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ORIGINAL ARTICLE

Clinical presentation and neural correlates of stroke-associated spatial delusions

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Abstract

Background and purpose: Incongruent beliefs about self-localization in space markedly disturb patients' behavior. Spatial delusions, or reduplicative paramnesias, are characterized by a firm conviction of place reduplication, transformation, or mislocation. Evidence suggests they are frequent after right hemisphere lesions, but comprehensive information about their clinical features is lacking.

Methods: We prospectively screened 504 acute right-hemisphere stroke patients for the presence of spatial delusions. Their behavioral and clinical features were systematically assessed. Then, we analyzed the correlation of their duration with the magnitude of structural disruption of belief-associated functional networks. Finally, we described the syndrome subtypes and evaluated whether the clinical categorization would be predicted by the structural disruption of familiarity-associated functional networks using an unsupervised *k*-means clustering algorithm.

Results: Sixty patients with spatial delusions were identified and fully characterized. Most (93%) localized the misidentified places closer to home than the hospital. The median time duration was 3 days (interquartile range = 1–7 days), and it was moderately correlated with the magnitude of structural–functional decoupling of belief-associated functional networks ($r = 0.39$, $p = 0.02$; beta coefficient regressing for lesion volume = 3.18, $p = 0.04$). Each clinical subtype had characteristic response patterns, which were reported, and representative examples were provided. Clustering based on structural disruption of familiarity- and unfamiliarity-associated functional networks poorly matched the clinical categorization (lesion: Rand index = 0.47; structural disconnection: Rand index = 0.51).

Conclusions: The systematic characterization of the peculiar clinical features of stroke-associated spatial delusions may improve the syndrome diagnosis and clinical approaches. The novel evidence about their neural correlates fosters the clarification of the pathophysiology of delusional misidentifications.

KEYWORDS
reduplicative paramnesia, spatial delusions, stroke

INTRODUCTION

In 1788, Charles Bonnet reported a peculiar form of spatial disorientation characterized by an incoherent belief of space mislocation [1]. Later, in 1903, Arnold Pick further characterized the syndrome and denominated it "reduplicative paramnesia" [2]. Pick described a 67-year-old woman who had been admitted to a clinic in Prague due to the subacute onset of cognitive and behavioral changes. Five months after her admission, she started to believe that she was not in Prague anymore, but in a replica of the original clinic that was located in her birthplace, "the suburb clinic." She could not be convinced otherwise and insistently tried to find explanations to justify her belief [2]. Since Pick's description, reduplicative paramnesias (also called spatial delusions or delusional misidentifications of space) were defined as a firm conviction of being in a different place from the real one, which does not change when the patient is confronted with clear counterfactual evidence [3, 4].

Different forms of spatial delusions have been described [5], representing different poles of pathological familiarity [6]. Place reduplication typifies hypofamiliarity for places and corresponds to the original description made by Pick, that is, the patients are convinced that they are in a replica of the original place. Chimeric assimilation is characterized by the fusion or combination of two different places (e.g., the hospital is inside the patient's home). In confabulatory mislocation, patients believe that they are in a place that is substantially different from the real one (e.g., believing to be at home instead of being at the hospital). Both embody place hyperfamiliarity [7].

At the structural and functional levels, spatial delusions are associated with a dual pattern of structural disconnection involving right frontothalamic and right occipitotemporal circuits [8], which prompts structural–functional decoupling of belief, familiarity, and place-associated functional networks [9]. At the clinical level, the striking incongruence between the patient's conviction and the surrounding environment may markedly disturb the patient's behavior [3, 10]. Although traditionally seen as a rare syndrome, evidence suggests that spatial delusions can be a frequent manifestation of right hemisphere lesions [11–13], particularly in the acute phase of right hemisphere strokes [8]. So far, the available knowledge about spatial delusions' clinical features is mainly based on case reports and small case series [3, 5]. Misdiagnosis of spatial delusions as delirium or psychomotor agitation may lead to erroneous approaches in terms of pharmacological treatment, behavioral interventions, and support of family members and caregivers.

Here, we systematically studied a large sample of patients with spatial delusions after right hemisphere acute stroke to shed light on their clinical presentation and pathophysiology. First, we aimed to characterize the clinical phenotype of spatial delusions and their subtypes. Second, we studied the neural correlates of these clinical features. Specifically, we hypothesized that there was a correlation between the duration of the reduplicative paramnesia and the magnitude of structural disruption of belief-associated functional networks and that the disturbances of familiarity-associated networks would predict the syndrome subtypes.

