



# The Effects of Vestibular Rehabilitation on Kinesiophobia and Balance with Individuals Who has Vestibular Hypofunction

Ebru Sever<sup>1</sup> · Gamze Kiliç<sup>1</sup> · Zeliha Candan Alğun<sup>1</sup>

Received: 23 August 2021 / Accepted: 6 November 2021  
© Association of Otolaryngologists of India 2021

**Abstract** The study aimed to examine the effects of vestibular rehabilitation on kinesiophobia, quality of life, dynamic visual acuity, and balance. Thirty vestibular hypofunction patients aged 18–65 years who were diagnosed by videonystagmography (VNG) voluntarily participated in the study. Before and after treatment Tampa Kinesiophobia Scale, World Health Organization Quality of Life Scale-Turkish Short Form, Tandem Stance Test, Dynamic Visual Acuity, Visual Analog Scale to measure dizziness, Subjective Visual Vertical and Subjective for verticality and horizontality perception Visual Horizontal tests were applied. The exercise program was applied for 8 weeks. Patients were observed in the hospital every two weeks. The exercises given in the session were given as home exercises, 3 times a day, for 10 repetitions. As a result of the study, statistical correlations were found tandem stance test, subjective visual vertical and subjective visual horizontal tests for the perception of verticality and horizontality, visual analog scale to measure the severity of dizziness, dynamic visual acuity, quality of life and tampa kinesiophobia scales ( $p < 0.05$ ). It can be said that vestibular rehabilitation improves the quality of life, balance, dynamic visual acuity, and overcomes kinesiophobia

in patients. Trial registration number: NCT05070936, Date of registration: 10/06/2021 (Retrospectively registered).

**Keywords** Balance · Dynamic visual acuity · Kinesiophobia · Vestibular hypofunction · Vestibular rehabilitation

## Introduction

Vestibular hypofunction is a disease that occurs when there is a partial or complete decrease in the functions of the vestibular organs or the vestibular nerve [1]. It is seen in two forms as unilateral vestibular hypofunction (UVH) and bilateral vestibular hypofunction (BVH) [2]. The peripheral and central system is known as the cause of vestibular hypofunction. Peripheral causes; pres by vertigo, cervicogenic dizziness, benign paroxysmal positional vertigo (BPPV), Meniere, vestibular neuritis, vestibular migraine, head trauma, acoustic neuroma. Central causes; It is known as multiple sclerosis, atypical Parkinson's, stroke, migraine, cerebellar disorder, head trauma, drugs, psychogenic and cardiovascular/autogenic conditions [3]. Symptoms such as dizziness, oscillopsia, postural instability, and gait disturbances are seen in patients with UVH. Symptoms such as oscillopsia, spatial orientation problems, cognitive impairment, postural instability, visual and gaze disturbances, and physical inappropriateness are seen in patients with BVH [2, 4].

Vestibular hypofunction treatment consists of vestibular rehabilitation, posturography training, virtual reality, and instrumental rehabilitation. One of the most valuable stages of vestibular rehabilitation is the education of the patient. The patient's adaptation to exercise and motivation is increased. Rehabilitation consists of three main exercises;

✉ Ebru Sever  
fztebrusever@gmail.com  
Gamze Kiliç  
fztgamzekilic@gmail.com  
Zeliha Candan Alğun  
calgun@medipol.edu.tr

<sup>1</sup> Department of Physiotherapy and Rehabilitation, İstanbul Medipol University, Kavacak South Campus, 34815 Beykoz, İstanbul, Turkey

these are gaze stabilization exercise, habituation exercise, and postural stabilization exercises [5].

Kinesiophobia is the condition in which the patient restricts her/his movements and activities because of the fear of being injured again after a painful experience [6]. If we consider the fear-avoidance model; A painful stimulus can produce a state of pain, which causes fear and anxiety, leading to avoidance behavior. If this situation continues for a long time, the person will isolate himself/herself from social life [7].

