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ORIGINAL COMMUNICATION

# Cognitive deficits in patients with a chronic vestibular failure

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**Abstract** Behavioral studies in rodents and humans have demonstrated deficits of spatial memory and orientation in bilateral vestibular failure (BVF). Our aim was to explore the functional consequences of chronic vestibular failure on different cognitive domains including spatial as well as non-spatial cognitive abilities. Sixteen patients with a unilateral vestibular failure (UVF), 18 patients with a BVF, and 17 healthy controls (HC) participated in the study. To assess the cognitive domains of short-term memory, executive function, processing speed and visuospatial abilities the following tests were used: Theory of Visual Attention (TVA), TAP Alertness and Visual Scanning, the Stroop Color-Word, and the Corsi Block Tapping Test. The cognitive scores were correlated with the degree of vestibular dysfunction and the duration of the disease, respectively. Groups did not differ significantly in age, sex, or handedness. BVF patients were significantly impaired in all of the examined cognitive domains but not in all tests of the particular domain, whereas UVF patients exhibited significant impairments in their visuospatial abilities and in one of the two processing speed tasks when compared independently with HC. The degree of vestibular dysfunction significantly correlated with some of the cognitive scores. Neither the side of the lesion nor the duration of disease influenced cognitive performance. The results demonstrate that vestibular failure can lead to cognitive impairments beyond the spatial navigation deficits described earlier. These cognitive impairments are more significant in BVF patients, suggesting that the input from one labyrinth which is distributed into bilateral vestibular circuits is sufficient to maintain most of the cognitive functions. These results raise the question whether BVF patients may profit from specific cognitive training in addition to physiotherapy.

**Keywords** Vertigo · Cognition · Vestibular failure · Vestibular rehabilitation · Attention · Memory

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## Introduction

The vestibular system maintains balance with the eyes, head, and body in the upright position and keeps the gaze in space constant during locomotion. The most obvious effects of an acute unilateral vestibular failure (UVF) are direction-specific vertigo, nystagmus, and instability of stance and gait. Evidence has been increasing that vestibular input also essentially contributes to higher cortical (cognitive) functions such as spatial memory and orientation, multisensory motion perception, and navigation [1, 2].

Several behavioral studies in rodents [3, 4] and humans [5] have demonstrated that visuospatial memory and

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cognition depend on vestibular function. Moreover, some patients with a vestibular disorder complain of a loss of memory and attentional focus [6–8]. These handicaps persisted when postural and ocular motor functions were restored by compensatory processes. To date, only a few studies have examined the extent of the vestibular system's influence on cognitive domains like memory and executive functions that do not focus on spatial memory and orientation. Some cognitive studies using the Wechsler Memory test in full on patients with vestibular failure have suggested that general memory and attention are not significantly affected [5]; in contrast, others have reported cognitive impairments such as dyscalculia, decelerated reaction time, or reduced visual short-term memory [9, 10]. These impairments seemed to be more severe in bilaterally affected patients (BVF), although very few studies directly compared the cognitive performance of patients with UVF and those with BVF [11–13]. Hence, the general effects of vestibular disorders on non-spatial cognitive performance are still being debated.

The aim of this group study was to ascertain whether the four main domains of cognition, i.e., executive function, working memory, processing speed, and visuospatial abilities, are impaired in chronic vestibular dysfunction and, if so, to what extent. Six cognitive tests were administered to patients with UVF or BVF and to healthy controls. The following questions were also addressed: (1) Is there a correlation between the degree of cognitive impairment and the severity of vestibular failure or time since disease onset? (2) Does the side of lesion in UVF patients cause a difference in cognitive performance? This is interesting because of the dominance of the right hemisphere and the ipsilateral right-sided pathways for cortical processing of vestibular information in right-handers [14, 15].

## Methods

### Patients and controls

Sixteen patients with a chronic UVF [mean age (SD) = 56 (10) years, 9 females, 7 with a left-sided lesion, 14 right-handers]; 18 patients with a BVF [mean (SD) = 57 (13) years, 9 females, 16 right-handers]; and 17 healthy controls [HC, mean age (SD) = 52 (14) years, 9 females, 16 right-handers] participated in the study (Table 1).

Patients were recruited from the German Center for Vertigo and Balance Disorders, Ludwig-Maximilians University, Munich, Germany, between January 2010 and December 2013. All patients were assessed neurologically and neuro-otologically on site (Table 2); tests included electronystagmography (ENG) with bithermal caloric testing, neuroorthoptic analysis by experienced orthopticians including the clinical head impulse test (HIT) and measurements of the subjective visual vertical (SVV). Caloric parameters represent low-frequency vestibular function, whereas the HIT represents high-frequency function. Inclusion criteria for the patients were a chronic disease lasting at least 6 months, no spontaneous nystagmus, and no tilts of SVV, which is indicative for an acute vestibular imbalance. The mean disease duration was 43 ± 29 months in BVF patients and 16 ± 10 months in UVF patients. BVF was characterized by the typical symptoms of gait imbalance in darkness and on uneven ground and one of the following responses consistent with prior findings [16, 17]: (1) bilateral pathological HIT and calorically elicited nystagmus with a mean peak slow phase velocity of <5°/s for each caloric irrigation on both ears; (2) bilateral pathological HIT and caloric responses >5°/s on one or both sides; or (3) normal HIT and loss of bilateral responses or reduced responses <5°/s to caloric irrigation on both sides. UVF was defined by the typical history of an acute onset of sustained vertigo with gait deviation and postural imbalance for several days that occurred at least 6 months before the examination and one of the following conditions: (1) pathological HIT and a reduction of the caloric response of the same affected ear compared to the unaffected ear (relative vestibular reduction, RVR) of >25%, (2) normal HIT and a unilateral RVR of >25%, (3) pathological unilateral HIT and RVR of <25%.

