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Visual Analytics for the Interpretation of Fluency Tests during Alzheimer Evaluation

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ABSTRACT

A possible way to evaluate the progress of Alzheimer disease is to conduct the Isaac set test [13,14]. In this activity, the patients are asked to cite the largest possible number of city names within a minute. Because the names are handwritten very quickly by a medical practitioner some cities are abbreviated or poorly written. In order to analyze such data, medical practitioners needs to digitize it first and clean the dataset. Because these tasks are intricate and error prone we propose a novel set of tools, involving interactive visualization techniques, to help medical practitioners in the digitization and data-cleaning process. This system will be tested as part of an ongoing longitudinal study involving 9500 patients.

CCS Concepts

• Human-centered computing~User centered design • Human-centered computing~Visual analytics • Human-centered computing~Visualization techniques • Social and professional topics~Personal health records • Information systems~Data cleaning • Applied computing~Document capture

Keywords

Alzheimer Disease, 3C Dataset, Electronic Health Records, Information Visualization, Data cleaning.

1. INTRODUCTION

According to a ministerial review from 2004, approximately 860,000 people are affected by Alzheimer’s disease in France. This figure is estimated to reach 1.3 million in 2020 and 2.1 million in 2040. This is why the study of Alzheimer’s disease has been identified as a major challenge for society. In the 3C cohort study [1], 9500 elderly people performed a set of tasks (lexical, cognition evaluation, sensory and motor assessments). They were longitudinally followed during a 22 year period and some of them developed Alzheimer’s disease (AD). Hence, the 3C project contains Electronic Health Record (EHR) that has been used to extract relevant information [2,8] regarding personal health.

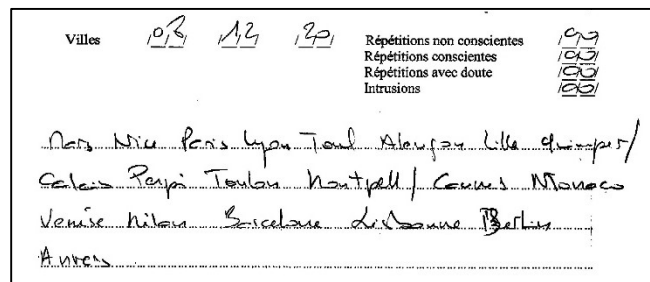


Figure 1. Sample of a fluency test result. The slashes represents timestamp separators (15, 30 & 60 seconds)

Our study focuses on one of the tasks performed by the patients in the 3C project: the lexical evocation task (called a fluency task). This fluency task is a part of the Isaac test set [13,14]. In this task, the patient is asked to cite the largest possible number of city names within a minute.

The lexical evocation task is directly connected to the concept of cognitive maps introduced by Tolmann [28] and echoed by O’Keefe and Nadel [22]. A cognitive map can be considered as a conceptual matrix in which episodes of life are recorded to be later accessed by user mental processes (i.e. fluency test). Moreover, according to O’Keefe and Nadel, hippocampal lesions distort spatial “imaging”. Since AD impacts the hippocampal region, we are strongly convinced that the evolution of the patient cognitive map will lead us to detect at an early stage the beginning of AD.

We hypothesize that being able to spatially and temporally map cited cities during the test will help neuropsychologists to analyze the evolution of the patient cognitive map. Therefore performing the digitization and cleaning of the fluency task is a great opportunity to study the effect of aging on the human brain.

The digitization process is not an easy task and will require special care. Because notes are taken by hand by a medical practitioner some cities are abbreviated or poorly handwritten (a sample is shown in figure 1). The first step toward analyzing this data is the digitization. This process involves first to transform the handwriting information into a list of cities with temporal timestamps. Secondly, one needs to clean the dataset from digitization errors as well as remove ambiguities between the misspelled cities or any other kind of confusion of data. Due to the complexity of these two tasks, no automatic method can be used. Furthermore some errors in the list of cities can also contain relevant information regarding the cognitive state of the patient

(e.g. some of them are called *intrusion* and will be detailed in the section 5 of this paper).

