Available online at www.sciencedirect.com

ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Single Case Report

Progressive macrographia for block letter writing: A case study

Semenza Carlo [a], De Pellegrin Serena [b], Facchini Silvia [c], Cecchin Diego [d], Manara Renzo [a,e], Shallice Tim [f,g] and Vallesi Antonino [a,h,*]

[a] *Department of Neuroscience & Padova Neuroscience Center, University of Padova, Padova, Italy*
[b] *Department of Neuroscience, University Hospital of Padua, Padova, Italy*
[c] *Department of Neuroscience, University of Padova, Padova, Italy*
[d] *Nuclear Medicine Unit, Department of Medicine - DIMED, University of Padova, Padova, Italy*
[e] *Neuroradiology Unit, University Hospital of Padova, Padova, Italy*
[f] *Institute of Cognitive Neuroscience, University College of London, UK*
[g] *Scuola Internazionale Superiore di Studi Avanzati — SISSA, Trieste, Italy*
[h] *IRCCS San Camillo Hospital, Venice, Italy*

A R T I C L E I N F O

Article history:
Received 16 March 2021
Reviewed 20 April 2021
Revised 10 May 2021
Accepted 13 September 2021
Action Editor Jean-Francois Demonet
Published online 24 September 2021

Keywords:
Megalographia
Working memory
Progressive macrographia
Neglect
Dysgraphia

A B S T R A C T

“Macrographia”, a relatively rare symptom generally following cerebellar diseases, consists of an abnormally large handwriting. The case reported in the present investigation shows several outstanding features. First, it is of the progressive variety, letters increase in size as one goes through the word towards the lower-right portion of space. Moreover, it is limited to one allographic variety, that is, block letters. This phenomenon is previously unreported, all allographic varieties being usually equally affected. Finally, no prominent cerebellar or basal ganglia abnormality could be demonstrated with structural MRI or PET. From a cognitive point of view, a peculiar combination of spatial attention, executive function and working memory deficits is proposed to account for the progressive misalignment and elongation of individual letters when specifically writing in block prints. From an anatomical perspective, the pattern of multifocal lesions, encompassing multiple cortical areas in both hemispheres and the corpus callosum, may support this multi-componential interpretation of the reported phenomenon.

1. Introduction

“Macrographia” (also called “megalographia”), a relatively rare symptom following neurological diseases, consists of an abnormally large handwriting. Macrographia was first reported by Thomas (1911) in the context of cerebellar lesions. A relation with cerebellar lesions was later confirmed by several authors (e.g., Bing, 1923; Haymaker, 1956; Holmes, 1917; Petitpierre,

* *Corresponding author*. Department of Neuroscience, University of Padova, via Giustiniani 2, 35128, Padova, Italy.
E-mail address: antonino.vallesi@unipd.it (V. Antonino).
https://doi.org/10.1016/j.cortex.2021.09.002
0010-9452/

1925). Macrographia appears indeed to be associated with several conditions resulting from cerebellar damage, including essential tremor (Martinez-Hernandez & Louis, 2014). Indeed, a role of the cerebellum in handwriting has also been confirmed by meta-analyses (Planton et al., 2013; Purcell et al., 2011). Other than in cerebellar diseases, macrographia has also been observed, however, in basal ganglia dysfunctions such as in Huntington disease (Hochheimer, 1936; Phillips et al., 1994) and in dystonic tremor (Bajaj et al., 2012).

Most authors have contrasted macrographia with the complementary symptom, micrographia (Bajaj et al., 2012; Beeson & Rapcsak, 2011; Letanneux et al., 2014), commonly observed, for example, in Parkinson's disease (Denes et al., 2005; Mariën & Manto, 2015). Macrographia and micrographia are sometimes classified, if mentioned at all, within the "peripheral agraphias" (Van Dun et al., 2015) under the label of "motor execution agraphias" and are usually associated with subcortical lesions (e.g., Mariën & Manto, 2015; Mody, 2017).

Abnormally large writing is not a feature reported in other types of "peripheral agraphia", that is, agraphias that, in contrast to "central agraphias", do not result from damage to the language system (Van Dun et al., 2015: according to this last distinction, macrographia cannot but fit within peripheral agraphias, no linguistic factors being of any influence).

The most frequent of peripheral dysgraphias, that is, apraxic agraphia, motor agraphia and spatial agraphia/dysgraphia (often accompanied by spatial neglect, Lorch, 2013; but see Cubelli et al., 2000) differ from macrographia in one important respect. In macrographia, letters are clearly written and readable, with little signs of distortion, imprecision or incompleteness: the main, if not the only, anomaly is the abnormal size. This speaks in favor of a different location of both the neural and the functional damage. Importantly, to the best of our knowledge, no report of selective macrographia for a specific type of allograph (e.g., cursive, block capital) has been previously published.

Bing (1923) also observed that in macrographia following a cerebellar lesion the height of letters progressively increased, thus mirroring the progressive decreasing of letter size very common to micrographia. Later authors indeed have distinguished within both macrographia and micrographia a consistent variant, in which the handwriting is consistently large or small, and a progressive variant, in which the patient is unable to maintain normal letter size for more than a few characters (Frings et al., 2010; Letanneux et al., 2014; Wilson, 1925). Progression, however, is hardly a frequent feature of macrographia, where as a rule the size is consistently large (Frings et al., 2010).

The only reported cases of progressive macrographia in fact appear in Bing (1923). The only case of his for which an example of writing is given is that of a twelve-year-old child affected by cerebellar paralysis (see Bing, 1923, Fig. 3). Writing was clearly shaky, being also affected by tremor, and letters progressively widened toward both the top and bottom, and the affected allograph that was reported was cursive. Whether other types of allographs were also affected is not specified.

The case reported in the present investigation is of the progressive variety but the writing is not shaky. Moreover it looks to be limited to one allographic script, that is, print writing (i.e., block letters), a phenomenon previously unreported in the literature about macrographia, all allographic scripts being usually equally affected. Concomitant symptoms and the pattern of preserved and impaired capacities may clarify the functional underpinnings of the phenomenon reported here. The combination of multiple anatomical lesions and PET-related metabolic activity, that do not seem to primarily affect either the cerebellum or the basal ganglia, but rather involve multiple cortical areas in both hemispheres and the corpus callosum, suggests that a different interpretation of the phenomenon may be required from that provided for the cerebellar variety.

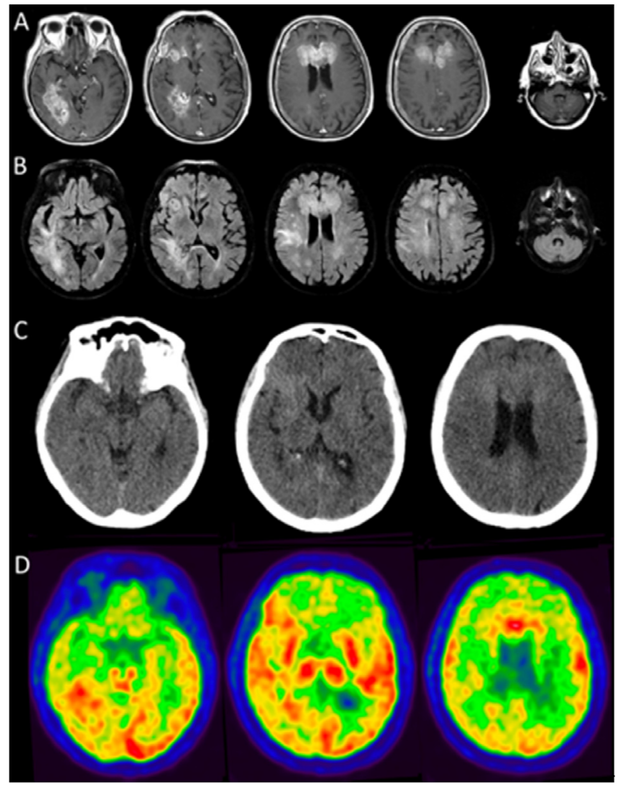

Fig. 1 – Panels A and B show contrast-enhanced T1-weighted and fluid attenuated inversion recovery axial images, respectively. Panels C and D show a standard low-dose Computed Tomography (CT) acquired for attenuation correction and anatomic localization, and ^{18}F-FDG Position Emission Tomography (PET), respectively. A multicenter malignant tumor is clearly visible in different cerebral locations (Panels A–C), with a corresponding intense hypermetabolism shown in PET (Panel D).

