Article

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# TOPOGRAPHICAL DISORIENTATION IN ALZHEIMER'S DISEASE

*Carla Cristina Guariglia[1], Ricardo Nitrini[2]*

**Abstract** – Topographical disorientation (TD) has not been as extensively studied as other frequent manifestations of Alzheimer's disease (AD). **Objective:** To verify the occurrence of TD and to identify the neuropsychological dysfunctions associated with TD in AD. **Method:** Thirty patients with probable AD, their caregivers and 30 subjects without dementia (controls) were interviewed with a questionnaire and evaluated with tests related to topographical orientation. **Results:** AD patients, even those with mild dementia, differ from controls in the questionnaire on topographical orientation and in most neuropsychological tests except for tests of spatial working memory, point localization, three dimension and nonsense figure copy. When the performances in the neuropsychological tests of patients with mild or moderate dementia were compared, only landmark recognition and route description were more impaired in moderate dementia. **Conclusion:** TD occurs even in mild dementia of AD, a finding apparently not explained by the impairments of more elementary spatial functions.

KEY WORDS: Alzheimer's disease, orientation, spatial perception, topographical disorientation, spatial working memory.

**Desorientação topográfica na doença de Alzheimer**

**Resumo** – Desorientação topográfica (DT) não tem sido tão exaustivamente estudada quanto outros sintomas frequentes da doença de Alzheimer (DA). **Objetivo:** Verificar a ocorrência de DT e identificar as disfunções neuropsicológicas associadas com a DT na DA. **Método:** Trinta pacientes com DA provável, seus cuidadores e trinta sujeitos sem demência (controles) foram entrevistados com um questionário e testes relacionados à orientação topográfica. **Resultados:** Pacientes com DA, mesmo aqueles com demência leve, diferiram dos controles no questionário de orientação topográfica e na maioria dos testes neuropsicológicos, exceto nos testes memória operacional espacial, localização de pontos, cópia de figuras sem sentido e de figura em três dimensões. Quando os desempenhos de pacientes com demência leve ou moderada foram comparados, apenas os testes de reconhecimento de marcos e descrição de rotas foram mais comprometidos na demência moderada. **Conclusão:** DT ocorre mesmo na demência leve da DA, um achado aparentemente não explicado pelo comprometimento das funções espaciais mais elementares.

PALAVRAS-CHAVE: doença de Alzheimer, orientação topográfica, desorientação topográfica, percepção espacial, memória operacional espacial.

Topographical disorientation (TD) can be defined as an impairment of finding the way in a familiar route, in learning new routes, recognizing places, describing verbally a route, using a map for self orientation, identifying landmarks or finding rooms in the house[1-7]. TD is very common in AD as dementia gets worse, but many times it is one of its first manifestations[1,2]. Henderson et al. observed that 38% subjects with mild dementia in AD had difficulty to recognize places and were lost in the neighborhood[1]. Topographical orientation is a broad concept, encompassing heading, optic flow, alocentric and egocentric orientations, landmark recognition and geographic orientation[3-7]. Heading is regarded as the general sense of direction, which is necessary to go from a place to a distant one, when both places cannot be seen at once[3]. Optic flow is the designation of the radial pattern of visu-

Behavioral and Cognitive Neurology Unit, Department of Neurology and CEREDIC (Reference Center for Cognitive Disorders), Hospital das Clínicas, University of São Paulo (USP) School of Medicine, São Paulo SP, Brazil: [1]Neurologist, Master in Neurology; [2]Associate Professor of Neurology.

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*Dr. Ricardo Nitrini – Rua Itapeva 378 / 93 - 01332-000 São Paulo SP - Brasil. E-mail: rnitrini@uol.com.br*

al motions that is formed when a subject moves through the environment[4]. These radial patterns, which have the subject in the center, give the direction of self-movement and permit the identification of the relative position of objects, according to the apparent slower visual speed of distant objects and the apparent faster visual speed of near objects[4].

