HOW DYSGRAPHIA IN ALZHEIMER'S PROGRESSES AND COMPARES TO OTHER WRITING DISORDERS

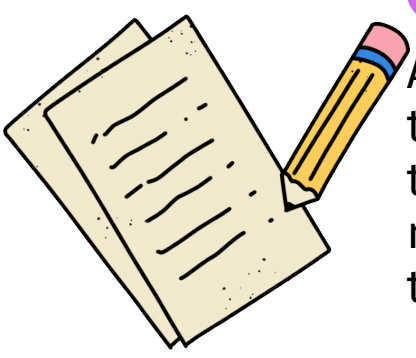
What is Alzheimer's?

- Alzheimer's Disease (AD) is a type of dementia
- It **affects behavior, thinking, and memory.**
- AD may affect the progression of **dysgraphia**, a neurological condition that affects writing.

Background

- Many symptoms of AD **progress linearly** with the disease.
- **The details of progression** in symptoms of comorbid diseases such as dysgraphia **is unknown.**

Methods



AD patients were given a set of writing tasks, then scored based on severity and type of spelling errors made. After 6-12 months, a portion of the patients were tested again.

Observations

- There was **high variability** in dysgraphia vs. AD progression
- AD patients' scores **spanned the dysgraphia spectrum**

Results

- Severity of dysgraphia **does not progress linearly** with severity of AD.
- Dysgraphic symptoms in AD patients is **very similar** to people with **brain damage.**

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Biology 469
Professor Bergstrom
Research Paper 3: Graphical Abstract

Alzheimer's Disease (AD) is a neurological disorder that is best known for its' effects on the memory of those affected. There is a wide range of symptoms experienced by people with Alzheimer's, not limited to mood changes, behavioral changes, the deterioration of memory, etc. A perhaps lesser-known symptom of AD is its' impairments on one's motor skills, which can cause other diseases such as dysgraphia. The paper I chose, "Multiple patterns of writing disorders in dementia of the Alzheimer type and their evolution", by Luzzatti et al. (2003), investigates the progression and pathology of dysgraphia in AD patients, as well as characterizing the symptoms relative to other conditions that may cause impairments in one's writing, such as brain damage.

In my graphical abstract, I chose to represent this with a purple infographic, as purple is the color of Alzheimer's. The infographic is divided up into five sections, each with a clear heading to guide readers. In my first section, "What is Alzheimer's?" I give a brief introduction to the pathology of the disease and how it relates to dysgraphia. Though the paper didn't explicitly give a description or introduction to AD in their abstract, I thought this would be appropriate and relevant to include in a graphical abstract targeting an audience of a non-scientific background (as the authors of the paper assume that their audience is one of a scientific background, with many that are experts in the field of AD research, or at least familiar with the disease). Then, with my "Background" section, I introduced a bit more information about dysgraphia in the context of AD, allowing readers to understand the significance of the question (which is in the title) of the paper. I then divided the methods, observations, and results sections into two different blocks (each with their own section), to help the reader separate the categories in a way that was easier to digest. "Methods" was in its' own section and kept relatively short, as the specifics of how the study was conducted may not have high relevance or garner high interest from the layman.

Each section of the graphical abstract has either one or two images next to it to help convey part of the meaning of the text, as well as help retain the interest of the reader. Every section (except for the "Methods" section) is broken up further with the use of bullet points.

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Multiple patterns of writing disorders in dementia of the Alzheimer type and their evolution

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Abstract

This paper reports the results obtained from a writing task given to 23 Italian patients suffering from mild to moderate dementia of the Alzheimer's type (DAT). Spelling performance was tested with a task that taps the sub-word-level (spelling of regular words and nonwords), and the lexical route (spelling of regular and irregular words), in line with contemporary models of writing. Each patient's performance was classified according to the emergence of dissociated patterns of damage between regular words and nonwords and between regular and irregular words.

The 23 DAT patients span the whole spectrum of dysgraphic taxonomy; five showed the characteristic pattern of impairment of surface dysgraphia, two showed the characteristics of phonological dysgraphia, while a mixed pattern (i.e. better performance on regular words compared to irregular words and regular nonwords) emerged in seven cases. Three patients presented undifferentiated writing disorders, two were completely agraphic, while four patients showed only minimal or no writing defects. The rate of dissociated impairments in the lexical and the sub-word-level routine is very similar to that observed after acute focal brain damage, which contradicts the hypothesis that degenerative brain damage selectively impairs writing performance along the lexical-semantic route.

To test the hypothesis that surface sub-word-level processing abilities are affected only during the evolution of the disease, nine patients were tested longitudinally after an interval of 6–12 months. Once again, the data showed high variability across subjects, and do not seem to support involvement of the sub-word-level spelling routine only at a late stage in the development of the disease.

Keywords: Dementia of the Alzheimer's type; Writing disorders; Spelling disorders; Phonological and surface dysgraphia

1. Introduction

The language impairment which emerges in dementia of the Alzheimer's type (DAT) is traditionally described as conforming to an almost standard pattern. However, clinical practice and the results of several group studies on DAT patients have shown that communication disorders lack homogeneity across patients, both at onset and during evolution of the disease [1,37].

Studies on writing impairments reflect the relative lack of consistency in the findings regarding verbal output. Early authors reported a precocious and fairly constant impairment of both reading and writing (e.g. [10]), but several studies found that in more than 40% of mild to moderate DAT patients spelling is preserved [3], or is affected only in the later stages of the degenerative disease [12,14]. Overall, the level of correlation of spelling performance with DAT severity seems to be fairly low, but it increases significantly in certain tasks such as the written description of pictures [21,24], or spontaneous writing of sentences [26], where a greater number of operations interact. Thus, it appears that phenomena such as inertia, morpho-syntactic impairment, visuo-spatial disorders or perseverative behaviour may interfere with the normal performance of the task.

1.1. Cognitive models of writing and dysgraphia

Recent studies on dysgraphia which follows acute brain damage have analysed spelling impairments in a cognitive neuropsychological frame. This approach requires that subjects use at least two independent spelling procedures: a *lexical route* based on access to stored lexical-semantic representations (i.e. the phonological input lexicon, the underlying semantic representations and the orthographic output lexicon), and a *sub-word-level routine* based on phonological-to-orthographic conversion rules. Once the

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appropriate orthographic string has been obtained it must be retained in a specific short-term memory store (the *graphemic buffer*), after which it will be addressed to peripheral output procedures, i.e. oral or written spelling, and subsequent hand-writing or typing motor control. The capacity of literate subjects to write irregular words, as well as unfamiliar words or legal nonwords (i.e. nonlexical but phonotactically plausible phonological strings) from dictation can only be explained by the use of at least two writing routes.

