the SMA were more strongly mobilized in adults than in children.

Interestingly, the effect of condition (writing words or letters) on the BOLD signal was similar for both groups. The middle occipital gyrus was the only region showing an interaction between group and condition. This effect is difficult to interpret given the non-specific function of this region. No interaction was found in the regions of the handwriting network. This might be due to the fact that both tasks are realized frequently at school: the differences in the processes which allow the writing of letters of the alphabet and words corresponding to the days of the week may already be established in 8- to 11-year-old children. Indeed, previous studies have shown that children process orthographic sequences in the same way as adults, when these sequences are frequent (Chase & Tallal, 1990; Gibson et al., 1962; McCandliss et al., 2003). An interaction effect between group and task could perhaps be observed if less frequent words, pseudowords, or words with higher spelling complexity were to be produced. Further neuroimaging research comparing adults and children during the production of various orthographic sequences is needed.

4.3 | Differential cerebellar and fusiform involvement with writing expertise

One portion of the right anterior cerebellum was more strongly activated in the adults than in the children. This part of the right cerebellum is reliably activated in studies involving writing and has been identified as specific to writing, relative to other manual motor

tasks (Planton et al., 2013). Case studies have shown that lesions in the right cerebellum can induce apraxic agraphia, in which patients can no longer access previously mastered motor programs (De Smet et al., 2011). More generally, researchers from the field of motor control assign to the cerebellum a role in the implementation of internal models that allow an automatic proactive movement coupled with performance monitoring (Koziol et al., 2014; Manto et al., 2012; Wolpert et al., 1998). This result therefore points towards the major role of the cerebellum in the acquisition of writing skills. Increasing reliance on a cortico-cerebellar loop with writing acquisition is predicted by the computational model of Grossberg and Paine (2000).

Group differences were also found in the left FuG with stronger activation for children than adults. Several studies have shown that the specificity of the left occipitotemporal region for letter strings emerges with reading acquisition (Brem et al., 2010; Centanni et al., 2017; Dehaene-Lambertz et al., 2018; Hannagan et al., 2015) and that the strength of activation correlates with the level of acquisition (McCandliss et al., 2003). The present finding of a stronger fusiform activation during writing in children than in adults might thus seem counterintuitive. In reading studies, the acquisition of functional specificity has been evidenced in younger children (James, 2010; James & Engelhardt, 2012). The involvement of the left FuG in writing acquisition has previously been suggested by Richards et al., (2011); in their study, the activation of this region differed between good and poor writers, and correlated with writing proficiency and spelling skills. It is thus possible that the maturation of the functional properties of the left FuG occurs in different time-windows for writing and reading. Further experiments comparing the role of this region in reading and writing processes, with various control conditions, and in different age groups, would be useful to explore this important issue.