We used a User Centered Design (UCD) [27] process and developed a set of tools (like an auto-completion algorithm, a confidence-based algorithm to support the data cleaning process and finally visualization tools to help knowledge extraction) to help medical practitioners during the digitization and cleaning process.

Our contribution relies on our interactive visualization system to help practitioners clean the patient records, trace modifications and remove ambiguities between digitization error and actual insights.

In the following section we present relevant the related work. Then we list the design requirements to fulfill the digitization and cleaning tasks. Next, we describe our software features and justify our implementation choices. Finally, we outline the strength of our design with specific cleaning scenarios.

2. RELATED WORK

Data cleansing, also called data cleaning, or data scrubbing is the process of correcting data by removing errors. The quality of the resulting cleansing is highly dependent of the intervention by a human domain expert to perform accurate cleaning [9]. This is also the case of the dataset we will have to clean where only an expert can perform the cleaning process.

Many tools also focus on the data cleaning process, such as TimeCleanser [11] which is specialized in time oriented data. Our data set is also time oriented since city citations are time ordered, but the majority of the cleaning process will operate on the city names and not on the temporality of the city citations. In our case, the cleaning process will operated mostly on the geographical aspect of the dataset.

Different taxonomy of the data quality problems exist [3,6,15,21,23,26]. However, none of them propose a solution in which inconsistent spatial data can be automatically cleaned.

Among the available data cleaning tool, we note that AJAX [10] provides a valuable framework including expressive and declarative language specifications to perform the data clean process. For instance, it supports mapping, matching, clustering and merging transformation. However in our study, very few errors are generic and only the individual investigation of the records can help to determine if they contain errors or ambiguities.

We investigated text recognition algorithms like A2iA [19], but the handwriting process with time restriction produced too many abbreviations and poor quality trails which hinder and prohibit the usage of automatic text recognition.

Bensalem et al. [4] and Buscaldi et al. [7] in their toponym disambiguation bases their analysis on the geographical as well as hierarchical relations (e.g. Paris is the capital of France and France is a country of Europe). In their work, the hierarchical relations is based upon the WordNet ontology [20]. However, the WordNet ontology was not precise enough to help us disambiguate toponyms for small villages of France.

3. DEFINITIONS

In this section we define important medical and technical terms.

Fluency Test: This is a task part of the Isaac test set [13,14]. In the fluency test, patients are asked to cite the largest possible number of city names within a minute. As the subject lists city names, the practitioner writes the cited cities and adds a marker at 15, 30 and finally 60 second intervals (the end of the test).

Citation: We make a distinction between two types of citations: *Verbal* and *Digitized* citations. Verbal citation is cited by the subject and then laid down on paper. Digitized citation is the verbal citation that has been digitized.

Intrusion: A word that is definitely not a city (e.g. Banana). This is one of the errors that can be present in the verbal and/or digitized citation. More details regarding errors and ambiguities are provided in section 5.

Paraphasia: A speech defect characterized by incoherence in the arrangement of a syllable or word. There are different types of paraphrases depending on the type of incoherence. (e.g. semantic, verbal or phonemic). For example saying “tiger” instead of “lion” is a semantic paraphasia.

Patient: The subject who performed the fluency test. The patient can be diagnosed as having dementia or not as a result of medical testing process which are outside of the scope of this paper.

Medical Practitioner: The person who supervised the fluency tests and annotated the cited cities on paper. He is a medical expert.

Digitizer: The person who will take the paper based record of the fluency test and enter the list of city citations in the software. This software contains many features to help the digitizer during the digitization process (these features will be explained in section 7.1).

Cleaner: The user who will employ our tools to perform data cleaning. The cleaner can also be a practitioner but he or she has specific skills regarding patient cognitive processes. He must be an expert to determine whether the investigated record contains errors or ambiguities and finally perform possible corrections.