HC were recruited by newspaper advertisement and word of mouth. No HC had a history of neurological illness or was on psychopharmacological medication. Neurological and neurootological examinations were normal including tests for spontaneous nystagmus (Frenzel's glasses), gaze-evoked nystagmus, positioning maneuvers, clinical HIT, and tests of stance and gait (Romberg test, Unterberger stepping test), while bithermal caloric testing and measurements of SVV were not performed. The study was approved by the local ethics committee of the Ludwig-Maximilians University, Munich. All subjects gave their informed written consent to participate in the study.

### Clinical data for correlation analyses

To determine whether the degree of cognitive impairment correlated with the severity of vestibular dysfunction in BVF patients, the mean peak slow phase velocity (SPV) calculated from the bithermal caloric irrigation of both ears was used as a measure of dysfunction. For UVF patients, the difference of the caloric response between the affected and unaffected ear was used (i.e., relative vestibular reduction, RVR). An asymmetry above 25% was considered pathological according to the Jongkees formula [18, 19]. Caloric parameters represent low-frequency

**Table 1** Demographic and examination data of patients with unilateral vestibulopathy (UVF), bilateral vestibulopathy (BVF), and healthy controls (HC)

| Group | Age | Gender | Handedness | Education[a] | MMSE[b] |
|---|---|---|---|---|---|
| UVF | 64 | f | r | 2 | 30 |
| | 59 | m | r | 2 | 28 |
| | 34 | m | l | 3 | 29 |
| | 59 | f | r | 1 | 30 |
| | 80 | m | r | 3 | 29 |
| | 59 | m | r | 2 | 30 |
| | 58 | f | r | 2 | 27 |
| | 39 | m | l | 2 | 28 |
| | 58 | m | r | 1 | 29 |
| | 57 | f | r | 3 | 30 |
| | 64 | f | r | 2 | 29 |
| | 46 | f | r | 3 | 30 |
| | 50 | f | r | 3 | 30 |
| | 63 | f | r | 3 | 29 |
| | 50 | m | r | 3 | 27 |
| | 62 | f | r | 2 | 29 |
| BVF | 71 | m | r | 3 | 29 |
| | 63 | f | r | 3 | 29 |
| | 67 | f | r | 3 | 28 |
| | 64 | m | r | 1 | 30 |
| | 59 | m | r | 3 | 20 |
| | 72 | m | l | 1 | 27 |
| | 53 | f | r | 2 | 28 |
| | 47 | m | r | 2 | 30 |
| | 30 | f | r | 3 | 29 |
| | 51 | m | r | 1 | 30 |
| | 70 | m | r | 2 | 28 |
| | 55 | f | r | 2 | 29 |
| | 36 | f | r | 1 | 30 |
| | 48 | f | r | 2 | 27 |
| | 59 | f | l | 2 | 29 |
| | 78 | m | r | 1 | 28 |
| | 45 | m | r | 3 | 29 |
| | 74 | f | r | 3 | 30 |
| HC | 71 | m | r | 3 | 30 |
| | 62 | f | r | 3 | 30 |
| | 30 | f | r | 2 | 29 |
| | 47 | m | r | 2 | 28 |
| | 60 | m | l | 3 | 29 |
| | 52 | m | r | 3 | 30 |
| | 60 | f | r | 2 | 28 |
| | 65 | f | r | 1 | 27 |
| | 29 | m | r | 3 | 30 |
| | 67 | m | r | 2 | 29 |
| | 29 | m | r | 3 | 29 |
| | 54 | f | r | 2 | 28 |
| | 44 | f | r | 2 | 30 |
| | 52 | f | r | 3 | 28 |
| | 33 | f | r | 2 | 29 |
| | 72 | f | r | 1 | 30 |

*f* female, *m* male, *r* right, *l* left, *b* bilateral, *MMSE* Mini-Mental State Examination

[a] Education (1 = Hauptschulabschluss (lowest school degree), 2 = Mittlere Reife (intermediate degree), 3 = Abitur (highest school degree)

[b] Max value = 30. Values 26–30 represent normal global cognition, no mild dementia, and only subjects with values >25 were included in the study

vestibular function, whereas the HIT represents high-frequency function. For the clinical HIT the scaling was 0 = not pathological, 1 = unilateral pathological, 2 = bilateral pathological with one side more pronounced, and 3 = bilateral pathological.