Observation of patients with acquired brain lesions has provided proof of two independent spelling procedures. Focal brain damage may cause writing disorders that appear to involve either routine selectively. Some patients cannot access lexical knowledge, but still make correct use of phonological-to-orthographic conversion rules, thus making a prevalence of phonologically plausible errors when writing irregular words, i.e. words with unpredictable spelling. Such a deficit is called *surface dysgraphia* or *lexical agraphia* [6,20]. Other patients can write words they have learned to spell in the past, whether regular or irregular, but are unable to write a legal nonword. This type of damage is usually known as *phonological dysgraphia* [5,34,39]. Impairment of the graphemic buffer causes an undifferentiated spelling disorder involving both retrieved and assembled orthographic strings, where word length effect is the most characteristic feature [9]. Finally, dysgraphia may result from damage beyond the graphemic buffer, i.e. to more peripheral levels of processing. These include the retrieval of letter shapes, and the corresponding hand-writing motor programs, and of letter names.

The results of a multiple single-case study on a sample of 52 Italian dysgraphic patients after acute focal brain damage [28] showed that approximately three-quarters of the aphasic patients suffer from disproportionate impairment either of the lexical route or of the sub-word-level spelling procedure, or of a mixed pattern of impairment (i.e. resulting in a better performance on regular words as opposed to irregular words and regular nonwords). Another 25% of the patients showed an undifferentiated impairment compatible with multiple foci of writing damage, selective damage to the graphemic buffer, or peripheral damage to the retrieval for letter shapes, etc.

1.2. Cognitive neuropsychological analyses of writing deficits in DAT

Several studies used a cognitive neuropsychological frame to describe the writing impairments emerging in DAT patients. Once again, results are inconsistent, but surface dysgraphia seems to be the most frequent form of damage, with preserved spelling of regular words and nonwords along the sub-word-level routine, and more severe impairment of irregular words, due to over-reliance on phoneme-to-grapheme conversion rules. This was the case of a Japanese patient ([19], case 1), who was no longer able to read and write Kanji ideograms, but was still able to read and write Kana syllabic characters. Surface spelling alone was also used by a German patient [13], who was still able to access German orthographic conversion rules, but without the orthographic lexical feedback necessary to select the correct version from the phonologically plausible alternatives (for example, the correct orthography of the German word [tsa:l] “number”, is *Zahl* and not *Zaal*, whereas that of the word [za:l], “hall”, is *Saal*, and not *Sahl*).

Recent investigations have attempted to verify whether the pattern of damage described for these subjects is applicable to the writing disorders of the entire DAT population. Rapcsak et al. [38] analysed the spelling performance of 11 DAT patients in writing regular words, irregular words, and nonwords. The results of the study would support a progressive involvement of the lexical spelling procedure and the relative preservation of the phoneme-to-grapheme conversion route, since the performance of all the 11 patients was significantly worse on irregular words, with a majority of phonologically plausible regularisation errors. In addition, five subjects also revealed a severe praxic-constructive writing deficit, which obliged the authors to use oral spelling to assess the orthographic abilities of the patients.

Several studies have confirmed the assumption that surface dysgraphia is the most typical writing disorder in DAT patients [11,18,25], in particular at disease onset [22,36] and in patients in which the first symptom of the degenerative disease was a progressive language impairment of the *semantic dementia* type (e.g. [23,41], see also [17] for a review).

On the other hand, however, other studies failed to find a similar homogeneity across patients or to confirm a prevalence of phonologically plausible regularisation errors, since a qualitative analysis of writing performance usually also shows substitution, perseveration and omission errors [4,21,24,27,33], and grapho-motor dyspraxic-dysgraphic damage, even in mild-to-moderate DAT forms. Furthermore, the spelling performance of those patients who made a majority of phonologically plausible errors does not seem to differ qualitatively from that of the control subjects and would therefore appear to be affected by a more general processing load effect of the degenerative disease [15,16] rather than by selective damage to the lexical spelling route.

In her detailed review of dysgraphia in dementia, Graham [17] refuted the assumption that a single pattern of spelling impairment is always associated with DAT. The author suggests that surface dysgraphia emerges as the most frequent pattern of impairment during the early stages of the disease, but subsequently, patients would tend to produce an increasing number of non-phonologically plausible errors (substitutions, omissions and perseverations) and of peripheral graphomotor errors. A similar evolution was also documented [22] in a DAT patient who showed regularity effects (regular words and nonwords were spelled better than irregular words, with phonologically plausible regularisation errors) in the early stage of the disease, followed by a precipitous deterioration in nonword spelling and by an increase of non-phonologically plausible errors.

1.3. Aims of the study

The aim of the present study is to analyse the presence, type and severity of spelling impairments in DAT patients. Firstly, the average pattern of dysgraphia observed in a sample of mild-to-moderate Italian DAT patients will be described. As the patients were expected to show a heterogeneous pattern of impairment, the spelling performance of each single subject was analysed. In addition, it will be verified if surface dysgraphia does actually occur as an early phenomenon, while the other dysgraphic patterns only emerge in the later phases of the disease. Finally, the hypothesis that different patterns of dysgraphia may co-occur with different types of language impairment will be verified, and the writing damage observed in DAT patients will be compared to that observed in patients suffering from acute focal brain damage.

2. Materials and methods

2.1. Subjects

Twenty-three Italian patients (11 males and 12 females) who were tested for DAT at the Department of Neurology of the Bergamo General Hospital, the Department of Neurology of the *Ospedale San Paolo* and the Geriatric Unit of the *Ospedale Policlinico* of the University of Milan participated in the study. All were diagnosed as probable DAT patients on the basis of the NINCDS-ADRDA criteria [31]. Table 1 summarises the characteristics of the participants. The mean age of the group was 68.4 years (S.D. = 6.6; median = 68; range = 56–80), with mean education 9.8 years (S.D. = 5.2; median = 8; range = 5–18). Mean length of illness was 25.6 months (S.D. = 17.3; median = 22; range = 6–84 months). Severity of the overall cognitive impairment was measured with the Milan overall dementia assessment (MODA) [8]. The MODA scores range from 0 to 100, 89.1 being the normality threshold. Table 1 gives the MODA scores equivalent to those of the Italian version of the mini mental state examination [32]: correspondence was estimated (by means of a linear regression equation) using the scores obtained by another sample of 22 demented patients who were given both the MODA and the mini mental state examination. Twenty-two patients obtained a performance ranging from 42.4 to 87.5 (median = 75.5; mean = 70.97; S.D. = 12.8), while one patient could not be assessed for overall dementia because of a general inability to understand the instructions; this however, contrasted with a still only moderate language and behavioural impairment in a more ecological context. All the patients were still autonomous in daily activities and none had been institutionalised.

