Writing-specific sites in frontal areas: a cortical stimulation study

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Object. The aim of this study was to determine whether cortical areas involved in the writing process are associated with reading or naming areas in patients undergoing surgery for brain tumors in frontal areas. This study was undertaken to spare all language areas found in patients during surgery.

Methods. Fourteen patients (eight women and six men [mean age 47 years] of whom 12 were right handed, two left handed, 12 monolingual, and two bilingual) who harbored brain tumors in the left (11 patients) or right (three patients) frontal gyri or in Rolandic areas, were tested by direct stimulation by using the awake surgery technique for direct brain mapping. Mapping of the frontal gyri was performed using naming, reading, and writing under dictation tasks in the appropriate language(s).

Considerable individual variability in language organization among patients was observed. Interferences in writing were found during direct stimulation in the frontal gyri, in cortical sites common or not common to interferences in naming or reading. In dominant regions, patterns of writing dysfunctions were variable and included writing arrest, illegible script, letter omissions, and paragraphia. These dysfunctions were nonspecific (stimulation-induced eye movements) in nondominant frontal regions and in Rolandic gyri (hand contractions). In the same patient, different writing impairments could sometimes be observed during stimulation of different sites. As is the case for naming or reading interference sites, writing interference sites could be extremely localized (1 cm² in diameter). In this group of patients, writing interference sites found in Broca areas were associated with other sites of language interference, whereas writing-specific interference sites were found twice in the dominant middle frontal gyrus.

Conclusions. In this series, we found that writing interference sites could be detected by direct cortical stimulation in dominant inferior and middle frontal gyri regardless of whether they were associated with naming or reading interference sites. Writing disorders elicited by direct stimulation in the frontal lobes are varied and probably depend on the functional status of the stimulated cortical area.

KEY WORDS • Exner area • writing-specific site • agraphia • brain mapping • cortical stimulation

In the second half of the 19th century, following works by Broca and Wernicke on language organization, several authors postulated that other aspects of language, such as reading and writing, could also be sustained by specific brain areas. Characterized as possibly specific disorders, writing disorders (agraphia) were described by some authors as early as the 1860s. Shortly thereafter, in 1881, Sigmund Exner reported on patients with brain lesions and isolated symptoms of agraphia. He postulated that lesions of the foot of the F2 could specifically produce writing impairments and attributed to this area the role of writing center. Since then, several other cortical zones, such as the dominant inferior parietal lobe, have also been hypothesized as being more specifically involved in writing. Modern approaches to brain organization with regard to writing schematically differentiate between a lexical system (based on whole-word retrieval involved in writing regular or irregular words) and a phonological system used to write unfamiliar words or pseudowords. In addition to this functional distinction, these two systems could be represented in different anatomical locations: a lesion of the angular gyrus leading to lexical agraphia and a lesion of the supramarginal gyrus causing phonological agraphia. In frontal areas, however, the existence of a specific writing center as defined by Exner lent itself to debate and is still contested.

Even though modern functional studies performed using fMRI imaging or positron emission tomography have sometimes been used to study brain organization of writing in the context of the dual writing code used in Japanese (Kanji versus Kana), direct cortical stimulation has rarely been used to test writing in patients undergoing neurosurgery. In this study, we analyzed results obtained
in 14 European language–speaking patients with brain tumors in whom direct cortical stimulation was used to detect writing areas in frontal regions.

**Clinical Material and Methods**

**Patient Population**

Between May 1999 and January 2004, we used intraoperative direct cortical stimulation in 14 patients with brain tumors (mean age 47 years; range 14–75 years) by using writing tasks. The goal of these brain mapping studies was to spare all language areas found during tumor removal. These patients were asked to perform naming, reading, and writing tasks while we performed surgery in the frontal gyri after standard mapping of the rolandic area, because the tumors were close to presumed Exner and Broca areas or close to the precentral gyrus. As suggested by other authors,42 it has been the policy of our department to perform, when feasible, the awake surgery technique with direct brain mapping in patients with brain tumors in whom functional areas are potentially at risk during surgery. Although infrequent, the right hemisphere can sometimes be involved in some language or neurocognitive tasks.5 Accordingly, some selected patients with brain tumors in the right hemisphere (for which removal was expected to be delicate for reasons such as mapping of the rolandic area was required or a bilateral language representation was suspected) were offered awake surgery with our standard brain mapping technique.17 We think that dominant and nondominant rolandic areas are better studied when patients perform naming or reading tasks for parts related to face or tongue movements and when they use hand movements for parts related to hand functions. The group of patients studied was heterogeneous in handedness and hemispheric lateralization of operated lesions. The dominant left frontal gyri was studied in 10 right-handed patients and the right frontal and precentral gyri were studied by cortical mapping in two other right-handed patients. In the two remaining left-handed patients the left and right frontal gyri were studied, respectively.

