Impaired navigation skills in patients with psychological distress and chronic peripheral vestibular hypofunction without vertigo

La comorbidità del deficit labirintico cronico e del distress psicologico sulla memoria visuo-spaziale

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SUMMARY

Few studies have focused on the role of the vestibular system for navigation and spatial memory functions in humans, with controversial results. Since most experimental settings were based on magnetic resonance imaging volumetry of the hippocampus and virtual navigation task on a PC, aim of this study was to investigate whether a well-compensated unilateral peripheral vestibular hypofunction in humans could interfere with navigation tasks while walking on memorized routes. A series of 50 unilateral labyrinthine-defective patients, without vertigo at the time of examination, and 50 controls were invited to visually memorize 3 different routes (a triangle, a circle and a square) on a grey carpet and then to walk along them clockwise and counter-clockwise (mental map navigation) with eyes closed. The same test was then repeated with eyes open (actual navigation) and a second time with eyes closed (mental navigation). Execution time was recorded in each test. In the same session, working spatial memory was assessed by the Corsi block test and all subjects completed the Symptom Check List (SCL-90) to assess depression and anxiety levels. Results showed that labyrinthine-defective patients presented higher levels of anxiety and depression and performed the Corsi block test with more difficulties than controls. All differences reached statistically significant level (p < 0.05). Moreover, patients needed more time than controls in the first and third navigation tasks (eyes closed). No difference was observed between clockwise and counter-clockwise walking, on all routes, either in patients or controls. Patients showed a greater improvement in the third navigation task, with respect to the first test, than controls, with no side-effect in relation to labyrinthine hypofunction. These data demonstrate that walking along memorized routes without vision is impaired by peripheral vestibular damage even if vestibular compensation prevents patients from suffering from vertigo and balance disturbances. This impairment could be due to a permanent deficit of visuo-spatial short-term memory as suggested by the Corsi block test results even if a residual sensori-motor impairment and/or an interference of psychological distress could not be excluded.

KEY WORDS: Vestibular disorder • Spatial memory • Visuo-spatial short-term memory • Memorized routes • Navigation • Anxiety

Questo studio è stato progettato allo scopo di verificare se la presenza di un deficit labirintico monolaterale (da lieve a severo) nell’uomo possa interferire negativamente con la memoria visuo-spaziale a breve termine tramite l’esecuzione di percorsi su traiettorie memorizzate. Dopo un esame oto-neurologico completo, 55 pazienti adulti affetti da deficit labirintico monolaterale stabilizzato, asintomatici per vertigine e 50 controlli sani sono stati istruiti a memorizzare visivamente tre differenti percorsi (un triangolo, un cerchio e un quadrato) disegnati su di un tappeto grigio e successivamente invitati a camminare sopra di essi sia in senso orario che antiorario (mental map navigation) con gli occhi chiusi. Lo stesso test è stato quindi ripetuto ad occhi aperti (actual navigation) e di nuovo ad occhi chiusi (mental navigation). È stato memorizzato il tempo di percorrenza di ciascun percorsodopo il ciascun soggetto è stato sottoposto al test dei blocchi di Corsi (test di verifica della memoria visuo-spaziale a breve termine) e ad un questionario psicometrico per la determinazione del distress psicologico (SCL-90 R). I pazienti affetti da deficit labirintico compensato hanno evidenziato livelli di ansia e depressione significativamente superiori ai controlli (p < 0,05) e maggiori difficoltà all’esecuzione del test dei blocchi di Corsi (p < 0,05). Inoltre i pazienti hanno impiegato un tempo di percorrenza significativamente superiore ai normali nella prima e nella terza sessione (ad occhi chiusi) (p < 0,05). Non sono invece emerse differenze significative tra le performance in senso orario e antiorario sia nei pazienti che nei controlli (p < 0,05). Infine i pazienti hanno mostrato un miglioramento della performance tra il primo e il terzo test di percorrenza rispetto ai normali (p < 0,05) indipendentemente dal lato della lesione labirintica. Ciò ha consentito di concludere che il camminare lungo percorsi memorizzati in assenza di visione è reso più difficile dalla presenza di un deficit labirintico stabilizzato e non più associato a sintomi vertiginosi. Si è ipotizzato che questa difficoltà possa essere dovuta ad un deficit della memoria visuo-spaziale a breve termine anche se un residuo difetto a livello vestibolo-spinale e/o un’inferiorità nella percepizione e nella percezione visiva possono non essere esclusi definitivamente.