Table 1
Description of the 23 DAT subjects and 20 control subjects who participated in the study

Case no.	Gender	Age (years)	Education (years)	Length of illness at the first evaluation (months)	General severity (MODA: range 0–100)	Equivalent to MMSE[a]
1	F	64	8	24	61.4	17
2	M	64	13	36	83.2	23
3	F	68	5	24	70.4	20
4	F	67	5	24	62.4	17
5	M	68	5	18	53.0	15
6	F	68	5	24	66.0	18
7	F	71	5	36	83.8	23
8	F	72	5	6	76.8	21
9	F	68	12	6	86.9	24
10	M	56	18	14	69.0	19
11	F	80	13	12	55.4	16
12	F	74	13	42	57.5	16
13	M	62	18	84	42.4	12
14	M	76	8	12	85.3	24
15	M	76	8	18	75.3	21
16	M	69	18	48	77.8	22
17	M	71	8	12	75.8	21
18	F	80	8	12	79.4	22
19	F	74	18	12	75.5	21
20	M	59	18	36	82.5	23
21	M	64	5	30	87.5	24
22	M	61	5	36	na	–
23	F	59	5	22	54.0	15
Mean (S.D.)		68.4 (6.6)	9.8 (5.2)	25.6 (17.3)	71.0 (12.8)	19.73 (3.48)
Control subjects	12M +8F	67.7 (4.4)	9.4 (4.0)	–	–	–

MODA, Milan overall dementia assessment; MMSE, mini mental state examination; na, not administered.

[a] Correspondence was estimated (by means of a linear regression equation) using the scores obtained by another sample of 22 demented patients who were given both the MODA and the MMSE.

Nine patients were re-examined after an interval of 6–12 months in order to follow the evolution of the writing impairment.

None of the patients had a history of learning disability or prior psychiatric illness. All patients had undergone medical, neurological and neurodiagnostic evaluation to exclude the possibility that the dementia symptoms might be attributed to a non-degenerative aetiology.

Presence and severity of the language impairment was assessed by the Italian version of the Aachen aphasia test (AAT) [30].

2.2. The test

The patients' spelling abilities were tested using three out of the five sections of the writing test developed by Luzzatti et al. [28,29]: (i) spelling of words with regular one-sound-to-one-letter correspondence; (ii) spelling of words with unpredictable orthography; (iii) spelling of nonwords with regular one-sound-to-one-letter correspondence. The lexical stimuli (categories (i) and (ii)) were matched for word frequency and length [29].

2.2.1. Words with regular one-sound-to-one-letter correspondence

In this section the spelling of 80 words with regular shallow orthography was tested. Different sources of lexical (*written word frequency* [7]) and of phonetic-phonological complexity (presence of *continuant* versus *plosive* consonants, stimulus *length*, presence of *consonant clusters*, *presence* of *geminate consonants*) were matched across item subsets [29].

2.2.2. Words with unpredictable transcription along the phonological-to-orthographic conversion routine

The second set of items consisted of 55 words, with an orthography which is not fully predictable by the application of regular sub-word-level spelling routines. The principal features of the Italian orthography are summarised in Appendix A.

2.2.3. Nonwords with one-sound-to-one-letter correspondence

The third set of items included 25 regular nonwords with a phonological and graphemic structure parallel to that of the

Table 2
Subtests of the writing task (from [28,29])

(i) Regular words with one-sound to one-letter correspondence ($n = 80$)	Continuance	Clusters	Doubled consonants	Syllables	n
Examples (translation)					
sole (sun)	Yes	No	No	2	10
lavoro (work)	Yes	No	No	3/4	10
senso (sense)	Yes	Yes (1)	No	2	10
valle (valley)	Yes	No	Yes	2	10
dito (finger)	No	No	No	2	10
prato (meadow)	No	Yes (1)	No	2	10
tappo (cork)	No	No	Yes	2	10
sponda (bank)	No	Yes (2)	No	2	10
(ii) Words with unpredictable transcription ($n = 55$)	Ambiguity	n			
Examples (translation)					
scena/scienza (scene/science)	[tʃ], [ʃ]: ± I	10			
paglia/balia (straw/nurse)	[ʎ]: GL/LI	10			
segno/genio (sign/genius)	[ɲ]: GN/NI	10			
libro/febbre (book/fever)	BR/BBR	10			
cuore/quota (heart/quote)	[kw]: CU/QU	15			
(iii) Nonwords with one-sound-to-one-letter correspondence ($n = 25$)	Continuance	Doubled consonants	Syllables	n	
Examples					
nise	Yes	No	2	5	
vimàne/ramàsola	Yes	No	3/4	5	
seffa	Yes	Yes	2	5	
tido	No	No	2	5	
nitta	No	Yes	2	5	
Categories	n	Word frequency			
(i) Regular words	80	47.4 ± 69.6			
(ii) Words with unpredictable transcription	55	47.6 ± 96.5			
(iii) Regular nonwords	25	–			
Total	160				

80 regular words. Nonwords were matched for length and phonological/orthographic structure with the regular words (i).

Table 2 summarises the principal aspects of the three sections of the writing task. Words and nonwords were presented separately. The 135 words were randomised for regularity, complexity, word frequency and length; the 25 nonwords for complexity and length. The examiner read each item aloud in a neutral tone of voice; each item could be repeated once on request. No feedback was provided; spontaneous repairs were accepted.

As the normative data of the test were based on younger subjects with a higher level of education [29], the patients' performances were compared to those of a new matched sample of 20 control subjects.

2.3. Statistical methods

As well as evaluating the average performance of the 23 DAT patients, the study aimed at revealing discrepancies in the ability to spell between the lexical and the sub-word-level procedures, the former being available for regular words and words with unpredictable spelling whose orthography had been learned in the past, the latter for regular words and nonwords.

Since DAT patients usually show further neuropsychological and neurolinguistic impairments which may cause a more diffuse level of deficits, the criterion for a disproportionate impairment of either of the spelling routes was that of a strong dissociation across tasks ([40], pp. 227–228). The choice is theoretically sound since no claim will be made for the existence of two separate routes of spelling (as this has already been extensively demonstrated), but only for a significantly more severe impairment of either of the two spelling routes.