2. Case description

A 75 years old right-handed Italian woman without any previous history of neurological problems was referred by her family to the Neurology Clinic of the Padova Hospital because of a space-time disorientation and a drop in mood for 1–2 months before hospitalization. Contrast enhanced T1-weighted and fluid attenuated inversion recovery (FLAIR) MRI sequences were acquired on a 3T Ingenia Philips whole-body scanner with a 32-channel head-coil. MRI sequences

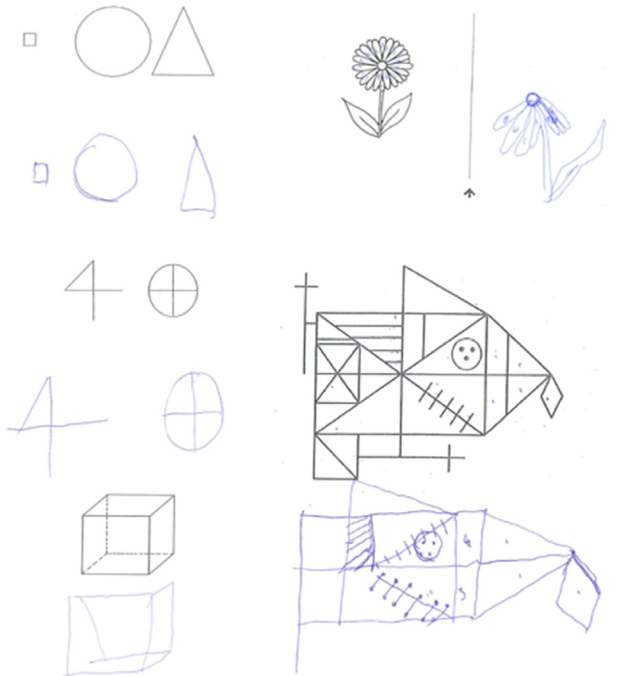

Fig. 2 – **Selected examples of copy tasks, including geometric shapes (some taken from Spinnler & Tognoni, 1987), simple objects, and Rey–Osterrieth complex figure. The model was shown in black, while the patient's copy was performed with a blue ink pen.**

(Fig. 1, Panels A, B) showed a multicenter malignant tumor involving the deep right temporo-parietal white matter, the right inferior frontal gyrus, the right anterior insula, the anterior cingulate cortex and the white matter of the forceps minor bilaterally. No lesion was detectable in the posterior cranial fossa (brainstem and cerebellum).

Additionally, ^{18}F-FDG PET/CT was acquired, using a PET/CT Ingenuity Philips scanner, for 15 min, 60 min after injecting 3 MBq/Kg of radiopharmaceutical. A standard low-dose CT was acquired for attenuation correction and anatomic localization. The PET scan revealed areas of intense hypermetabolism corresponding to the regions of contrast enhancement shown by MRI in the right temporo-parietal white matter, right inferior frontal gyrus, insula and corpus callosum bilaterally. Interestingly a clear hypometabolism of the frontal cortex (including premotor area) bilaterally was evident (Fig. 1, Panel D, second and third columns from the left), probably due to a disruption of frontal white matter tracts resulting in cortical disconnection. Similar hypometabolic findings were also evident in the right temporo-polar cortex.

The patient underwent a standard protocol of paper-and-pencil neuropsychological assessment. She was also tested more specifically for dysgraphia and neglect based on her manifest symptoms. The tests used followed the standard procedure in our clinic when the diagnosis needs to be carried out in more depth; different pencil and paper tests are given until a clear interpretation is achieved.

Whenever applicable, we report all data exclusions, all data inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study.

2.1. *Standard neuropsychological testing*

The patient was administered a comprehensive series of standardized neuropsychological tasks. The Oxford Cognitive Screen (OCS; Demeyere et al., 2015; Mancuso et al., 2016) was used as an initial brief screening instrument. OCS is composed

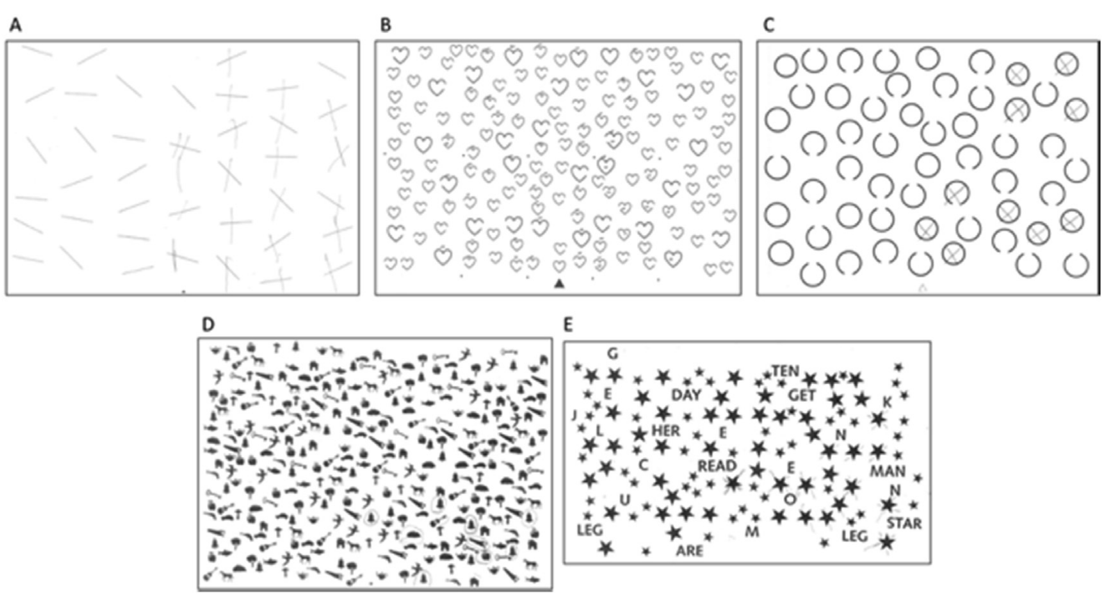

Fig. 3 – **Visual Search task performance examples. A) Albert Test: cross each line; B) Broken Hearts test (from Oxford Cognitive Screen): mark complete hearts among hearts broken on the left or in the right side; C) Modified gap detection test: mark fully-outlined circles but not circles broken on the top or on the bottom; D) Bells test: mark bells among other objects; E) Stars cancellation test: mark big stars among small stars and verbal stimuli.**

of tasks on language, visual attention, spatial neglect, praxis abilities, visual and verbal memory, calculation, number reading and executive functions. More specific tests were also administered to better evaluate distinct cognitive functions. Verbal memory was assessed using the Prose Memory Test (immediate and delayed recall) and Interference Memory test (Mondini et al., 2011). Forward and backward digit span and the Corsi block-tapping test were administered to measure short-term memory and working memory both for the verbal and visuospatial components (Monaco et al., 2013). The Trail-Making-Test, forms A and B, was used as a measure of selective attention and switching abilities (Mondini et al., 2011), Rey-Osterrieth complex figure Copy (Caffarra et al., 2002) and Drawing Figure Copy tests (Spinnler & Tognoni, 1987) were used for a preliminary assessment of visuospatial functions and praxis abilities.

Language abilities were assessed through the Phonemic Fluency test (Mondini et al., 2011) and the Esame Neuropsicologico per l'Afasia (ENPA; Capasso & Miceli, 2005), a detailed Italian-standardized battery, covering all language functional components (comprehension, repetition, reading, writing, naming) applied to different linguistic units (words, non-words and sentences, nouns and verbs).

3. Results

The results of the standard neuropsychological battery are reported in Table 1.

3.1. *Visuospatial tasks*

Different tasks were administered evaluating visuospatial functions and praxic skills. In copy tasks involving single elements (Spinnler & Tognoni, 1987), the patient was asked to copy simple (square, rhombus, four-pointed star) and complex (cube) geometric shapes. The patient was also asked to copy a drawing of a real object (i.e., a flower). The copy of figures was correct for simple figures, but became disorganized for complex figures with tridimensional structure (a cube) or made up by different elements (Fig. 2). The patient ignored elements in the left part of the space (e.g., left leaf of the flower, Rey copy left elements), and in some cases also in the upper part (e.g., see cube and flower petals). The patient transposed some details in a wrong position (Fig. 2, Rey copy). She also occasionally showed perseveration and a closing-in effect (Fig. 2, Rey copy). Copying a sequence of square, circle, triangle did not show any effect of progressive elongation (Fig. 2, upper left).

3.2. *Visual search tasks*

In a simple visual search task (Albert, 1973), the patient had to cross all the segments randomly arranged on the sheet (Fig. 3, A). More complex visual search tasks of this kind were also administered (OCS-Visual Search, Demeyere et al., 2015; BIT, Wilson et al., 1987), in which the patient was asked to search a specific target stimulus among randomly arranged distractors. The tests were repeated changing the type of stimulus: complete hearts among hearts broken on the left or on the right side (OCS-Broken Hearts test, Fig. 3, B), complete circles between circles broken on the top or on the bottom, that is, a version of the gap detection test modified to detect possible signs of vertical allocentric neglect (Fig. 3, C), the bells among other objects (Vallar et al., 1994, Fig. 3, D), big stars among small stars and verbal stimuli (modified Star cancellation test from BIT; Fig. 3, E).

In all these tests, the patient used a particular searching behavior, starting from the center and moving towards the lower right corner of the space, while ignoring many targets located in the left and upper sections of the sheet. Left neglect was documented in standardized visual search tasks (Table 1). Furthermore, the patient showed left-ward allocentric neglect signs (OCS-Broken Hearts test scores reported on Table 1 and Fig. 3, B).

