Journal of Otology 17 (2022) 1–4

Contents lists available at ScienceDirect

Journal of Otology

journal homepage: www.journals.elsevier.com/journal-of-otology/

The diagnosis of central vestibular disorders based on the complementary examination of the vestibulospinal reflex

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A R T I C L E I N F O

Article history:
Received 5 May 2021
Received in revised form
29 June 2021
Accepted 1 July 2021

Keywords:
Unsteadiness
Central vestibular disorder
Vestibulospinal reflex
Ultrasound-computer-craniocorpography

A B S T R A C T

Objectives: Stance and gait unsteadiness along with vertigo contribute to a central vestibular disorder. For objective analysis ultrasound-computer-craniocorpography (US-COMP-CCG) can be used. Aim of the study was to characterize the unsteadiness in central vestibular disorders and discuss the possible diagnostic usage of US-COMP-CCG.

Methods and results: Hundred-and-ninety patients (70 male and 120 female, mean age ± SD, 58.94 ± 15.27) suffering from central vestibular disorder and 230 healthy control patients (78 male and 152 female, mean age ± SD, 50.94 ± 15.27) were enrolled. Stance and gait analysis was according to vestibulospinal tests of US-COMPCCG. IBM SPSS V24 software was used for statistical analysis. Mann-Whitney*U* test and Chi-square test were used, along with sensitivity and specificity categorization. The significance level was $p < 0.05$. According to schematic and statistical analysis instability and postural sway were increased in the vertigo population and statistically significant difference was shown. Upon categorical analysis significant correlation was detected [standing test: longitudinal sway ($p < 0.00001$), lateral sway ($p < 0.00001$), forehead covering area parameters ($p = 0.0001$); stepping test: longitudinal deviation ($p = 0.05$), lateral sway ($p = 0.011$) parameters].

Conclusions: Clinicians should consider that postural instability is prominently present in this population and might be of a diagnostic importance.

1. Introduction

Vertigo and dizziness attribute the 20–30% of the daily clinical practice symptoms (Mostafa et al., 2014). The two main types of vestibular disorders resulting in dizziness can be defined as peripheral and central vestibular pathologies (Dunlap et al., 2019), according to its origin, whereas the correct differentiation among them and diagnosis can be complex (Strupp, 2011). Central vestibular disorder is attributed mostly to strokes, intracranial tumors, degenerative disorders and metabolic conditions (Choi and Kim, 2017), whereas vestibular migraine may also be considered. Patients with central vestibular disorder complain of balance disorders along with dizziness complaints (Strupp and Brandt, 2008).

Balance control is based on a multisensory interaction, integrating proprioceptive, visual and vestibular signals (Takakusaki, 2017). Asymmetry in the balance input into the vestibular centres is achieved by an injury to the central or peripheral vestibular system (Walker and Zee, 2000), which may be presented anywhere from the labyrinths to the central vestibular system (Brandt and Dieteric, 2017). Based upon epidemiological studies the central causes are accountable for almost one-fourth of the dizziness experienced by patients visiting the daily clinical practice (Karatas, 2008). The most important structures of the central vestibular system playing a key role are the vestibular nuclear complex and the cerebellum. The vestibular nuclear complex is thought to be functioning as a sensory integration center with neural outputs which are important for controlling eye and postural movements and for spatial orientation (Furman and Whitney, 2000). Whereas the vestibulocerebellum is having a leading role in modulating vestibular responses, coordinating the movement, and having fine-tuning sensory balance responses (Koziol et al., 2014). Consequently, disturbances in the system result in loss of postural stability and

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Peer review under responsibility of PLA General Hospital Department of Otolaryngology Head and Neck Surgery.

https://doi.org/10.1016/j.joto.2021.07.001
1672-2930/

discoordination of stepping patterns (Snijders et al., 2007). These disturbances can be measured based on the vestibulospinal reflex (Schniepp et al., 2019), using for example the craniocorpography (Gomez-Angel et al., 2000) or posturography (Falls, 2019). Ultrasound-computer-craniocorpography (US-COMP-CCG) is applicable for the objective examination of the vestibulospinal reflex, whereas it analyses the head and body movements under the strain of different test profiles applying the standing test (Romberg) and the stepping test (Unterberger-Fukuda) (Maihoub et al., 2019). Therefore, thorough spherical evaluation of central dizziness can add up to our understanding on the function of the central vestibular system to assure our daily activities.

