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Pure Agraphia Associated with a Frontal Meningioma on Left Superior Frontal Gyrus

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Abstract: *Background*: The existence of cerebral area specifically involved in coding for writing movements in the left middle frontal gyrus is a matter of debate. We present a rare case of pure agraphia associated with a left frontal meningioma. The location of the lesion associated with this disorder could help to feed this debate. *Method*: We report a case of pure agraphia in a 69-year-old man. The patient had a writing disorder evolving over several months with a dominant, left frontal lesion. On neuropsychological evaluation, the writing difficulties were present whatever the nature of the writing (spontaneous, dictation, coping). The writing disorder was isolated, with no features of aphasia, alexia or limb apraxia. Phonological and lexical processing was preserved. The imaging showed a probable frontal meningioma restricted to the foot of the first and second left frontal circumvolutions (MNI coordinates /barycenter of the lesion: x=-19.8, y=1.5, z=52.2). *Results*: The patient was operated and the whole lesion was removed. After surgical resection, the patient's writing disorder improved. Other components of language assessed were the same as before the surgery and showed no disturbances. The pathological study concluded on an OMS grade II atypical meningioma. *Conclusion*: We think that the disorder presented by our patient was related to the disturbance of the frontal graphemic center located in the Exner area. Here, we describe and analyze his condition through a neuro-anatomical and a cognitive approach.

Keywords: Agraphia, Exner, Frontal Graphemic Center

1. Introduction

The term "agraphia" was first used by Ogle in 1867 to describe the inability to write correctly [1]. Less than two decades later, Exner theorized that a writing disorder without any other language impairment could be associated with the lesion of a circumscribed frontal cortical area [2, 3]. Since then, the posterior part of the middle frontal gyrus (corresponding to Brodmann Area 6) has been referred to as the "Exner area" and the concept of "pure agraphia" (written language disorder that occurs without oral language, reading ability, motor ability or praxis being affected) has become a subject of interest.

Although Exner's point of view was supported by some early research, more recent authors associated agraphia with lesions in other brain areas [4–7]. The possibility of finding a writing disorder without any other language impairment was challenged [3] on the basis of surgical and neuroimaging cases. Pure agraphia reports are rare and the existence of a frontal "Graphic motor image center" located in the foot of middle frontal gyrus (as theorized by Exner) is still a matter of debate [7–12].

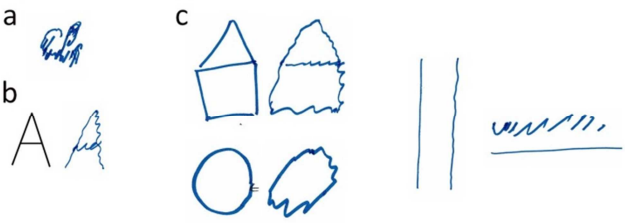
In this paper, we report the case of a patient with pure agraphia associated with a meningioma located on the foot of the middle and superior frontal gyri. The case is of interest for two particular reasons. First, it presents a new case of a rare disorder: pure agraphia. Second, the location of the lesion associated with this disorder could help to feed the debate concerning the mechanisms underlying writing production and the existence of a frontal writing center. In this paper, we discussed these issues and made a brief review of the frontal brain structures involved in writing.

2. Case Presentation

A 69-year-old, right-handed man (MC) was addressed to our consultation for the recent finding of an intracranial meningioma. He had received 12 years of formal education and had been working as an electrician and a restaurant manager. He had no previous history of brain disease or mental illness and no previous surgery or long-term medication. MC reported a difficulty in writing that had been evolving for several months. Progressively, he had become unable to write his name correctly or even sign a check. He spontaneously reported no other language impairment.