Since the neglect scores for the upper versus lower vertical space are not standardized in the tests we administered, we used an alternative statistical approach to document signs of upper vertical neglect in our patient (Table 2), despite we did not specifically collect performance data from healthy controls on these tasks (usually at ceiling or near-ceiling). A two proportion *z*-test was used to compare each pair of proportions of omissions for the upper versus lower space, but also more specifically within the left hemifield, right hemifield and, when enough target stimuli were available, also in the midline. Similar analyses were performed for commission errors, when these occurred, for the OCS-Broken Hearts test, Bells test (Vallar et al., 1994) and the modified version of the gap detection test.

The results of these tests showed that the proportion of omissions was significantly higher for the upper visual field as a whole than for the lower one in the Broken Hearts test, Bells test, Star Cancellation test (all ps $< .05$), but numerically also in the other tests (*p*-value range: .129/.3707). When the visual fields were fractionated further, vertical neglect for the upper versus lower field emerged statistically in the midline (Broken Hearts Test, gap detection test, $ps < .05$) and right visual field (Bells test, Star Cancellation test, $ps < .05$; and, as a trend, Albert test, Broken Hearts Test, gap detection test, *p*-value range: .0793/.1711). In the left visual field, instead, upper and lower targets were equally neglected apart from non-significant trends in the Broken Hearts (p=.0885) and Star Cancellation ($p = .1251$) tests.

Commission errors with distractors showed instead the opposite pattern, that is, their proportion was significantly higher for the lower field than for the upper field in the Bells test ($p = .0281$), with similar non-significant trends also occurring in most of the other tests (P-value range: .1379/.1949) with the exception of the gap detection test. When the visual fields were fractionated further, commission errors were significantly higher in the lower versus upper midline for the (left-)Broken Hearts Test ($p = .0192$), in the lower versus upper right field for the Bells test ($p = .0344$) and, as a non-significant trend, in the lower versus upper right-field for the (right-)Broken Hearts Test ($p = .1515$) and down-broken circles of the gap detection test ($p = .1423$). No difference in terms of commission errors emerged for the lower versus upper left field (all $ps > .2643$).

3.3. *Spontaneous speech, naming, repetition and reading*

Spontaneous speech was intact both phonemically and syntactically. However most often the patient spoke only if

Table 1 – Results of the standard neuropsychological tests. Cut-off values are reported when available. The Esame Neuropsicologico per l'Afasia (ENPA) battery also reports (in parenthesis) the number of errors over the total number of items for each subtest.

Test	Correct Score	Cut-off	Performance
Oxford Cognitive Screen			
Picture Naming	4	3.10	Normal
Semantics	3	3	Normal
Orientation	3	3.90	Impaired
Visual Field	3	4	Impaired
Sentence Reading	15	14.70	Normal
Number Writing	3	2.90	Normal
Calculation	2	3.40	Impaired
Visual Search-Broken Hearts test	25	44.50	Impaired
Egocentric component	−3	< −3	Borderline
Allocentric component	16	>2	Impaired
Imitating Meaningless Gestures	8	9	Impaired
Verbal Memory	0	2.60	Impaired
Episodic Memory	0	3.50	Impaired
Executive functions	0	3	Impaired
Memory Interference (ENB-II)			
10 sec	5	4	Normal
30 sec	3	4	Impaired
Prose Memory (ENB-II)			
Immediate recall	0	8	Impaired
Delayed recall	0	10	Impaired
Digit Span			
Forward	3.13	4.26	Impaired
Backward	0	2.65	Impaired
Spatial Span			
Forward	1.24	3.46	Impaired
Backward	0	3.17	Impaired
Trail Making Test (ENB-II)			
A	152″	69″	Impaired
B	NE	188″	Impaired
Phonemic Fluency (ENB-II)	3	10	Impaired
Rey Figure (Copy)	18.50	28.87	Impaired
Drawing Figure copy test	7.5	7.75	Impaired
Bells Test (Vallar et al., 1994**)**			
Total omissions	29	5	Impaired
Right minus left	5	5	Borderline
Line crossing (BIT) hits	17/36	34	Impaired
Right space	17/18		
Left space	0/18		
Star cancellation (BIT) hits[a]	12/54	51	Impaired
Right space	12/27		
Left space	0/27		
ENPA			
Repetition words (10/10)	9.80	8.80	Normal
Repetition nonsense words (3/5)	2.50	2.00	Normal
Repetition sentences (3/3)	3	3.00	Normal
Reading words (9/10)	6.40	6.40	Normal
Reading nonsense words (1/5)	1.00	4.00	Impaired
Reading sentences (0/2)	.10	1.30	Impaired
Writing words (8/10)	8.10	6.30	Normal
Writing nonsense words (3/5)	2.30	1.40	Normal
Writing sentences (1/2)	.60	.60	Normal
Naming words (9/10)	9.00	8.20	Normal
Naming verbs (7/10)	7.10	6.10	Normal
Naming colors (5/5)	5	4.00	Normal
Comprehension words (18/20)	18.60	18.40	Normal
Comprehension sentences (8/14)	7.80	11.60	Impaired

[a] In this test, the standard instruction would be to cross the little stars, however we varied this instruction by asking the patient to cross the big stars, in order to check whether neglect signs were still present even with bigger targets. Thus, the standardized cut-off should be interpreted with caution in this case.

stimulated. Sometimes speech was interrupted at mid-sentence because of anomia for low frequency words and proper names. Repetition was normal both when assessed informally at bedside and when tested with specific ENPA items (Table 1). Word reading was preserved, but reading of nonsense words and sentences was impaired by substitution or addition of phonemes in the initial portion of the words.

3.4. *Writing*

3.4.1. *Writing to dictation*

The patient was asked to write to dictation different verbal stimuli: meaningful words (N = 9) and pseudowords (N = 5) intermixed between each other (Fig. 4, A), meaningful words only (N = 10, Fig. 4, B) and sentences (Fig. 4C–E), in both uppercase print (N = 2, Fig. 4C–D) and lowercase cursive (N = 3, Fig. 4, E). Spontaneous writing of relatively familiar (400) and unfamiliar (708, 15,200) Arabic numbers was also tested (Fig. 4, F).

The performance was normal (see Table 1) for words, non-words and sentences written in lowercase cursive as far as the graphic form was concerned (Fig. 4, E). Writing of Arabic numbers was also flawless (Fig. 4, F), suggesting a dissociation with number-specific macrographia reported in some aphasic patients (Fradis & Leischner, 1985). Prompted by an anonymous reviewer, we also performed an error analysis on the patients' written material. When writing in block print, some spelling errors emerged in both words and non-words, including letter and tract perseverations, omissions, insertions, deformations and substitutions for words (see Table 3 for more details, and Figs. 4–6, for the patient's specific written material).

Notably, in uppercase print writing, both for words and sentences, the patient progressively elongated the letters towards the bottom, proceeding from the left to the right part of the stimulus most of the time (Fig. 4B–D). Elongation towards the top was seldom observed. Both single words and non-words were tested for uppercase print writing on a single occasion (dictation task), but it seems that the phenomenon was not shown when words were administered together with non-words (Fig. 4, A) or soon after (first part of Fig. 4, B). This was the only instance in which no macrographia was observed for uppercase print writing.

Table 2 – Number of mistakes (omissions or commissions) that the patient made (out of the total number of stimuli) for each portion of space in the different visual-search tests. The results of two proportion *z*-tests are also reported to compare relevant pairs of proportions.