## Neuropsychological assessment

Handedness was defined according to the Edinburgh Inventory Laterality Index [20]. Global cognitive function was measured with the Mini-Mental Examination [21], and general intelligence function was assessed using the Multiple Choice Word Fluency Test (MWT-B).

The patients answered the Vertigo Symptom Scale VSS [22], a questionnaire that evaluates the two sub-scales vertigo and related symptoms (VER) as well as somatic anxiety and autonomic arousal (AA).

A battery of well-established neuropsychological tests was used to assess the cognitive domains of processing speed, short-term memory, executive function, and visuospatial abilities:

*The Test for Attentional Performance (TAP)*: *Alertness and Visual Scanning.* A computer-controlled battery of attentional tests consisting of several sub-tests.

*Visual Scanning*: The subject was asked to quickly push a button when detecting a critical target on a 5 × 5 matrix. The reaction time was a value of visuospatial abilities.

*Alertness*: When a cross appeared in the middle of the screen, the subject had to push a button as fast as possible. The test measured the alertness and thus cognitive processing speed.

*Whole report based on the Theory of Visual Attention (TVA)*: After a short fixation period, a column of five different, red or green letters appeared on the computer screen to the left or right of the fixation point for variable short exposure times. The task was to report as many letters as possible. Depending on the test person's accuracy in different exposure duration conditions, the parameters visual

**Table 2** Clinical data of patients with unilateral vestibulopathy (UVF) and bilateral vestibulopathy (BVF)

| Diagnosis | Duration[a] | Lesion | VER | AA[b] | HIT[c] | RW[d] | LW[d] | RC[d] | LC[d] | MCR[e] | RVR[f] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *UVF* | | | | | | | | | | | |
| PVD | 9 | l | 0.63 | 0.53 | 0 | 21.1 | 3.7 | 14.2 | 3.7 | | 65 |
| PVD | 29 | r | 1.47 | 1.40 | 1 | 1 | 30 | 4 | 25 | | 83 |
| PVD | 14 | l | 0.58 | 1.33 | 1 | 6.8 | 4.5 | 10.2 | 4.4 | | 31 |
| PVD | 8 | r | 0.58 | 1.87 | 1 | 2.2 | 16 | 0 | 12 | | 85 |
| PVD | 13 | l | 1.05 | 0.27 | 1 | 15.8 | 1.1 | 26 | 2.5 | | 84 |
| PVD | 36 | l | 0.58 | 1.67 | 1 | 10.3 | 3.5 | 17.6 | 2.2 | | 66 |
| PVD | 8 | l | 0.74 | 1.47 | 1 | 17.1 | 3.3 | 32.8 | 3 | | 78 |
| PVD | 34 | l | 0.11 | 0.93 | 0 | 11.7 | 0.9 | 13.5 | 1.6 | | 82 |
| PVD | 15 | r | 0.47 | 1.20 | 1 | 7 | 7.2 | 6.9 | 13.6 | | 20 |
| PVD | 6 | r | 0.95 | 1.87 | 1 | 1.3 | 12.5 | 0.3 | 8 | | 86 |
| PVD | 16 | r | 0.16 | 0.27 | 1 | – | – | – | – | | – |
| PVD | 9 | r | 0.47 | 1.20 | 1 | 2.2 | 14.8 | 4 | 19.3 | | 69 |
| PVD | 32 | r | 0.32 | 0.47 | 0 | 6 | 8.6 | 4.9 | 10 | | 26 |
| PVD | 6 | r | 0.63 | 1.27 | 0 | 5.2 | 12.8 | 8 | 11.4 | | 29 |
| PVD | 6 | r | 0.63 | 2.00 | 1 | 6 | 15.7 | 6.1 | 15.5 | | 44 |
| PVD | 12 | l | 0.42 | 1.60 | 1 | 15.3 | 11.4 | 9.8 | 9.2 | | 10 |
| *BVF* | | | | | | | | | | | |
| BVP, UE | 26 | b | 1.47 | 1.67 | 3 | 2.7 | 0.4 | 0 | 1.7 | 1.2 | |
| BVP, UE | 69 | r > l | 0.11 | 0.00 | 3 | 1.2 | 0.2 | 0.6 | 0 | 0.5 | |
| BVP, MD | 48 | b | 0.47 | 1.73 | 3 | – | – | – | – | – | |
| BVP, UE | 42 | r > l | 0.26 | 1.07 | 2 | 3.7 | 0.5 | 2.3 | 3.2 | 2.4 | |
| BVP, UE | 134 | b | 1.05 | 1.87 | 3 | 4.3 | 4.2 | 10.6 | 4.1 | 5.8 | |
| BVP, MD | 54 | l > r | 0.16 | 0.60 | 3 | 1.4 | 3.4 | 2.1 | 1.6 | 2.1 | |
| BVP, UE | 27 | l > r | 0.47 | 0.80 | 1 | 3.7 | 3.3 | 2.4 | 2.3 | 2.1 | |
| BVP, UE | 29 | b | 0.68 | 2.00 | 1 | 1.1 | 0.2 | 1 | 1.4 | 0.9 | |
| BVP, VN | 20 | b | 0.21 | 1.47 | 3 | 0 | 1.2 | 0.7 | 1.8 | 0.9 | |
| BVP, UE | 81 | b | 0.47 | 1.67 | 3 | 2.1 | 7.6 | 3 | 2.9 | 3.9 | |
| BVP, UE | 44 | l > r | 0.68 | 2.27 | 2 | 2.3 | 3.9 | 3.2 | 3.8 | 3.3 | |
| BVP, UE | 61 | b | 0.63 | 1.87 | 3 | 1.5 | 1.1 | 2.4 | 2.3 | 1.8 | |
| BVP, UE | 25 | b | 0.89 | 1.27 | 3 | 3.5 | 0.6 | 3.3 | 2.4 | 2.5 | |
| BVP, AO | 37 | r > l | 0.58 | 1.33 | 0 | 2.1 | 2.9 | 2.3 | 2.1 | 2.4 | |
| BVP, UE | 29 | l > r | 0.89 | 1.53 | 3 | 5.5 | 4.8 | 4.6 | 5 | 5.0 | |
| BVP, UE | 48 | b | 0.79 | 2.00 | 1 | 0 | 1 | 1.4 | 0.8 | 0.8 | |
| BVP, UE | 9 | b | 1.47 | 1.33 | 3 | 8.3 | 4.3 | 5.9 | 6 | 6.1 | |
| BVP, UE | 6 | b | 0.26 | 1.47 | 0 | 0 | 0.2 | 0 | 0.3 | 0.1 | |