Egocentric and alocentric orientations are important skills for topographical orientation. Egocentric orientation permits the subject to know his position in relationship with the surroundings objects in the environment[5-7]. It depends on the position of the subject, because an object located on the right side of the subject can be turned to the left side if the subject walks and changes his/her position. Conversely, alocentric orientation is the spatial relationship between landmarks, which is independent of the perspective of the subject[6,7]. For instance, both egocentric and alocentric orientations participate in finding the route from the bed to the bathroom, in the dark. Egocentric orientation is responsible for the relationship between the subject and the bed that can be changed if the subject turns to the right or to the left side, but the relationship between the bathroom's door and the bed is always constant and depends on alocentric orientation. Landmark recognition is the skill to recognize salient features of the environment, such as buildings of the neighborhood[2,6]. Geographical orientation is the ability to establish the direction and distance between distant places like cities in a map[8].

Topographic orientation is also dependent of other functions such as visual attention, spatial working memory and visuospatial perception, and for that reason many brain areas are related to it. In the rat, pyramidal cells of the hippocampus have a pattern of action potentials which is distinctively related to the particular area of space where the rat is, and for that they were called "place cells"[9]. It is not clear whether there are place cells in the human hippocampus but the posterior hippocampi are larger in London taxi drivers, who should pass a rigorous examination on street names and routes to obtain their license, than in controls[10]. There are data to support that parieto-occipital areas are linked to optic flow processing[4] and parahippocampal gyrus is related to landmark recognition[6], while lesions of the retrosplenic cortex are associated with heading impairment[3].

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The objective of this study was to verify the occurrence of TD in AD patients and to identify which alterations of basic neuropsychological functions were related to this occurrence.

## METHOD

Thirty patients with probable AD, following NINCDS-ADRDA criteria[11], and with mild or moderate dementia defined by scores in the Mini-mental state examination above 14, and 30 control subjects were evaluated. All participants had been living in São Paulo city at least for the past 5 years, had 8 or more years of schooling to avoid educational bias and were fluent in Portuguese. Subjects with aphasia, focal cerebral damage, vision or auditory impairment were excluded.

Subjects and patients were recruited from the Behavioral and Cognitive Neurology Unit of the Department of Neurology and CEREDIC (Reference Center for Cognitive Disorders), Hospital das Clínicas, University of São Paulo School of Medicine, São Paulo, Brazil.

Patients and control subjects were submitted to the Mini-mental State Examination[12,13], digit-span and to the Brief Cognitive Battery that includes visual perception, naming, immediate memory, delayed recall, verbal fluency and clock drawing tests[14-16].

Patients and control subjects were evaluated with a questionnaire on topographical orientation and a task battery developed for this study. The questionnaire contained questions on topographical orientation with 11 questions, from which only three questions that are less influenced by the subjects' autonomy to walk to different places were selected. These questions were: (1) Has the patient ever get lost? (2) Is the patient able to go out in the neighborhood? For instance, is he able to go out to closest grocery? (3) Is the patient able to go to out to far places? Each question scored one point and the total score ranges from 0 to 3, higher scores being associated with more impaired orientation.

Landmark agnosia was evaluated showing seven pictures from famous Brazilian landmarks (Alvorada's Palace - Brasília, Lacerda's lift - Salvador, Farol da Barra - Salvador, Rio de Janeiro shore - Rio de Janeiro, Congresso Building - Brasília, Hercilio Luz bridge - Florianopólis, Ouro Preto - Minas Gerais) and 15 pictures from famous places at São Paulo city (São Paulo Museum of Art - MASP, Central Railway Station, Paulista Avenue, Italia Building, Flags Monument - Ibirapuera Park, Ipiranga Museum, Bandeirantes Palace, São Paulo Theatre, Copan Building, Martinelli Building, Consolação Church, America Latina Memorial, Liberdade district, Paissandu square, Julio Prestes Railway station). Subjects had to name the place or give its location. Each corrected answer was scored one point.

For route recognition evaluation the patient was asked to describe a route from his own house to the closest grocery (commercial store where people by common items such as bread,

milk, cheese, matches, etc - in Brazil, the bakery at the corner of the street) and the possible scores were zero, 0.5 and 1, which higher scores corresponding to better performance.