Logistic regression analysis was applied to the profile of each patient and the major variables that might have affected the performance were included within a linear model. The units were the 160 stimuli of the test and the dependent variable for each stimulus was dichotomous (passed or failed). The model included both categorical (i.e. regular words, words with unpredictable orthography and nonwords) and continuous variables (word frequency and difficulty (expressed as the number of control subjects who wrote the stimulus correctly [29])).

The analyses permitted detection of the patients' dysgraphic patterns by comparing their performance on words with one-sound-to-one-letter correspondence to that (i) on nonwords with comparable phonological and orthographic complexity; and (ii) on words with unpredictable transcription. The analyses were written as a macro-instruction of the generalised linear model program (GLIM 3.77) of Aitkin et al. [2] and were performed for each patient using a multiple single-case approach.

As a single-case diagnostic procedure was used, overall protection for the whole set of patients was not adopted [42].

The significance level was set at 0.1 for each effect under study due to the fact that one of the two conditions in the comparisons was always easier a priori (regular words are by definition easier than irregular words or nonwords). As such, the rejection of the null hypothesis is to be expected only with a difference in favour of regular words, and in such cases it is customary to adopt a significance threshold corresponding to $P = 0.10$. Analyses always included covariance by word frequency and item difficulty and therefore any observed dissociation is stronger than, and not simply proportional to, the difference observed among control subjects.

3. Results

3.1. Group study (first assessment)

Table 3 summarises the mean performance of the (normal) control subjects and of the 23 DAT patients on the three sections of the writing task. As a group, the latter made more spelling errors than the control subjects, and particularly when writing both words with unpredictable transcription and nonwords.

3.2. Analysis of the single-case profile: type of dysgraphia

Using models that assume at least two spelling procedures, the ability to write regular words was compared with the ability to spell both nonwords and words with unpredictable transcription. A sub-word-level and/or lexical impairment was diagnosed when the ability to spell nonwords or words with unpredictable transcription was significantly different from the ability to spell regular words.

Table 3
Performances of the 23 DAT patients and 20 control subjects on the three sections of the writing task

Sections of the test	Mean percentage (S.D.)	
	DAT patients	Control subjects
(i) Regular words with one-sound-to-one-letter correspondence	79.5 (29.6)	98.2 (2.8)
(ii) Words with unpredictable transcription[a]	65.0 (29.2)	86.6 (12.0)
(iii) Nonwords with one-sound-to-one-letter correspondence	60.7 (32.1)	93.3 (6.9)

[a] For details, see Table 2 and Appendix A.

The patients were classified by comparing the impairment of the sub-word-level and of the lexical route as follows:

No significant difference between *regular words*, *words with unpredictable spelling* and *nonwords*	Undifferentiated writing disorders
Words with unpredictable spelling significantly more impaired than *regular words*	Surface dysgraphia
Nonwords significantly more impaired than *regular words*	Phonological dysgraphia
Words with unpredictable spelling and *nonwords* significantly more impaired than *regular words*	Mixed dysgraphia

Table 4 shows the profiles of each of the 23 DAT patients, sorted by performance on the three sections of the writing task, that were analysed by means of logistic regression analysis, following a multiple single-case approach. Table 5 summarises the error analysis for each single patient (phonologically plausible versus non-plausible errors).

Two patients showed a disproportionate impairment for nonwords (cases 20, 21), which suggests damage to the sub-word-level routine. Case 20 produced some semantic and morphological substitutions and showed a significant frequency effect (*deep dysgraphia*). Case 21 showed a disproportionately severe impairment in writing nonwords (*phonological dysgraphia*) and, while he also misspelled a few words with unpredictable transcription most of his

Table 4
Single-case analysis of the 23 DAT patients: logistic regression analysis, after covariance for word frequency and item difficulty

Case	Type of language impairment	Regular words with one-sound to one-letter correspondence (correct (%))	Comparisons of regular words with						WF	L
			Nonwords			Words with unpredictable transcription				
			Correct (%)	χ^2	*P*-value	Correct (%)	χ^2	*P*-value		
Phonological dysgraphia										
20	B	31	0	9.9	0.002	26	<1	ns	+	−
21	B	88	8	22.7	<0.0001	67	<1	ns	+	+
Surface dysgraphia										
3	A	94	84	<1	ns	75	1.829 (9.9)	0.176, ns (0.002)	+	+
4	A	91	96	<1	ns	69	4.7	0.030	−	−
5	W–A	49	48	<1	ns	18	5.5	0.019	−	−
7	A	95	88	1.3	0.256, ns	71	5.2	0.023	+	−
18	N	99	84	<1	ns	84	5.0	0.025	+	−
Mixed (phonological and surface) dysgraphia										
1	B	89	40	4.4	0.037	60	3.6	0.059	+	+
6	A	83	44	1.7 (11.0)	0.187, ns (0.001)	46	13.4	0.0002	+	−
8	N	96	80	3.1	0.080	65	9.7	0.002	+	−
12	W–B	65	40	2.3 (3.9)	0.128, ns (0.048)	42	4.0	0.045	−	−
13	W	88	48	2.7	0.098	66	4.5	0.034	+	−
14	A	90	64	8.3	0.004	73	4.4	0.037	−	−
15	A	95	72	4.4	0.037	84	<1 (4.8)	ns (0.029)	+	−
Undifferentiated writing disorders										
2	N	95	88	<1	ns	87	1.292	0.256, ns	+	−
11	A	89	84	<1	ns	86	<1	ns	+	−
19	N	93	68	2.0	0.164, ns	87	<1	ns	+	−
No writing impairment or minimal defect										
9	N	99	84	1.3	0.249, ns	95				
10	A	99	88	<1	ns	96				
16	A	100	96			100				
17	N	100	92			98				
Agraphia										
22	A	0	0			0				
23	B	0	0			0				

In four patients significance only emerged without covariance for word frequency and item difficulty (results of the analysis are given in brackets). Word frequency (WF) and length (L) effects are also reported. Type of language impairment: B, Broca's aphasia; W, Wernicke's aphasia; A, anomic aphasia; N, no language impairment or minimal defect.