4.4 | Other differences between adults and children

The stronger activation of the IFG pars opercularis/insula and of the ACC in children is another important result of the present study. With its ideal connection to the motor cortex, the ACC plays a prominent role in online monitoring, primordial in motor learning,
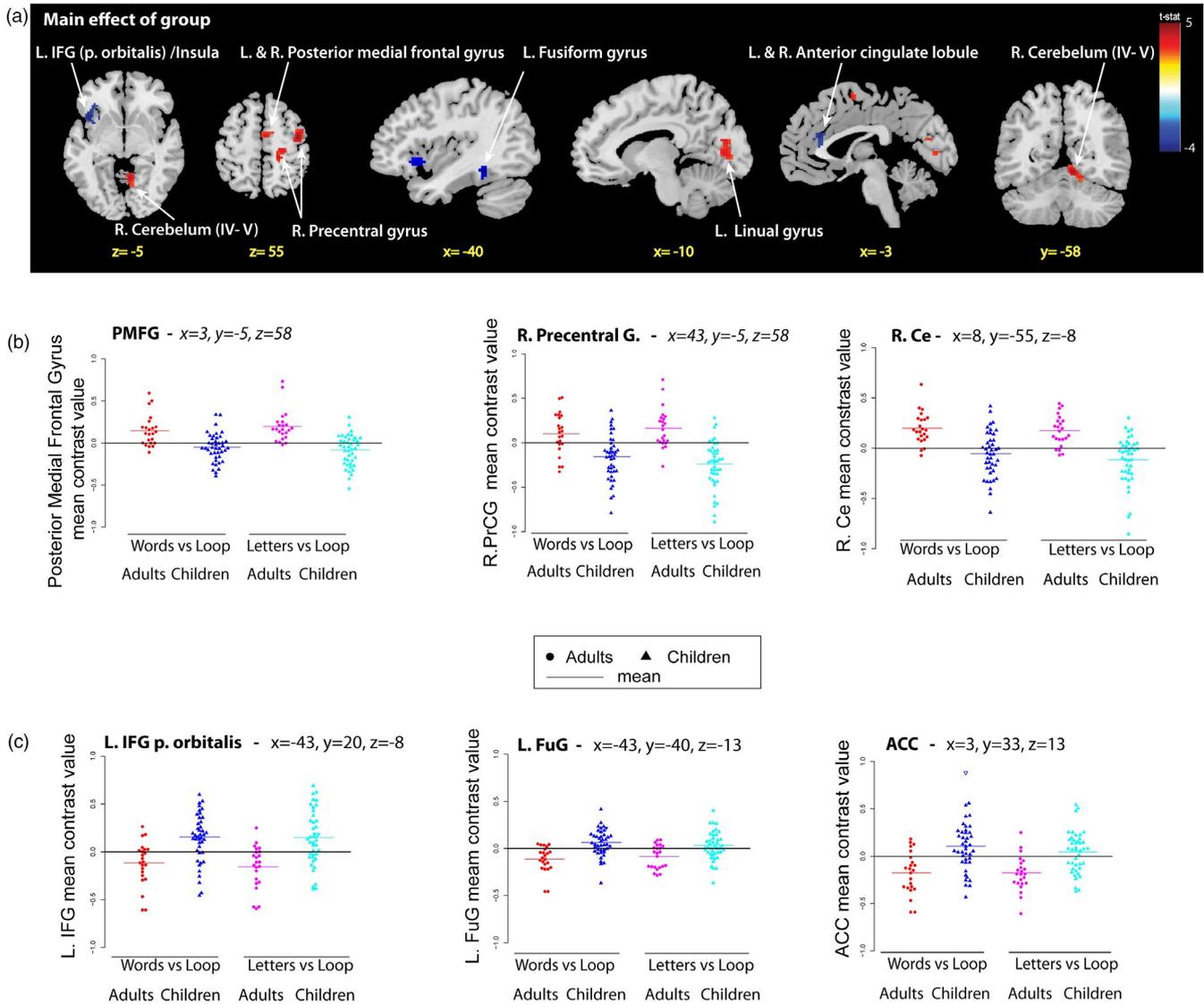
FIGURE 3 Results of the whole brain contrast for the main effect of group, and mean contrast values in the activated clusters. (a) Blue: regions preferentially activated for children. Red: regions preferentially activated for adults, displayed on axial, sagittal, and coronal slices. (b & c) Individual mean contrast values for several of the regions presenting group differences. b – Regions preferentially activated for adults and c – Regions preferentially activated for children. Results are displayed for the two contrasts: Words versus Loops (red and blue) and Letters versus Loops (pink and cyan), and for the two groups: Adults (dots) and Children (triangles). The mean values for each contrast are represented by a line of the corresponding color. The contrasts are displayed at a threshold of $p < .001$, uncorrected for multiple comparisons at the voxel-level and $p < .05$, FWE-corrected for multiple comparisons at the cluster-level. Mean contrast value for each cluster has been extracted from the individual contrasts computed at the first level using the SPM12 MarsBar toolbox. Abbreviations: R: right; L: left; G: gyrus; IFG: inferior frontal gyrus; PMFG: posterior medial frontal gyrus; Ce: cerebellum; FuG: fusiform gyrus; ACC: anterior cingulate lobule.