Albert Test/Line Crossing (BIT) - omissions (Fig. 3A)					Z Score test results	
	Left	midline	Right	Tot	Upper versus Lower (left)	$z = \text{NaN}$
Upper	8/8	1/2	1/8	10/18	Upper versus Lower (midline)	$z = 1.155$, $p = .1251$
Lower	9/9	0/2	0/9	9/18	Upper versus Lower (right)	$z = 1.093$, $p = .1379$
	17/17	1/4	1/17		Upper versus Lower (tot)	$z = .334$, $p = .3707$
OCS Broken Hearts Test (Full hearts) - omissions (Fig. 3B)						
	Left	midline	Right	Tot	Upper versus Lower (left)	$z = 1.348$, $p = .0885$
Upper	6/10	4/5	8/10	18/25	Upper versus Lower (midline)	$z = 1.897$, $p = .0287$
Lower	3/10	1/5	5/10	9/25	Upper versus Lower (right)	$z = 1.406$, $p = .0793$
	9/20	5/10	13/20		Upper versus Lower (tot)	$z = 2.554$, $p = .0054$
OCS Broken Hearts Test (left-broken hearts) - commissions (Fig. 3B)						
	Left	midline	Right	Tot	Upper versus Lower (left)	$z = .469$, $p = 3199$
Upper	4/10	2/5	3/10	9/25	Upper versus Lower (midline)	$z = -2.070$, $p = .0192$[a]
Lower	3/10	5/5	4/10	12/25	Upper versus Lower (right)	$z = -.469$, $p = .3199$
	7/20	7/10	7/20		Upper versus Lower (tot)	$z = -.860$, $p = .1949$
OCS Broken Hearts Test (right-broken hearts) - commissions (Fig. 3B)						
	Left	midline	Right	Tot	Upper versus Lower (left)	$z = -.626$, $p = .2643$
Upper	1/10	0/5	0/10	1/25	Upper versus Lower (midline)	$z = \text{NaN}$
Lower	2/10	0/5	1/10	3/25	Upper versus Lower (right)	$z = -1.026$, $p = .1515$
Tot	3/20	0/10	1/20		Upper versus Lower (tot)	$z = -1.0426$, $p = .1492$
Modified gap detection test (full circles) - omissions (Fig. 3C)						
	Left	midline	Right	Tot	Upper versus Lower (left)	$z = \text{NaN}$
Upper	3/3	3/3	1/5	7/11	Upper versus Lower (midline)	$z = 2$, $p = .0227$
Lower	3/3	0/1	0/4	3/8	Upper versus Lower (right)	$z = .949$, $p = .1711$
Tot	6/6	3/4	1/9		Upper versus Lower (tot)	$z = 1.126$, $p = .1292$
Modified gap detection test (up-broken circles) - commissions (Fig. 3C)						
	Left	midline	Right	Tot	Upper versus Lower (left)	$z = \text{NaN}$
Upper	0/6	0/1	0/4	0/11	Upper versus Lower (midline)	$z = \text{NaN}$
Lower	0/3	0/2	0/3	0/8	Upper versus Lower (right)	$z = \text{NaN}$
Tot	0/9	0/3	0/7		Upper versus Lower (tot)	$z = \text{NaN}$
Modified gap detection test (down-broken circles) - commissions (Fig. 3C)						
	Left	midline	Right	Tot	Upper versus Lower (left)	$z = \text{NaN}$
Upper	0/5	NA	0/4	0/9	Upper versus Lower (midline)	NA
Lower	0/4	NA	1/4	1/8	Upper versus Lower (right)	$z = -1.069$, $p = .1423$
	0/9	NA	1/8		Upper versus Lower (tot)	$z = -1.093$, $p = .1379$
Bells test - omissions (Fig. 3D)						
	Left	midline	Right	Tot	Upper versus Lower (left)	$z = \text{NaN}$
Upper	9/9	NA	9/9	18/18	Upper versus Lower (midline)	NA
Lower	8/8	0/1	3/8	11/17	Upper versus Lower (right)	$z = 2.823$, $p = .0024$
	17/17	0/1	12/17		Upper versus Lower (tot)	$z = 2.769$, $p = .0028$
Bells test - commissions (Fig. 3D)						
	Left	midline	Right	Tot	Upper versus Lower (left)	$z = \text{NaN}$
Upper	0/77	0/5	0/70	0/152	Upper versus Lower (midline)	$z = \text{NaN}$
Lower	0/59	0/3	3/65	3/127	Upper versus Lower (right)	$z = -1.818$, $p = .0344$[a]
	0/136	0/8	3/135		Upper versus Lower (tot)	$z = -1.905$, $p = .0281$[a]
Modified Star Cancellation test (BIT) - omissions (Fig. 3E)						
	Left	midline	Right	Tot	Upper versus Lower (left)	$z = 1.151$, $p = .1251$
Upper	14/14	NA	11/15	25/29	Upper versus Lower (midline)	NA
Lower	10/11	NA	3/11	13/22	Upper versus Lower (right)	$z = 2.328$, $p = .0099$
	24/25	NA	14/26		Upper versus Lower (tot)	$z = 2.201$, $p = .0139$

[a] It should be noted that the direction of the effect for commissions (i.e., more errors for lower space than for upper space) was opposite to the direction for omissions (i.e., more for upper space than for lower space).

3.4.2. *Writing by copy*

These tasks included copying various verbal stimuli with different allographs, in particular: single lowercase cursive letters (N = 10, Fig. 5, A), single lowercase block letters (N = 10, Fig. 5, B), lowercase block words (N = 3, Fig. 5, C), uppercase block words (N = 6, Fig. 5, D), and sentences (N = 3, Fig. 5, E). In a further task, compound words (N = 2) and sentences (N = 2) were presented where the first part of the stimulus was written in lowercase cursive and the second part in uppercase print or vice versa (Fig. 5, F). The patient was instructed to copy the stimulus exactly as she saw it.

Copy tasks of uppercase print words and sentences showed the same graphical effect of progressive elongation of elements (Fig. 5D–E). Interestingly, progressive macrographia was present also with lowercase block letters (Fig. 5, C). Some omissions (Fig. 5, D, first and last words) and repetitions (Fig. 5,

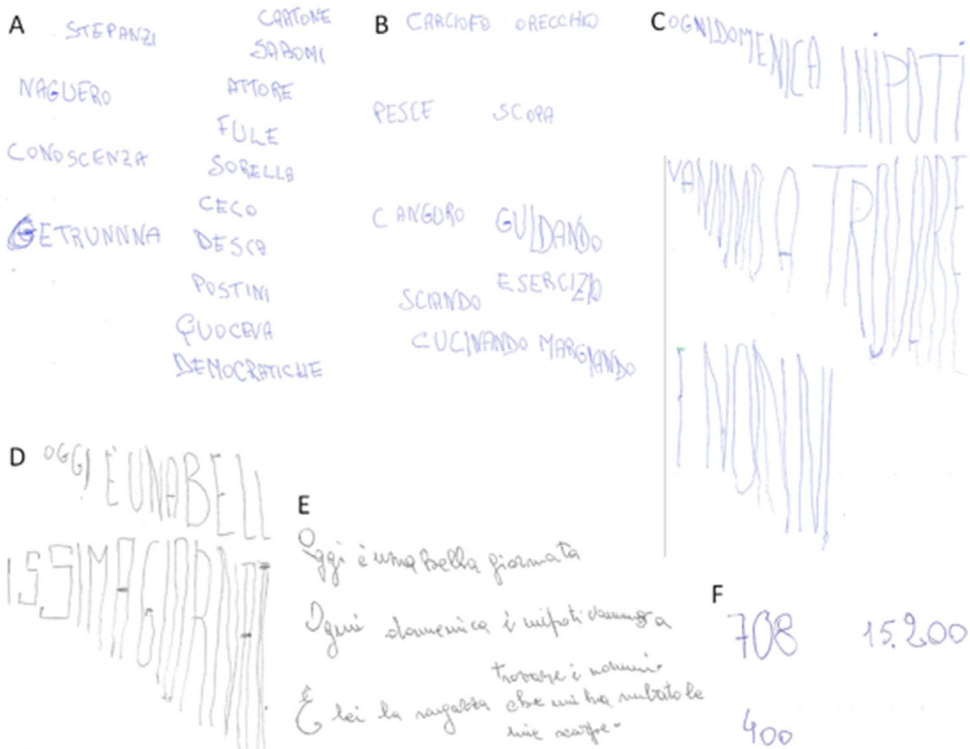

Fig. 4 – All instances of writing on dictation are shown here. The patient was always explicitly requested to write with a specific allograph (lowercase cursive or uppercase print). A: Meaningful words and pseudowords in uppercase print (ENPA items); B: Meaningful words only, in uppercase print (ENPA items); C and D: sentences in uppercase print taken from ENPA or invented by the examiner, respectively; E: Sentences in lowercase cursive: the first sentence was invented by the examiner like in D, while the other two sentences were taken from ENPA; F: Arabic numbers taken from the Oxford Cognitive Screen.

E bottom word) of letters, especially in the left part, also emerged. The copy of lowercase cursive and capital single letters was basically intact (Fig. 5A–B).

In copy tasks where a change of allograph was required at mid-word, once again the patient wrote correctly in lowercase cursive, but she switched to progressive macrographia when the second part of the word was written in uppercase capital letters (capoSTAZIONE) (Fig. 5, F). This effect was not evident with the second part written in lowercase (ARCObaleno) (Fig. 5, F). The patient was mostly anosognosic with respect to her own deficits.

3.4.3. *Writing simple sentences to describe pictures*

Finally, the patient was also asked to freely write simple sentences in uppercase print (N = 2, Fig. 6A–B) and lowercase cursive (N = 3, Fig. 6, C) to describe images taken from the Aachen Aphasia Test (AAT).

Progressive macrographia is noticeable in uppercase print writing (Fig. 6A–B), but not in lowercase cursive writing (Fig. 6, C). In Fig. 6, A, letter perseverations, distortions and substitutions are also shown (the intended sentence was: “Il pescatore ha pescato un grosso scarpone”; also see Table 3).

Despite the patient's progressive macrographia is already evident upon visual inspection, we wanted to also provide some quantification of the phenomenon. To that purpose, we used the segments of one of the sentences written to dictation in uppercase print as a case example (Fig. 4, C). First, we documented the positive slope for each of the three sentence segments through a Pearson correlation analysis between the ordinal number of each letter (1, 2, 3 etc.) and its length (measured as the vertical distance between the highest and lowest boundaries of the letter in cm) in the patient (Fig. 7). The same analyses were performed with the handwriting of the same sentence produced by a control individual with comparable demographic characteristics. As shown in Fig. 7, panel B, while the patient always showed a significantly positive correlation (all $rs > .905$, all $ps < .014$), which indicates that the letter length was progressively increased from one letter to the next one, the control individual showed a mixed pattern of positive and negative correlations that never reached significance (all $ps > .15$). Correlations obtained by the patient and control were also tested against each other for each segment, and resulted significantly different for the first two segments ($z = 5.949$, $p < .001$and $z = 5.988$, $p < .001$, respectively), and not for the last segment ($z = .863$, $p = .194$), perhaps because it was too short.