Table 5
Error analysis on words with unpredictable spelling (multiple errors in a single word were counted separately)

Case	Type of errors	
	Phonologically plausible errors	Non phonologically plausible errors
Phonological dysgraphia		
20	0	44
21	2	15
Surface dysgraphia		
3	11	3
4	10	7
5	23	30
7	14	3
18	9	0
Mixed (phonological and surface) dysgraphia		
1	6	18
6	22	10
8	15	5
12	4	15
13	7	7
14	3	11
15	6	3
Undifferentiated writing disorders		
2	6	1
11	4	3
19	5	2
No writing impairment or minimal defect		
9	2	1
10	1	1
16	0	0
17	1	0
Agraphia		
22	–	–
23	–	–

spelling errors did not involve the foci with unpredictable orthography.

Five patients (cases 3–5, 7, 18) showed a predominant writing impairment for words with unpredictable spelling, which indicates damage to the lexical route (*surface dysgraphia*). The qualitative analysis of the errors for all these patients was in line with the statistical outcome, though cases 4 and 5 made significantly more spelling errors on phonemes with regular transcription when writing words with unpredictable spelling, and case 5 also showed several upper/lowercase alternations (*allographic errors*), thus pointing to a peripheral component of dysgraphia.

Other seven patients (cases 1, 6, 8, 12–15) showed a mixed pattern of impairment, i.e. disproportionate impairment in writing words with unpredictable transcription and nonwords, and preserved spelling of regular words. The same pattern of impairment has already been described in focal brain damaged patients [28] under the label of "*mixed*(*phonological and surface*) *dysgraphia*". When writing words with unpredictable spelling, cases 1 and 14 made several unexpected spelling errors on phonemes with regular transcription, which would appear to indicate an effect of overloading. Cases 6 and 12 also showed marked impairment on nonwords, which justifies their being included in the "mixed" group even if the difference with respect to regular words only emerged in the absence of covariance for difficulty. Case 8, made several expected errors on words with unpredictable transcription and only a moderate number of errors on nonwords. Case 13 also made several allographic errors. Case 15 was only mildly dysgraphic, but made several errors on nonwords and made phonologically plausible errors on irregular words.

Three patients (cases 2, 11, 19) presented an *undifferentiated writing deficit*. Four patients (cases 9, 10, 16, 17) showed no, or minimal, spelling impairment. Two patients (cases 22, 23), on the other hand, were completely agraphic.

Table 4 also shows the effect of the relevant psycholinguistic variables on the writing performance of the DAT patients. *Word frequency* had significant effect in the large majority of the patients, whereas *word length* was significant in only three patients (cases 1, 3, 21).

3.3. Follow-up study

Table 6 summarises the performance of the nine DAT patients who were re-examined after 6–12 months from the first assessment. Overall, the group performance worsened only slightly (one-tailed paired t-test = 2.1; d.f. = 8; P = 0.037), but with much variability across subjects, since some patients were almost unchanged, whereas other showed a steep decline. With respect to the three sections of the writing task, there is a significant mean decline for nonwords (one-tailed paired t-test = 2.9; d.f. = 8; P = 0.01), and a clear trend for regular words (P = 0.051).

Given the wide range in the levels of performance which emerged across the subjects, a multiple single-case analysis is clearly more informative than a group analysis. Table 7 shows the results of the task comparisons, carried out on the individual performance for the second evaluation. Once again, in order to classify the patients according to the main dysgraphic patterns, a combined criterion, i.e. the concurrence of clinical and statistical principles, was followed.

Table 8 summarises the evolution of the nine patients who received a follow-up examination. Several remarks can be made:

(i) the surface dysgraphic patients continued to show a preponderance of spelling disorders for words with unpredictable transcription;
(ii) two of the three patients with minimal defects tended towards phonological dysgraphia;
(iii) of the mixed dysgraphic cases, one patient (case 6) showed no change in his pattern of spelling disorder, another patient (case 1) suffered a further breakdown of the sub-word-level routine and in a third patient

Table 6
Performances of the nine DAT patients re-examined at 6–12 months from the first assessment on the three sections of the writing task

(a) Mean percentages (S.D.) at the first and the second assessment and results of paired *t*-test	First assessment	Second assessment	Paired *t*-test (d.f. = 8); one-tailed *P*-value
Sections of the test			
(i) Regular words with one-sound-to-one-letter correspondence	93.1(5.5)	80.0 (22.9)	1.84; 0.051
(ii) Words with unpredictable transcription	77.1 (17.5)	65.6 (30.0)	1.69; ns
(iii) Nonwords with one-sound-to-one-letter correspondence	74.2 (21.8)	60.0 (26.6)	2.90; 0.010
Total score	82.6 (11.4)	70.2 (24.8)	2.06; 0.037

(b) Individual performances of the nine DAT patients re-examined at 6–12 months from the first assessment	First assessment				Second assessment			
	Regular words with one-sound-to-one-letter correspondence	Words with unpredictable transcription	Nonwords	Total	Regular words with one-sound-to-one-letter correspondence	Words with unpredictable transcription	Nonwords	Total
Case								
1	89	60	40	71	35	22	0	26
2	95	87	88	89	94	89	64	86
3	94	75	84	82	91	71	60	77
4	91	69	96	80	88	71	80	77
6	83	46	44	63	83	47	52	65
9	99	95	84	91	99	93	88	92
10	99	96	88	94	94	95	72	89
13	88	66	48	73	41	11	36	27
16	100	100	96	100	95	91	88	93
Mean (%)	93.1	77.1	74.2	82.6	80.0	65.6	60.0	70.2

Table 7
Single-case analysis of the nine DAT patients with a follow-up examination (see Table 4 for details)

Case	Type of language impairment	Regular words with one-sound to one-letter correspondence (correct (%))	Comparisons of regular words with						WF	L
			Nonwords			Words with unpredictable transcription				
			Correct (%)	χ^2	*P*-value	Correct (%)	χ^2	*P*-value		
Phonological dysgraphia										
1	B	35	0	12.8	0.004	22	<1	ns	+	+
2	N	94	64	<1 (10.56)	ns (0.001)	89	<1	ns	+	−
10	A	94	72	<1 (5.0)	ns (0.025)	95	<1	ns	+	+
16	A	95	88	5.3	0.021	91	<1	ns	−	−
Surface dysgraphia										
3	A	91	60	1.7	0.192, ns	71	5.2	0.022	+	−
4	A	88	80	<1	ns	71	2.8	0.094	+	−
13	W	41	36	<1	ns	11	9.4	0.002	+	−
Mixed (phonological and surface) dysgraphia										
6	A	83	52	2.3 (7.2)	0.131, ns (0.007)	47	13.5	0.0002	+	−
No writing impairment or minimal defect										
9	N	99	88	<1	ns	93				

(case 13) the pattern of impairment evolved to a disproportionate impairment of the lexical route;

(iv) the patient who was formerly diagnosed with an undifferentiated writing disorder (case 2) evolved to a disproportionate impairment of the sub-word-level routine.