For the evaluation of egocentric orientation, the examiner pointed to five objects in the examination room and then the subject was asked to close his/her eyes and then point to the location of each of the objects. After a distraction task, the subject was asked to point to the objects again. The performance was scored one to five depending on the number of correct pointed items in the immediate and in the delayed task.

Geographical orientation was evaluated asking the patient to point to five capital cities in the Brazil map (Porto Alegre, São Paulo, Manaus, Brasília, Recife). It was scored one to five depending on the number of correct pointed cities.

Point localization was evaluated showing to the subject a card with 25 points arranged in columns. Then five cards, each one with only point located in different positions were presented to the subject, who should point to the right position of the point in the 25 point card. Scores range from 0 to five correct located points.

Line orientations judgment was evaluated with Benton's line orientation test[17], using only two subtests each one with two lines (lines 4 and 5; lines 3 and 10) out of the thirty lines of the original test.

Geometric relationships were evaluated asking subjects to copy four non-sense drawings[18]. Each correct draw was scored one point.

Mental imagery was evaluated with four 3 dimensional figures of blocks, where the subject has to count the number of blocks[18]. Scores ranged from 0 to 4. Mental rotation was evaluated with the Christensen parallelogram test, which has 10 parallelograms in different orientations. Scores ranged from 0 to 10[19].

Complex spatial functions were evaluated by asking the subject to copy a three dimensional cross and to draw a sketch of his/her house. Scores were zero, 0.5 and 1, for each of the tests.

Spatial working memory was evaluated through the spatial span using the Corsi's block tapping test[20,21].

Unilateral negligence was evaluated with a non verbal cancellation test[22].

According to the scores in Mini-mental State Examination, patients were classified into mild dementia (scores above 19) or moderate dementia (scores ranging from 15 to 19).

This study was approved by the Ethics Committee of the Hospital das Clínicas, University of São Paulo and written informed consent was obtained from all subjects or the caregivers when appropriate.

**Statistical analysis**

Chi-square test was used to verify the difference among categorical variables and the Mann-Whitney test was used for quantitative variables. The Statistical Package for the Social Sciences for Windows, version 10.0 (SPSS Inc) was used for statistical analysis. The value of statistical significance accepted was 0.05.

## RESULTS

Patients and control subjects were not different regarding educational level and gender, although patients with dementia were older than control subjects. When patients were divided into mild and moderate dementia groups, there was no difference between them regarding age, educational level and gender (Table 1).

The performances in the topographical orientation questionnaire and in tests related to topographical orientation are presented in Table 2. There were differenc-

*Table 1. Demographic data and performance of control subjects. AD patients and AD patients with mild or moderate dementia in the Mini-mental State Examination (MMSE). verbal fluency and digit span tests.*

| | Control subjects N=30 | Patients N=30 | p | Mild dementia patients N=15 | Moderate dementia patients N=15 | $p^1$ | $p^2$ | $p^3$ |
|---|---|---|---|---|---|---|---|---|
| Gender | 21 W<br>9 M | 15 W<br>15 M | 0.94 | 6 W<br>9 M | 7 W<br>6 M | 0.128 | 0.271 | 0.715 |
| Ages – Median (Minimum–Maximum) | 68.5 (59–88) | 75 (54–95) | 0.009 | 76 (60–95) | 74 (54–88) | 0.016 | 0.67 | 0.345 |
| Years of schooling – Median (Minimum–Maximum) | 8.0 (8–17) | 11 (8–17) | 0.634 | 8 (8–17) | 11 (8–16) | 0.428 | 0.999 | 0.267 |
| MMSE – Median (Minimum–Maximum) | 29 (27–30) | 20 (15–26) | <0.001 | 23 (21–26) | 17 (15–19) | <0.001 | <0.001 | <0.001 |
| Verbal fluency – Median (Minimum–Maximum) | 17 (9–26) | 10 (3–18) | <0.001 | 10 (5–18) | 9 (3–17) | <0.001 | <0.001 | 0.436 |
| Digit span – Median (Minimum–Maximum) | 6 (4–8) | 3 (0–7) | <0.001 | 4 (0–7) | 3 (0–5) | 0.001 | <0.001 | 0.174 |

N: total number; W: women. M: men; p: comparison between dementia patients and controls; $p^1$: comparison between mild dementia patients and controls; $p^2$: comparison between moderate dementia patients and controls; $p^3$: comparison between mild and moderate dementia patients.