**Preoperative and Postoperative Assessments**

All patients in this series underwent pre- and postoperative language examinations to rule out specific language deficits. This testing, which involved all languages used by the patients, included the evaluation of written and oral understanding, naming, oral fluency, reading, dictation, repetition, written transcription, calculation, and object handling by using appropriate tests.10 These tests were standardized for all patients and have been used for many years by speech therapists and neurologists at our institution who specialize in aphasic disorders. We used a short version of the Boston Naming Test, which contains 50 items that the patient has to name so that a naming or aphasic disorder can be detected immediately. Possible category-specific defects were also evaluated with a subset of specific naming categories (vegetables, wild animals, tools, and so forth). Writing was evaluated by dictating short sentences to patients. The numbers of errors and the patients’ handwritten calligraphy were evaluated both quantitatively and qualitatively (by comparing pre- and postoperative handwriting samples). Writing was also evaluated by asking patients to copy written material, such as isolated letters, words, and numbers. Dysphasic patients in whom the number of errors increased by greater than 10% in the naming tests were excluded from this study. The degree of handedness of the patients was assessed using the Edinburgh Handedness Inventory test.29 Handedness was assessed (from +100 for completely right-handed patients to −100 for completely left-handed patients) by asking patients what hand they usually prefer to use to perform various daily acts. Twelve of our patients were right handed and the other two were strongly left handed. All but two patients were natives of France. One of these, born in Morocco, learned Arabic as a first language but spoke, read, and wrote French fluently. Another patient, 67 years of age, whose first language was English, was an English–French interpreter in the British Army. After retiring from the army, he came to live in southern France. He also spoke, read, and wrote French fluently. Postoperatively as well as preoperatively, the patients were asked to perform the same tests so that any language problem might be checked. The results (with special mention of possible writing difficulties based on the intraoperative findings) were compared.

**Cortical Mapping Procedures**

The patients all underwent surgery in which the awake surgery technique was used.29,40 They were each placed supine and a three-point head fixation device was applied. After their heads were fixed and rotated 30˚ opposite to the side of the craniotomy, their heads and shoulders were slightly raised (a 10–20˚ incline) so that they could feel comfortable and be able to watch their hands while writing. We used a neuronavigational system (Stealth Station; Sofamor Danek, Surgical Navigation Technologies, Broomfield, CO) in all patients. The brain was exposed in a standard fashion. Intraoperative cortical stimulation was used to localize areas of the functional cortex after the afterdischarge threshold was determined using electrocorticography. The cortex was directly stimulated by using the bipolar electrode of a cortical stimulator (1-mm electrodes separated by 5 mm; Newmedic International s.a.s., Toulouse, France). The current amplitude was progressively increased by 1 mA increments beginning at 2 mA. We used a procedure of stimulation that included biphasic square wave pulses of 1 msec at 60 Hz, with a maximum train duration of 4 seconds. Anatomical relationships among the rolandic sulcus, the precentral gyrus, and the F3, F2, and F1 regions were defined by means of neuronavigation using 3D reconstructions of the brain. During surgery, the patients were initially asked to perform two different tasks: a naming task to search for an anomia (that is, “This is a . . .”) and a reading task (that is, various basic sentences that had no connection among them and had not been previously rehearsed). Then the patients were asked to write a dictated text by using the hand they usually used for writing. The patients used a pencil to write horizontally on A4 sheets of paper, which lay on a stiff pad that a nurse had presented to them vertically. The patients could see what they were writing when something was dictated. Cortical sites (on F1, F2, and F3) were randomly selected and tested under direct stimulation during the naming, reading, and writing tasks. For the writing task, we started dictating a sentence at each given cortical site and direct
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stimulation was applied for less than 4 seconds while the patients were writing. Induced difficulties were pointed out to the surgeon. When a functional site was located, it was marked by a 0.25-cm² sterile label and another area was tested. Our strategy was to spare the language areas found using this test during tumor removal by avoiding resection of tumor tissue located within 1 cm from eloquent cortex (distance between the resection margin and the nearest functional site). All the patients and their families gave their informed consent to this study of language areas by direct brain mapping.