Altogether, none of the patients who formerly showed surface dysgraphia evolved to phonological dysgraphia, and no convergent progression toward mixed dysgraphia emerged.

3.4. Types of dysgraphia and clinical-demographic aspects

Clinical peculiarities which would able to characterise the two major types of writing impairment, phonological and surface dysgraphia, were sought out through an analysis which was done on all patients classified with either type of dysgraphia, either at the first or second assessment. More explicitly, the phonological dysgraphia group included two patients from the first assessment (cases 20, 21) and four cases (1, 2, 10, 16) which became phonological dysgraphics at the second assessment. The surface dysgraphia group also included six patients, five (cases 3–5, 7, 18) from the first assessment and one (case 13) from the second assessment. Table 9 summarises the demographic and clinical data of the subjects suffering from the two types of dysgraphia.

Table 8
Evolution of the nine patients with a follow-up examination

Case	First assessment	Second assessment
9	No dysgraphia or minimal defect	No dysgraphia or minimal defect
10		Phonological dysgraphia
16		Phonological dysgraphia
2	Undifferentiated writing disorders	Phonological dysgraphia
1	Mixed dysgraphia	Phonological dysgraphia
6		Mixed dysgraphia
13		Surface dysgraphia
3	Surface dysgraphia	Surface dysgraphia
4		Surface dysgraphia

The phonological dysgraphia group contained five males and one female and the surface dysgraphia group numbered two males and four females (Fisher exact test, $P = 0.24$, ns). Surface dysgraphic patients tend to be older than phonological dysgraphic subjects (two-tailed *t*-test = 2.2; d.f. = 10; $P = 0.055$), the two groups of patients did not differ with respect to education, length of illness and dementia severity.

3.5. Route impairment and type of language impairment

Table 9 also reports the distribution of phonological and surface dysgraphic patients by type of aphasia. In five of the six cases suffering from *surface dysgraphia* the writing impairment was associated to *fluent language disorder*, while a non-fluent language impairment emerged only in the phonological dysgraphia group: in three patients the language disorder assumed the features of a Broca's aphasia, one of which with agrammatism.

3.6. Cross-sectional study of the relation between type of dysgraphia and DAT severity

The aim of this section is to analyse the relationship of DAT severity with a disproportionate impairment of either spelling procedure. The analysis was carried out on dysgraphic patients only (cases 9, 17 were excluded); fully

Table 9
Demographic and clinical data of the six phonological and six surface dysgraphic patients on the first and/or second assessment

Case	Gender	Examination	Type of language impairment	Age	Education (years)	Length of illness (months)	General severity (MODA)
Phonological dysgraphia							
1	F	Second	B	64	8	30	33.4
2	M	Second	N	64	13	42	80.3
10	M	Second	A	56	18	20	67.9
16	M	Second	A	69	18	54	76.3
20	M	First	B	59	18	36	82.5
21	M	First	B	64	5	30	87.5
Mean (S.D.)				62.7 (4.2)	13.3 (5.2)	35.3 (10.7)	71.3 (18.0)
Surface dysgraphia							
3	F	First + second	A	68	5	24	70.4
4	F	First + second	A	67	5	24	62.4
5	M	First	W–A	68	5	18	53
7	F	First	A	71	5	36	83.8
13	M	Second	W	62	18	90	32.4
18	F	First	N	80	8	12	79.4
Mean (S.D.)				69.3 (5.5)	7.7 (4.8)	34.0 (26.1)	63.6 (17.3)
t-test (d.f. = 10)				2.17; $P = 0.055$	1.8, ns	0.37, ns	0.16, ns

Type of language impairment: B, Broca's aphasia; W, Wernicke's aphasia; A, anomic aphasia; N, no language impairment or minimal defect.

agraphic cases (cases 22, 23) were not included, due to the inadequacy of these patients to test for disproportionate impairment of either spelling route. Therefore, 17 cases from the first evaluation and two from the second entered the study.

Testing the hypothesis of a relationship between general DAT severity and the degree of impairment to the lexical or the sub-word-level spelling route, required an index which could reflect a disproportionate damage of the two procedures. The parameter that expresses this difference in the logistic regression model, describing the spelling ability of each single patient, is an appropriate tool. The regression coefficient of each patient was further normalised by dividing the estimated value by its standard error [2]. This parameter has been called the route index (RI). Positive RI values indicate a disproportionate impairment of the lexical

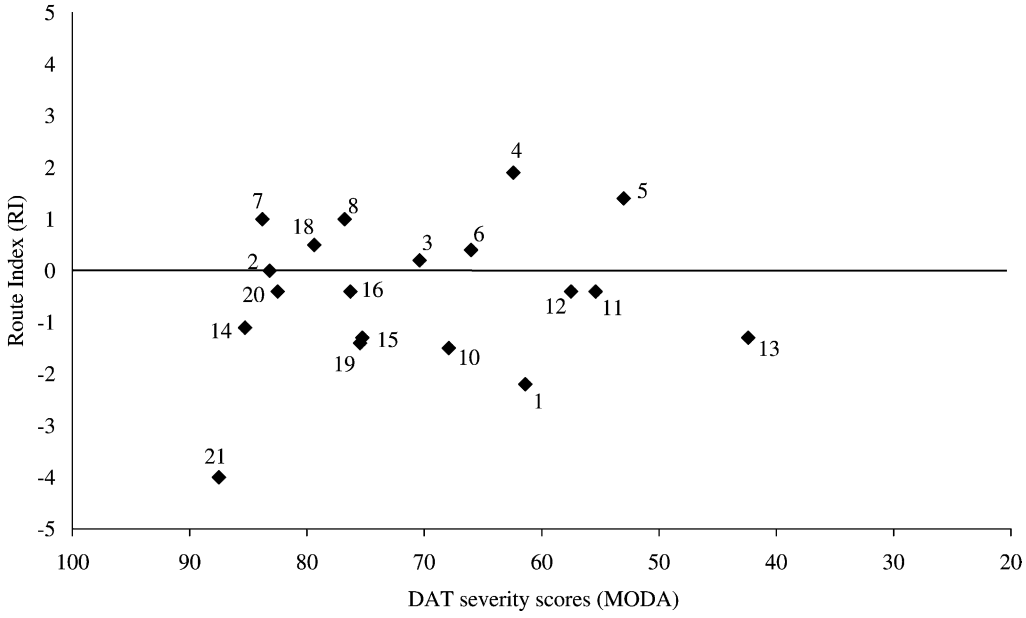

Fig. 1. Plot of the normalised RI values against the DAT severity scores: positive and negative RI values are evenly scattered with respect to DAT severity scores. Negative RI values indicate a lexical route advantage, whereas positive values indicate an advantage of the sub-word-level routine. Highest severity score (MODA) indicates best performance.