On neurological examination, the patient was alert, oriented and cooperative. He had no significant cognitive functions impairment. He was able to walk by himself but had diffuse paresis of his right leg (4/5 on muscle testing - Medical Research Council power scale- of tibialis anterior, triceps surae, quadriceps and iliopsoas). No motor deficit of the right hand (he was able to button his shirt, tinker at home, and use his knife and fork without difficulty), of the left hemibody or of the face was detected. There was no tone disturbance and no sensory deficit. Reflexes were present and symmetrical. The patient had no visuospatial impairment or praxis disorders. He had no involuntary movements or sensory disturbance. However, he had an objective writing disorder and he was conscious of his difficulty. There was no rest tremor of the limbs but, when he wanted to write, his right hand (dominant hand) began to show fine trembling and he was unable to finalize the movement.

On pre-operative neuropsychological examination, a French adaptation of the Boston Diagnostic Aphasia Examination test (BDAE) was used to assess language [13]. The conversational and expository components of speech were conserved and the patient's spontaneous speech was fluent. His auditory comprehension was normal. Oral expression was conserved. MC was able to pronounce words correctly or repeat single words and sentences and he showed no dysarthria. Words articulation was not impaired. During the Oral Naming on Visual Presentation test (DO80), the patient's score was 78/80 (normal value for his age) [14]. Reading (words/sentences) was not disturbed. Recognition of written letters was conserved after changes of case and typography. Reading comprehension was conserved; the patient was able to correctly recognize words that were presented orally or spelled among a multiple choice of written words, or match written words with images. The patient continued to play Scrabble regularly with his wife and friends, an activity suggesting intact orthographic skills. He had also no difficulty while typing. This was confirmed with the BDAE evaluation: letters were poorly formed but substitutions and inversions were absent; oral and written spelling of regular words, irregular words (those whose spelling–sound relationships violate at least one such correspondence) and ambiguous words (ex: ball as a round object or a formal dance) were correct, which is in favor of preserved lexical processing. Pseudo-words were also correctly spelled, indicating a preserved phonological pathway.



Samples of CM's spontaneous writing using his right, dominant hand.

Figure 1. *a. The patient's spontaneous attempts to write his name. He manages, laboriously, to write the first two letters "Cl".* ***b.*** *Examples of the letter "A" copied by the patient using his right, dominant hand.* ***c.*** *Copy drawing productions: a house, a circle, a horizontal straight line, and a vertical straight line. Curiously, the vertical straight line was less difficult to reproduce than the horizontal straight line.*

Concerning writing production, the patient was unable to write correctly. His hand was not stable and presented fine oscillations each time he tried to write. He could grasp the pen correctly but, as he said, "as soon as I put pen to paper, it becomes impossible for me to control my hand's movement" (Figures 1a-b). The patient's writing disorder was present whatever the nature of the writing (letter, words, sentence, signature). Spontaneous writing, writing to dictation and copying were equally affected. Even drawing a straight line or a simple geometric shape was difficult for him (Figure 1c). The shaking observed during writing was absent at rest or during other kinds of fine hand movement (e.g., eating, folding a paper or putting a key into a lock). Furthermore, the patient showed no disturbance when he was tested on fine and rapid movements (finger-nose test and hand tapping test). Because of his difficulty in forming letters, MC quickly became exhausted and it was difficult for him to write a whole word in one go. However, when he succeeded in writing, he did not appear to make grammatical or orthographic errors, be it for regular words (e.g., page), irregular words (e.g., yacht) or pseudo-words words (e.g., "cartule"). Writing with the left hand (non-dominant hand) was possible and the patient did not experience difficulties in "controlling his (non-dominant) hand's movement". The visuo-constructive praxic abilities of the patient were preserved; the clock-drawing test was not impaired and he had no difficulty in reproducing the spatial configuration of objects (eg.: cube). However, when his abilities to reproduce a figure by drawing were tested line crossings and misplacement were noted, caused by the same

fine tremor as seen during writing (the line was twisty, especially vertical lines).