METHODS

Study design and patient selection

This research work is a subanalysis of a prospective, cumulative, case–control study that we performed from December 2016 to February 2020 in a stroke unit of a tertiary university hospital in Lisbon, Portugal [8]. The study aimed to investigate the neural basis of spatial delusions after stroke. Spatial delusions are right hemisphere syndromes [4]. Four hundred patients admitted within the acute phase (≤72 h) of right hemisphere stroke (ischemic or hemorrhagic) were screened for the presence of spatial delusions. An additional 104 cases were recruited from March 2020 to June 2021. Patients with dementia, acute confusional state (delirium), and decreased level of consciousness were excluded (the full description of exclusion criteria is detailed in Table S1).

The screening was performed in the first 72 h of admission and then at regular intervals of 48 h until the patients' discharge, using the systematic approach detailed in the following section. Patients with the syndrome whose phenomenological presentation was fully registered were selected for this study.

The study was approved by the Joint Ethics Committee of the Lisbon Academic Medical Centre.

Screening and phenotypic characterization of reduplicative paramnesia

Patients were asked if they knew where they were, specifically the type of building (hospital), the city (Lisbon), and the city district. If the patients did not know or gave a wrong answer, their correct location was explained, namely that they were in a hospital, which was called "Hospital de Santa Maria" and was located in Lisbon, more specifically in "Campo Grande/Cidade Universitária" (city district). When the patients disagreed, counterevidence was systemically shown to convince them otherwise. The questions and confrontations were tailored to the subtype of reduplicative paramnesia. When the patients believed they were in a place other than a hospital (i.e., confabulatory mislocation), they were asked: Question 1) why health care professionals would be in the referred place; Question 2) why medical equipment (oxygen masks, infusion tubes, vital signs monitor) would be there; Question 3) why the patients' clothes and bed sheets were labeled "Hospital de Santa Maria"; Question 4) why other patients would be in the referred place; Question 5) in which home division they would be (in the case they believed they were at home/living house); and Question 6) why it would be possible to see from the window distinct landmarks, such as Alvalade Stadium (the stadium of a leading football club in Portugal), the Lisbon airport, or Lisbon University (for those whose clinical condition allowed them to stand and to show them the window view).

For patients presenting chimeric assimilation, in addition to the questions referred to above, they were asked: Question 7) whether they had noticed or heard about any construction work in the referred place; and Question 8) why a hospital would be constructed inside that place.

For patients presenting with place reduplication, Questions 3 and 6 were posed. In addition, they were asked: Question 9) why "Lisbon" would be written next to the hospital logo; and Question 10, how many "Hospital de Santa Maria" they thought there were.

The diagnosis of reduplicative paramnesia was made when the patients maintained the belief of mislocation after exposure to the abovementioned counterevidence.

Clinical characterization

Demographic, clinical, and reduplicative paramnesia-related variables were collected (detailed in Table S2).

The geodesic distances between the misidentified place, the patients' home, and "Hospital de Santa Maria" were calculated and the relative distance of the misidentified place to the patient's home and to "Hospital de Santa Maria" ($r\Delta$) was determined:

$$r\Delta = \frac{\Delta place\_hospital}{\Delta place\_hospital + \Delta place\_home}$$

where $\Delta place\_hospital$ = the distance between the misidentified place and the "Hospital de Santa Maria" and $\Delta place\_home$ = the distance between the misidentified place and the patient's home (values closer to 1 represent mislocation closer to the hospital; values closer to 0 represent mislocation closer to the patient's home).

Neuroimaging correlations

Stroke lesions were defined based on brain magnetic resonance imaging (MRI; preferentially) or on computed tomography (CT) performed 24–72 h after stroke onset (MRI, $n = 22$; CT, $n = 38$). Magnetic resonance images were acquired with a Philips Achieva 3-T or Philips Intera 1.5-T scanner. CT images were acquired with a Philips Brilliance 64-channel scanner. The delineation was done manually on axial slices with a thickness of 3 mm in the patient's native space by a researcher with clinical experience in acute stroke lesion analysis. The researcher was blind to clinical variables. Lesions were normalized to a common space, MNI152 [14]. For MRI, the diffusion-weighted imaging was the sequence of reference for delineation [15]. T1 images were registered to MNI152 space through linear (affine transformation, 12 degrees of freedom) and nonlinear transformations, using the FMRIB Software Library functions "flirt" and "fnirt" [14]. For CT images, the registration was made to the CT-derived MNI152 template using a linear transformation [16]. Finally, the registration deformation fields were applied to the lesion masks.