Conditions of Validation

To be accepted as a language location, the language sites that we located were meticulously tested at least three times. Sites that did not demonstrate any reproducible language interference were not included in this study. Intraoperative photographs of the brain were obtained, demonstrating sites of positive cortical stimulation—those marked L for a language-essential site (a naming interference site as defined by Ojemann, et al.29), R for a reading-interference site, and W for a writing-interference site) sites that produced no change or interference in language were marked N. For the sake of clarity of the intraoperative pictures, cortical sites producing no naming, reading, or writing impairments were not all systematically noted by a sterile label. The cortical mapping procedures were all videotaped, the patients’ oral answers were recorded using a microphone placed near their mouths (as evidence of each patient’s cortical organization and so that the patient’s responses could be further analyzed in team meetings), and the writing production of the patients was recorded as well. Finally, it must be emphasized that we qualified a site as “writing-specific” when no interference in naming or reading was found at that site; however, we cannot completely exclude the possibility that other functions not tested in this study could be revealed by stimulation in our writing-specific sites.

Results

Each of our 14 patients underwent three different brain mapping studies in which naming, reading, and writing tasks were conducted in French. In Cases 2 and 14, naming, reading, and writing tasks were also tested in Arabic and English, respectively. In all, 48 different brain mapping studies were performed and 26 functional sites were found (23 in frontal areas, one in the superior temporal gyrus, and two in additional sites for the second language). All the patients in this series were very cooperative in performing all tasks. The difficulty in tumor removal mainly depended on the presence of language areas in the surgically treated region. In this series, the total number of cortical sites studied for each patient varied from eight to 22 (mean 14). Three gyri—F1, F2, and F3—were studied using cortical stimulation mainly in their posterior portions, within a limit of 6 cm from the precentral sulcus.

Interference in naming or reading, which were not due to eye-induced movements, were found 15 times and interference in writing, also not due to eye-induced movements, 16 times (two times in one bilingual patient [Case 2]) in common or different frontal sites. Repeated eye movements, which were not directly classified as interferences in speech, were also identified and were mainly located in the F2. These eye movements, which were induced by stimulation of frontal areas (as in Cases 6, 8, 9, and 11–14) impaired normal reading and/or writing. Vocalization phenomena were found twice when stimulation was delivered over the precentral gyrus but they were very brief. For all patients in this study, the strongest current that did not evoke afterdischarges ranged between 3 and 6.5 mA. No patient experienced a generalized seizure intraoperatively. Stimulation over the precentral gyrus, and sometimes over the postcentral gyrus, led to interferences in articulation (also called “motor” effects) accompanied by a sharp speech arrest with mouth or face contractions. In this study, these cortical sites located within the pre- and postcentral gyri were not included in the data in this study. Descriptions of brain mapping studies, patients, and examples of interferences in writing are summarized in Figs. 1 and 2 and in Table 1.

Naming and Reading Tasks

Naming and reading tasks were performed normally in all patients in this series, but at least one naming or reading interference site was found in all patients, some of which were associated with eye-induced movements. Naming and reading interference sites were generally located in common sites but were sometimes task specific. In the frontal gyri (F3, F2, and F1), interference in naming consisted of pure anomia (the patient said: “I know the name but I can’t pronounce it . . .” or “Yes, this is a . . . what’s the name? . . . A . . .”) or speech arrest without perceptible face or tongue contractions. Anomia sites were generally found in the dominant F3. Interferences in reading were composed of reading arrest, paraphasias, or repetitive hesitation during reading. They were usually found in dominant F2s and F3s. Eye movements were mainly associated with sites in the F2, and with impaired naming and especially reading.