Table 10
Type of dysgraphia in DAT patients and in acute onset aphasic patients [28]

	Phonological dysgraphia (%)	Surface dysgraphia (%)	Mixed dysgraphia (%)	Undifferentiated writing disorder (%)	Agraphia (%)
21 DAT patients (present study)	4 (19)	5 (24)	7 (33)	3 (14)	2 (10)
52 acute onset aphasic patients [28]	7 (13)	18 (35)	11 (21)	16 (31)	0

route, negative RI values a disproportionate impairment of the sub-word-level routine. Fig. 1 plots RI normalised values against DAT severity scores.

Positive and negative values are evenly scattered with respect to DAT severity scores. Linear regression analysis was applied to the data. RI was the dependent variable, while the MODA score constituted the independent variable. No DAT severity effect emerged either for the non-normalised ($F(1, 17) = 1.7$, ns) or the normalised RI values ($F(1, 17) < 1$).

3.7. Patterns of dysgraphia in DAT patients and in aphasia after acute focal brain damage

The results obtained from the DAT sample were compared to those obtained in a previous study from a sample of aphasic patients after acute left hemisphere brain damage [28]. All DAT patients showing a spelling impairment on the first evaluation ($n = 19$), plus those in which the spelling deficit only emerged at the second evaluation ($n = 2$) were included in this comparison. Table 10 compares the distribution of type of dysgraphia by aetiology among the patients.

The incidence of the major dysgraphic patterns found in DAT patients (i.e. phonological, surface or mixed dysgraphia, undifferentiated writing disorders, and agraphia) is very similar to that found in aphasic patients after focal brain damage ($\chi^2 = 8.3$ (d.f. $= 4$); $P = 0.082$, ns). This similarity is even more striking if the rates of disproportionate impairment for the sub-word-level and the lexical spelling procedure (i.e. phonological and surface dysgraphia) are considered (Fisher's exact value < 1, ns).

4. Discussion

The writing abilities of a group of 23 DAT patients were studied, nine of whom were tested again after an interval ranging in length from 6 month to 1 year. The patients' writing performance was tested by three of the five tasks developed by Luzzatti et al. [29] to evaluate writing skills in a contemporary cognitive neuropsychological frame. The main findings of the study can be summarised as follows.

A specific dissociated pattern of performance does not emerge from the mean profile obtained from the 23 patients who participated in the study, and the minor differences which emerged across subtasks are simply an amplification of the general difficulty effect observed in control subjects.

The performance of the DAT patients was then analysed using a multiple single-case approach, which confirmed that spelling impairments are rather frequent, as 19 patients out of 23 (83%) showed impaired performance when writing single words and nonwords to dictation. The type of spelling impairment differed across subjects and was distributed all along the standard cognitive taxonomy, i.e. with a disproportionate impairment of either the lexical route or the sub-word-level routine.

Two patients in particular showed predominant damage to the writing of nonwords and relative preservation of the lexical route (*phonological dysgraphia*), while five patients showed predominant damage to lexical writing of irregular words and relative preservation of the sub-word-level route (*surface dysgraphia*). Impaired writing of both nonwords and irregular words, with relative preservation of regular words (i.e. with *mixed* features of phonological and surface dysgraphia) was recorded in seven patients. This pattern of impairment may be explained as being the result of two separate functional lesions, one at the level of the auditory-to-phonological conversion level, the other of the orthographic output lexicon. However, there are two other possible explanations for this same pattern of damage. Firstly, the interaction of the two partly damaged spelling routes may be successful when writing regular words: while neither of the two impaired spelling routes is sufficient alone when writing words with unpredictable orthography or nonwords, when they interact, performance with regular words is significantly better. Secondly, the pattern of damage may show the so-called "horse race effect". Either of the two partly damaged spelling routes can still succeed in writing a certain rate of regular words: the better performance on regular words can be attributed to the fact that these items have a higher chance of being spelled correctly, as two independent "race horses" increase a priori the chances that the words may be spelled correctly (see [28], p. 1731), and not to a positive interaction between routes. Among the patients with mixed writing disorders, a qualitative analysis of the responses permitted the identification of a case of peripheral dysgraphia. Three subjects showed a mild *undifferentiated spelling impairment*. This type of impairment is compatible with multiple foci of writing damage, selective damage to the graphemic buffer or peripheral damage to the retrieval for letter shapes. However a graphemic buffer impairment could be ruled out by the absence of a length effect, and peripheral damage by a qualitative analysis of the errors made by the three patients. In two further patients the disorder was so severe, to the extent that it affected the single letter level,

that they were not even able to spell out their own name. The impairment of these two *fully agraphic* patients appeared to be characterised by the association of central and peripheral (plus dyspraxic) types of spelling deficit. In other four patients, on the other hand, clear evidence of a writing impairment was absent and only *minimal deficits* could be detected.

This pattern of distribution does not confirm the pattern of dysgraphia reported in previous papers (see [17] for a review). Even if no unique type of impairment emerges from the literature, surface dysgraphia is said to be the most common pattern of writing disorder associated with DAT (e.g. [38]). This finding has been considered a typical aspect of progressive cognitive deterioration characterising the evolution of dementia. Spelling disorders would start in the early phase of the disease, showing progressive lexical and/or semantic deterioration, while more automatic sound-to-spelling conversion routines would be rendered ineffective only at a later stage. This can be applied quite successfully to patients affected by semantic dementia [23,41], but does not seem to be generalisable to all mild-to-moderate DAT patients, where individual cognitive and linguistic abilities may deteriorate separately. In particular, semantic, lexical, and sub-word-level processing abilities may dissociate giving rise to various patterns of writing disorder. Finally, the relatively shallower orthography and, therefore, the much larger reliance on the sub-word-level spelling procedure used in the early phases of acquisition of Italian orthography could partly account for these conflicting findings.