To compute the structural disconnection pattern of each lesion, we used a tractwise approach [17]. Using the tool "Disconnectome" from the software package BCBtoolkit (www.bcblab.com), each lesion was overlapped with a group of 178 healthy subjects' tractography from the Human Connectome Project 7-T dataset [18]. Tractographies were obtained using a whole-brain deterministic approach in StarTrack software (https://mr-startrack.com), applying a spherical deconvolution methodology, specifically a damped Richardson–Lucy algorithm. They were made available with the BCBtoolkit (http://www.bcblab.com). The full details of preprocessing are described in Karolis et al. [19]. A voxelwise probability of disconnection was calculated [20]. The voxels were included in the disconnectome map if they were disconnected in >50% of healthy subjects' tractographies [20].

It has been demonstrated that delusional misidentifications are associated with structural–functional decoupling of belief and familiarity-associated functional networks [9, 21]. Neurosynth is a validated brain-mapping platform that performs large-scale automated extraction of meta-analytic functional maps of terms of interest [22]. We used Neurosynth to obtain the meta-analytic maps of the terms "belief," "familiar," and "unfamiliar." Association test maps were extracted [22]. The maps are corrected for multiple comparisons applying a false discovery rate of 0.01. Then, we computed the volumetric spatial overlap of these meta-analytic maps with the individual stroke lesion and with the structural disconnectome maps.

The Spearman correlation between the duration of spatial delusions and the structural disruption (either lesion or structural disconnection) of belief-associated networks was calculated. Lesion volume is an important confounder in the establishment of lesion–behavior associations [23, 24]. A regression analysis was performed to investigate whether the putative correlations were independent of lesion volume. In addition, we computed a voxelwise beta-coefficient map using the linear regression function of scikit-learn [25], to analyze which voxels' lesion or disconnection best predicted the duration of the phenomenon.

To evaluate the classification performance of cases based on the structural disruption of familiarity-associated networks, we performed an unsupervised machine learning partition using the *k*-means clustering algorithm from scikit-learn [25]. The number of clusters to form was defined as three (the number of clinical subtypes of reduplicative paramnesia). The variables included in the model were the structural disruption (either lesion or structural disconnection) of "familiar" specific regions and the structural disruption of "unfamiliar" specific regions. Then, we calculated the Rand index to determine the similarity between the familiarity-derived clustering and the clinical subtype classification (1 meaning perfect agreement and 0 meaning no agreement). An alternative analysis was computed in which we defined the number of clusters to form as two, considering confabulatory mislocation and chimeric assimilation to be a unique category of hyperfamiliarity syndromes and place reduplication to be a hypofamiliarity syndrome [7]. The first presentation was considered for patients with more than one subtype of reduplicative paramnesia.

Statistical analysis

The Spearman correlation, linear regression, and *k*-means clustering were applied as explained above. When the residuals of the linear model were not normally distributed, a quantile regression was performed.

Alpha levels were set at 0.05 for statistical significance. The statistical software packages scipy.stats 1.7.1, Stata 14, and scikit-learn 0.24 [25] were used.

RESULTS

Clinical and demographic features

Sixty patients with spatial delusions were identified and fully characterized (the flowchart of patients' inclusion is available in Figures S1 and S2). Fifty-seven had an ischemic stroke (95%), and three had a hemorrhagic stroke (5%). Their median age was 81 years (interquartile range [IQR] = 73–85, range = 55–93), and the female/male ratio was 31/29. The median National Institutes of Health Stroke Scale at admission was 14 (IQR = 12–18) and at discharge was 8 (IQR = 3–12). The median admission time was 8 days (IQR = 6–12, range = 2–46). The affected territories are reported in Table S3.

The median time of diagnosis of reduplicative paramnesia was 1 day after stroke (IQR = 1–3 days, range = 0–7 days). Nineteen patients (32%) had at least one observation in which they were oriented in space before the manifestation of reduplicative paramnesia. Twenty-eight patients (47%) spontaneously expressed that they had previously been in the (original) "Hospital de Santa Maria" before being brought to the place where they believed they were.

Subtypes of reduplicative paramnesia and places of mislocation

Confabulatory mislocation was the most frequent presentation subtype (n = 36, 60%), followed by place reduplication (n = 16, 27%) and chimeric assimilation (n = 8, 13%). Most patients maintained the same subtype during the period of spatial delusion (n = 48, 80%). Most places of mislocation were closer to the patient's home than to the hospital (n = 56, 93%; Figure 1).