*PVD* peripheral vestibular deficit after vestibular neuritis, *VN* vestibular neuritis, *BVP* bilateral vestibulopathy, *UE* of unknown etiology, *MD* after Meniere's disease, *AO* of auto-immunological origin, *r* right, *l* left, *b* bilateral, *VER* Vertigo Scale, *AA* autonomic anxiety, *HIT* head impulse test, *RW* right ear, warm water, *LW* left ear, warm water, *RC* right ear, cold water, *LC* left ear, cold water, *MCR* mean caloric response, *RVR* relative vestibular reduction

[a] Duration since onset of disease in months

[b] AA = 0.30 ± 0.40 in controls [22]

[c] 0 = not pathological, 1 = unilaterally pathological, 2 = bilaterally pathological, more pronounced on one side, 3 = bilaterally pathological

[d] Values from caloric irrigation in °/s from both ears with cold water: 30 °C and warm water: 44 °C

[e] Mean caloric irrigation from (RW, RC, LW, LC) in °/s, values <5 considered pathological

[f] In %, Jongkees' formula [18]: values >25 considered pathological

short-term memory capacity *K* (amount of objects in the VSTM) and the visual processing speed *C* (elements/s) were estimated using TVA-based mathematical modeling [23].

*The Stroop Color and Word Interference Test*: To measure processing speed, the first two conditions required subjects to rapidly read and name a set of words and color bars [24]. In the third interference condition, the subject had to name the color of a word that designated a different color. The main outcome was the time needed to read the text in the interference condition; this measured the executive function.

*Corsi Block Tapping Test: forward and backward.* Nine blocks were arranged on a small board. Both tasks required the subject to observe the sequence of blocks tapped by the experimenter and then to repeat the sequence in the same order (CBT) or backward (BST). There were two runs, and a maximum of 14 points per task could be achieved. The CBT assessed short-term and working memory; the BST measured executive function [25].

### Data analysis

The mean for each task condition was calculated for all three groups. Normal distribution of data were verified with the Shapiro–Wilk test. Where necessary, a log transformation was applied to obtain normality. A simple two-sided *t* test for independent variables was used to examine the differences between the means of UVF vs controls and BVF vs controls in each task. To compensate for alpha inflation, a stepwise Bonferroni–Holm correction was made with an initial *p* level of 0.008. Furthermore, an N-way analysis of variance (ANOVA) was performed to examine the relationship between group and experiment. Subsequently, a one-way ANOVA was conducted to compare the effect of the vestibular dysfunction on the cognitive performance within all three groups. Post hoc comparisons were performed using the Tukey HSD test. The non-parametric Mann–Whitney *U* test was chosen to compare the effect of left- or right-sided lesions in UVF patients. The relationship between severity of vestibular dysfunction or disease duration and task performance was tested with Pearson's correlation for interval scaled values and Kendall-Tau-b correlation for ordinal-scaled values. Statistical analyses were performed with SPSS 22 (SPSS Inc., Chicago, USA).

## Results

Groups did not differ significantly in age, sex, or handedness. All subjects performed the experiments properly. None of the participants had a Mini-Mental State Examination (MMSE) or Mehrfach Wortschatz Test (MWT) value below normal. Thus, all 51 subjects were included in the analysis.