Two of the surface dysgraphic patients, when writing words with unpredictable spelling, showed a high rate of spelling errors also on phonemes with regular transcription (i.e. in that part of an irregular word which does not present any orthographic ambiguity) besides the expected rate of phonologically plausible errors. This pattern of error indicates that the high processing load involved in the attempt to retrieve lexical representation—required for spelling word segments with unpredictable transcription—may subtract standard resources from the sub-word-level processing routine, thus causing a higher rate of errors also on completely predictable word segments: a pattern of damage that cannot be accounted for by a mixed type of impairment, since regular nonwords are spelled significantly better than unpredictable words.

Other phenomena, such as perseveration, apraxia, short-term memory, attention and graphomotor disorders, interact with the classic central dysgraphic deficits.

The study also aimed at comparing the spelling impairment observed in DAT patients to that observed in aphasic patients after acute focal brain damage. Extremely differentiated disorders covering the entire taxonomy of writing deficits emerged from the analysis of the profiles of the individual patients. Excluding patients with no writing disorders, phonological dysgraphia emerged in 19%, and surface dysgraphia in 24%, of the dysgraphic subjects. These figures are quite similar to those obtained from acute brain damaged patients (13 and 35%, respectively). As in dysgraphia which occurs in conjunction with acute focal brain damage, mixed dysgraphia is also found here, which can probably be explained as an interaction between the two, partially damaged writing procedures. This is in line with an interpretation of DAT impairment in terms of a very differentiated deterioration of cognitive abilities that does not conform to any fixed pattern, i.e. that can hit different cognitive processes in different stages of the disease, and simply testifies to the relatively frequent focal onset of DAT.

Given the low number of patients studied, caution is required when making firm assumptions regarding the association between spelling disorders and types of language impairment. However, five of the six patients suffering from surface dysgraphia were affected by fluent aphasia (and one of the patients did not show any language impairment), while the language impairment of three of the six phonological dysgraphic patients showed the features of a non-fluent aphasia. No similar association emerged for the spelling impairment of aphasic patients caused by acute focal brain damage. This discrepancy may be explained by the different pathogenesis underlying the spelling impairment. An obvious difference is that cortical atrophy (at least in an early stage) usually involves different cortical domains, and does not imply subcortical disconnection phenomena, which is associated with acute focal (vascular) brain damage.

The analysis of the relationship of DAT severity with the degree of impairment to the lexical or the sub-word-level spelling route did not show any specific pattern of evolution, nor was there any evidence of surface dysgraphia evolving into phonological dysgraphia. In other words, this study did not confirm previous findings (e.g. [25]), showing a predominance of surface dysgraphia in the earliest stages of dementia and of phonological dysgraphia in the later stages. These previous findings were explained assuming a deep to surface progression of the degenerative disease, which first involves semantic conceptual knowledge, then lexical knowledge, and more peripheral sub-word-level procedures only at a later stage. The cross-sectional data recorded in this study do not supply evidence in favour of a proportionate sub-word-level decline with respect to severity, and/or of any transition from surface to phonological dysgraphia. To the contrary, the distribution of dysgraphia patterns all along the severity distribution was almost uniform, with phonological dysgraphia already emerging in mild DAT patients, and surface dysgraphia in severe cases also. Moreover, re-examination of nine patients after a 6–12 month interval confirmed a wide variation in the pattern of evolution of the disease and no specific progression of the impairment to the sub-word-level routine. While in two patients the impairment was seen to evolve to produce more marked damage to the spelling of nonwords, the evolution of another group of patients was toward predominant impairment to the lexical procedure.

These results are in line with a possible independent decline of the two spelling routes. DAT is a diffuse

degenerative disease, which however may arise focally. According to (i) the functional unit (and anatomical area) which is initially involved and (ii) the disease progression modality, different patterns of spelling impairment may emerge.

In conclusion, classification of spelling disorders according to contemporary cognitive models reveals different patterns of impairment which cover the entire taxonomy of writing disorders. Moreover, little correlation has been found between the type of dysgraphia and dementia severity. Therefore, the hypothesis of a progressive deterioration, initially of the semantic, then of the lexical, and finally of more surface abilities, would not appear to be generally applicable to all DAT patients. On the contrary, the data from this study appears to sustain Pick's hypothesis that DAT is a mosaic of circumscribed cognitive deficits [35]. In other words, there would be focal onset distributed through various cerebral areas, also for the different language sub-units, with the overall cognitive degeneration only appearing at a later stage of the disease.

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Appendix A

Italian is usually said to have a shallow, i.e. regular orthography. This is actually true for the large majority of Italian words, and this regularity is also said to influence the mechanisms underlying acquisition and normal spelling processing [28,29]. However, there is still a certain number of Italian words whose orthography cannot be derived from the application of sub-word-level conversion rules. This happens in particular for some consonants having more than one possible orthographic solution, though only one is correct for a certain lexeme. The syllable [ʃe], for instance, is usually transcribed by the sequence SCE. However, there are some words in which it is conveyed by the graphemic string SCIE (e.g. [ʃentsa] = SCIENZA, science). The same applies to the syllables [tʃe] and [dʒe] which in certain cases are transcribed by the sequence CIE and GIE (CIELO, sky and IGIENE, hygiene) instead of the more regular CE and GE (*CELO and *IGENE). Following linguistic convention, an asterisk (∗) denotes spelling errors arising from the over-reliance on sub-word-level phoneme-to-grapheme conversion rules. The phonemic group [kw] may be transcribed by the orthographic sequences QU, CU, CQU. The general rule is that the syllables [kwa], [kwi] and [kwe] are transcribed by the sequences QUA, QUI and QUE (e.g. QUALE, which, QUINDI, thus, QUESTO, this), while the syllable [kwo] is transcribed by the sequence CUO (e.g. CUORE, heart). There are, however, some exceptions, for example [kwɔta], quota, height is spelled QUOTA instead of *CUOTA. The segments [ʎ]–[lj] and [ɲ]–[nj] that are phonologically distinct in Tuscan and central-southern pronunciation, are homophones in north-western Italian, so much so that the spelling of words like *balia* [baʎa]/[balja], nurse (BALIA and not *BAGLIA), or *geranio* [dʒeraɲo]/[dʒeranjo], the geranium (GERANIO and not *GERAGNO), is not predictable along the phoneme-to-grapheme conversion routine. The pronunciation of plosive phones that are followed by liquid consonants ([l] and [r]) or by the semiconsonant [j] are homophone to their doubled counterpart, thus rendering uncertain the transcription of words such as [libro], book (LIBRO and not *LIBBRO), [febre], fever (FEBBRE and not *FEBRE), [biblico], biblical (BIBLICO and not *BIBBLICO), and [publico], public (PUBBLICO and not *PUBLICO).

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