*Table 2. Performance in the questionnaire and in tests related to topographical orientation (median, minimum and maximum values).*

| | Control subjects N=30 | Patients N=30 | p | Mild dementia patients N=15 | $p^1$ | Moderate dementia patients N=15 | $p^2$ | $p^3$ |
|---|---|---|---|---|---|---|---|---|
| Topographical orientation questionnaire | 0 (0–1) | 1 (0–3) | <0.001 | 3 (0–3) | <0.001 | 1 (0–3) | <0.001 | 0.161 |
| City landmarks | 10 (0–15) | 4 (0–9) | <0.001 | 6 (2–9) | 0.001 | 2 (0–6) | <0.001 | <0.001 |
| Brazil landmarks | 5 (0–9) | 2.5 (0–8) | <0.001 | 4 (0–8) | 0.210 | 1 (0–4) | <0.001 | <0.001 |
| Route description | 1 (0–1) | 1 (0–1) | 0.001 | 1 (0–1) | 0.150 | 0.5 (0–1) | <0.001 | 0.018 |
| Egocentric orientation (immediate) | 5 (3–5) | 4 (1–5) | <0.001 | 4 (2–5) | 0.001 | 4 (1–5) | <0.001 | 0.798 |
| Egocentric orientation (delayed) | 5 (2–5) | 3 (0–5) | <0.001 | 3 (1–5) | <0.001 | 3 (0–5) | <0.001 | 0.518 |
| Brazil map | 4 (1–5) | 2 (0–5) | <0.001 | 2 (0–5) | 0.012 | 2 (0–5) | <0.001 | 0.323 |
| House drawing | 1 (0–1) | 0.5 (0–1) | <0.001 | 0.5 (0–1) | 0.002 | 0 (0–1) | 0.001 | 0.237 |
| Point localization | 4.5 (0–5) | 4 (0–1) | 0.041 | 4 (1–5) | 0.334 | 3 (1–5) | 0.017 | 0.182 |
| Line orientation | 4 (0–4) | 3 (0–4) | 0.006 | 3 (0–4) | 0.008 | 3 (0–4) | 0.045 | 0.399 |
| Non sense drawing | 4 (0–4) | 4 (0–4) | 0.062 | 4 (0–4) | 0.212 | 4 (0–4) | 0.052 | 0.495 |
| Mental imagery Test | 3 (0–4) | 1 (0–4) | 0.007 | 1 (0–4) | 0.025 | 1 (0–4) | 0.034 | 0.846 |
| Parallelogram orientation | 3.5 (0–8) | 2 (0–5) | 0.001 | 2 (0–3) | 0.012 | 1 (0–5) | 0.003 | 0.269 |
| 3D drawing | 0.5 (0–1) | 0.5 (0–1) | 0.299 | 0.5 (0–1) | 0.502 | 0.5 (0–1) | 0.304 | 0.789 |
| Cancellation task | 2 (0–6) | 1 (0–5) | 0.264 | 1.5 (0–5) | 0.530 | 1 (0–4) | 0.238 | 0.719 |
| Corsi's block | 5 (3–7) | 4 (0–6) | 0.010 | 4 (3–6) | 0.080 | 4 (0–5) | 0.015 | 0.480 |

p: comparison between patients and controls; $p^1$: comparison between mild dementia patients and controls; $p^2$: comparison between moderate dementia patients and controls; $p^3$: comparison between mild and moderate dementia patients.

es between patients and control subjects in all tests except non sense drawing, cancellation test and three dimension figure copy.

When patients with mild dementia were compared with control subjects there was no difference in the recognition of Brazil landmarks, route description, point localization, Corsi's block tapping test as well as in non sense drawing, cancellation test and three dimension figure copy.

The comparison between mild and moderate dementia patients showed that there was no difference between them in the majority of the tests, except for São Paulo city landmarks, Brazil landmarks and route description.

## DISCUSSION

The results of the questionnaire showed that TD was present even in mild dementia of AD. Other authors that have applied questionnaires for topographical orientation in AD had reported similar findings[2,3,23].