4. Discussion

This case of macrographia presents with a pattern of unique characteristics. First of all, it is progressive. Second, it

Table 3 – Errors made by the patient when requested to write are reported here (organized in error categories). Most of the errors occurred when writing in uppercase block print. See Figs. 4–6 for the concrete instances of the reported errors.

Type of error for each task	Number of errors	Total number of stimuli of the same kind
Letter perseverations		
Task: writing single words/non-words on dictation (uppercase block)	Tot: 1	9 words, 5 non-words
An extra "N" in the non-word "GETRUNNA" (Fig. 4A)	1	
Task: writing sentences by copy (uppercase block)	Tot: 3	14 words in 2 sentences
An extra "E" inserted in the word "MELE" (Fig. 4C)	1	
An extra "N" in the word "VANNO" (Fig. 4C)	1	
An extra horizontal tract for the letter "E" (Fig. 4C)	1	
Task: writing sentences to describe pictures (uppercase block)	Tot: 8	13 words in 2 sentences
First letter "E" is repeated (and deformed) in the word "PESCATO" (Fig. 6A)	1	
Various letters ("R", "R", "O", "OSSO") are repeated (and sometimes deformed) in the word "GROSSO" (Fig. 6A)	6	
Letter "S" is repeated in the word "SCARPONE" (Fig. 6A)	1	
Letter omissions		
Task: writing on dictation (uppercase block)	Tot: 2	9 words, 5 non-words
Letter "I" in the word "CIECO" (Fig. 4A)	1	
Letter "I" in the non-word "DESCIA" (Fig. 4A)	1	
Task: writing by copy (uppercase block)	Tot: 3	6 uppercase block words
Letter "A" in the word "MARE" (Fig. 5D)	1	
Letters "L" and "F" in the word "ELEFANTE" (Fig. 5D)	2	
Task: writing by copy a compound sentence with a mixture of lowercase cursive and uppercase block		2 single compound words, + 9 words in 2 sentences
Most letters in the last two sentences, with letters for last sentence written in a sort of double tract (task not completed) (Fig. 5F)	Task not completed	
Task: writing sentences to describe pictures (uppercase block)	Tot: 1	13 words in 2 sentences
Letter "A" in the word "HA" (Fig. 6A)	1	
Letter Insertions		
Task: writing sentences to describe pictures (uppercase block)	Tot: 2	13 words in 2 sentences
Letters "GN" are inserted between the words "UN" and "GROSSO" (Fig. 6A)	2	
Letter Deformations/Substitutions		
Task: writing single words/non-words on dictation (uppercase block)	Tot: 2	9 words, 5 non-words
Letter "G" instead of "CQ" in the word "NACQUERO" (Fig. 4A)	1	
First letter "C" becomes a mixture of "C" and "Q" in the word "CUOCEVA" (Fig. 4A)	1	
Task: writing by copy (uppercase block)	Tot: 1	6 words
Letter "M" in the word "MARE" (Fig. 5D) written in lowercase instead	1	
Task: writing sentences to describe pictures (uppercase block)	Tot: 6	13 words in 2 sentences
Letter "C" becomes similar to an "E" in the word "PESCATORE" (Fig. 6A)	1	
First letter "E" becomes (twice) a mixture of "E" and "P" in the word "PESCATO" (Fig. 6A)	2	
First letter "S" in "GROSSO" becomes a mixture of E and S, another letter is not easy to identify (mixture of "O" and "R") (Fig. 6A)	2	
A mixture of letter "C" and "A" is produced instead of "CA" in the word "SCARPONE" (Fig. 6A)	1	
Task: writing sentences to describe pictures (lowercase cursive)	Tot: 1	17 words in 3 sentences
Letter "u" in the word "lui" was first mispelled as "a" and then self-corrected (Fig. 6C)	1	

concerns only block letters, while cursive style is unaffected. Finally, unlike in previously described cases, in terms of neurological damage, a multifocal cortical damage is present but no cerebellar lesion could be demonstrated even with very sensitive neuroimaging techniques able to characterize both structural (MRI) and metabolic (PET) features. This previously unreported pattern calls for an interpretation which can account for each of these three characteristics. We shall discuss each of these unique features in the following sub-sections.

4.1. *Progressivity: why is there a strong correlation between lengthening of neighboring letters towards the bottom-right field?*

Progressivity is common in the mirror phenomenon of micrographia, especially in Parkinson's disease patients (e.g., Kanno et al., 2020; Kim et al., 2005; Letanneux et al., 2014), but also described in a single case of left basal ganglia stroke (Barbarulo et al., 2007), and in another single case with Wilson's Disease, where the phenomenon was modulated by

Fig. 5 – Examples of writing by copy. A–B: single letters; C and D: words presented in lowercase and uppercase block letters, respectively; E: sentences; F: compound words and sentences where the first part of the stimulus was written in lowercase cursive and the second part in uppercase print or vice versa.

cognitive load (Auclair et al., 2008). To the best of our knowledge, progressivity for macrographia was by contrast previously reported only once in Bing (1923), or considered just as an exclusion criterion (not further documented) in a study on progressive micrographia in Parkinson's disease (Kanno et al., 2020). Noticeably, unlike in the patient described by Bing (1923), in the present case, the progressive elongation of letters as the patient goes through the word happens only toward the bottom and not also toward the top (apart from rare occasions), suggesting a completely new type of symptom.

The graphic motor planning processes produce the required motor plans, specifying the size and ordering of the strokes (Rapcsak & Beeson, 2000). These abstract motor plans for each font and case are presumably stored in long-term memory. Although these plans define certain visual properties of a given allograph, such as the direction, the sequence and relative size of the strokes, they do not specify absolute stroke size or duration. They therefore allow for the possibility of elongation.

A cognitive explanation for this phenomenon may be particularly related to the peculiar characteristics of the neglect syndrome also found in the patient: in some, although not all, other tasks administered in this investigation, the patient's visuo-spatial attention and motor behavior are abnormally attracted towards the lower-right quadrant (e.g., more omissions in upper-left field, and a tendency for more commissions in lower-right field, see Table 2). The presence of neglect for the upper-left field during visuo-motor tests strongly suggests a contribution of this spatial attention deficit to the gradual attraction towards the lower-right field during writing behavior.

It is however possible that the influence of neglect progressively also increases because of concomitant impairments in other cognitive processes supporting writing skills, namely a very low spatial short-term memory capacity, weak

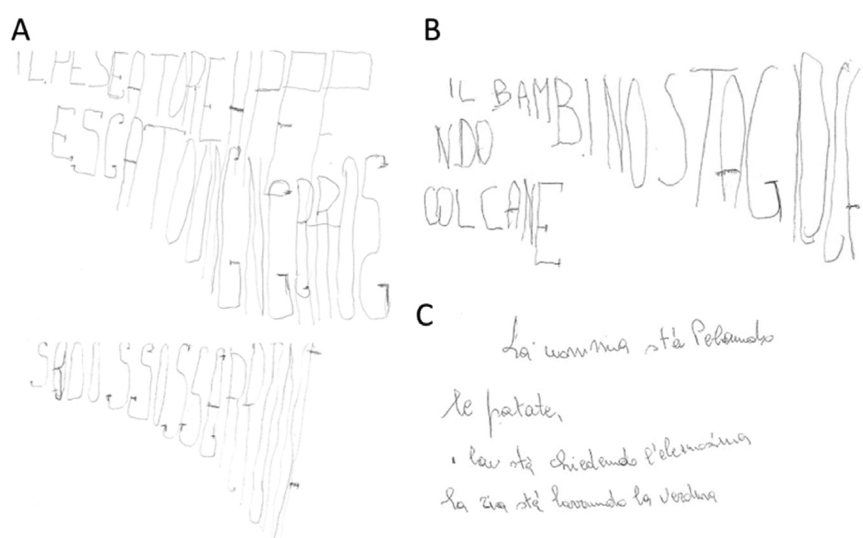

Fig. 6 – The patient was requested to write simple sentences in uppercase print (A–B) and lowercase cursive (C) to describe pictures taken from the Aachen Aphasia Test (AAT).