Writing Tasks: Overall Results

Writing interference sites (with no visible hand contraction) were found in frontal areas in all but two patients (Cases 7 and 13). In the following section we focus on writing interference data found in the F1, F2, and F3 regions. Writing impairments were also found during stimulation over the hand area in the precentral gyrus but were

<table>
<thead>
<tr>
<th>Type of Writing Error</th>
<th>No. of Patients</th>
<th>Location of Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>writing arrest</td>
<td>4</td>
<td>F1 0 F2 3 F3 1</td>
</tr>
<tr>
<td>word or letter substit.</td>
<td>4</td>
<td>F1 0 F2 2 F3 2</td>
</tr>
<tr>
<td>illegible script</td>
<td>3</td>
<td>F1 0 F2 1 F3 2</td>
</tr>
<tr>
<td>perseveration</td>
<td>2</td>
<td>F1 0 F2 2 F3 0</td>
</tr>
<tr>
<td>paragraphia</td>
<td>1</td>
<td>F1 0 F2 0 F3 1</td>
</tr>
</tbody>
</table>

*For each patient, different types of errors could be found. Nonspecific errors due to eye movements are not included in this table.
due to hand or finger contraction; this type of interference was considered nonspecific.

None of our patients had the same pattern of language cortical organization; that is, none of them had the exact same localization for naming, reading, and writing interference areas. A high variability in language organization among patients was found, even in well-defined language areas such as the Broca area. For instance, when the Broca area could be tested, we did not always find essential language or writing sites in this area, as in Cases 7 and 8.

The interferences in writing that we observed and their apparent causes varied. The shape and organization of writing during the operation had to be cautiously analyzed because patients were not in as comfortable a writing position as they had been during preoperative tests. In the F1, F2, and F3 regions, interferences in writing during cortical stimulation varied and consisted of writing arrests, irregular letter shapes, errors in letter selection, repetitions, or paragraphias. In a given patient, different writing impairments could be observed during stimulation of different sites.

Writing interference sites could be common to naming or reading interference sites, but sometimes they were specific to writing (as in Cases 1 and 2). Among 23 writing interference sites found in frontal areas and one site in the temporal lobe (Case 7), two were writing specific (both in F2); five included impaired writing and reading equally; nine included impaired writing, reading, and also naming; and eight dealt with eye movements. In our two bilingual patients, the writing impairments induced by stimulation were similar in both languages (letter substitutions in Case 2 and illegible scripts in Case 14 due to eye movements).

Finally, writing interference sites were extremely localized (1 cm² in diameter). As in naming or reading interference sites, the margins of these writing interference sites were usually sharply defined, with displacement of an electrode in an adjacent cortical area located in the same gyrus producing no more interference.

Writing Tasks: Specific Results

In this section we describe specific writing impairments found in our patients according to their handedness and the region studied.

During stimulation over the dominant F2 region in the patients in Cases 1 and 2, we found irregular handwriting and occasionally words that were impossible to decipher. The main feature of these patients’ writing disturbances was orthographic errors involving incorrect letter selections or phonemic substitutions. In the patient in Case 2, these error patterns were observed both in French and in Arabic (Fig. 3). In Cases 4 and 6, writing disturbances during stimulation over dominant F2 regions involved letter or word repetitions, use of upper-case letters within words, or writing arrest.