UVF patients exhibited an autonomic anxiety (AA) value of 1.2 (0.5) [mean (SD)] and BVF patients, 1.4 (0.5). The scale ranged from 0 to 4, with values of 0.30 (0.40) for controls (18). The vertigo value (VER) was 0.61 (0.32) for UVF and 0.64 (0.39) for BVF patients. This was well below the values of patients with an acute organic vestibular disorder, 1.06 (0.64) [22].

### Neuropsychological results

Overall, BVF patients performed significantly worse than HC for at least one of the measures in all of the tested domains (Fig. 1; Table 3). When directly compared to controls, UVF patients performed significantly worse than HC in the alertness and visual scanning test. However, the effect was no longer significant when the performance of

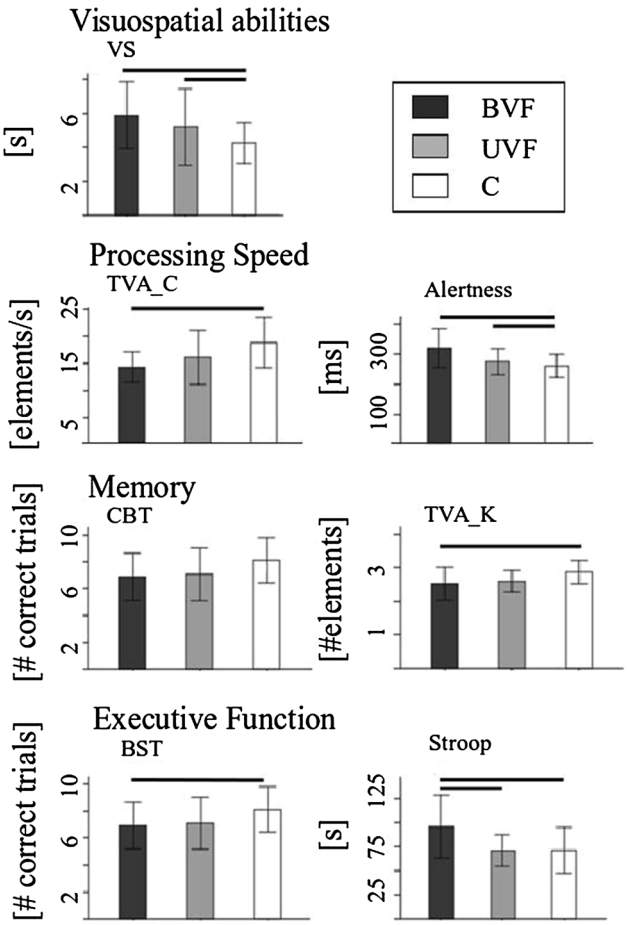


**Fig. 1** Graphical overview of mean performances in applied cognitive tests. Statistically significant differences highlighted with lines. *BVF* bilateral vestibular failure, *UVF* unilateral vestibular failure, *C* healthy controls, *VS* visual scanning, *TVA C* cognitive processing speed, *TVA k* visual short-term capacity, *CBT* Corsi Block Tapping

**Table 3** Mean performance on applied cognitive tests including standard deviation (SD) and statistical test results

| Cognitive domain | Visuospatial abilities | Processing speed | | Memory | | Executive function | |
|---|---|---|---|---|---|---|---|
| | VS (s) | Alert (s) | TVA_C[a] | TVA_k[b] | CBT[c] | Stroop (s) | BST[c] |
| Mean performance | | | | | | | |
| BVF | | | | | | | |
| Mean (SD) | 5.9 (1.9) | 0.32 (0.06) | 14.3 (2.7) | 2.5 (0.5) | 7.4 (1.2) | 95.9 (31.8) | 6.9 (1.7) |
| UVF | | | | | | | |
| Mean (SD) | 5.2 (2.2) | 0.28 (0.04) | 15.1 (6.1) | 2.6 (0.3) | 7.7 (1.8) | 71.0 (16.0) | 7.1 (1.9) |
| HC | | | | | | | |
| Mean (SD) | 4.2 (1.2) | 0.26 (0.03) | 18.8 (4.4) | 2.9 (0.3) | 7.5 (1.3) | 71.3 (23.1) | 8.1(1.6) |
| *T* test | | | | | | | |
| BVF vs HC | | | | | | | |
| *p* value | 0.003 | 0.004 | 0.001 | 0.02 | 0.85 | 0.007 | 0.04 |
| UVF vs HC | | | | | | | |
| *p* value | 0.007 | 0.03 | 0.98 | 0.53 | 0.67 | 0.48 | 0.70 |
| ANOVA: *F*(*df*, 2, 49) | | | | | | | |
| *p* value | 0.05 | 0.004 | 0.009 | 0.03 | 0.91 | 0.008 | 0.11 |
| Post hoc: Tukey HSD | | | | | | | |
| BVF vs HC | | | | | | | |
| *p* value | 0.04 | 0.005 | 0.007 | 0.03 | 0.98 | 0.01 | 0.11 |
| UVF vs HC | | | | | | | |
| *p* value | 0.35 | 0.72 | 0.17 | 0.12 | 0.96 | 0.99 | 0.23 |
| UVF vs BVF | | | | | | | |
| *p* value | 0.53 | 0.03 | 0.43 | 0.88 | 0.90 | 0.02 | 0.95 |