and in complex motor control (Carter, 1998; Gehring et al., 1993; MacDonald, 2000). In children, the structural patterns of the ACC are related to cognitive control efficiency (Cachia et al., 2014). The anterior insula is also implicated in performance monitoring as well as in domain general focal attention (Klein et al., 2013; Nelson et al., 2010). The combined stronger activation of the insula and the ACC in children could therefore be compatible with a performance monitoring account, with this system engaged in children but not in adults during writing. Alternatively, these activations could relate to

additional linguistic processing in the child group: in children aged around 11, the two regions are commonly activated in spelling and phonological tasks, and their response is sensitive to the conflict between phonological and orthographic information (Bitan et al., 2007). Furthermore, the study of Gimenez et al. (2014) pointed towards a role of the IFG/insula in the link between phonological processing and writing proficiency in children.

Two motor areas (supplementary motor area (SMA), and the right precentral gyrus) were found to be preferentially activated

TABLE 2 Results of the main effect of group at the whole brain level, MNI space, $p < .05$, FWE-corrected for multiple comparisons at the voxel- and cluster-level. The "Contrast" column shows significant pairwise t-tests between Adults and Children for voxels located at the local maxima ($p < .001$).

| Location		Cluster size	Stats, t-value	MNI Coordinates			Contrasts
				x	y	z	
Main effect of group							
Frontal							
Right	Precentral gyrus	161	5.5472	38	−10	50	Adults versus children
Right	Precentral gyrus	152	4.7785	20	−33	55	Adults versus children
Right/Left	Posterior medial frontal gyrus		4.5594	3	−5	58	Adults versus children
Right	Superior frontal gyrus		3.9558	20	−18	70	Adults versus children
Left	Inferior frontal gyrus (pars Orbitalis)/Insula	76	4.4635	−43	18	−5	Children versus adults
Left	Anterior Cingulate lobule	76	4.1973	−3	33	23	Children versus adults
Temporal							
Left	Fusiform gyrus (SVC)	38	4.7512	−40	−40	−13	Children versus adults
Occipital							
Left	Lingual gyrus/Calcarine	126	4.3426	−10	−78	5	Adults versus children
Cerebellum							
Right	Anterior cerebellar lobule (IV–V)	134	5.1063	8	−58	−8	Adults versus children
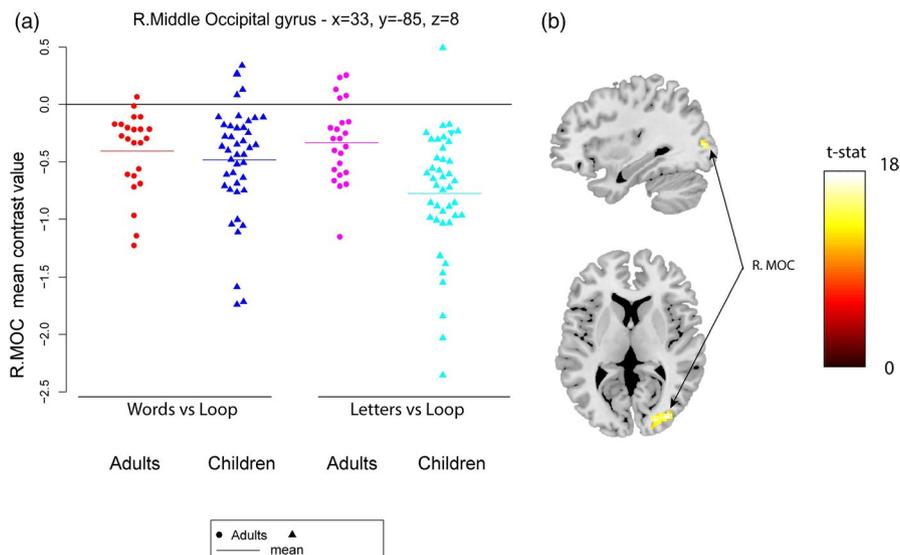
FIGURE 4 Interaction between Group and Condition in the right middle occipital gyrus (a) Position and t-stat of the activation of the right middle occipital cortex on sagittal (top) and axial (bottom) slices. (b) Individual contrast values within the middle occipital cluster. Results are displayed for the two contrasts: Words versus Loops (red and blue) and Letters versus Loops (pink and cyan) and for the two groups: Adults (dots) and Children (triangle). The contrasts are displayed at a threshold of $p < .001$, uncorrected for multiple comparisons at the voxel-level and $p < .05$, FWE-corrected for multiple comparisons at the cluster-level. Mean contrast value for each cluster has been extracted from the individual contrasts computed at the first level using the SPM12 MarsBar toolbox. Abbreviations: R: right; MOC: middle occipital cortex.
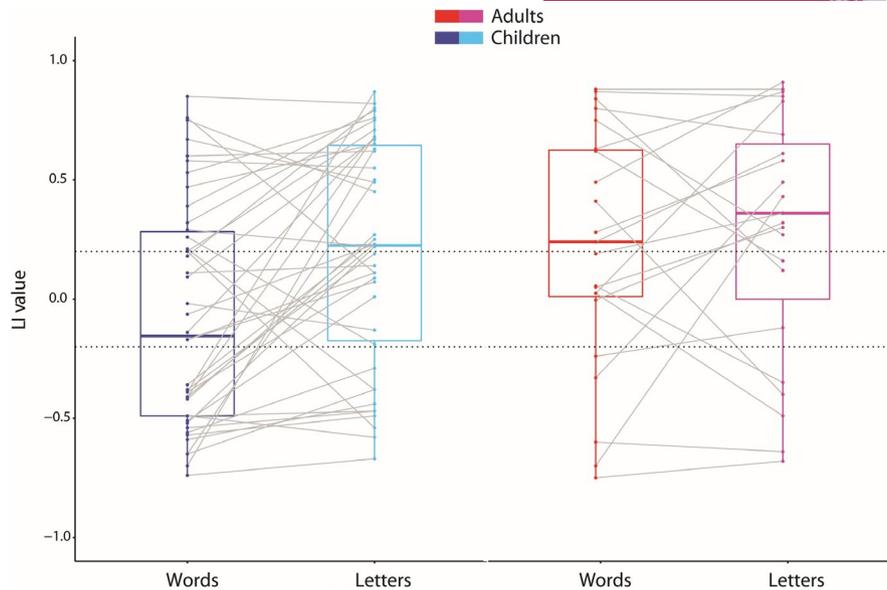
FIGURE 5 Results of the laterality analysis. Laterality indexes are displayed for all participants for the two contrasts: Words versus Loops and Letters versus Loops and for the two groups: Adults (red and pink) and Children (blue and cyan). The median values and the quartiles for each contrast are represented by a boxplot superimposed on the individual values. The dotted lines mark the values that correspond to thresholds for left (LI > 0.2) and right (LI < −0.2) lateralization.