Stimulation over dominant F3 regions led to different results: in Cases 3 and 10, the stimulation of different cortical sites over this area produced different types of writing.
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<table>
<thead>
<tr>
<th>Case No.</th>
<th>Patients Handed</th>
<th>Gyri studied by direct stimulation - Type of tumor</th>
<th>Type of writing impairment found during stimulation of frontal areas</th>
<th>Examples of text dictated - Underlined: stimulation</th>
<th>Examples of writing interferences or of no writing impairment (cases 7, 11, 13) in frontal areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35/F Right handed (+90)*</td>
<td>Left frontal/ F2 - Atypical meningioma</td>
<td>1) Substituted or omitted letters</td>
<td>Le livre et le lis. Imaginez le a ma place. Un peu de rien du tout.</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>47/F Right handed (+90)*</td>
<td>Left frontal/ F2 and F1 - Metastasis</td>
<td>1) Substituted letters (French- Arabic) 2) Writing arrest (French)</td>
<td>French/Arabic: La voiture est bleue ou rouge. J'aime bien cette musique.</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>50/F Right handed (+100)*</td>
<td>Left frontal/ F2 and F3 - Cavernoma</td>
<td>1) Word substitution 2) Paragraphias 3) Illegible script</td>
<td>La chaise est jolie. Le vent du nord souffle fort. L'éléphant d'Afrique. J'aime bien cette musique.</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>14/F Right handed (+90)*</td>
<td>Left frontal/ F1 and F2 - Astrocytoma grade III WHO</td>
<td>1) Perseverated letters</td>
<td>Le pain tendre est bon. Le vent.</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>67/F Right handed (+100)*</td>
<td>Left frontal/ F3 - Astrocytoma grade III WHO</td>
<td>1) Illegible script</td>
<td>Silence d'or. J'ai repoussé mon fusil</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>50/M Right handed (+80)*</td>
<td>Left frontal/ F1 and F2 - Astrocytoma grade III WHO</td>
<td>1) Writing arrest 2) Perseverated words</td>
<td>La chaise est jolie. Le vent du nord souffle fort. Le pain tendre est bon.</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>75/M Right handed (+60)*</td>
<td>Left frontal/ F3 - Astrocytoma grade IV WHO</td>
<td>No impairment in frontal areas</td>
<td>La chaise est jolie. Le vent du nord souffle fort. L'éléphant d'Afrique a de</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 2. Data on interference in patients’ writing during stimulation of the F1 through F3. Asterisk indicates that the Edinburgh Handedness Inventory test was used. Dagger indicates that typical paraphasias were found when there was stimulation of a cortical site in the superior temporal gyrus. WHO = World Health Organization.
During stimulation of this site the patient was unable to read what she had just written.

In Case 12, in which the right hemisphere was studied while the patient was writing with her left hand, the stimulation caused writing impairments (illegible script) over a cortical area (the right F2) along with reading arrests and induced eye movements.

In Cases 13 and 14, in which the right hemisphere was studied while the patients were writing with their right hands, stimulation over the posterior portion of the right F2 and the precentral gyrus did not specifically disturb writing (no semantic, orthographic, or other writing disturbance); writing was only disturbed by stimulation-induced eye movements.

**Postoperative Evaluation**

All our patients underwent a postoperative language ev-

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<table>
<thead>
<tr>
<th>Case No.</th>
<th>Patients Handedness</th>
<th>Gyri studied by direct stimulation - Type of tumor</th>
<th>Type of writing impairment found during stimulation of frontal areas</th>
<th>Examples</th>
<th>Examples of text dictated - Underlined: stimulation</th>
<th>Examples of writing interferences or of no writing impairment during stimulation (cases 7, 11, 13) in frontal areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>52/F Right handed (+30)*</td>
<td>Left frontal/F1 and F2 – Astrocytoma grade III WHO</td>
<td>1) No specific impairment except when induced eye movements - example here (Writing arrest)</td>
<td>D’Afrique, <em>je suis arrivé.</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>39/M Left handed (+50)*</td>
<td>Left frontal/ F2 and F3 – Metastasis</td>
<td>1) Illegible script</td>
<td><em>La voiture est bleue ou rouge</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>22/M Right handed (+100)*</td>
<td>Left frontal/ F2 and F3 – Ganglioloma</td>
<td>1) Word or letter substitution 2) Writing arrest</td>
<td><em>Le vent du nord souffle fort.</em>  <em>L’éléphant d’Afrique</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>35/F Right handed (+100)*</td>
<td>Left frontal/ F2 and F3 – Cavernoma</td>
<td>No impairment except when induced eye movements</td>
<td><em>Le pain tendre est bon.</em>  <em>Le vent du nord souffle fort.</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>43/F Left handed (-80)*</td>
<td>Right frontal F1 and F2 – Astrocytoma grade III WHO</td>
<td>1) Writing arrest</td>
<td><em>La chaise est jolie. Le pain tendre est bon.</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>68/M Right handed (+90)*</td>
<td>Right frontal F1 and F2 – Metastasis</td>
<td>No impairment except when induced eye movements</td>
<td><em>Je suis au fond du jardin.</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>67/M Right handed (+90)*</td>
<td>Right frontal F1, F2, and F3 – Metastasis</td>
<td>No specific impairment (French-English) except when induced eye movements - example here in English.</td>
<td>_French: _la chaise est jolie. English: <em>I grew up in the Falklands</em> (without and after induced eye movements)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Fig. 2. (continued, see p 797).**
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Fig. 3. Case 2. Location and patterns of writing interference in the F2 in a 47-year-old bilingual (French–Arabic) right-handed woman with a small left rolandic lesion (metastasis) in the upper portion of the precentral sulcus, who experienced a single partial seizure. Born in Morocco, this patient lived in France for many decades and wrote and spoke both languages fluently. No aphasic disorder or hand motor deficit was noted preoperatively. A: Examples of preoperative handwriting in French and Arabic. The patient exhibited no writing disorder; her calligraphy was preserved and she had no difficulty writing in response to dictation or while copying a text (either in French or in Arabic). B: Intraoperative photograph showing a zone (W) in which the patient displayed several writing problems in both French and Arabic (intensity of stimulation 3.6 mA). This zone is located at the foot of the F2, according to the probe of the neuronavigational system with 3D anatomical reconstructions. Stimulation over the precentral gyrus identified the hand area (H) contraction of individual or all fingers and a thumb area (T). Blue thread indicates the rolandic sulcus. C: Orthographic errors, letter substitutions, or repetitions were noted in both French and Arabic (underlined in red). No speech impairment was noted in this zone. D: Stimulation of another zone [N] produced no writing disorder under stimulation. E: Three-dimensional intraoperative reconstruction of the patient’s brain showing the neuronavigational probe over the exact area where interferences in writing were found.