*UVF* unilateral vestibular failure, *BVF* bilateral vestibular failure, *HC* controls, *VS* visual scanning, *Alert* alertness, *TVA C*: cognitive processing speed, *TVA k*: visual short-term capacity, *CBT* Corsi Block Tapping, *BST* Backwards Block Tapping, *df* degrees of freedom

[a] Elements processed per second

[b] Number of elements stored in visual short-term memory

[c] Number of correct trials of a maximum of 12

all groups was compared (ANOVA): The one-way ANOVA revealed that BVF patients differed significantly from UVF patients in the Stroop and the Alertness condition. The results of the N-way ANOVA analysis were not significant considering group ($F = 1.75$, $p = 0.176$, $df = 2$) and experiment ($F = 0.05$, $p = 0.9994$, $df = 6$). However, the interaction between group and experiment was significant ($F = 3.9$, $p = 0$, $df = 12$). Post hoc comparisons, following the one-way ANOVA, using the Tukey HSD test indicated that performance in BVF patients was significantly different from HC in the Alertness, Visual Scanning, Stroop, and TVA whole report and from UVF patients in the Alertness and Stroop test. The Tukey test further revealed no significant differences between UVF patients and HC. The mean performance of BVF was always worse than in UVF. The mean values including standard deviations and results from statistical analysis from all conducted tests are depicted in Table 3. In addition, in visual scanning, the mean of the total number of errors (standard deviation) showed 3.6 (2.2.) errors in HC, 5.3 (6.6) errors in UVF, and 7.6 (5.8) errors in BVF. A two-sided *t* test revealed a significant difference between HC and BVF ($p = 0.02$).

In brief, BVF patients were significantly impaired in all of the examined cognitive domains: visuospatial abilities, processing speed, short-term memory, and executive function. UVF patients exhibited impairments in their visuospatial abilities and in one of the two processing speed tasks.

### Unilateral VF: right- vs left-sided lesion

The means of the test performances of UVF patients with a left- ($n = 7$) or a right- ($n = 9$) sided lesion did not significantly differ.

### Correlation analysis

The results from caloric stimulation and HIT were correlated with the cognitive scores (Table 4; Fig. 2).

Significant correlations were found for both BVF and UVF patients. BVF patients showed significant correlation for caloric response and performance in the visuospatial task. In UVF patients, the reduction of caloric response (RVR) correlated significantly with one processing speed task, one executive function, and one memory task, while the HIT correlated significantly with one processing speed task, one executive function, and the visuospatial task. There were no correlations between time since disease onset and the cognitive scores (Table 3). This was also the case in the analysis of the subgroup with a similar disease duration (each $n = 9$; BVF $23 \pm 9$ months; UVF $22 \pm 9$ months).

## Discussion

We explored the functional consequences of vestibular disorders for four cognitive domains: visuospatial abilities, processing speed, short-term memory, and executive function. BVF patients exhibited significant deficits in all four examined domains. UVF patients were affected in their visuospatial abilities and in one of the two processing speed tasks when compared to healthy controls; independently, moreover, they also showed a functional declining trend in the other tests. Thus, our results demonstrate that the cognitive impairments associated with vestibular failure go beyond the domain of spatial cognition, stressing the implications of vestibular failure for non-spatial cognitive processes. Moreover, the UVF patients had considerably better results than the BVF patients, suggesting that one intact labyrinth—the afferent input of which is fed into the bilaterally organized central vestibular system—is sufficient to maintain the measured cognitive functions.

Earlier studies presented evidence that spatial memory and navigation were impaired in patients with vestibular loss. Similarly, animal behavioral studies showed that unilateral [4] and bilateral [3] vestibular deafferentation led to spatial memory deficits. Studies using a virtual version of the Morris Water Task on patients with vestibular failure also demonstrated navigational impairments in complete [5] as well as incomplete BVF [13]. This had been shown earlier in simple path integration tasks [26, 27]. These results may indicate that a lack of vestibular input alters hippocampal functions. Indeed, patients with a chronic complete BVF developed significant atrophy (16%) of the hippocampus relative to controls [5]. Such atrophy of the hippocampal formation was also seen in incomplete BVF [13] and complete UVF [35]. Our current findings add further weight to the view that vestibular function and cognitive visuospatial skills are strongly connected, since visuospatial abilities were impaired in UVF and BVF patients.