Inspector: The user in charge of checking the correctness of the cleaned data. The inspector is involved in our process after the cleaner. He must be a medical expert regarding patient cognitive processes (e.g. a neuropsychologist).

4. A USER CENTERED DESIGN PROCESS

To accelerate the development process of our digitization and cleaning tools, we applied a user centered design process (UCD) [27]. In this design process, we involved users as much as possible in the tool developments.

Different kinds of users were involved in this project: the practitioners who ran the tests, the patients who took the tests, the digitizer who will carry out the digitization, the cleaner who cleans the data, the inspector who validates the cleaned data and finally the neuropsychologists who analyzes the results. All of these categories of users were involved in the design process during the development of the tools. We recorded interviews with practitioners and digitizers and we conducted numerous call conferences with one specific inspector and one neuropsychologist.

In total we spent one day with the practitioners located in Bordeaux, and we conducted many discussions with three practitioners, two cleaners, and one inspector. We spent up to twenty hours of discussion time on the phone to assess our tools. We conducted one brainstorming with two HCI experts, one cognitive science expert also author of this paper, a practitioner and a cleaner. We conducted one design walkthrough (human computer interface validation) with one cleaner. Finally we spent three hours installing and detailing our tools for one cleaner.

These sets of interviews and brainstormings helped us to analyze errors and to refine the design requirements of our solution.

5. ERRORS AND UNCERTAINTIES

Exploring, analyzing and building statistics on a large cohort of patients requires taking into account errors during the digitization and cleaning process. Therefore we need to quantify, analyze and justify each error that may occur during the processes from the digitization to the analysis phase. This led us to define ways to compute a confidence value for a digitized cited city names with regards to possible errors.

5.1 Types of Error

Thanks to the UCD design process and the numerous discussions with the practitioners, we have identified three different types of error detailed in table 1.

Table 1. Error types identified in our study

Type	Sub-type (with details)
Patient errors	- Semantic paraphasia (lexical substitution) - Verbal paraphasia (phonetic substitution) - Intrusion - Repetition - Undetermined others...
Uninterpretable errors	- Unreadable city name (on paper) - Incomplete test (e.g. a whole part of the test is missing)
Digitization errors	- Wrong city (copy error) - Unknown city (city not in our database)

In addition to correcting the digitization and uninterpretable error types, the data cleaning step can also be used to identify patient specific errors. For example, in our particular case, some digitization errors (such as a wrong city) can in fact be a patient error (for example, Toulouse and Toulouse are two existing cities but can also be a verbal paraphasia error).

5.2 Confidence Values

The confidence value can be computed using multiple criteria. Thus, in our study we have identified three types of confidence: spelling, phonetic and Euclidian based distance.

5.2.1 Spelling-based

The first confidence value is spelling. Multiple cities have the same name, for example there are more than 10 different cities whose name start by “Chalons” and are orally referred as “Chalons” without the rest of their proper name. There is a large possibility of typing errors (e.g. misspelling). Thus, it is probable that the digitizer made a mistake. From these two errors, it is necessary to remove any ambiguity. Our solution is to define a string-distance-based confidence. This confidence is based upon the Damereau-Levenstein [9,16] distance and allows us to get the list of city with similar spellings. We define the confidence as such:

$$Card(\{city \mid d(citedCity, city) < thresholdValue\})$$

With the threshold being the minimum allowed string distance between the cited city and another.

5.2.2 Phonetic-based

Relatively similar to the spelling-based confidence, the phonetic-based confidence uses a phonetic comparison between two words. We choose to implement the metaphone algorithm [24,25] suitable for the French language. In this algorithm the listed city names are translated into a key. Thus, we can find phonetically similar cities

by comparing their keys. We define our confidence as the string distance between two city keys.

$$Card(\{CityKey \mid d(citedCityKey, cityKey) < threshold\})$$

With the threshold being the minimum allowed phonetic distance

5.2.3 Euclidian-distance-based

From our experience, only lexically based confidences may not be sufficient to detect potential errors. Thus, we have defined a third confidence level based on the Euclidian distance of the city from the preceding and the following one. During the task of verbal fluency, people tend to list cities near to each one’s following routes itinerary as theorized in vista space concepts [18] and revealed during our interviews with practitioners. Thus, if a cited city is far from the other, it may highlight a potential digitization error.