Two days after surgery, one patient (Case 3) began to display typical expressive aphasia, making grammatical errors and neologisms although her letters were well shaped (Figs. 4 and 5). These symptoms disappeared 1 week after surgery and everything went well after 6 weeks. In Case 4, the patient’s handwriting was slightly modified after surgery: she made a few spelling errors and her letters were not as well shaped as they had been preoperatively. In this young patient with a large high-grade astrocytoma, we found a cortical site involved in reading and writing in the left F2. This site was spared although the area of cortectomy was close to it (between 1 and 2 cm). This slight writing disorder persisted 3 weeks postoperatively and was worsened by radiotherapy given to treat her high-grade astrocytoma (Fig. 6). Nevertheless, no deterioration in oral reading was noted in any other patient. Writing was normally performed by all patients postoperatively.
V. Lubrano, F. E. Roux, and J. F. Démonet

Among the abilities acquired by a human being as a result of education, writing is a major step in language acquisition and one of the most complex processes (written words are “symbols of symbols” according to John Hughlings Jackson20), possibly linked to phylogenetically recent cortical zones.11 It involves multiple functional systems, for example, visual or auditory input processing, language analysis, spacial organization of hand gestures, gesture planning, and highly specific hand movements forming letter shapes. Writing includes not only handwriting but also typing (sometimes the primary form of writing in our computer-based modern societies) and remains in practice closely associated with reading. It is worth remembering that there are many writing systems distributed among the world’s languages, spanning from ideographic characters and syllabograms to alphabet letters or number signs. Such a diversity of factors has not made easy the differentiation of the brain’s functional and anatomical substrates of writing. Since the first reports on agraphia,3,14,28 some cases of selective impairments of writing have been observed.17,32 Authors of most of these reports have hypothesized that the functional components of writing could be partially separated into selective pathways within the cerebral lobes.7–9,14,32,35 Indeed, like reading, writing has been postulated to involve a dual route model.2,35,39 Whereas supramarginal and posterior temporal gyri could be the neuroanatomical substrates of the phonological process (sound–letter or phoneme–grapheme conversion), lesions of the angular gyrus were more likely to be involved in symptoms of lexical agraphia (the whole-word retrieval process),2,35,39

language was noted. In Case 9 a left-handed patient who underwent surgery in the right frontal lobe to remove a small lung metastasis from the precentral gyrus, demonstrated incomplete facial palsy 2 months after surgery accompanied by language articulation difficulties (including reading). This patient’s writing was considered normal.