It is difficult to compare our data with findings from other studies, most of which only measured the cognitive performance of patients with UVF. One study with BVF patients examined general memory function [5] using the Wechsler Memory Scale; only one of nine patients had an impaired memory index, whereas the Doors test revealed an impaired visual recognition memory in four of the nine patients. The TVA test of the BVF patients in our current study revealed that the visual short-term memory capacity was impaired. However, in contrast to an earlier study with UVF patients [28], we did not find any difference between

**Table 4** Correlation coefficients with $p$ values in parentheses

| Cognitive domain | Visuospatial abilities | Processing speed | | Memory | | Executive function | |
|---|---|---|---|---|---|---|---|
| Test | VS (s) | Alert (s) | TVA_C[a] | TVA_k[b] | CBT[c] | Stroop (s) | BST[c] |
| HIT[d] | 0.31 (0.02) | 0.23 (0.93) | −0.07 (0.62) | −0.19 (0.16) | −0.08 (0.58) | 0.31 (0.03) | −0.07 (0.61) |
| RVR[e] | 0.27 (0.32) | 0.14 (0.60) | −0.53 (0.04) | −0.50 (0.05) | 0.00 (0.75) | 0.44 (0.00) | −0.55 (0.03) |
| MCR[f] | 0.48 (0.04) | 0.14 (0.58) | 0.12 (0.63) | −0.42 (0.08) | −0.05 (0.85) | 0.17 (0.50) | −0.12 (0.64) |
| Duration[g] | 0.11 (0.52) | 0.02 (0.90) | −0.04 (0.84) | 0.10 (0.57) | 0.12 (0.52) | 0.17 (0.34) | −0.09 (0.62) |

Cognitive performance correlated with vestibular responsiveness

*HIT* head impulse test, *RVR* relative vestibular reduction, *MCR* mean caloric response, *VS* visual scanning, *Alert* alertness, *TVA C* cognitive processing speed, *TVA k* visual short-term capacity, *CBT* Corsi Block Tapping, *BST* Backwards Block Tapping

[a] Elements processed per second

[b] Number of elements stored in visual short-term memory

[c] Number of correct trials of a maximum of 12

[d] Including values from unilateral and bilateral vestibular patients (Kendall-Tau-b correlation analysis)

[e] Including values from unilateral vestibular patients only (Pearson's correlation analysis)

[f] Including values from bilateral vestibular patients only (Pearson's correlation analysis)

[g] Duration of disease since onset in unilateral and bilateral vestibular patients (Pearson's correlation analysis)

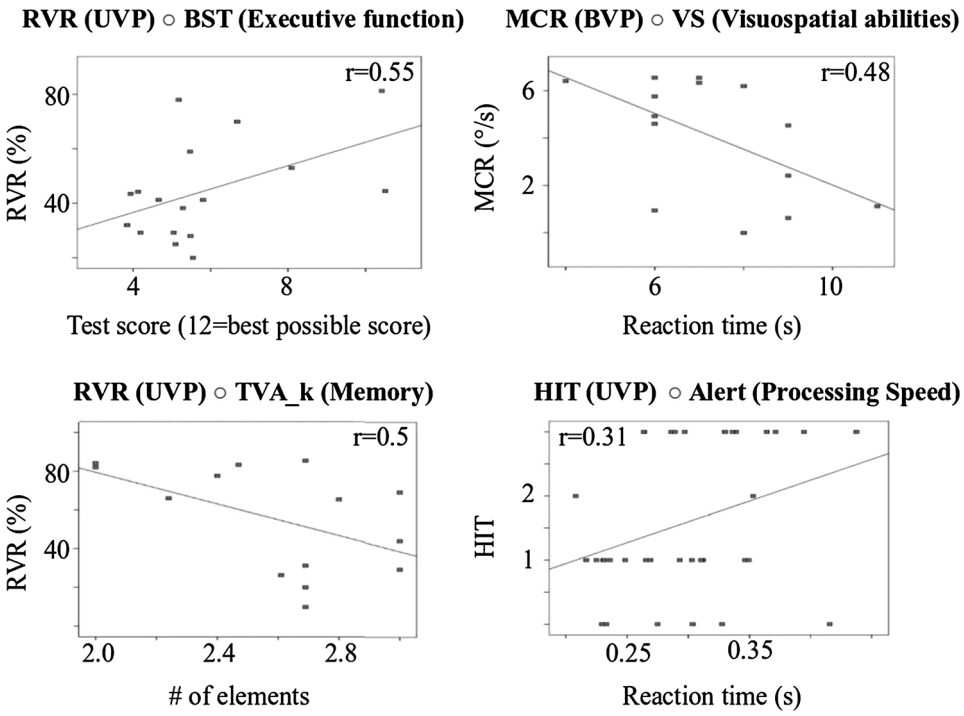


**Fig. 2** Scatter plots of selected significant correlation analyses of vestibular responsiveness and cognitive performances including correlation coefficients (*r*). *HIT* head impulse test, *RVR* relative vestibular reduction, *UVP* unilateral patients, *MCR* mean caloric response, *BVP* bilateral patients, *VS* visual scanning, *TVA C* cognitive processing speed, *TVA k* visual short-term capacity, *CBT* Corsi Block Tapping, *BST* Backwards Block Tapping

patients and controls in the forward version of the Corsi Block test. This might indicate that patients in our study were able to use strategies, like verbal rehearsal, to compensate for short-term memory deficits in the task, but it was not possible in the TVA whole report with very short exposure times.