Let Center be the geographical position between the B, preceding city and F, the following one of our cited city and G, the geographical position of this city. We define our Euclidian based confidence as:

$$\frac{d(G, Center)}{\|BF\|}$$

Normalizing our Euclidian based confidence, allows us to spot a divergent city from the preceding and following ones.

6. DESIGN REQUIREMENTS

This section presents the design requirements to achieve the digitization and the cleaning tasks. First, we analyze the digitization requirements and then the cleaning one’s. Requirements associated with the digitization process are abbreviated “Rd” and then those with the cleaning process “Rc”. All the requirements associated with the two tasks were collected during the UCD process

6.1 Digitization Process Requirements

During the digitization process, the digitizer needs to retrieve the list of digitized cited cities.

Rd1: Multiple solutions were available to us such as; character recognition, verbal recognition or typing. Due to the poor writing quality of the tests (figure 1), we were not able to use the character recognition. Concerning verbal recognition, as the tests are in French, we needed a French-based grammar recognition. However, we were unable to find an efficient and open source French-based grammar. Thus, finally we choose to digitize the fluency test by manual typing.

Rd2: Manual typing does not solve by itself the need to digitize a correct dataset. Some cities might have the same name (e.g. London, UK and London, CA). To avoid such indetermination, the user must be able to digitize a city to a unique name.

Rd3: The digitizer must specify the separators between cities listed during a period of 0 and 15 seconds, 15 and 30 seconds and 30 and 60 seconds.

Rd4: The digitizer must be able to specify an intrusion.

6.2 Cleaning Process Requirements

Rc1: Each digitized and cleaned fluency test must be validated by an inspector. To enhance his validation work, we want him to be able to look through any modification that the cleaner might have made and to validate or reject each test. Thus, we need to provide him with the list of each modification as well as allowing him to display the original digitized dataset.

The following requirements concern the cleaner tasks.

Rc2: The cleaner must be able to correct a digitized city and specify the error type. Thus, he must have interaction means to achieve his task. In the continuity of our digitization process, the cleaner must be able to solve any city-name indetermination problem (i.e. the system must allow the addressing of a unique city name).

Rc3: However, allowing him to fill-in a unique city name, means using a database of existing cities. If a city is missing from such a database, the cleaner need to be able to add one directly.

Rc4: Finally, as some errors are not known in advance, the system must give the cleaner the opportunity to find new errors. Thus, he must be able to explore the dataset in order to study prospective analysis methods.

6.3 Fluency Test Dataset

The fluency test dataset contains the recording of the cities listed by a patient during a test (e.g. "Paris, Bordeaux, Toulouse, Lyon, etc..."). This list of cited cities is separated into three sub-lists which consist of the cited cities during three different periods (see table 2). Tests are linked through the patient id.

Table 2. Fluency test field names and semantics

Field name	details
testId	The unique id of the test
Id	The unique id of a patient
BirthDate	The birthdate of a patient
TestDate	The date of the test
City15	The cited cities between 0 and 15 seconds
City30	The cited cities between 15 and 30 seconds
City60	The cited cities between 30 and 60 seconds

The cited city field includes the cited city name, the real name and the geographical position (latitude and longitude).

7. TOOLS

This section details the basic features of the two tools we developed in order to fulfill the previously identifier requirements; the digitization and data cleaning tools.

7.1 Digitization Tool

The digitization tool has two panels. The main panel shows the list of the fluency test records with values (figure 2 - top). The digitizer can import and export the digitized data at any time via two buttons.