PAROLE CHIAVE: Disordini vestibolari • Memoria spaziale • Memoria visuo-spaziale a breve termine • Percorsi memorizzati • Navigazione • Ansia
Introduction

Humans have two major sources of information to mentally build a topographic representation of an environment (spatial memory), namely information acquired during actual exploration within the environment and visually exploring a map. Therefore, humans can perform a navigation task on memorized routes using a mental topographic representation of the environment learned from actual navigation (mental navigation task) or learned from a map (mental map task).

A parietofrontal network (superior frontal sulcus, the middle frontal gyrus, the pre-SMA and the intraparietal sulcus) 1, which is thought to reflect the spatial imagery components of the topographical task, is activated during both mental navigation and map navigation tasks. The posterior cingulate cortex is activated in the mental navigation condition involving topographical tasks, but not in the mental map task 2. The neural substrate for navigation also includes a right hippocampal area that is activated during both mental and map navigation tasks, and by the parahippocampal gyrus which is bilaterally activated only during mental navigation 3,4.

The role of the vestibular system, for navigation and spatial memory, has been extensively investigated in animal (for a review see Stackman et al. 5) but not in man. In one of the few studies in this area, spatial memory was examined in patients with bilateral vestibular failure due to neurofibromatosis type 2 after bilateral vestibular neurectomy 6. Significant spatial learning and memory deficits were shown in 12 patients as compared to 10 healthy controls. Surprisingly, the hippocampus was the only area of the brain to show atrophy - measured using functional magnetic resonance imaging (fMRI) – correlated with the presence of vestibular paresis > 25% according to Jonekees formula 12, as a consequence of previous vestibular neuritis diagnosed according to Strupp’s criteria 12;

1. unilateral labyrinthine hypofunction (documented by the presence of vestibular paresis > 25% according to Jonekees formula) as a consequence of previous vestibular neuritis diagnosed according to Strupp’s criteria 12;
2. no spontaneous and/or positional nystagmus (observed by video-oculography);
3. no vertigo attack in the last 6 months;
4. no other disequilibrium symptom (dizziness, fainting, drop attack) in the last 3 months;
5. normal daily work activity and social behaviours.

Exclusion criteria were:

1. musculoskeletal disorders potentially conditioning upright stance and dynamic gait control;
2. neurological diseases as diagnosed by neuroimaging (computed tomography (CT) and MRI);
3. otosurgical procedures;
4. Ménière’s disease (or other hydropic recurrent syndromes);
5. benign paroxysmal positional vertigo;
6. use of neuroleptics and benzodiazepines in the week before examination;
7. age under 20 or over 80 years.

Patients were compared with normal subjects (controls) recruited among hospital staff personnel on the basis of no history of vertigo/balance disorders and a negative otorhino-laryngological examination. The control group comprised 26 (52%) males and 24 (48%) females, mean age 52 years (range: 20-70, SD = 11.02). Controls were well-matched for sex (p = 0.316) and age (p = 0.347) with the patient group.

Informed consent was obtained from all participants before examination and the protocol was reviewed by the Ethics Committee of the AUSL of Modena.

Methods

Neuropsychological test for visuo-spatial short-term memory

To test short-term memory for visuo-spatial information, patients and controls were both submitted to the Corsi block test, which has been extensively used, for this purpose, in patients suffering from various neuropsychological disorders 13-15. Adapted from Milner 16, our apparatus for the Corsi block test consisted of 9 black blocks (4x4x4 cm) irregularly positioned on a black board (32x25 cm). The examiner touched a sequence of blocks at a rate of one block every two seconds. Participants were required to reproduce the sequence by touching the same blocks in the same order. To facilitate presentation and scoring, the sides of the block facing the examiner were numbered from one to nine: these numbers were not visible to the participant. Immediately after each tapped sequence, the subject attempts to reproduce it, progressing until no longer accurate. The final score was the total number of correct trials.
Anxiety and depression levels
The revised version of the Symptom Check List-90 (SCL-90 R), a valid and reliable psychiatric multidimensional self-report inventory, was the tool designed to screen for 9 symptoms of psychopathology. It contains 90 items intended to measure symptom intensity on 9 different subscales that describe a tendency to somatization, obsessivity-compulsivity, interpersonal sensitivity, depression, hostility, anxiety, paranoid ideation, phobic anxiety and psychotism. Each item of the questionnaire is rated by the patient on a 5 points scale of distress from 0 (none) to 4 (extreme). Only the subscales for depression and anxiety were used in this study.