Patients with confabulatory mislocation most frequently believed that they were at home (n = 27, 75%), followed by believing they were in their relative's home or vacation home (n = 4, 11%) or in another hospital or clinic (n = 2, 6%). The remaining three were mislocated in extravagant places: an ambulance, a former bus garage, and a social security office. Of these, 14 patients (39%) changed the place of delusional mislocation during their presentation; five (14%) changed to a chimeric assimilation subtype, five (14%) changed to a place reduplication subtype, and four (11%) changed the place of confabulatory mislocation.

All patients with place reduplication were convinced they were in a branch of "Hospital de Santa Maria" (n = 9, 56%) or in a replica of the hospital (n = 7, 44%) located in another place. During the period of spatial delusion, three (19%) changed the location of the reduplicated building and one (6%) changed to a confabulatory mislocation form.

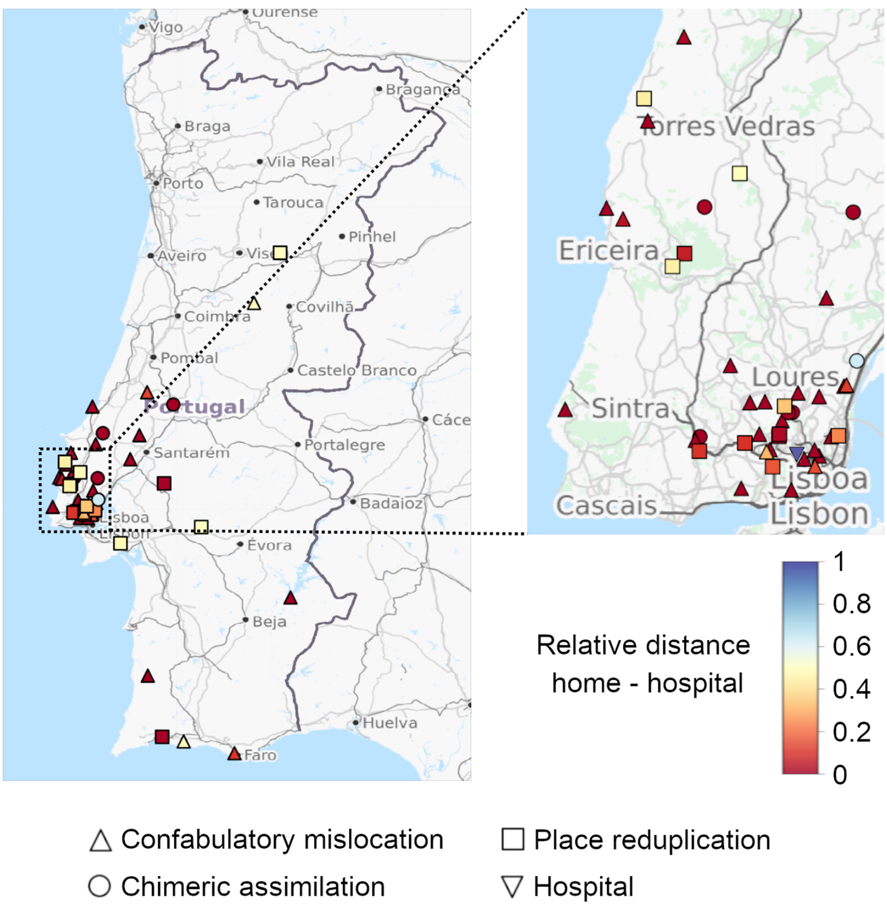

FIGURE 1 Map representation of the mislocation places' geographical location (https://www.openstreetmap.org). The color gradient represents the relative position of the mislocation place. Values closer to 1 represent mislocation closer to the hospital; closer to 0 means closer to the patient's home. Only the first is shown in patients presenting more than one place of mislocation

Regarding the patients presenting chimeric assimilation, three (38%) believed their home had been transformed into a hospital, three (38%) that a relative's home had been transformed into a hospital, and two (25%) that the hospital was inside their home. One patient (13%) changed his delusional belief to a place reduplication form.

Overall, 19 patients changed the place of mislocation during the period of reduplicative paramnesia (32%). The second place of mislocation was significantly closer to the hospital in the majority of patients ($n = 11$, 58%; distance difference: median = 28.86 km, range = 0.39–201.26 km) and farther in four patients (21%; distance difference: 0.08 km, range 0.01–2.03 km; $p < 0.01$). The remaining four changed the misidentification belief, but the geographical position of the misidentified place remained the same (21%).