**Discussion**

Among the abilities acquired by a human being as a result of education, writing is a major step in language acquisition and one of the most complex processes (written words are “symbols of symbols” according to John Hughlings Jackson20), possibly linked to phylogenetically recent cortical zones.11 It involves multiple functional systems, for example, visual or auditory input processing, language analysis, spacial organization of hand gestures, gesture planning, and highly specific hand movements forming letter shapes. Writing includes not only handwriting but also typing (sometimes the primary form of writing in our computer-based modern societies) and remains in practice closely associated with reading. It is worth remembering that there are many writing systems distributed among the world’s languages, spanning from ideographic characters and syllabograms to alphabet letters or number signs. Such a diversity of factors has not made easy the differentiation of the brain’s functional and anatomical substrates of writing. Since the first reports on agraphia,3,14,28 some cases of selective impairments of writing have been observed.17,32 Authors of most of these reports have hypothesized that the functional components of writing could be partially separated into selective pathways within the cerebral lobes.7–9,14,32,35 Indeed, like reading, writing has been postulated to involve a dual route model.2,35,39 Whereas supramarginal and posterior temporal gyri could be the neuroanatomical substrates of the phonological process (sound–letter or phoneme–grapheme conversion), lesions of the angular gyrus were more likely to be involved in symptoms of lexical agraphia (the whole-word retrieval process),2,35,39

![Writing Interference Sites](image-url)
After Exner’s formulation, the hypothesis of the existence of a writing center ("graphic motor image center") located in the foot of the F2 received much attention. It was indeed tempting, in decades following the discovery of the Broca area as a premotor region adjacent to the mouth region of the primary motor cortex, to hypothesize that, in the same manner, an area located rostral to the hand area (the Exner area) could be specifically involved in writing. Nevertheless, this hypothesis has been contested and more than 130 years after its initial description, the existence of a writing center in the F2 remains controversial and, until recently, supported by only a few studies.

The main facts leading us to think that a writing center could be specifically localized in the dominant F2 are based on case reports of patients with brain injury who preferentially or specifically lost their ability to write. Pure agraphia (writing impairment with preserved oral language) had been observed in patients with frontal lobe lesions. In clinical practice, symptoms of agraphia, which are usually associated with lesions in the frontal lobes, consist of agrammatic symptoms (a typical syndrome associated with Broca aphasia) or poor grapheme production with letter omissions and substitutions. Gordinier detailed a very interesting case of a woman with a glioma located at the base of the left middle frontal convolution; she had no upper-limb motor deficit and no form of language impairment other than complete agraphia. More recently, among the most striking cases of selective writing impairments, Anderson and colleagues described the case of a woman with a small lesion in the foot of the F2 who had severely impaired letter writing and reading, although she was able to read and write numbers easily. This dissociation between two different language categories is interesting to consider by reference to cases of Japanese patients with frontal lobe damage. Tohgi, et al. described a man with a lesion of the F1 and F2 regions who had a marked preserved ability to write Kanji (ideographic characters), whereas his ability to write Kana (sublexical characters) was perturbed.

In only a few activation studies have the neuroanatomical systems involved in writing been specifically exam-
Interestingly, investigators using fMR imaging have repeatedly found that the anterior portion of the superior parietal lobe and the posterior portions of the F1 and F2 are specifically activated during a writing task. These investigators have postulated that the Exner frontal area could be the substrate of pure agraphia symptoms. Using fMR imaging in 12 volunteers, Matsuo and associates found, along with activations of the fusiform and regions around the intraparietal gyri, significant activation within the frontal lobe of the Exner area.

Direct Cortical Stimulations and Writing

Longer than 40 years after the first report about the use of writing tasks during cortical stimulation in neurosurgical patients, few direct cortical stimulation studies focusing on frontal gyri involvement in the writing process have been published. Lesser, et al., studied oral language and writing functions by using subdural grids in the frontal lobes in three patients. They did not identify a zone that produces writing impairment without concomitant impairment of other motor acts or speech, and they denied that the Exner area could be separated from the Broca area. Penfield and Roberts said that they used writing tasks during some brain mappings, but “the number of such tests were too few to draw general conclusions.” Nevertheless, they asserted that writing arrests were noted in anterior and posterior speech areas. They also agreed that a writing center could be found in the frontal gyri, because one of their patients exhibited transient writing impairments after removal of a lesion from the F2 and F3 regions. These transient postoperative writing disturbances were mainly composed of omitted words within a sentence or badly written words.