Kinesiophobia has often been examined in studies in disease states that cause pain. The number of studies examining the relationship between vestibular rehabilitation applied in vestibular pathologies and kinesiophobia is limited. Therefore; this study aimed to examine the effect of VR on kinesiophobia, quality of life, dynamic visual acuity, and balance in individuals with VH.

## Methods

Thirty patients aged between 18 and 65 years with positive VNG test were admitted to otolaryngology clinic with complaints such as turning from the head, balance problems, and falling. Inclusion criteria for the study; Individuals with vestibular hypofunction diagnosed by VNG test and patients aged between 18 and 65 years. Exclusion criteria from the study; Patients with visual impairment and neurological involvement, individuals with wavy vertigo, ataxia, or other lesions causing oscillopsia, dementia, patients with severely limited mobility and unable to walk without using a walker, cane, or orthosis. Patients were evaluated before and after rehabilitation. Tampa Kinesiophobia Scale, World Health Organization Quality of Life Scale-Short Form Turkish Version, Dynamic Visual Acuity, tandem stance test, Visual Analogue Scale to measure dizziness Subjective Visual Vertical and Subjective Visual Horizontal tests for verticality and horizontality perception were applied.

*Videonystagmography*; Bithermal caloric test, one of the most important components of the VNG test, is the gold standard for the diagnosis of vestibular hypofunction [8]. With this test, the vestibulo-ocular reflex was evaluated by giving thermal stimuli. While the patient was lying in the supine position, with the head flexed at 30 degrees, 8 L of air at 50 degrees and 24 degrees Celsius, respectively, were sent to both eardrums in 60 s with 5 min rest intervals. Involuntary eye movements were recorded for 120–140 s and the results were calculated by graphing [9].

## Applied Evaluations

*Demographic Data Form*: Sociodemographic characteristics and clinical conditions; Name, surname, age, smoking and alcohol consumption, illnesses and/or surgeries,

medications used, whether have a history of falling, their frequency, fear of heights, and whether they are uncomfortable with the dark, etc. was questioned.

*Tandem Stance Test*: The patient placed the heel of one foot directly on the tip of the other foot, extended his hands in front of him parallel to the ground, and tried to maintain this position for 30 s without support. The test is finished when it maintains 30 s. If he could not, how many seconds he did, that second was noted. This test was applied first with eyes open and then with eyes closed, and the values were examined separately.

*Subjective Visual Vertically (SVV) Test and Subjective Visual Horizontally (SVH) Test*: A line in a bright or obvious color tone was placed inside the bucket. An angle indicator is placed at the bottom of the bucket. A weight hung from the middle of the bucket. The patient was asked to align the vertical line horizontally and the horizontal line vertically by holding the bucket from both sides and turning it to the right or left side so that the patient's face was facing the inside of the bucket. If there was a deviation from 0 degrees, this was recorded [10].

*Dizziness Evaluation*: The Visual Analogue Scale (VAS) was used to evaluate the severity of dizziness. It is a score between 0 and 10 cm on the Visual Analog Scale. 0 cm: I have no dizziness, 10 cm: I have a lot of dizziness. If the scoring is between 1 and 4 cm; mild vertigo, 4–8 cm; moderate vertigo, if it is between 8 and 10 cm; classified as severe vertigo [11].

*Tampa kinesiophobia scale (TKS)*: It measures fear of movement and fear of re-injury. A 4-point Likert scoring (1 = strongly disagree, 4 = strongly agree) is used. It consists of 17 questions. After reversing the 4th, 8th, 12th, and 16th items, the total score is calculated. It gets a total score between 17 and 68. A high score shows high kinesiophobia [12].

*World Health Organization Quality of Life Scale-Turkish Short Form (WHOQOL-BREF-TR)*: Developed by WHO. Validity and reliability were obtained by Eser et al. There are two versions of the scale, long (WHOQOL-100) and short (WHOQOL-27) form. The scale measures physical, mental, social and environmental well-being and consists of 26 questions. When the Turkish version (question 27 is the national question), the perimeter score is called Perimeter-TR. In this situation Perimeter-TR area score is used instead of perimeter score. Each area is evaluated on its own. Area scores are calculated between 4 and 20. The higher the score, the higher the quality of life [13].