On Imaging, brain magnetic resonance images (MRI) showed an extra-axial lesion that had developed at the expense of the cranial convexity. The lesion was located in the pre-rolandic region, over the foot of the first and second frontal circumvolutions (Figure 2a). The lesion was spontaneously hypointense on T1 sequences and was highly enhanced after gadolinium injection. There was a slight hypersignal on FLAIR sequences corresponding to perilesional oedema. A left parietal convexity meningioma was evoked.

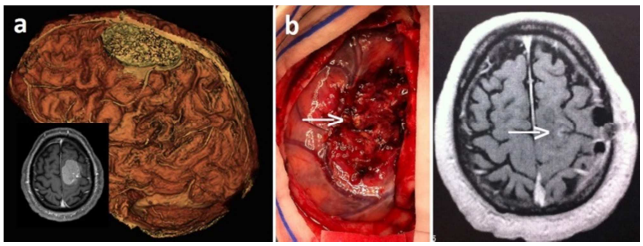


Figure 2. *a. Axial MRI slice and 3D reconstruction of the meningioma located in the superior frontal gyrus.* ***b.*** *Intraoperative image showing the main zone of cortical compression on the lateral part of the superior frontal gyrus, close to the superior/middle frontal gyrus sulcus correlated with MRI zone of edema (arrows). MNI coordinates identified with an intraoperative neuronavigational system were x=-19.8, y=1.5, z=52.2.*

The patient was operated and the whole lesion was removed. The lesion had no clear cleavage plane and the separation from the cortex was carried out cautiously (Figure 2b). There were no postoperative complications. The paresis of the left leg recovered (5/5 on muscle testing) and the patient was able to walk normally a few days after the surgery. He was discharged to home on day five. The pathological study concluded on a WHO grade II atypical meningioma and close monitoring was decided upon.

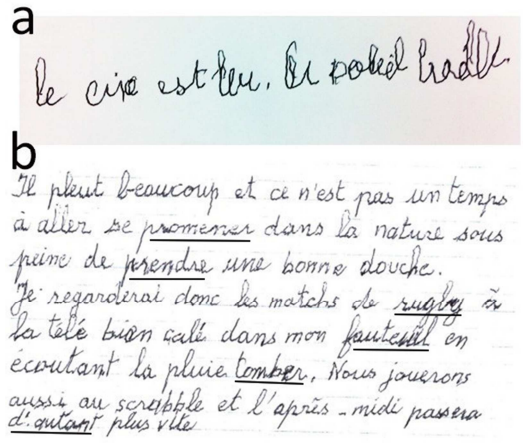


Figure 3. *a. The patient's writing under dictation 3 days after surgery: "le ciel est bleu, le soleil brille" (the sky is blue, the sun is shining). b. The patient's spontaneous writing one month after surgery. The writing production of the patient is greatly improved, he is able to write more easily. The graphism of the letters keeps some sinuosity (underlined). There are no grammatical or spelling errors.*

On postoperative neuropsychological assessment, the patient's writing was improving progressively. He was able to write letters, words and sentences more easily. The graphic quality of his letters was not perfect but he had recovered enough control of his fine hand movements to produce fairly legible handwritten script. (Figures 3a-3b). Other components of language assessed were the same as before the surgery and showed no disturbances (Table 1). The post-operative MRI showed no residual tumor.

Table 1. *Scores of the language battery. We used a French adaptation of the Boston Diagnostic Aphasia Examination test (HDAE-F) and the Oral Naming on Visual Presentation test (DO80).*

	Before the surgery	After the surgery
Reading words (HDAE-F)	10/10	10/10
Reading sentences (HDAE-F)	10/10	10/10
Basic dictation (HDAE-F)	10/10	10/10
Word graphic evocation (dictation of words) (HDAE-F)	5/5	5/5
Syntactic and grammatical spelling	4/4	4/4
Spelling words	8/8	8/8
Oral denomination (DO80)	78/80	79/80