The results of direct cortical stimulation in our group of patients showed that interferences with writing could be found during direct stimulation in the posterior portion of the frontal gyri. These interferences in writing were found with a high degree of individual variability; rarely writing specific; variable in their expression (from writing arrest to paragraphia) in dominant regions; and sometimes also due to stimulation-induced eye movements in nondominant or dominant frontal regions. We think that this variability is related to the intrinsic organization of the language cortex and reflects the fact that writing is a complex human function involving several language subcompone-
Writing-specific sites in frontal areas

ments. Furthermore, this highly individual variability in the three language components studied (naming, reading, and writing) among the patients of this series could be considered a limitation in the establishment of a general model of language implementation in the brain.

It must be acknowledged that writing is not always easy to test by direct cortical stimulation because the patients' posture is not truly comfortable. The task also requires a cooperative patient with no significant preoperative motor and language deficits. Furthermore, the fact that the F2 and F3 regions can also be involved in reading or eye movements are factors of confusion in the analysis of specific writing disorders. In this study, we arbitrarily separated the data obtained during stimulation of the precentral gyrus (writing impairment due to hand or finger contractions) from those of the frontal gyri. Nevertheless, considering that the foot of the F2 and the precentral gyrus are considered to be distinct anatomical entities, this distinction could not be substantiated in terms of cytoarchitecture: the border between Brodmann’s Areas 4 and 6 lies within the precentral gyrus. The posterior portion of the precentral gyrus, which is classified as Brodmann Area 4, belongs to the rolandic sulcus. The anterior portion of the precentral gyrus and the foot of the F2 were classified by Brodmann as Area 6. This different cellular organization can clearly be confirmed by direct cortical stimulation: contractions of the whole hand or individual fingers are obtained by applying stimulation close to the rolandic sulcus and much less frequently by applying it close to the precentral sulcus. Additional functional studies (neuroradiographic and/or direct cortical stimulation) could clarify the topography of subareas in the F2 and the precentral gyrus that are responsible for impairments of hand gesture related to writing.

Overall, the small number of patients tested during writing tasks, as described in the literature or in the current study, as well as the high interindividual variability of language organization do not allow us to draw general conclusions about the existence of a writing center in the dominant F2 in all patients. More research has to be done. Nevertheless, because writing can be specifically impaired in some patients in the F2, a writing task could be useful in selected cases during brain mapping when testing dominant F2 regions. On the contrary, in the present study, interferences in writing found in the Broca area were associated with other interferences in language, limiting the real usefulness of writing tasks during direct brain mapping in the dominant F3.

Conclusions

The organization of linguistic functions within the Broca and Exner areas is extremely variable among individuals. Direct cortical stimulation in these regions can disclose small functional areas involved in naming, reading, or writing. Often involved either in naming, reading, or writing tasks, these small functional cortical areas are sometimes task specific. Furthermore, other functional cortical areas can be found within or very close to these regions, such as areas involved in eye movements (in the F2), or articulation or hand movements (in the precentral gyrus). Writing disorders elicited by direct stimulation in the frontal lobes are variable, depending on the functional status of the cortical area that is stimulated and reflecting the complexity of the writing function. Although rare, the finding of writing-specific areas with direct cortical stimulation is possible in the F2. The occurrence of a specific and isolated writing disorder in this region would require a small lesion that damages specific areas involved in the writing process but spares cortical areas involved in other linguistic tasks. This rare condition could explain why writing disorders are rarely found isolated in the Exner area. The authors believe that, in selected patients surgically treated for brain tumor or epilepsy, writing tasks could be used in addition to naming and reading tasks, especially in the dominant F2.

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References


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42. Taylor MD, Bernstein M: Awake craniotomy with brain mapping as the routine surgical approach to treating patients with supratentorial intraxial tumors: a prospective trial of 200 cases. *J Neurosurg* 90:35–41, 1999.


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