The aim of the study was to characterize the unsteadiness in patients suffering from central vestibular disorder and discuss the possible diagnostic usage of US-COMP-CCG.

2. Methods and materials

2.1. Subject group

This investigation was a prospective study, in which 420 patients were selected in the period of 2 years, who were referred with dizziness complaints in our tertiary referral Neurotological Department. Inclusion criteria were based on the previous documented neurology findings and the neurotology examinations, including electronystagmography (ENG) with bithermal caloric test, video-head impulse test (vHIT), brain imaging (e.g., MRI) and US-COMP-CCG, as well as complementary examinations were carried out (e.g. pure tone audiometry, BERA, ultrasound imaging of carotid and vertebral arteries). Central vestibular lesions in the neurotology practice were defined by the brain MRI examination, which have shown lacunar or diffuse ischemic lesions of the central vestibular pathways, leading to the depiction of abberations of the central vestibular system including the exact anatomical localization. Bithermal caloric test with ENG registration was also applied, which indicated hyperreaction of the contralateral horizontal canals and superior parts of the vestibular nerve, which is usually registered in case of central vestibular disorders (Szirmai and Keller, 2013). vHIT showed no abnormality in these cases but helped in the definitive discrimination between peripheral and central dizziness. Exclusion criteria for the selection of the participants were medications that could influence the vestibular system, physical limitation, and influence of alcohol and/or drugs, as well as patients diagnosed with peripheral disorders.

According to the results of the former examinations, 190 patients (70 male and 120 female, mean age $\pm$ SD, 58.94 $\pm$ 15.27) suffering from a central vestibular disorder were enrolled. Based on the medical documentation, 37% had generalized ischemia, 25% vertebrobasilar insufficiency, 17% vascular encephalopathy, 4% multiple sclerosis, 3% acoustic schwannoma (including those cases, which were reaching the brainstem), 1% probable migraine vestibulopathy.

230 subjects (78 male and 152 female, mean age $\pm$ SD, 50.94 $\pm$ 15.27) with no vestibular complaints, who were referred to neurotology because of hearing loss and/or tinnitus were also investigated. This was defined as our control group. Dizziness or instability was absent, and the complete neurotological examination as well as the complementary examinations did not show any pathological aberration.

2.2. Ultrasound-computer-craniocorpography (US-COMP-CCG)

US-COMP-CCG (ZEBRIS Coordinate Measurement System®, Isny, Germany) can provide an objective assessment of the gait and stance stability through the vestibulospinal tract examination. Subjects complete the standing test (Romberg) and stepping test (Unterberger-Fukuda) for a duration of 1 minute with closed eyes, whereas the position related to the starting and end point is recorded. The position of markers that are located at the anterior and posterior vertex of the subject's head, left and right shoulder are analyzed with the aid of ultrasound (Seiwerth et al., 2018). As a result of the procedure, two graphs are drawn and four parameters for each test are calculated. Standing test is evaluated by the longitudinal and lateral sway in cm, the torticollis angle in degrees, and the forehead covering area in cm^2. Whereas, stepping test is evaluated by the longitudinal deviation and lateral sway width in cm, the angular deviation and the self-spin in degrees (Maihoub et al., 2019). The longitudinal sway as well as longitudinal deviation calculates the sway of the patient from front to back, where a sway of more than 10 cm is considered as abnormal. The lateral sway calculates the sway from side to side, where a measurement of more than 10 cm is considered abnormal. The torticollis angle (abnormal considered above 0° emphasizing the side) and forehead covering area (normal range up to 50°) is based on the interrelated movement pattern between the longitudinal axis of the skull, in combination with the frontal and occipital markers, with the transverse axis of the shoulders. During the angular deviation, the patient might deviate to one side of his original sagittal axis (normal range up to 45°), whereas the self-spin is calculated based on the patient's rotation around his own vertical axis (normal range up to 45°).