One explanation for our finding of impaired non-spatial cognition may be the changes in functional and structural connectivity that evolve due to missing vestibular input. The vestibular network has widespread cortical areas in the posterior parietal operculum, the insula, the retroinsular cortex, the temporo-parietal junction, the sylvian fissure, and the cingulate cortex [29]. Their functions and the extent to which they are connected to other networks have been only partly elucidated [30]. The temporo-parietal junction, for example, is involved in attentional processes [31]. The vestibular system projects further to many areas besides the parietal cortex and the hippocampus. The vestibular input is also projected to the retrosplenial, entorhinal, and perirhinal cortices, which play an important role in different memory processes [32]. Unilateral and bilateral vestibular damage leads to a complex cascade of neural changes and cortical reorganization due to processes that compensate for the missing vestibular input [13, 33–36].

UVF patients seemed to have less non-spatial cognitive impairments than BVF patients. Although no significant effects were found in the between-group analysis, when independently compared to HC, they performed significantly worse in one of the processing speed tasks (Alertness). Moreover, other cognitive domains seem to be hampered, since their mean performance was worse than that of HC in five of the seven cognitive scores (Fig. 1). This agrees with the findings of a few other studies. In dual-task experiments on postural control during cognitive tasks, UVF patients performed worse on the cognitive tasks than the controls, not only while standing but notably also while seated [10, 37].

The cognitive tasks in the dual-task experiments were reaction time and backward counting tasks. Hence, they examined processing speed and executive control. As the reaction time-based alertness task was the only processing speed measure affected in UVF patients in our study, UFV patients seem to have particular problems with speeded motor responses but not with fast perceptual information uptake as measured in the whole report or the Stroop test.

The few studies that directly compared cognitive performance in UVF and BVF patients are in agreement with our findings of more pronounced impairments in BVF patients [11, 12, 38]. The graduated difference between HC, UVF, and BVF patients suggests that—due to the bilaterally organized vestibular system with several midline crossings in the brainstem and through the splenium of the corpus callosum [39]—one intact labyrinth is able to send sufficient information to both hemispheres and thus supports the maintenance of most functions tested here. One might suspect that the poor performance of BVF patients could be biased by the longer mean disease duration; however, there were no correlations between the degree of cognitive impairment and disease duration and

this was also true for a subgroup analysis with similar disease durations in UVF and BVF patients. This suggests that the impairment occurs early after the breakdown of vestibular function.

Although the Vertigo Scale VER in the VSS of our patients was lower, the autonomic anxiety scale AA was as high as in patients with acute organic vestibular disorders [22]. This finding emphasizes that non-organic impairments persist after postural and oculomotor functions are restored by compensatory processes.

Moreover, the magnitude of cognitive impairment and the vestibular responsiveness significantly correlated in some of our tasks. In BVF patients vestibular caloric responsiveness and cognitive performance significantly correlated in the visuospatial task, whereas in UVF patients it correlated in two processing speed tasks: one executive function and one memory task. Results from the HIT correlated in both patient groups significantly with two processing speed tasks, one executive function and the visuospatial task.

Our data cannot simply be explained by age-related decline of vestibular function in the otherwise healthy elderly, since the test results were compared to age-matched controls. This is important since a study on the elderly reported significant associations between vestibular decline (measured by vestibular-evoked myogenic potentials) and visuospatial, working memory, and attention factor scores [40].

Since the vestibular system exhibits a hemispheric right-sided dominance in right-handers [14], we also tested whether the side of the lesion has an influence on cognitive performance. In some spatial navigation tasks, patients with a right-sided lesion had a tendency to perform worse than patients with a left-sided lesion [12]. Compensated UVF patients had a significant decrease in the volume of the left posterior hippocampus and the right superior temporal gyrus, irrespective of the side of the lesion [35]. In contrast, another study found volume reductions in the superior temporal gyrus in patients with complete unilateral deafferentation ipsilateral to the affected ear [41]. However, the cognitive performance of the UVF patients in our experiments was not influenced by the side of the lesion. This finding may be due to the small number of cases (seven left vs nine right).

A limitation of the study is that the neuropsychological tests preferably included visual measures. To make a stronger case for cognitive impairment, future studies should include non-visual cognitive measures.

## Conclusions

In conclusion, our study provides evidence of widespread cognitive impairment after chronic bilateral and even unilateral vestibular failure. Apart from visuospatial abilities, short-term memory, executive function, and attention are significantly impaired when vestibular input is missing. The extent to which these cognitive deficits are relevant for aspects of daily life such as driving a car or working on a computer has up to now been unclear. The current findings may also have implications for the rehabilitation of these patients. They raise the question of whether the treatment of BVF patients should include not only physiotherapy for balance control, but in addition specific cognitive training.

**Compliance with ethical standards**

**Conflicts of interest** PP had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis and reports no disclosures. MW, KF, MR, TB, and MD report no disclosures.

**Ethical statement** The study was approved by the local ethics committee of the Ludwig-Maximilians University, Munich. All subjects gave their informed written consent to participate in the study.

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