Although our patients with mild dementia have TD, they were not impaired in point localization, non sense drawing and three dimension figure copy when compared to control subjects. Other studies have also reported that spatial and visual perception may not be involved in early stages of AD[23,24] . These findings suggest that TD in AD is not directly caused by disturbances of less complex spatial and visual functions.

Spatial memory tasks results showed that spatial working memory disturbances are present in patients with dementia compared to controls. However, spatial working memory was not different in patients with mild dementia and controls in this study. These findings are different from another study which verified that were statistical difference in Corsi's block tapping test between mild dementia patients and control subjects[25]. It is possible that impairment of spatial working memory did not contribute to TD in the patients with mild dementia in this study.

Conversely, egocentric and alocentric orientation, landmark recognition, route description, geographic orientation, house drawing, line orientation and mental rotation are impaired in patients with mild dementia in this study.

Egocentric orientation was significantly impaired in AD patients in this study, similarly to the findings of Monacelli et al.[5]. There was no difference between mild and moderate AD patients, showing that patients have egocentric disorientation in early stages of AD.

Landmark recognition was also different between control subjects and AD patients, even in mild dementia of AD, in accordance with other studies. Monacelli et al.[5] evaluated landmark recognition in the hospital hall while Uc et al. tested landmark identification during actual driving[26]. Both studies showed that failure in landmark recognition was present in mild AD.

Honda et al. evaluated route description by normal adults verifying that the intelligibility of the route description depends on their knowledge of the environment relationships[27]. In this sense, the failure of route description by our patients suggests that they have alocentric disorientation, and that this disturbance occurs in the early stages of AD.

Landmark recognition and route description were more severe in moderate than in mild dementia in our study. Although this study did not follow AD patients longitudinally, these findings suggest that landmark recognition and route description failures are responsible for the worsening of TD in moderate compared to mild dementia.

Geographic orientation in a Brazil map showed difference between the groups. This task identified difficulty in mild dementia patients suggesting that the impairment also occurs since the early stages of AD[9].

House drawing results showed difference between mild dementia patients and control subjects. Liu et al. studied drawings of mild dementia patients' houses and the results were similar to this study[28]. The results of this test may be influenced by impairment of constructional praxis in AD, but difficulty in drawing the relationship between rooms in the house can be also interpreted as an alocentric disorientation.

Although route description and house drawing are probably based on different mental faculties, both may be interpreted as alocentric tests. In our study AD patients with mild dementia were impaired in these tasks, suggesting that alocentric disorientation contributed to TD in these cases.

Line orientation test showed difference between patients with mild dementia and controls. These results are different from Uc et al., who also compared line orientation test between mild dementia patients (mean MMSE=26) and aged-matched control subjects and he did not find difference[26]. Although elementary visual and perception tests apparently were not responsible for TD in AD, more complexes spatial procedures as mental imagery and mental rotation seems to contribute to TD, as it was seen on the results of the tests of parallelogram rotation and mental imagery tests (counting hidden blocks). Kurylo et al. found similar results in mental rotation test between control subjects and AD patients[24].

These results may be explained by the course of the spread of the pathological process in AD. Once the disease starts, the hippoccampal cells area affected and the spreading of the pathological lesions to parahipocampal gyri may cause landmark recognition[6]. The involvement of the retrosplenic cortex may lead to heading impairment[3] and as the pathological process affects the parietal cortex, the optic flow may be disrupted[4].

This study has several limitations. The diagnosis of TD was based only on a questionnaire, which revealed that almost all patients have TD. An environmental test probably would be able to diagnose TD and to classify its severity. Another limitation was due to the small number of individuals when the patients were divided into mild and moderate dementia.

Besides these limitations it was possible to see that TD differentiate patients from control subjects, even in early stages of AD, while visual and spatial perceptions do not seem to contribute to TD in the early stages of AD. Landmark recognition, egocentric and alocentric orientation are early impaired in AD and do contribute to cause TD in these patients. Landmark recognition and route description impairments are more severely involved in moderate dementia, probably accounting for the worsening of TD usually seen in moderate compared to mild dementia of AD patients.

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