Navigation session
- TASK 1. Walking on visually memorized routes (navigation task based on mental map).
  Patients and controls were invited to carefully observe a grey carpet on the floor in front of them at a distance of 1 meter on which a blue triangle path (route 1), a yellow circle path (route 2) and a red square were traced (Fig. 1). The carpet was composed of thin foam rubber and the routes were marked with narrow bands of colour so that plantar sensitivity of patients could not be triggered by walking on them. Each side of the carpet was 2.2 meters in length.
  Each participant was requested to carefully observe the 3 routes and instructed to memorize them. They were then positioned by the assistant on the lower right corner and invited to walk along the single route blindfold and come back to the starting point both clockwise and counterclockwise sequentially. The assistant verbally corrected the subject’s trajectory. The entire trial was carried out barefoot, in a silent room.
  The assistant recorded the time taken by subjects to perform each task.
- TASK 2. Walking on visible routes (actual navigation).
  Each participant was then invited to repeat the same 3 routes (yellow circle, blue triangle and red square), both clockwise and counter-clockwise, with eyes open, in order to provide them with a visual, vestibular and somatosensory feedback. The time taken for each session was also recorded.
- TASK 3. Repetition of walking on memorized and physically executed routes with eyes closed (navigation task based on mental map and actual navigation).
  Finally, patients and controls were requested to repeat, in the same order, the first walking exercise again, with no visual input. Time performances were also recorded.

Statistical analysis
The non-parametric Mann-Whitney test was adopted to statistically test the null hypothesis that the mean scores of the Corsi block test as well as SCL-90 R subscales for anxiety and depression were equal between groups. Comparison between parametric variables, such as the time of navigation performances, were computed by t-test procedures. The statistical significance level was set at p < 0.05, in all cases.

Results
Neuropsychological battery
The Corsi block test score was significantly higher (p < 0.005) in controls (7.2 ± 0.9) than in patients (6.0 ± 1.2), thus indicating a reduced ability of visuo-spatial short-term memory in labyrinthine-deficient patients. The latter also showed significantly higher levels of anxiety and depression (rough scores: 20.8 ± 5.2 and 29.1 ± 6.7, respectively) as revealed by the SCL-90 R subscales if compared to controls (16.7 ± 4.9 and 20.3 ± 5.8) (p < 0.005).

Navigation performances
No differences in time performance was found between right and left labyrinthine-deficient patients during the clockwise and counter-clockwise navigation tasks based on mental map and both mental map and actual navigation (t-test, p > 0.05), thus excluding the possibility that the side of the labyrinthine damage might play a role. No differences were found in controls for the same clockwise and counter-clockwise navigation tasks (t-test, p > 0.05).

Task 1: patients took a longer time than controls in all the navigation tests based on mental map and both mental map and actual navigation (t-test, p > 0.05) (Table I).
Task 2: no differences were found between the pathological sample and the control group in the actual navigation tasks (i.e., with eyes open) (p > 0.05).

Table I. Time scores (expressed in seconds) of clockwise (cw) and counter-clockwise (ccw) navigation (route 1: yellow triangle, route 2: blue circle, route 3: red square) in Task 1 in labyrinthine-deficient patients and controls.

<table>
<thead>
<tr>
<th>Routes</th>
<th>Patients</th>
<th>Controls</th>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>1 cw</td>
<td>26.0</td>
<td>9.9</td>
</tr>
<tr>
<td>2 cw</td>
<td>23.5</td>
<td>10.4</td>
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<tr>
<td>3 cw</td>
<td>31.3</td>
<td>12.5</td>
</tr>
<tr>
<td>3 ccw</td>
<td>21.9</td>
<td>11.2</td>
</tr>
<tr>
<td>2 ccw</td>
<td>20.4</td>
<td>7.8</td>
</tr>
<tr>
<td>3 ccw</td>
<td>28.2</td>
<td>11.6</td>
</tr>
</tbody>
</table>

Fig. 1. Grey carpet with route 1 (black triangle), route 2 (white circle) and route 3 (gray square). Each side of carpet was 2.2 meters in length.
Task 3: on the contrary, patients took a longer time than controls in all the navigation tasks based on both mental map and actual navigation (p < 0.005) (Table II). Comparison of time scores for the 3 routes, before (Task 1) and after actual navigation (Task 3), revealed a significant improvement for all the tests, both in controls and in labyrinthine-defective patients (p < 0.005) (Table III).