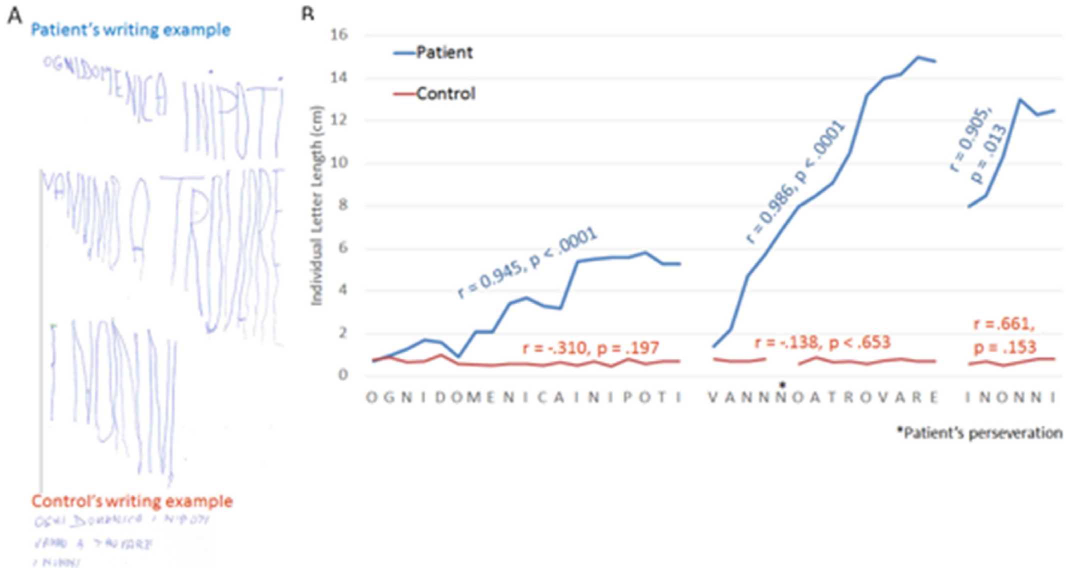

Fig. 7 – Panel A. Examples of patient's and control's performance when asked to write to dictation the sentence: "OGNI DOMENICA I NIPOTI/n VANNO A TROVARE/n I NONNI". Panel B. Results of the Pearson correlation analyses performed on the writing to dictation. Each letter is shown in the *x*-axis and its length (in cm) in the *y*-axis.

attention and executive functions (e.g., McCutchen, 2011; Racine et al., 2008), a multifaceted pattern of deficits that is compatible with the patient's multifocal (fronto-temporo-parietal) cortical and white-matter lesions. All these factors would possibly have an increasing influence in determining the size of the effect: the control over the size would thus progressively weaken, increasing the effect of the abnormal attraction toward the bottom.

The strong sequential dependency between the lengths of the letters in neighboring positions deserves further discussion. As far as writing is concerned, the key point, if the stored engram (allograph) is intact, is when to stop one stroke and begin the next one. The patient was fairly slow, so that writing a stroke, when the effect was occurring, took a couple of seconds or so. Since the patient suffers from neglect of the left and upper visual fields and has impaired verbal and spatial working memory capacity, there may be little influence of letters on the left of the one she is currently writing or previous ones on its size. The exception is the letter immediately to the left of the one she is writing. This assumption about the preceding letter would explain why it can act as a guide to the size of the current letter, and so result in a strong sequential dependency between the lengths of the letters in neighboring positions (note that the patient's Corsi score is 1 and not 0). It would also explain why moving back to the top of the next letter is not basically affected.

In summary, one way to cognitively account for elongation in this patient is as an unusual form of neglect dysgraphia selective for the block print allograph (cf., Baxter & Warrington, 1983), but with deficits of executive functions, spatial attention and working memory components involved as well. Thus, in contrast to micrographia, the progressive macrographia case described here could not be interpreted in the framework of extrapyramidal or cerebellar disorders. A difficulty in sensorimotor integration and a lack of motor control might also partially contribute to the fact that the action does not stop when it should, and some strokes are exaggeratedly elongated (Feder & Majnemer, 2007), in this case towards the non-neglected lower-right space.

The influence of all these factors may, however, vary according to the type of case and font, as the phenomenon is clearly present only when handwriting occurs in block capitals, an issue that will be dealt with in the next sub-section (4.2).

4.2. *Specificity of progressive macrographia for the block script handwriting and sparing of cursive script*

The specificity of the disturbance for block print writing stands as a unique feature of this case and needs to be explained. In this respect, a number of characteristics distinguishing block print writing from cursive must be considered. Block letter writing is likely to be a more difficult, and less automatic writing schema (especially in cultures where it is not the primary way of handwriting) with respect to cursive and number writing (e.g., Semeraro et al., 2019). In fact, in Italy, print writing, although occasionally used for taking short notes, becomes much less common soon after the acquisition of writing skills, while lowercase cursive becomes the most prevalent handwriting style across the whole lifespan. Another peculiarity of writing in print is that the pen must be picked up between strokes so making the writing more challenging, choppier and jerkier than cursive in terms of fine-motor movements. Being more discontinuous and less fluid than cursive, it might trigger more errors and so be increasingly sensitive to spatial disorders. Print writing also requires much more space between letters than cursive writing (which might be relevant for neglect-related factors). Print writing in fact is indeed thought to be more prone to errors in patients with dysgraphia than cursive writing (Silveri et al., 1999). In normal circumstances, adults write faster in cursive mode than in print mode (Gates & Brown, 1929; Graham & Miller, 1980; Gray, 1930).

The literature does in fact report a number of cases of "allographic agraphia" whereby the main deficit is a selective inability to produce written letters in a specific case and/or font. Some of them concern specifically the printing of capital letters (Menichelli et al., 2008, 2012; Venneri et al., 2002). These cases support the idea that the information about the font and case of letters, the procedures for accessing them and implementing their writing may be represented with sufficient neural and functional independence that brain damage can selectively affect one type of case or font, leaving the others intact (Exner, 1881). Importantly, the same reasoning may hold for Arabic numbers, which are indeed spared in the present case. Menichelli et al. (2012) argued that the allographic retrieval process for word-like letter sequences is largely implicit and based on the inherent mechanisms of procedural memory rather than declarative memory. In cursive writing, single letters in a word-like sequence are graphically connected, unlike in print writing, where each letter is not connected to neighboring letters. A relatively higher reliance on implicit cognitive processes than on explicit ones may thus be sufficient to support cursive writing. Indeed, cursive writing might still rely on procedural memory, which in turn may rely on the patient's intact basal ganglia and cerebellar regions (Doyon et al., 2009; Menichelli et al., 2012), although we cannot totally exclude that the connectivity of the underlying circuits is impaired as a consequence of lesions elsewhere in the brain. In summary, the specificity of this phenomenon may derive from the fact that intact procedural memory circuits might be sufficient to sustain more practiced and automatized cursive handwriting and make this writing style more resilient to impaired spatial attention and working memory.

Apart from the spatial attention and working memory deficits already discussed above, there is another complementary factor that might help to account for the specificity of these findings, that is, energization difficulties. Energization is the ability to voluntarily invest attention to optimize behavior for achieving a goal. It is needed for controlled initiation and maintenance of responses, and it is sustained by superior medial prefrontal structures (Paus, 2001; Stuss et al., 1995; Stuss & Alexander, 2007). Thus, we might cautiously speculate that the patient also suffers from a severe energization failure. An energization deficit is compatible, behaviorally, with spontaneous speech inertia, as the patient most often spoke only in answer to the examiners' questions and, anatomically, with medial frontal lesions involving (abnormally hypermetabolic) anterior cingulate and callosal structures, and with hypometabolism in premotor regions. This would leave the patient unable to voluntarily concentrate, leaving room for neglect deficits to progressively affect the size of writing, especially for the most difficult writing style, that is, block capital handwriting. That the latter was the most difficult writing style for our patient is also corroborated by the fact that all types of errors occurred almost exclusively with this writing style (Table 3). Moreover, the patient's known right frontal lesion might have produced failure of performance monitoring (Shallice & Cipolotti, 2018; Stuss & Alexander, 2007; Vallesi, 2021), which would in turn exacerbate the problem. The patient appeared indeed unaware of her progressive macrographia. A note of caution should of course be used when discussing anatomo-clinical relationships in this patient with multifocal lesions.

4.3. *Anatomical differences from previous cases of macrographia*

A remarkable feature of the present case is the absence of visible cerebellar and basal ganglia damage. Macrographia is often reported following cerebellar and/or basal ganglia lesions (Bing, 1923; Frings et al., 2010; Manto, 2018), although it still needs to be better explained at the cognitive level. In the case reported here, neuroimaging data suggest that the source of this special case of progressive macrographia stems from cerebral lesions instead of cerebellar ones.

Traditionally, the peripheral components of the writing process have been associated with the left intraparietal sulcus, the left superior parietal lobule, the left premotor area, and the bilateral supplementary motor area (SMA) (Beeson et al., 2003). There is a consensus about the kinematic representations of graphomotor trajectories in parietal regions (Seitz et al., 1997) and the translation of these commands in specific motor patterns by premotor areas (Beeson & Rapcsak, 2011). These areas seem to be largely preserved in the present case, which may explain why the writing of letters is preserved and, with the exception of progressive macrographia, letters are relatively well formed.

In contrast, a deep right temporoparietal white matter lesion may be responsible for spatial neglect, to which the right frontal lesion may also contribute. The right temporal lesion and hypometabolism may also explain the patient's profound spatial working memory defect. Finally, the widespread bilateral frontal damage extending to forceps minor is conceivably responsible for the dysexecutive component of the phenomenon. In combination, these multifocal lesions and their functional consequences may have led to the particular case of macrographia reported here, that remarkably appears in absence of conspicuous cerebellar lesions.