2.3. Statistical analysis

Statistical analysis was carried out using IBM SPSS V24 software. According to Shapiro-Wilk test the parameters did not show normal distribution; therefore Mann-Whitney*U* test was used (non-parametric test). Categorical analysis was performed by using Chi-square test. The significance level was specified as $p < 0.05$. To illustrate the results boxplots were included, ROC curves were drawn and based on area under curve the sensitivity and the specificity parameters were calculated.

3. Results

To determine which parameter of US-COMP-CCG could be specific for central vestibular disorder based on the balance dysfunctions, boxplots were drawn, and the parameters were contrasted to the results of the control group.

According to Fig. 1, the boxes of longitudinal sway, lateral sway and forehead covering area parameters of standing test of the central vestibular disorder group are showing higher values than those of the control group, indicating a difference between the parameters, and the results are statistically significant, suggesting a strong difference between the two groups. However, in case of torticollis angle parameter no obvious difference could be seen, which is also confirmed based on the statistical analysis ($p = 0.97$). These two facts indicate that a patient suffering from a central vestibular disorder will not exhibit a deviation to the sides but rather a movement of body from back to front with tendency of increased unsteadiness and increased fall rate.

As shown in Fig. 2, all boxes of the stepping test parameters of central vestibular disorder group have visible difference than those of the control group, and the statistical analysis also indicates a strong difference in all cases.

Based on the analysis, all parameters of the stepping test, and most parameters of the standing test (excluding the torticollis angle parameter) may be useful in the diagnosis of central vestibular disorders. To analyze how the US-COMP-CCG can differentiate the normal and pathologic patients, the outcome of the tests was

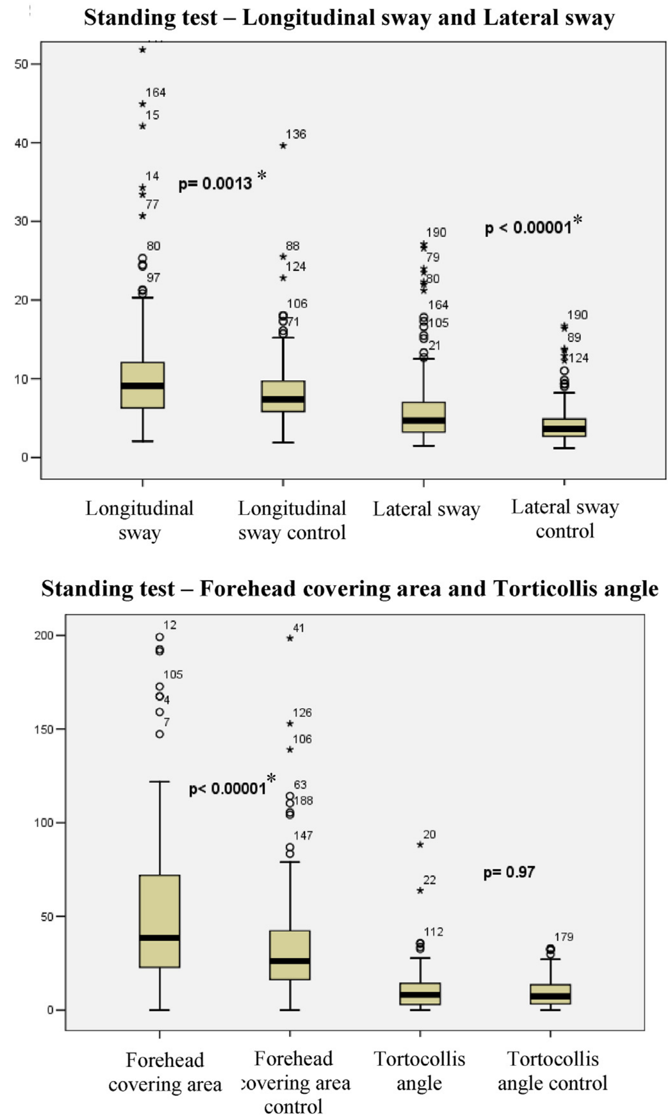

Fig. 1. Boxes showing the parameters of standing test. A box could be lower or higher than another; this could indicate a difference. Interpretation: the median value is shown by the line, which divides the boxes into two parts. The box represents the 50% of the data, and the whiskers are showing the lower and upper 25%, excluding outliers. The results of the non-parametric test are also included, * indicates statistically significant difference.