for adults. The SMA is involved in movement control; its activation is reliably observed in writing tasks but its contribution is considered non-specific (Palmis et al., 2019; Purcell, Napoliello, et al., 2011; Rapp & Dufor, 2011; Rapp et al., 2016). More generally, it is often mobilized in language production tasks (Longcamp et al., 2019). Its stronger activation in expert adults is consistent with studies showing its critical role in coordination with complex and overlearned movements (Gerloff, 1997; Goldberg, 1985; Toni et al., 1998).

The ipsilateral precentral gyrus is reliably found activated during unimanual tasks. Its involvement has been interpreted as the result of an interhemispheric balance that promotes better control of movement. Several studies have evidenced ipsilateral BOLD activations for more complex tasks or for tasks with increased demands in precision (Buetefisch et al., 2014; Verstynen et al., 2005). fMRI does not discriminate neural excitation from neural inhibition, thus the exact functional role of the ipsilateral activation in unimanual tasks is not completely clear. However, TMS investigations have shown that the inhibition of motor cortex ipsilateral to the hand realizing the task improves the performance (Buetefisch et al., 2011; Kobayashi et al., 2003). Thus, learning to write could be associated with a better mobilization of the ipsilateral motor cortex. Furthermore, the primary motor cortex is the locus of important plastic changes with motor learning (Galea et al., 2011; Hardwick et al., 2013; Pascual-Leone et al., 1995). Even if it is not considered as being part of the core of the handwriting network, several studies have demonstrated its preferential activity for handwriting over motor control tasks (Kadmon Harpaz et al., 2014; Planton et al., 2017; Purcell, Napoliello, et al., 2011). This could suggest a greater role of the primary motor cortex in expert handwriting than usually thought.