Table II. Time scores (expressed in seconds) of clockwise (cw) and counter-clockwise (ccw) navigation (route 1: yellow triangle, route 2: blue circle, route 3: red square) in Task 3 (no vision after visually guided Task 2) in labyrinthine-defective patients and controls.

<table>
<thead>
<tr>
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<th>Patients</th>
<th>Controls</th>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>cw</td>
<td>17.6</td>
<td>7.6</td>
</tr>
<tr>
<td>2 cw</td>
<td>16.2</td>
<td>6.5</td>
</tr>
<tr>
<td>3 cw</td>
<td>24.3</td>
<td>10.0</td>
</tr>
<tr>
<td>ccw</td>
<td>17.1</td>
<td>8.8</td>
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<tr>
<td>2 ccw</td>
<td>16.4</td>
<td>11.3</td>
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<tr>
<td>3 ccw</td>
<td>23.7</td>
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The overall improvement between Task 1 and Task 3, as expressed by the difference in the total time that each subject took to walk along the 6 routes in the 2 tasks, was statistically higher in subjects with labyrinthine hypofunction than in controls. The total time reduction was 35.9 seconds (SD = 28.6) and 10.3 seconds (SD = 9.6), respectively (p < 0.005).

Discussion

Data emerging from this study show that subjects suffering from labyrinthine hypofunction, even if well compensated, exhibit impaired visuo-spatial short-term memory (as demonstrated by the Corsi block test results) if compared to subjects with normal vestibular function, well-matched for sex and age. This result suggests that peripheral vestibular information contributes to the cortical and sub-cortical processes that provide visuo-spatial working memory, thus supporting recent clinical evidence for cognitive dysfunction in humans following vestibular damage also if tested without any concurrent motor task to which vestibular reflexes may contribute, such as walking.

In particular, the first navigation task, based on a mental map scan, resulted in significant impairments in labyrinthine-deficient patients, as compared to controls, thus suggesting that peripheral vestibular information may contribute also to the cortical and hippocampal processes that humans activate during mental map navigation.

It is worthwhile pointing out that since we found no difference between navigation performances, clockwise and counter-clockwise, in labyrinthine-deficient whether left or right patients, a residual vestibulo-spinal impairment would not appear to contribute to navigation difficulties. On the other hand, there is no reasonable explanation for a unilateral peripheral vestibular defect might interfere with spatial memory and navigation functions without left or right specificity. More information will hopefully become available once a more “neuromatational” pathway, from the vestibular end-organ to the hippocampus, is defined in humans.

Furthermore, the improvement in performance following the navigation task seems to confirm that acquired somatosensory, vestibular and visual feedback information, produce better navigation modalities. This “learning effect” has been shown to depend more on cortical activity than on improvement in the sensory control of posture. Many anatomical and electrophysiological studies have demonstrated that there are many pathways from the vestibular nucleus to limbic and neocortex areas concerned with learning and memory (see Wiener & Berthoz for a review).

On the other hand, a higher level of anxiety, as demonstrated in labyrinthine-deficient patients, could potentially interfere with cognitive task performance, particularly for walking without vision. Therefore, further studies are needed to investigate the affective-cognitive impairment of patients following peripheral vestibular damage. Furthermore, a video-recording system, to monitor patient’s accuracy during walking, would corroborate these data.

Conclusions

Results of this study provide further demonstration of the relationships between peripheral vestibular and function cognitive functions.

Chronic peripheral vestibular damage seems to be related to a deterioration in cognitive function with particular regard to the visuo-spatial short-term memory.

A likely explanation for this interaction is that vestibular...
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information is necessary to the cortical areas and hippocampus in order to perform mental map tasks and mental navigation and that actual navigation on memorized routes could be impaired by lack of this kind of information in non-visual conditions.

It should be pointed out that if vestibular damage really causes cognitive dysfunction in humans, most patients may not be aware of this impairment. The association of chronic vestibular damage with psychological distress could once more be a reason for focusing on the links between the labyrinth and those anatomical regions, such as the limbic network and the prefrontal right area, that subserve both attentional demand for memorization and emotion.

References

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