4.4. *Limitations*

The influence of a possible contribution of "central" linguistic components to this case of macrographia could not be safely assessed as the patient became progressively untestable. Thus, the question of whether there is any interaction between linguistic and non-linguistic writing mechanisms remains unanswered. This is a limitation of the present study. Indeed, while increase in size, elongation and progressivity allow speculations to be made about more peripheral aspects of writing, the phenomena suggesting a central involvement are rather scanty. Some of the errors made are graphene substitutions, while others look like errors of the type found in surface dyslexia; they could derive from coexisting, independent disturbances that can be expected in a patient with multiple lesions. It is hard to establish, in fact, whether these errors come from a meaningful interaction of central components with peripheral ones, even if they seem to appear mostly in the block print handwriting. They could simply emerge more conspicuously when the task is harder for the patient. In fact, graphemic errors were found by Trojano and Chiacchio (1994) in a patient who showed relatively spared lowercase cursive writing with respect to uppercase print writing (where several types of errors were present, including letter deletions, substitutions, insertions and transpositions). The authors attributed such errors to a deficit in the graphemic output buffer which however revealed itself to different degrees in the two handwriting styles.

As another limitation, all of our accounts were solely based on structural/metabolic neuroimaging data. Additional functional neuroimaging data (e.g., task-related and resting-state functional MRI) would have been desirable, if feasible at all, to more directly demonstrate many of the (functional) anatomo-clinical hypotheses put forward to explain our patient's peculiar behavior, but she rapidly became untestable and further investigation could not be carried out.

5. Conclusions

In conclusion, this single case of progressive macrographia highlights that the processes involved in writing in block letters can be partially dissociated from those involved in cursive handwriting. More specifically, the theoretically-relevant possibility arises from this case study that a mixture of intact spatial attention, executive functions and working memory processes is necessary to write properly in block letters while keeping the spatial distribution of the written product in the page under control and avoiding progressive misalignment and elongation of individual letters. Future research should experimentally manipulate each of these cognitive processes in writing tasks to disentangle their specific weight in this phenomenon.

Ethics statement

The patient was always compliant and gave her oral informed consent to participate to the neuroimaging session and the neuropsychological testing that was conducted for diagnostic purposes, as a follow-up of routine neuropsychological evaluation. This study was approved by the Ethics Committee of the Padua University Hospital (Prot. N. 0017052). Given the highly time-sensitive nature of the clinical case under study, no part of the procedures or analyses were pre-registered prior to this neuropsychological assessment being carried out. The conditions of our clinical evaluation do not allow public data archiving for this case study. Qualified researchers seeking access to the data should contact the corresponding author. Data will be shared with named individuals following completion of a data sharing agreement and approval of the local research ethics committee.

Credit author statement

Semenza Carlo: Conceptualization, Methodology, Investigation, Writing-Original draft preparation, Writing-Reviewing and Editing, Supervision, Project administration.

De Pellegrin Serena: Conceptualization, Investigation, Formal analysis, Resources, Data curation, Writing-Reviewing and Editing.

Facchini Silvia: Investigation, Data curation, Formal analysis, Writing-Reviewing and Editing.

Cecchin Diego: Investigation, Formal analysis, Writing-Reviewing and Editing.

Manara Renzo: Formal analysis, Writing-Reviewing and Editing.

Shallice Tim: Conceptualization, Writing-Original draft preparation, Writing-Reviewing and Editing.

Vallesi Antonino: Conceptualization, Methodology, Validation, Formal analysis, Resources, Data curation, Writing-Original draft preparation, Writing-Reviewing and Editing, Visualization, Supervision, Project administration.

Acknowledgments

This work was in part supported by the “Department of Excellence 2018-2022" initiative of the Italian Ministry of University and Research (MIUR) awarded to the Department of Neuroscience – University of Padua.

REFERENCES

Albert, M. L. (1973). A simple test of visual neglect. *Neurology, 23*(6), 658–664. https://doi.org/10.1212/WNL.23.6.658

Auclair, L., Siéroff, E., & Kocer, S. (2008). A case of spatial neglect dysgraphia in Wilson's Disease. *Archives of Clinical Neuropsychology, 23*(1), 47–62. https://doi.org/10.1016/j.acn.2007.08.011

Bajaj, N. P. S., Wang, L., Gontu, V., Grosset, D. G., & Bain, P. G. (2012). Accuracy of subjective and objective handwriting assessment for differentiating Parkinson's disease from tremulous subjects without evidence of dopaminergic deficits (SWEDDs): An FP-CIT-validated study. *Journal of Neurology, 259*(11), 2335–2340. https://doi.org/10.1007/s00415-012-6495-5

Barbarulo, A. M., Grossi, D., Merola, S., Conson, M., & Trojano, L. (2007). On the genesis of unilateral micrographia of the progressive type. *Neuropsychologia, 45*(8), 1685–1696. https://doi.org/10.1016/j.neuropsychologia.2007.01.002

Baxter, D. M., & Warrington, E. K. (1983). Neglect dysgraphia. *Journal of Neurology, Neurosurgery, and Psychiatry, 46*(12), 1073–1078.

Beeson, P. M., & Rapcsak, S. Z. (2011). Agraphia. In J. S. Kreutzer, J. DeLuca, & B. Caplan (Eds.), *Encyclopedia of clinical neuropsychology* (pp. 55–60). Springer. https://doi.org/10.1007/978-0-387-79948-3_851.

Beeson, P. M., Rapcsak, S. Z., Plante, E., Chargualaf, J., Chung, A., Johnson, S. C., & Trouard, T. P. (2003). The neural substrates of writing: A functional magnetic resonance imaging study. *Aphasiology, 17*(6–7), 647–665. https://doi.org/10.1080/02687030344000067

Bing, R. (1923). Über einige bemerkenswerte Begleiterscheinungen der “extrapyramidalen Rigidität”(Akathisie-Mikrographie-Kinesia paradoxa). *Swiss Medical Weekly, 53*, 167–171.

Caffarra, P., Vezzadini, G., Dieci, F., Zonato, F., & Venneri, A. (2002). Rey-Osterrieth complex figure: Normative values in an Italian population sample. *Neurological Sciences, 22*(6), 443–447. https://doi.org/10.1007/s100720200003