3. Discussion

3.1. Cortical Regions Involved in Writing

Pure agraphia is defined as agraphia that is either isolated or associated with symptoms that cannot explain the writing impairment (no hand motor deficit, aphasia or apraxia) [15]. In this case, the patient had an isolated writing disorder with no features of aphasia or alexia, solely difficulty in forming letters (graphemes) and simple geometrical shapes. In clinical practice, pure agraphia (spelling impairment with preserved oral language) has been observed in patients with frontal lobe lesions [16–18]. Damage to BA6 has been shown to result in difficulties in spelling words with letters in the right sequential order (graphemic buffer syndrome) and in allographic processing difficulties, i.e., in the shaping of letters [9, 19]. This BA6 is located in the frontal lobe in front of the primary motor cortex in humans. The middle frontal gyrus where the meningioma of our patient was located is included in the BA6. In the monkey, this area roughly correspond to the area F7 of the nomenclature.

Exner's initial evidence of a writing disorder emphasized the implication of the posterior part of the middle frontal gyrus [2, 8]. Exner's view has been significantly propagated and the supposed "frontal graphemic motor image center" is

referred to as "Exner Area": a region immediately superior to Broca area and anterior to the primary motor cortex involved in hand movement [20]. However, Exner described a very small number of patients with agraphia (only four cases of his "own collection") and only one had an isolated lesion in the posterior part of the left middle frontal gyrus [3]. Later, a few authors supported the existence of a writing center in the frontal lobe [8–12], [21] whereas agraphia was described in patients with lesions in multiple cerebral sites including: the parietal lobe [6], the perisylvian region [7], the left occipital lobe [22] and basal ganglia [23].

In contrast to the clinical anatomic approach, cognitive psychology supports functional models of writing production. These models define different stages whose the final step is the graphic gesture [24]. Two levels of writing mechanisms are distinguished, namely central and peripheral levels. The central level belongs to the language functional architecture *per se* and involves a two-route feature, with a sublexical processing (operating the conversion of phonemes into graphemes) and lexical processing (translating auditory word forms to their written counterparts, an especially important process in orthographically opaque languages such as English or French) [25, 26]. Agraphia due to the impairment of these central mechanisms ("linguistic agraphia") is frequently associated with aphasia, letters being usually well-formed while spelling errors (phonological and/or lexico-semantic) dominate. A reverse pattern is observed when agraphia relates to impairment of the peripheral level of writing processes, hence yielding to peripheral or apraxic agraphia; agraphic deficits mainly involve allography, grapheme or letter shaping. These functional distinctions have to a certain extent anatomical correlates: a lesion of the left angular gyrus induces frequently a lexical agraphia, while a lesion of the left supramarginal gyrus is associated with sublexical (or phonological) agraphia [27, 28]. Our patient did not make spelling errors on language assessment. His phonological and lexico-semantic writing mechanisms were preserved.

Peripheral agraphia can be related to a purely mechanical disturbance of gesture execution (lesion of the motor cortex) or a more complex disturbances that were classically described as specialized apraxia. Roeltgen and Heilman addressed the functional relationship between praxis and writing processes [26]. They postulated that writing and praxis are separated and that engrams used for skilled motor movements are distinct from those used for guiding motor programming in grapheme production. They coined "apractic agraphia" as an abnormal grapheme shaping with otherwise normal praxis [26]. Thus, ideomotor limb apraxia and apractic agraphia are considered as two distinct and dissociable entities [29]. It has also been suggested that the existence of a frontal graphemic area responsible "for guiding motor programming in grapheme production" [26] could account for this dissociation.

We think that our patient's features of agraphia with his meningioma was located in the posterior part of the superior premotor cortex, was consistent with the disturbance of a region we termed the "graphemic/motor frontal area" – GFMA [30]. The GFMA area (located in BA6) is located just rostral to the hand area in the primary motor cortex. This GFMA could represent a functional interface between abstract orthographic representations and the generation of motor commands matching our patient impairments, characterized by ill-formed letters, slow handwriting, or handwriting arrest.