Name of the misidentified place

Eighteen patients (30%) named the place that was misidentified as “Hospital de Santa Maria”. In these cases, reduplicative paramnesia was uncovered when they were asked about their location (i.e., the city or town in which they were). The majority ($n = 15$) expressed that it was because they were in a replica or in a branch of the original hospital (i.e., place reduplication). The remaining three patients believed that there was a hospital ward inside their homes (i.e., chimeric assimilation), also named “Hospital de Santa Maria”.

Duration of spatial delusions and disruption of belief-associated networks

The median duration of reduplicative paramnesia was 3 days (IQR = 1–7 days, range = 1–29 days; Figure 2a). In 23 cases, the patients were discharged still presenting reduplicative paramnesia.

The duration of reduplicative paramnesia was moderately correlated with the volume of structural disconnection overlapping the belief-associated functional network (Spearman correlation = 0.39, $p = 0.02$; Figure 2b), and this association was independent of lesion volume (beta coefficient = 3.18, 95% confidence interval = 0.12–6.24, $p = 0.04$). The voxelwise linear regression revealed that higher beta-coefficients mostly overlapped inferior temporal white matter fibers of the left hemisphere (Figure 2c), that is, the disconnection of these fibers had a stronger association with the duration of reduplicative paramnesia. No independent association was found with lesion overlap ($p = 0.53$).

The lesion and the structural disconnection overlap maps are available in Figure S3. The belief-associated meta-analytic functional map, derived from 83 studies, is available in Figure S4.

Semantic knowledge about the location of places and spatial routes

All patients were able to say their own address, and the majority knew the location of the (original) “Hospital de Santa Maria” ($n = 52$, 87%).

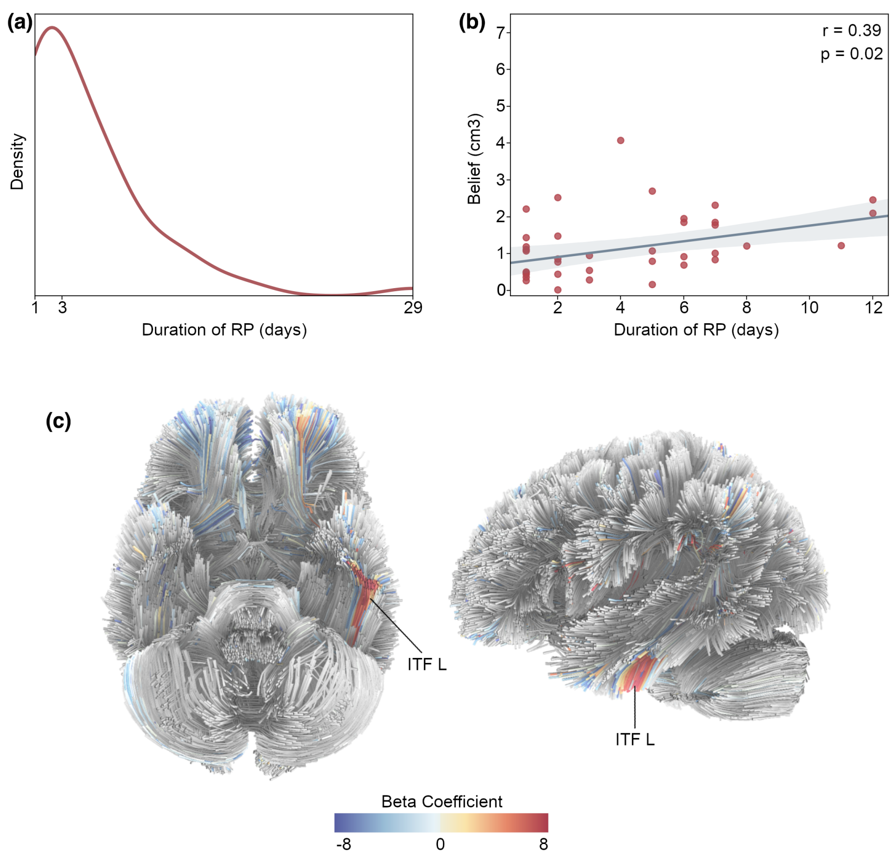

FIGURE 2 Reduplicative paramnesia duration. (a) Density distribution of the duration of reduplicative paramnesia. (b) Relationship between the duration of reduplicative paramnesia and the structural disconnection of the belief network expressed in the volume of overlap. The blue line represents the robust regression line, and the blue shadow, the 95% confidence interval. (c) Tract representation of the beta-coefficient values obtained in the voxelwise linear regression between the duration of reduplicative paramnesia and the structural disconnection of the belief network. The colormap represents the projection of the beta-coefficient map on a white matter tract template, using DSI Studio (https://dsi-studio.labsolver.org). ITF, inferior temporal fibers; L, left; *r*, Spearman correlation; RP, reduplicative paramnesia