To add test results, the digitizer uses a form and manually enters the names [Rd1] and fills in the data of the fluency test (see table 2). To allow the digitizer to bind a city name with a unique city, we have implemented an auto-completion algorithm based on a city database [Rd2]. The city database is composed of the major international cities [29] and all French towns [30]. When a town is missing, the digitizer can still override the auto-completion. In that case, the digitizer is warned with an orange feedback. Moreover, he can specify an intrusion with a right click on the text box [Rd4].

While entering the listed cities, the digitizer can see the geographical polyline formed by the fluency test (at the bottom-right of figure 2). This tapered polyline shows the location of each city (known in the database) and the direction of the polyline [12]. With this visualization, he is able to see whether a city seems erroneous or not (i.e. a city too far from the previously listed ones).

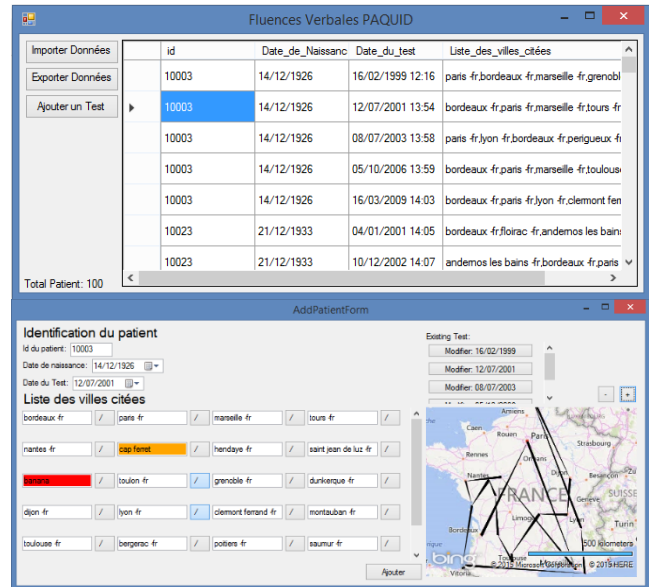


Figure 2. The digitization tool. On top is the list of tests, below is form to add a fluency test. Each city is typed in combo-boxes. Unknown cities are orange, and intrusions words red.

The timestamp of the fluency test (each 15, 30 & 60 seconds) is displayed in the interface with slash buttons allowing the digitizer to put the three slashes initially in the paper-based test [Rd3].

Finally, by typing an existing test ID, the digitizer is able to load an existing test and modify it using the top-right box.

7.2 Cleaning Tool

Our cleaning tool (figure 3) is composed of three main panels; the histoSelector panel, the citation panel and the detail panel. In the following subsections, we detail each component.



Figure 3. The cleaning tool. On the left the HistoSelector panel, and on the right the Citation Panel. The cleaner can change the confidence with combo box above the citation panel.

7.2.1 The HistoSelector Component

To filter and explore the dataset during the cleaning process [Rc4], we display histograms showing the distribution of values of each dataset attribute (figure 4). The cleaner can select the dataset attribute to be displayed by right clicking on the histogram name.

To find new insights or errors in the dataset, we have chosen a selection paradigm based on a brushing interaction [17]. Users draw a bounding box (a one dimension brushing technique) and can modified it by sliding the bounds of the selection. Multiple boxes can be specified, and they can be removed with a brush stroke with the right button of the mouse pressed (i.e. the erase mode).