The junction of the left superior and middle frontal gyri is commonly referred to as Exner's area [3] and could correspond to Exner's initial observations and be associated with so called "pure agraphia". Accordingly, neuroimaging studies showed BA6 activity during specific linguistic spelling tasks -e.g., long word spelling- [31–33], as well as in sensorimotor spelling tasks related to finger or hand movements [34, 35]. More recent neuroimaging data underlined the importance of this area as a handwriting-specific area that is involved in handwriting only and not in, for example, oral spelling [36].

Recent approaches using functional imaging [37] and/or awake surgery [30, 38] revealed additional elements in favor of the involvement of the frontal lobe in writing. Roux et al. [30] used direct cortical stimulation (12 patients) and functional magnetic resonance (22 healthy volunteers) to study the frontal areas involved in writing. The converging results from the 2 different methods showed an activation cluster specific to word handwriting, lying in the F1/F2 sulcus, anterior to the hand primary motor area (Brodmann Area 6). This region was named the "graphemic/motor frontal area" (GMFA) [30] and its Talairach coordinates (x, y, z: -26, -6, 42) were very close to those of the case described here (x, y, z:-19, 1, 52) and to another case (x, y, z: -23, 3, 61) we tested by electrostimulation during awake surgery [39]. A meta-analysis of neuroimaging data [40] pointed out that the frontal area the most repeatedly activated during writing is located in the posterior part of F2; here again, the MNI coordinates of peak activation are very close to those of our patient (x, y, z: -22, 8, 54). Planton and al.[36] regarded the GMFA as an interface between abstract orthographic representations of words (sequences of graphemes) and motor programs enabling the transcoding of graphemes into allographic letter strings – in other words an interface between abstract orthographic representations and the generation of motor commands. This area is located in front of the primary hand area (a primary area involved in basic hand movements such as flexion or extension) but in the frontal lobe. Thus, this frontal lobe is involved in highly integrated processes and among them in the final process of writing. Writing information could come from the parietal lobe and could be integrated in the GFMA and the primary motor cortex as support of basic hand movements. Another group [41], investigating single letter writing, identified a region specifically associated with the representation of the letter shape within the left frontal lobe (between the left superior frontal sulcus and pre-central gyrus), a location highly congruent with the GMFA. These results were in close alignment with those previously found for words. A similar

viewpoint was adopted by Purcell et al. to account for the activation of this area in a bimanual typing task [42].

3.2. Subcortical Pathways

Little is known about the subcortical pathways involved in writing. Croisile et al. emphasized the role of white matter fiber pathways in writing and reported an interesting observation of a patient with pure agraphia following a left frontal hematoma [15]. The anatomical location of the hematoma was of interest since it was "a deep lesion which has not affected the frontal and parietal cortices". They proposed a disconnection hypothesis with an interruption during transfer of writing (but not practic) information between the intact parietal and frontal cortices. The authors concluded on a very selective disruption in the pathways linking the temporo-parietal and frontal cortices involving only fibers used for writing. Motomura et al. reported the first case of transient agraphia and alexia elicited through intraoperative direct subcortical stimulation [43]. They combined the results of intraoperative mapping with a postoperative DTI tractography. The tract found to be implicated consisted of the deep portions of the dorsal IFOF. Finally, Klein et al. have studied the fibre connectivity of Exner's area and argued in favour of a neuro-functional and neuro-structural dissociation of Exner's area with a dorsal and a ventral connecting pathways [44]. This sheds light on a new component of the neural counterparts of writing production and emphasizes the role of white matter bundles.

4. Conclusion

We have reported a case of pure agraphia in a patient with a left frontal meningioma located in the "Exner" area. The writing disturbances observed were isolated with no disturbance of other components of language. The writing of the patient improved after surgery. Our report is in favor of the existence of a frontal writing area, the GMFA. Most recent works highlight the involvement of subcortical pathways. This has not been analyzed in our work but seems to be an interesting research track to explore in further studies.

Disclosure of Interest

The authors report no conflict of interest.

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