TABLE 1 Representative descriptions of patients with confabulatory mislocation

Why are health care professionals here?
"You are the doctor from Hospital de Santa Maria. You came here to take care of me. I was there before. How did you know the address of my home? Did you find it well?"
Why is medical equipment here?
"Usually, this equipment exists in the hospitals. It is similar to the one I had in Hospital de Santa Maria. The hospital should have put it here. Nowadays, technology can be anywhere. This building is my home, but many things should have been brought from Hospital de Santa Maria."
Why does it say "Hospital de Santa Maria" on your bed sheets and hospital clothes?
"These clothes should have come in the ambulance. When the ambulance was called, the clothes should have been put inside."
Why are other patients in this room?
"These patients shoul have come with me in the ambulance, with the permission of the doctors and the nurses. It would be rude to send them away from my home."
What do you think about this window view? The building, the stadium…
"I had never noticed that I could see the sports stadium from home. But if I were in Hospital de Santa Maria, I would also see Benfica's stadium."

TABLE 2 Representative descriptions of patients with place reduplication

Why does it say "Hospital de Santa Maria" on your bed sheets and hospital clothes?
"This shall be a duplication of the service provided by Hospital de Santa Maria. The name is the same, but it covers other geographical areas."
Why does it say "Lisbon" next to the hospital logo?
"I had not read it. They made a mistake. They should have put the name of this town."
How many "Hospital de Santa Maria" do you think there are?
"There is only one. The original one. This is a dependency, not the main one. They might have built this one for the periods when the main one is full. Hospital de Santa Maria is much bigger than this one."
What do you think about this window view? The building, the stadium…
"These buildings are not typical of this district. I had never seen them. The architecture is similar the original Hospital de Santa Maria. I am going to put on my glasses, so that you do not say I am confused or disoriented. I might have lost some cognitive abilities after the stroke, but my spatial orientation is intact. The proof that it is possible to see Sporting's Stadium from this district is that I am seeing it."

Twenty-eight patients (47%) were able to correctly describe the spatial route between two or more points of interest (home–"Hospital de Santa Maria", place of mislocation–home, place of mislocation–"Hospital de Santa Maria").

Orientation in time

Most patients correctly knew the current year (*n* = 48, 80%) and month (*n* = 49, 82%).

Specific phenomenology of confabulatory mislocation

Representative descriptions of patients with confabulatory mislocation are presented in Table 1.

The most frequent answers are presented in Table S4.

Specific phenomenology of place reduplication

Representative descriptions of patients with place reduplication are presented in Table 2.

The most frequent answers are presented in Table S5.

Specific phenomenology of chimeric assimilation

Representative descriptions of patients with chimeric assimilation are presented in Table 3.

The most frequent answers are presented in Table S6.

Clustering based on familiarity-associated functional networks

The *k*-means clustering results based on the volume of lesion and volume of structural disconnection overlapping familiarity- and unfamiliarity-associated functional networks are presented in Figure 3. The familiarity- and unfamiliarity-associated meta-analytic functional maps, derived from 275 and 183 studies, respectively, are available in Figure S4.

The Rand index was 0.47 for lesion maps and 0.51 for structural disconnection maps (poor similarity). The classification similarity remained low when the number of clusters was reduced to two: lesions maps, Rand index = 0.64; structural disconnection maps, Rand index = 0.56.

DISCUSSION

In this work, we analyzed the clinical phenomenology and neural correlates of stroke-associated spatial delusions. First, we characterized the

TABLE 3 Representative descriptions of patients with chimeric assimilation

Why does it say "Hospital de Santa Maria" in your bed sheets and hospital clothes?
"That's because Hospita is here and my home is here too. Please open the door because my maid should be arriving. The house is mine. The hospital is not mine."
Why are other patients in this room?
"I do not know these patients. I do not know what they are doing here. They should have been brought here when I was sleeping. Probably, there were not enough beds at the hospital and they were sent here."
Have you noticed or heard about any construction work?
"It's strange how they have done it so quickly. They transformed my home into a hospital. In the future, I might make some profit from this."
Why would a hospital be built inside your home (or in your relatives' home)?
"Maybe the hospital was full and they used this space. The other patients were brought here too. You are asking me all these questions to see if my mind is fine, but I assure you that it is."
What do you think about this window view? The building, the stadium...
"My building is very similar to Hospital de Santa Maria. It should have been designed by the same architect. Everything with public funds, maybe..."