4.5 | Lack of leftward lateralization in the words writing condition in children

Finally, the lateralization analysis indicates that the hemispheric activations induced by the tasks were balanced differently in the two groups. This is in line with previous data showing an evolution of lateralization patterns with cognitive development (Szaflarski et al., 2006) and a relationship between lateralization and task performance from late childhood to adolescence (Everts et al., 2009). This also confirms that proficiency in writing could be indexed by the lateralization of the networks involved in the task (Planton et al., 2017). From that perspective, the difference in lateralization between the two tasks in children, and the difference between children and adults during words writing are noteworthy. This distinct lateralization pattern for words in children could suggest that the brain networks underlying writing are less mature for the production of words than letters in middle school-aged children. Possibly, this occurs because words have a stronger linguistic component: Everts et al. (2009) showed that the functional asymmetry induced by a word production task continues to increase during adolescence.

4.6 | Possible confounds in the interpretation of the present results

The interpretation of the present results, nonetheless, has some limitations, as would any brain imaging study in children.

The first possible confound is the general difference in task difficulty for the two groups. This raises a question on the nature of the activation of prefrontal regions. Although we made sure that the absence of visual feedback was not disabling for the performance

of the two groups, maybe writing while lying down in the scanner environment is a source of more difficulties for children than adults (Chartrel & Vinter, 2006; van Doorn & Keuss, 1993). Thus, prefrontal activations could highlight a compensatory recruitment of regions involved in attention and monitoring due to the difficulty induced by the absence of feedback. However, it is important to point out that although there is an overall difference in performance between adults and children, the patterns of behavioral differences between the conditions of interest and the control conditions are similar for both groups. It is therefore unlikely that the effects are related to differences in the general task difficulty between groups. Further investigations are necessary to determine whether the differential implication of the ACC and inferior frontal cortices in the task for the two groups is related to a difference in the nature of the control processes implemented specifically for writing, or whether it is "artifactual" (induced by the particular conditions of writing in an unusual posture).

Another important possible confound is the difference in head movements between the two groups. Increased noise due to head movements in children has been counterbalanced by a larger number of participants included in this group. In addition, careful data de-noising and verification procedures were implemented to minimize the possible effects of noise induced by head movements. However, the fact remains that the possible effects of head movements are a major drawback of any brain imaging study that compares adult to child participants.

A final possible confound regarding both the behavioral and fMRI data is the writing style used by our participants. All the children still followed the French school guidelines and wrote in cursive, whereas the adults wrote using a mix of cursive and script. The choice of this mixed style by many French adults may support the optimization of writing performance (van der Plaats & van Galen, 1991). It is thus difficult to fully distinguish the contribution of this change in writing style from the differences observed between adults and children in the present study. At the brain level, the existence of specific neural correlates of allographic selection is debated; studies where this aspect has been specifically tested (Rapp & Dufor, 2011; Rapp & Lipka, 2011) did not evidence any association between patterns of brain activation and the selection of letter case.

5 | CONCLUSION

The handwriting network of adults and of typical 8- to 11-year-old children is composed of the same five key regions. The organization of the main handwriting network of children is thus already established and very similar to that of adults. Despite this general similarity, our data point towards a major role of the cerebellum, primary motor cortex, and prefrontal regions in the acquisition of writing skills. In addition, they highlight a complex pattern of maturation in the FuG with writing acquisition, and a specific lateralization profile for the words writing task in children. This first study of the neural underpinning of writing in typically developing children opens important perspectives for the study of brain specificities in children with orthographic or motor learning difficulties during writing tasks.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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