Capasso, R., & Miceli, G. (2005). *Esame Neuropsicologico per l'Afasia - E.N.P.A.* Springer-Verlag Italia. www.springer.com/gp/book/9788847001527.
Cubelli, R., Guiducci, A., & Consolmagno, P. (2000). Afferent dysgraphia after right cerebral stroke: An autonomous syndrome? *Brain and Cognition, 44*(3), 629–644. https://doi.org/10.1006/brcg.2000.1239
Demeyere, N., Riddoch, M. J., Slavkova, E. D., Bickerton, W.-L., & Humphreys, G. W. (2015). The Oxford Cognitive Screen (OCS): Validation of a stroke-specific short cognitive screening tool. *Psychological Assessment, 27*(3), 883–894. https://doi.org/10.1037/pas0000082
Denes, G., Signorini, M., & Volpato, C. (2005). Post graphemic impairments of writing: The case of micrographia. *Neurocase, 11*(3), 176–181. https://doi.org/10.1080/13554790590944636
Doyon, J., Bellec, P., Amsel, R., Penhune, V., Monchi, O., Carrier, J., Lehéricy, S., & Benali, H. (2009). Contributions of the basal ganglia and functionally related brain structures to motor learning. *Behavioural Brain Research, 199*(1), 61–75. https://doi.org/10.1016/j.bbr.2008.11.012
Exner, S. (1881). *Untersuchungen über die Localisation der Functionen in der Großhirnrinde des Menschen.* Vienna: Braumüller.
Feder, K. P., & Majnemer, A. (2007). Handwriting development, competency, and intervention. *Developmental Medicine and Child Neurology,* 49(4), 312–317. https://doi.org/10.1111/j.1469-8749.2007.00312.x
Fradis, A., & Leischner, A. (1985). Number agraphia. *European Archives of Psychiatry and Neurological Sciences, 235*(2), 82–91. https://doi.org/10.1007/BF00633477
Frings, M., Gaertner, K., Buderath, P., Christiansen, H., Gerwig, M., Hein-Kropp, C., Schoch, B., Hebebrand, J., & Timmann, D. (2010). Megalographia in children with cerebellar lesions and in children with attention-deficit/hyperactivity disorder. *Cerebellum (London, England), 9*(3), 429–432. https://doi.org/10.1007/s12311-010-0180-y
Gates, A. I., & Brown, H. (1929). Experimental comparisons of print-script and cursive writing. *Journal of Environmental Radioactivity, 20*(1), 1–14. https://doi.org/10.1080/00220671.1929.10879960
Graham, S., & Miller, L. (1980). Handwriting research and practice: A unified approach. https://doi.org/10.17161/FOEC.V13I2.7428.
Gray, W. H. (1930). An experimental comparison of the movements in manuscript writing and cursive writing. *The Journal of Economic Perspectives: a Journal of the American Economic Association, 21*(4), 259–272. https://doi.org/10.1037/h0075967
Haymaker, W. (1956). Robert Paul bing, 1878-1956. *A.M.A. Archives of Neurology and Psychiatry, 76*(5), 508–510. https://doi.org/10.1001/archneurpsyc.1956.02330290052006
Hochheimer, W. (1936). Zur Psychologie des Choreatikers. *J Psychiatr, 47*, 49.
Holmes, G. (1917). The symptoms of acute cerebellar injuries due to gunshot injuries. *Brain: a Journal of Neurology, 40*(4), 461–535. https://doi.org/10.1093/brain/40.4.461
Kanno, S., Shinohara, M., Kanno, K., Gomi, Y., Uchiyama, M., Nishio, Y., Baba, T., Hosokai, Y., Takeda, A., Fukuda, H., Mori, E., & Suzuki, K. (2020). Neural substrates underlying progressive micrographia in Parkinson's disease. *Brain and Behavior, 10*(8), Article e01669. https://doi.org/10.1002/brb3.1669
Kim, E.-J., Lee, B. H., Park, K. C., Lee, W. Y., & Na, D. L. (2005). Micrographia on free writing versus copying tasks in idiopathic Parkinson's disease. *Parkinsonism & Related Disorders, 11*(1), 57–63. https://doi.org/10.1016/j.parkreldis.2004.08.005
Letanneux, A., Danna, J., Velay, J.-L., Viallet, F., & Pinto, S. (2014). From micrographia to Parkinson's disease dysgraphia. *Movement Disorders, 29*(12), 1467–1475. https://doi.org/10.1002/mds.25990
Lorch, M. (2013). Written language production disorders: Historical and recent perspectives. *Current Neurology and Neuroscience Reports, 13*(8), 369. https://doi.org/10.1007/s11910-013-0369-9
Mancuso, M., Varalta, V., Sardella, L., Capitani, D., Zoccolotti, P., Antonucci, G., & Italian OCS Group.. (2016). Italian normative data for a stroke specific cognitive screening tool: The Oxford Cognitive Screen (OCS). *Neurological Sciences, 37*(10), 1713–1721. https://doi.org/10.1007/s10072-016-2650-6
Manto, M. (2018). Cerebellar motor syndrome from children to the elderly. *Handbook of Clinical Neurology, 154*, 151–166. https://doi.org/10.1016/B978-0-444-63956-1.00009-6
Mariën, P., & Manto, M. (2015). *The linguistic cerebellum.* Academic Press.
Martinez-Hernandez, H. R., & Louis, E. D. (2014). Macrographia in essential tremor: A study of patients with and without rest tremor. *Movement Disorders, 29*(7), 960–961. https://doi.org/10.1002/mds.25894
McCutchen, D. (2011). From novice to expert: Language and memory processes in the development of writing skill. *Journal of Writing Research, 3*(1), 51–68. https://doi.org/10.17239/jowr-2011.03.01.3
Menichelli, A., Machetta, F., Zadini, A., & Semenza, C. (2012). Allographic agraphia for single letters. *Behavioural Neurology, 25*(3), 233–244. https://doi.org/10.3233/BEN-2012-119008
Menichelli, A., Rapp, B., & Semenza, C. (2008). Allographic agraphia: A case study. *Cortex; a Journal Devoted To the Study of the Nervous System and Behavior,* 44(7), 861–868. https://doi.org/10.1016/j.cortex.2007.06.002
Mody, M. (2017). *Neural mechanisms of language.* Springer.
Monaco, M., Costa, A., Caltagirone, C., & Carlesimo, G. A. (2013). Forward and backward span for verbal and visuo-spatial data: Standardization and normative data from an Italian adult population. *Neurological Sciences, 34*(5), 749–754. https://doi.org/10.1007/s10072-012-1130-x
Mondini, S., Mapelli, D., Vestri, A., Arcara, G., & Bisiacchi, P. (2011). Esame neuropsicologico breve 2 *(II)*. Raffaello Cortina Editore. http://www.raffaellocortina.it/scheda-libro/sara-mondini-daniela-mapelli-alec-vestri/esame-neuropsicologico-breve-2-9788860304193-870.html.
Paus, T. (2001). Primate anterior cingulate cortex: Where motor control, drive and cognition interface. *Nature Reviews. Neuroscience, 2*(6), 417–424. https://doi.org/10.1038/35077500
Petitpierre, M. (1925). Über den Antagonismus zwischen der "parkinsonistischen" Mikrographie und der cerebellaren Megalographie. *Schweiz Arch Neurol Psychiatr, 17*, 270–282.
Phillips, J. G., Bradshaw, J. L., Chiu, E., & Bradshaw, J. A. (1994). Characteristics of handwriting of patients with Huntington's disease. *Movement Disorders, 9*(5), 521–530. https://doi.org/10.1002/mds.870090504
Planton, S., Jucla, M., Roux, F.-E., & Démonet, J.-F. (2013). The "handwriting brain": A meta-analysis of neuroimaging studies of motor versus orthographic processes. *Cortex; a Journal Devoted To the Study of the Nervous System and Behavior, 49*(10), 2772–2787. https://doi.org/10.1016/j.cortex.2013.05.011
Purcell, J. J., Turkeltaub, P. E., Eden, G. F., & Rapp, B. (2011). Examining the central and peripheral processes of written word production through meta-analysis. *Frontiers in Psychology,* 2, 239. https://doi.org/10.3389/fpsyg.2011.00239
Racine, M. B., Majnemer, A., Shevell, M., & Snider, L. (2008). Handwriting performance in children with attention deficit hyperactivity disorder (ADHD). *Journal of Child Neurology, 23*(4), 399–406. https://doi.org/10.1177/0883073807309244
Rapcsak, S. Z., & Beeson, P. M. (2000). Agraphia. In L. J. G. Rothi, B. Crosson, & S. Nadeau (Eds.), *Aphasia and language: Theory and practice* (pp. 184–220). Guilford Press.

Seitz, R. J., Canavan, A. G., Yágüez, L., Herzog, H., Tellmann, L., Knorr, U., Huang, Y., & Hömberg, V. (1997). Representations of graphomotor trajectories in the human parietal cortex: Evidence for controlled processing and automatic performance. *The European Journal of Neuroscience, 9*(2), 378–389. https://doi.org/10.1111/j.1460-9568.1997.tb01407.x

Semeraro, C., Coppola, G., Cassibba, R., & Lucangeli, D. (2019). Teaching of cursive writing in the first year of primary school: Effect on reading and writing skills. *Plos One, 4*(2), Article e0209978. https://doi.org/10.1371/journal.pone.0209978

Shallice, T., & Cipolotti, L. (2018). Prefrontal cortex and neurological impairments of active thought. *Annual Review of Psychology, 69*(1), 157–180. https://doi.org/10.1146/annurev-psych-010416-044123

Silveri, M. C., Misciagna, S., Leggio, M. G., & Molinari, M. (1999). Cerebellar spatial dysgraphia: Further evidence. *Journal of Neurology, 246*(4), 312–313. https://doi.org/10.1007/s004150050353

Spinnler, H., & Tognoni, G. (1987). *Standardizzazione e taratura italiana di test neuropsicologici: Gruppo italiano per lo studio neuropsicologico dell'invecchiamento*. Masson Italia Periodici.

Stuss, D. T., & Alexander, M. P. (2007). Is there a dysexecutive syndrome? *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 362*(1481), 901–915. https://doi.org/10.1098/rstb.2007.2096

Stuss, D. T., Shallice, T., Alexander, M. P., & Picton, T. W. (1995). A multidisciplinary approach to anterior attentional functions. *Annals of the New York Academy of Sciences, 769*, 191–211. https://doi.org/10.1111/j.1749-6632.1995.tb38140.x

Thomas, A. (1911). *La fonction cérébelleuse*. Doin et fils.

Trojano, L., & Chiacchio, L. (1994). Pure dysgraphia with relative sparing of lower-case writing. *Cortex; a Journal Devoted To the Study of the Nervous System and Behavior, 30*(3), 499–501. https://doi.org/10.1016/s0010-9452(13)80345-0

Vallar, G., Rusconi, M. L., Fontana, S., & Musicco, M. (1994). Tre test di esplorazione visuo-spaziale: Taratura su 212 soggetti normali. *Arch Psicol Neurol Psichiatr, 55*, 827–841.

Vallesi, A. (2021). The quest for hemispheric asymmetries supporting and predicting executive functioning. *Journal of Cognitive Neuroscience, 33*(9), 1679–1697. https://doi.org/10.1162/jocn_a_01646

Van Dun, K., Vandenborre, D., & Marien, P. (2015). Cerebellum and writing. In P. Mariën, & M. Manto (Eds.), *The linguistic cerebellum* (pp. 149–198). Academic Press.

Venneri, A., Pestell, S. J., & Caffarra, P. (2002). Independent representations for cursive and print style: Evidence from dysgraphia in Alzheimer's disease. *Cognitive Neuropsychology, 19*(5), 387–400. https://doi.org/10.1080/02643290143000204

Wilson, S. A. K. (1925). Some disorders of motility and of muscle tone, with special reference to the corpus striatum. *Lancet, 206*(1–10), 53–62. https://doi.org/10.1016/S0140-6736(01)20638-2, 169–178; 215–219; 268–276.

Wilson, B., Cockburn, J., & Halligan, P. (1987). Development of a behavioral test of visuospatial neglect. *Archives of Physical Medicine and Rehabilitation, 68*(2), 98–102.