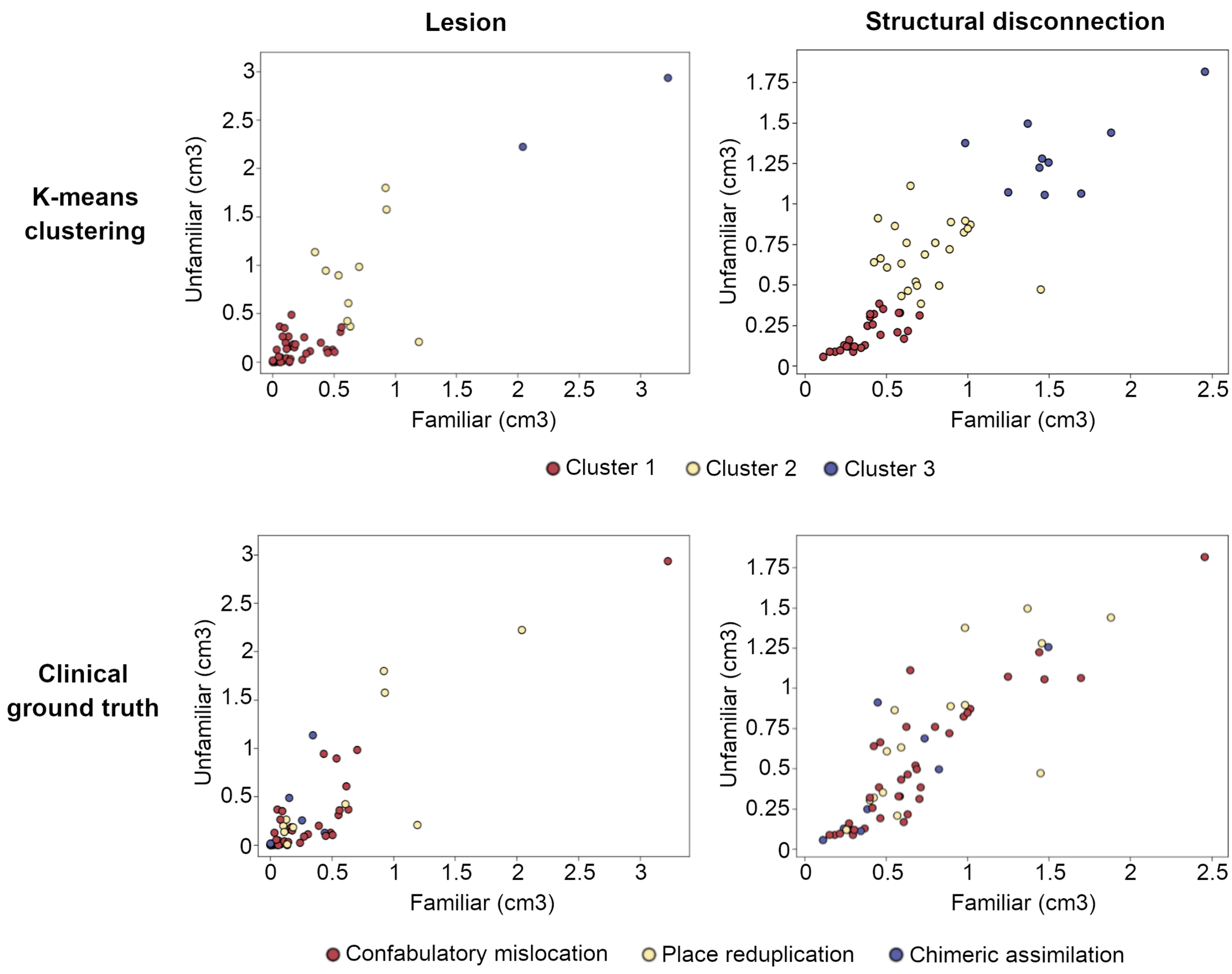

FIGURE 3 Reduplicative paramnesia subtypes and familiarity-associated functional networks. Clustering of reduplicative paramnesia cases based on the volume of the lesion (top left) and of structural disconnection (top right) overlapping familiarity- and unfamiliarity-associated functional networks are compared with the ground truth classification based on clinical presentation (bottom)

location of misidentified places and described the general phenotypic features of the syndrome. We demonstrated that the duration of spatial delusions is moderately correlated with the structural decoupling of belief-associated functional networks. Second, we reported associated clinical features, such as the patients' knowledge about the location of the misidentified places and their orientation in time. Third, we described the most common patterns of patients' response according to spatial delusion subtypes and provided representative examples to facilitate recognition and diagnosis. Finally, we showed that case clustering based on structural disruption of familiarity/unfamiliarity-associated functional regions poorly matches the clinical classification.