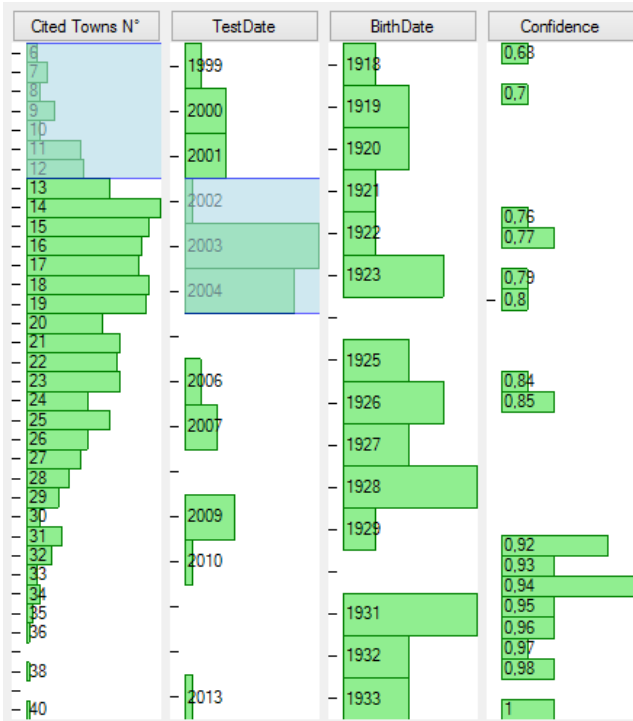


Figure 4. Histogram Panel. By drawing boxes on the histograms, a cleaner has selected all patients who revealed only a low number of towns during the 2002-2004 tests. A selection in one histogram updates all histograms to its right.

We maintained the classical reading pattern (left to right) in such a way that the selections or modifications of one histograms directly modify its neighbor's values. Nesting multiple histogram allows the user to refine a query depending on multiple dataset's attributes.

Thus, the fluency tests selected through the histograms are displayed in the citation panel.

7.2.2 Citation Panel

The citation panel is the representation of each fluency test in our cleaning tool (figure 5) [Rc1].

One row corresponds to one fluency test. The row is composed of coloured squares which correspond to each cited city with its confidence value. Two parameters are displayed in these squares.

First, the saturation of each square is bound to the state of validation of the city. If the city has been validated then it has a low saturation value. In the other hand, if it is not validated, the saturation is at its full value. As saturation is a dissociative visual parameter [5], encoding the validation state of a city through saturation allows the visual emergence of the not validated cities.

Secondly, the color of each square is bound to the confidence value of the city. The associativity of the color improves pre-attentive selection [5] allowing users to instantly visualize a group of low confidence cities that need to be reviewed. Our color range is defined by five levels of confidence with a color generator [31]. The colors are green for confidence values over 80%, then light-green (60-80%), yellow (40-60%), orange (20-40%), and red for confidence values lower than 20%.

Finally, clicking on a colored square opens up the detail panel.

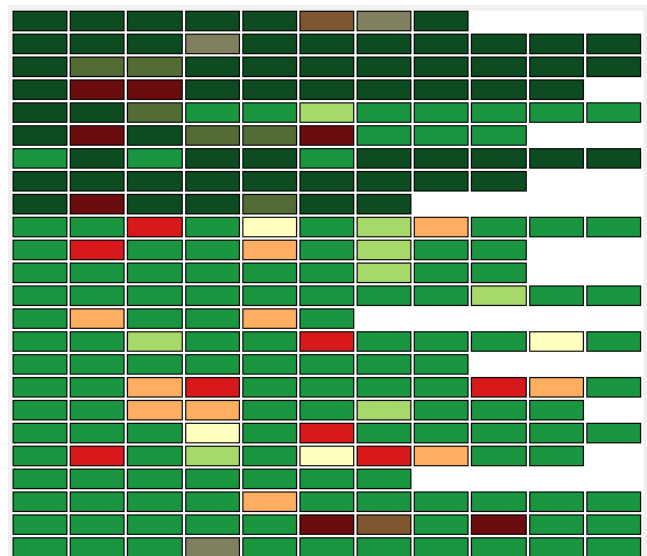


Figure 5. Citation panel. Displays the confidence of each digitized city encoded in five levels of color (red to green). A validated city is de-saturated (top of the figure).

7.2.3 Detail Panel

The detail panel allows the user to correct a potential error in a digitized city. This panel is composed of four main parts.

The first part, at the top of the form, displays the values associated with the city (PatientId, BirthDate, TestDate, Confidence value and the actual digitized cited city). In this first part, the user is able to correct the city name (via the Correct City textbox) and fill-in the error type [2]. Each textboxes has personalized auto-completion algorithm. The cleaner is also able to add a city to the database via the "City not in DB" button [Rc3]. The second part displays the list of cities lexically similar to the cited one.