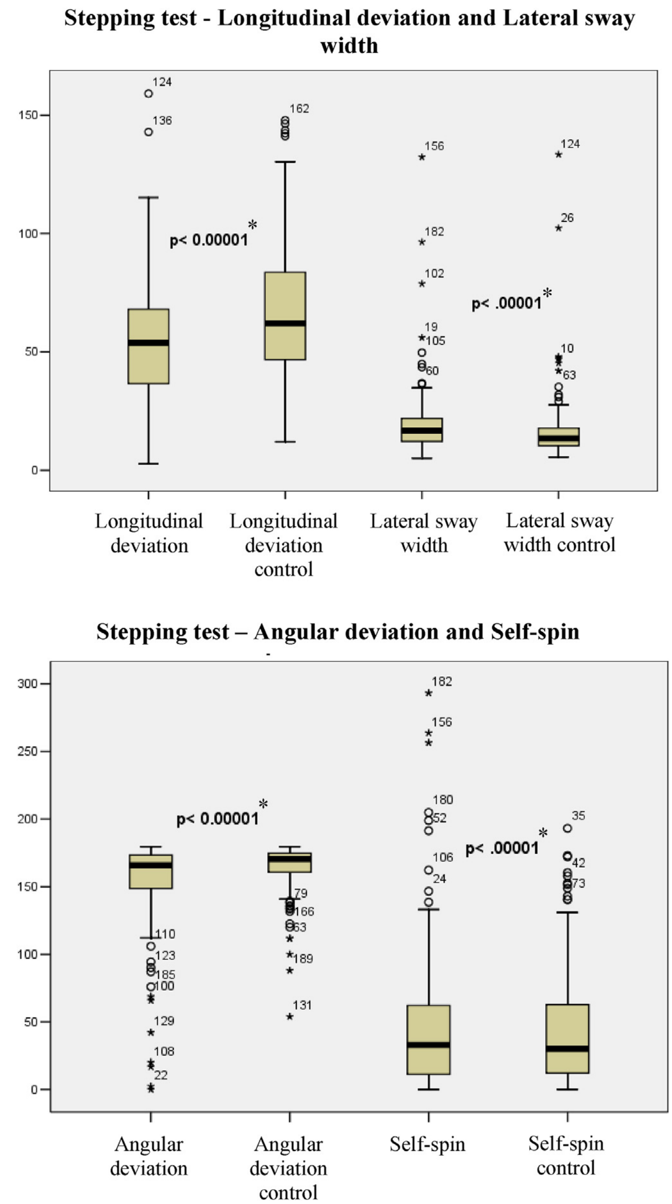

Fig. 2. Boxes showing the parameters of stepping test. The results of the non-parametric test are also included, * indicates statistically significant difference.

contrasted to the outcome of the complete neurotological examination. For the analysis, categorical analysis (i.e., based on the normal parameters of US-COMP-CCG, the examined patient was normal/not and based on complete neurotological examination belongs to the normal group or not) was carried out by Chi-square test. The results are shown in Table 1. Normal parameters were based on our previously published data (see the material and methods section).

Based on Chi-square test correlation between the result of US-COMP-CCG (normal/pathologic value) and final results were detected in cases of longitudinal sway, lateral sway, forehead covering area parameters of standing test, and of longitudinal deviation and lateral sway width parameters of stepping test. Irrevocably, it can be concluded that even though there is significant difference between most parameters of control and central disorder groups, categorical analysis indicates that standing test is more specific for central vestibular disorders, since most of the parameters showed similar results contrasted to the other neurotological examinations.