The large majority of patients localized the misidentified place closer to their homes than to the hospital. Limbic-related models of delusional misidentifications support that misidentified stimuli tend to be emotionally relevant for patients [26], and an association between spatial delusions and structural disconnection of limbic structures has been established [8].

Belief, as a neural process, can be defined as the integration of perceived information with internal representations of personal significance and emotional value [27]. Distinct neural systems in the prefrontal cortex and the limbic system mediate the states of assent, dissent, and uncertainty [28, 29]. Deregulations of belief processes seem to be a cardinal condition for delusional misidentifications [27, 30]. As our phenomenological analysis showed, patients recognize that the surrounding environment looks like "Hospital de Santa Maria" but still do not believe they are there. For the first time, we showed that the magnitude of structural disconnection of belief-associated functional networks is correlated with the duration of reduplicative paramnesia. Interhemispheric unbalance models propose that delusional misidentifications result from right hemisphere damage and left hemisphere unleashing [6]. Whereas previous evidence shows that the emergence of spatial delusions is predicted by disconnection of right temporal regions [8, 9], here we showed that the disconnection of left temporal regions best predicts the syndrome's duration. This result may provide structural–functional support to the role of left hemisphere dysfunction in the pathophysiology of reduplicative paramnesia [6, 31]. This effect might be mediated by contralateral hemisphere diaschisis [32].

The erroneous beliefs and the disturbed mechanisms of implicit memory and recognition overwhelm the patient's semantic knowledge about the spatial localization of misidentified places [26, 33, 34]. In our sample, all patients were able to say their own address and the large majority knew the location of (the original) "Hospital de Santa Maria". The maintenance of correct orientation of time in most patients evidences the spatial specificity of the syndrome.

The strong emotional valence associated with reduplicative paramnesia, evident in the pioneer and in subsequent descriptions [2, 11, 35], manifests at opposite poles of pathological familiarity [6]. However, the clustering classification based on structural disruption of familiarity/unfamiliarity-associated functional networks had a poor capacity to predict clinical subtype classification. Finer functional interactions between familiarity-associated brain regions and psychological factors might be crucial to determine this phenomenological divergence [36].

Knowledge about the phenomenological features of the syndrome is important to make an appropriate diagnosis and to avoid misinterpretations of patients' general cognitive status. Nearly one third of the patients called "Hospital de Santa Maria" to the misidentified place, which may contribute to the underdiagnosis of the syndrome. Simple questions, such as asking in which town/district patients are, might be crucial for the diagnosis and should be performed during the neurological examination, especially in patients with right hemisphere lesions. In addition, in at least one third of the patients, the syndrome was not hyperacute, that is, the patients were oriented in space for at least 1 day before the emergence of reduplicative paramnesia, and nearly half spontaneously said that they had previously been in the (original) "Hospital de Santa Maria" before being brought to the place where they were at that moment. The physiopathological reason for this deferred onset remains to be clarified but may be due to delayed diaschisis [32].

As a limitation of our study, we were not able to conduct a prospective follow-up of patients after their hospital discharge. In addition, the study was performed in a tertiary stroke unit and may not represent the entire stroke population. Finally, in a considerable proportion of patients, MRI was not performed. However, modern CT scanners also provide high-resolution images suitable for stroke lesion analysis studies [15].

In conclusion, our work reports a systematic description of the peculiar clinical features of stroke-associated spatial delusions, which may boost the awareness and the proper diagnosis of the syndrome. It also contributes to a better understanding of the neural background of delusional misidentifications by providing novel evidence about the neural correlates of the syndrome.

AUTHOR CONTRIBUTIONS

Pedro N. Alves: Conceptualization (equal), data curation (lead), formal analysis (lead), funding acquisition (lead), investigation (lead), methodology (equal), visualization (lead), writing–original draft preparation (lead). Ana C. Fonseca: Conceptualization (equal), methodology (equal), writing–review and editing (equal). Teresa Pinho-e-Melo: Conceptualization (equal), writing–review and editing. Isabel P. Martins: Conceptualization (equal), methodology (equal), project administration (lead), supervision (lead), writing–review and editing (equal).

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CONFLICT OF INTEREST

None

DATA AVAILABILITY STATEMENT

The anonymized data supporting this study's findings are available on request from the corresponding author. The data are not publicly available due to ethical approval restrictions and because their containing information could compromise the privacy of research participants.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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