The third part shows the cited cities preceding and following the selected city and displays the distance between them. This geographical distance is enhanced by displaying the polyline formed by the fluency test associated with the selected city centered on the selected one. With this visualization, the user is able to geographically place and check the location of the city and to compare it with the following and preceding one as well as with the whole fluency test.

The last part of the detail panel (at the bottom) is an image display of the original paper-based test. This allows the cleaner to check if the city was really written or not, especially in the case of a city with a low confidence value but in which the digitized city was indeed cited by the patient (refer to figure 7 for an example).

Once the correction of the city has been performed, the user can validate or cancel his changes.

8. SCENARIO

This section describes four scenarios of use. The first two describe a true-positive and a false-positive detection. The third one shows how the cleaner can explore the dataset and find unrevealed erroneous data. Finally the last scenario illustrates the validation process performed by one inspector. The typical meta-scenario is as follows:

While a patient 'V' executes the task of verbal, a practitioner 'W' writes down each cited city on a paper. At 15", 30" and 60" the practitioner writes down a slash to timestamp the cited cities.

By selecting the right criteria, he is able to display the tests to be cleaned, thus allowing him to focus on those tests. Then, the cleaner selects the first red square showing a very low confidence value on a citation.

In the detail panel, he sees the information concerning the citation (shown in figure 7). The digitized citation shows the city of Algiers in Algeria. The previous cited city is Pau and the following is Bougue. Thus, the Euclidian distance is relatively high.

To confirm the inaccuracy of the digitized citation, the cleaner takes a look at the original citation at the bottom of the detail panel in figure 7. However, ‘Y’ sees that the city that was written down on paper during the test is Algiers. He concludes the low confidence level was a false-positive one. Finally, he validates the correctness of the digital citation by clicking the “validation” button.

Since the confidence based criteria cannot always be true, this use-case highlights the way a cleaner can detect and resolve a false-positive result thanks to the confidence algorithm.

8.3 Detect Outliner Subsets Scenario

In this use-case the cleaner ‘Y’ wants to detect a subset of outliers in the data to be cleaned. In this particular use-case, he wants to investigate the relationship between the length of the fluency tests and the year of the test.

‘Y’ initially decides to bind a first histogram to the fluency test length (the number of cited cities). By clicking on the tag name of the histoSelector component, he is able to change its binding. Then, he repeats the operation on the following histoSelector component (directly on the right of the previous one) binding it to the year of the test. With this configuration the cleaner is able to visualize the distribution of the test years depending on the selected fluency test lengths (figure 4).

Then he selects the fluency test with a low number of listed cities by brushing the histoSelector component. During the brushing sequences, the cleaner can directly see the repartition of test dates. ‘Y’ discovers that the majority of tests with a low number of listed cities were performed in 2003-2004. Moreover, with the citation panel, the cleaner finds that all these low numbered tests are missing the 30 to 60 second parts. Thus, the cleaner can conclude the presence of an error in the test protocol during the tests in the period from 2003 to 2004.

This use-case illustrates how the cleaner can detect outlier subsets through exploration of data properties. Exploring and interacting with the dataset helped him find unpredicted errors.

8.4 Track Modifications Scenario

We detail a scenario where an inspector ‘Z’ wants to validate corrections made by the cleaner ‘Y’ during the cleaning process.

Once the cleaner has finished the cleaning process, the inspector can validate or invalidate these modifications. To achieve this objective, he starts binding the first histoSelector to the modified attribute and the second to the validated attributes. Then by selecting the modified but invalidated fluency tests (via the two configured histograms) ‘Z’ displays the list of modifications requiring validation in the citation panel.