Based on area under curve of ROC curves, specificity and sensitivity parameters for each test were determined (Table 2.). As shown, parameters of standing test are more specific, while parameters of stepping test are more sensitive. Based on the analysis, the highest specificity was detected in case of lateral sway parameter of standing test (96.5%, which is almost a perfect parameter) and the most sensitive parameter is the angular deviation of the stepping test (98.9%). This fact indicates the necessity to combine the two examinations, and the most important parameters based on the analysis are the lateral sway and angular deviation parameters.

4. Discussion

In this study, we aimed to characterize the balance unsteadiness

Table 1
Results of the categorical analysis. The * indicates statistically significant difference.

Parameter	Chi-square test p value
Longitudinal sway (cm)	<0.00001*
Lateral sway (cm)	<0.00001*
Forehead covering area (degrees)	0.0001*
Torticollis angle (cm^2)	0.55
Longitudinal deviation (cm)	0.05*
Lateral sway width (cm)	0.011*
Angular deviation (degrees)	0.20
Self-spin (degrees)	0.63

Table 2
Sensitivity and specificity parameters for each test.

Parameter	Sensitivity (%)	Specificity (%)
Longitudinal sway (cm)	46	76
Lateral sway (cm)	19.4	96.5
Forehead covering area (degrees)	49.2	69.6
Torticollis angle (cm^2)	1.05	43.5
Longitudinal deviation (cm)	61.3	29.6
Lateral sway width (cm)	86.9	23.04
Angular deviation (degrees)	98.9	0
Self-spin (degrees)	78.5	19.6

in patients suffering from central vestibular disorder and discuss the possible diagnostic usage of vestibulospinal tests in these cases. Imbalance is more likely to be caused by central vestibular disorders rather than a peripheral vestibular one. US-COMP-CCG is a quick, non-invasive, relatively inexpensive tool suitable for the complementary diagnosis of central vestibular pathologies based on its objective measurement. Postural instability influences everyday activities, and it has been shown that the vestibular symptoms correlate with prospective disability (Breivik et al., 2013). Patients presenting initially with dizziness and instability, attributed to subsequent cerebrovascular or cerebellar events, is higher than expected in the everyday practice (Della-Morte and Rundek, 2012; Chase et al., 2012). Based on a recent study of Gimmon et al. (2017) the investigation of balance in vestibular disorders presented an impaired gait pattern in comparison to the healthy controls. In the current study, the incidence of patients with central vestibular disorder combined with gait instability was high. Patients consistently showed increased postural sway throughout both tests as compared with healthy controls. These findings supported implantation of US-COMP-CCG in gait function evaluation, and our results supported the former stating based on the schematical and analytical results that we concluded. Schniepp et al. (2019) concluded in their study that a comprehensive clinical assessment of gait performance based on a quantitative characterization of gait impairments can assist clinical decision making for the initial diagnosis and prognosis in patients, therefore strengthening the necessity of proper gait analysis. Moreover, Vanni et al. (2017), by using among others the evaluation of gait and standing position on patients with dizziness and unsteadiness, were able to reinforce the urgency to combine the examinations to raise the diagnostic accuracy.

Limitations of this study include that further vestibular evaluation would have been valuable to confirm subclinical vestibular dysfunction, whereas their correlation with postural instability remains to be explored. Patients suffering from peripheral vestibular disorders were also not investigated in the current study.

5. Conclusion

In this study, we reinforced the recommendation to perform vestibular tests in daily clinical practice for the investigation of postural instability in patients suffering from central vestibular disorders. Clinical evaluation of imbalanced patients should include both objective measures of balance and conventional tests. Therefore, based on this information a diagnosis improvement and not establishment is acquired. A prognosis and a successful follow up along with outcome assessment is also more achievable. Although, based on the sensitivity and specificity parameters, US-COMP-CCG cannot be used by itself, but as a part of complete neurotological examination, including other tests.

Declaration of competing interest

The Author(s) declare(s) that there is no conflict of interest.

Funding Acknowledgements

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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