Within these tests, the inspector can explore and click on each ones. He chooses to click on the first test and check the digitized cited city. Thus, ‘Z’ opens the detail panel. In the detail panel he sees that the corrected city name is Damascus. By clicking on the button next to the versioning number (left arrow “<” in figure 8), he sees that

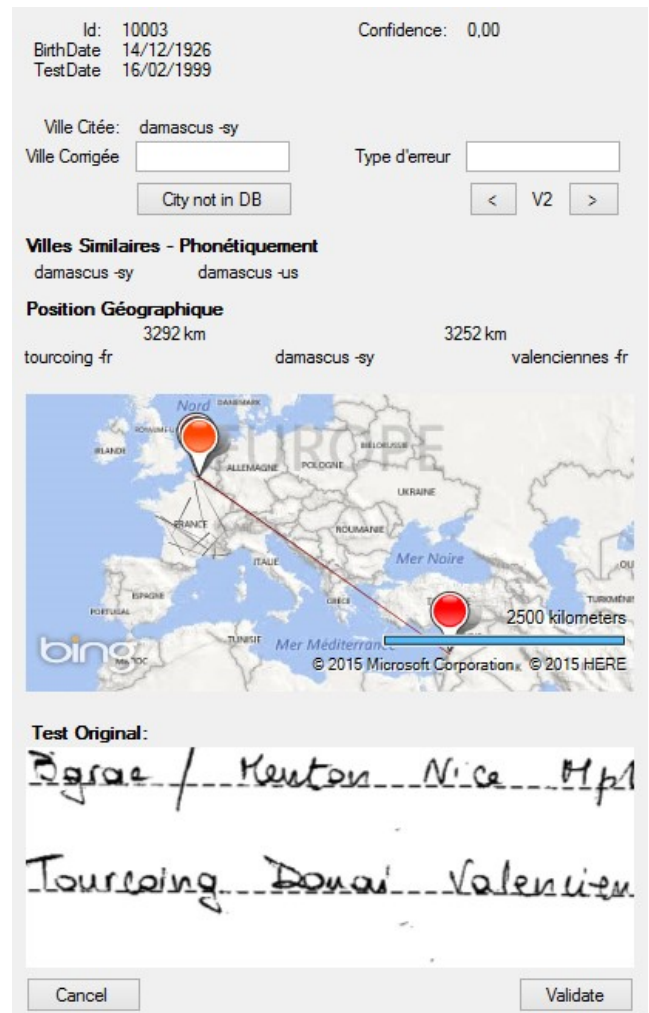


Figure 8. Validation of a cleaned test. In this case, the cleaned city is Damascus but the original cited city was Douai. The expert can invalidate the modification and make a new correction to the data.

the initial value of the digitized cited city was a city unknown in the database named “Damas” (the French name for Damascus).

Via the original test view in the bottom of the detail panel, “Z” checks that Damascus is indeed written in the original test. However the expert does not read “Damas” but “Douai” a French city near the preceding and following cities. Thus, he corrects the cited city a second time to the known city of Douai. Finally, he corrects and validates his change with the “Validate” button.

Through this use-case, we see how the validation of the inspector can spot errors made during the cleaning process and double check the corrections. This enables the correctness of the clean dataset to be improved.

9. CONCLUSION & FUTURE WORK

The study of Alzheimer’s disease is a unique opportunity to work on an unexploited handwritten dataset. In the digitization and cleaning process the main difficulty is to reduce ambiguities between errors induced by our own cleaning/digitization process and errors made by the patient during the verbal fluency test. Processing and identifying these errors cannot be achieved with an automatic algorithm due to its variability. Thus it must be carried out by users.

To solve this problem we developed two tools that help users during the digitization as well as the cleaning steps. As an example, these tools have helped the people in charge of the digitization process by allowing them to directly input known city names into an existing database. In the cleaning process, our tool helps the user to solve the ambiguity problems inherent to city names (having multiple cities with the same name) as well as solving problems from our digitization process (missing city names).

Our work can be further improved and extended in many aspects. For instance, other confidence tests could be investigated: the homonic test or the toponym test are good candidate to extend the available tools to detect issues in our database. We believe that the tools described in this paper can be useful to provide cleaner data and facilitate the study of Alzheimer disease progression.

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