*Dynamic Visual Acuity*: It was done using the Snellen test. He was seated in a chair 3 m away from the chart. The patient was initially asked where he read on the eye chart on the wall while the head was fixed, and it was recorded. Then, while the patient's head was turned to the

right and left rapidly 2 times per second, the patient was asked to continue reading on the eye board and the answers were recorded [4].

**Vestibular Rehabilitation Program:** Vestibular rehabilitation consisted of a total of 4 sessions, rearranged every 15 days. These exercises were prepared gradually to increase the vestibulo-ocular reflex and vestibulospinal reflex. The following exercises were done with the patients: both sitting and standing gaze stabilization exercises, neck joint range of motion exercises, 20 min walks outside, walking backward both open-and-closed eyes, and walking in tandem with both open-and-closed eyes. The therapist gave the patients a home exercise program. It was emphasized that the exercises should be applied as 10 repetitions. After the session, the exercises shown to the patients were explained in written form and given as home exercises. They were also asked to do home exercises 3 times a day, 10 repetitions, for 15 days. Evaluation of the patients was done at the beginning of the first session and the 4th session. Thus, 3 separate exercise sessions and a home exercise program were applied to the patients.

**Statistical Analysis:** The data obtained in the research were analyzed using the Statistical Package for Social Sciences (SPSS) Windows 25.0 program. The collected information was interpreted by using the frequency, percentage values, median, minimum, maximum, mean, and standard deviation, which are descriptive statistics. The normal distribution of the data was made using the Shapiro–Wilk test. It was observed that the WHOQOL-BREF scale and Tampa Kinesiophobia scale had normal distribution, and the dizziness and tandem posture test values did not show normal distribution. To test whether the scores of two quantitative correlated variables differed significantly from each other, a dependent sample t-test was used for normally distributed variables, the Wilcoxon test was used for non-normally distributed variables, and the McNemar test was used to examine the variation of two dependent groups in different periods. In cases where the error rate was determined in all tests and  $p < 0.05$ , the difference between the groups was considered statistically significant. Comments were made in the light of the tables created by the analysis of the data.

## Results

Thirty people who met the inclusion and exclusion criteria completed the study. The mean age of the participants in the study was  $46.10 \pm 11.80$ . It was determined that 80.0% of the participants were female and 20.0% were male. It was determined that 23.3% of them smoked and those who used alcohol did not. It was observed that 36.7% of the patients had BVH and 63.3% had UVH. After eight weeks

of vestibular rehabilitation, improvements were observed in the tandem stance test eyes open/eyes closed tests ( $p < 0.05$ ). SVV and SVH test scores were found to be statistically significant in sitting, hard and soft surfaces ( $p < 0.05$ ). The mean vertigo severity (VAS) decreased from  $7.15 \pm 1.36$  to  $1.06 \pm 2.02$ . The results of the tandem stance test, SVV and SVH tests, dizziness, and dynamic visual acuity parameters are shown in Table 1. It was found that their quality of life improved and their kinesiophobia decreased ( $p < 0.05$ ). Quality of life and kinesiophobia parameter results are shown in Table 2.

## Discussion

Vertigo, nausea, vomiting, dizziness, nystagmus, and imbalance in gait and posture are prominent symptoms in vestibular hypofunction [14]. In our study, 30 patients were admitted to the hospital with these symptoms, and after an 8-week vestibular rehabilitation program, complaints of loss of balance, kinesiophobia, and dizziness were decreased, and VOR gain and quality of life increased.

Vestibular hypofunction, dizziness, and loss of balance are among the most common problems in individuals over 60 years of age [15]. Considering recent studies, it was concluded that vestibular losses can also be seen in children, and it was stated that the female gender is a risk factor [16, 17]. Since it is a disease that affects all age groups, individuals between the ages of 18–65 with vestibular hypofunction were included in our study. The mean age of the subjects in our study was found to be 46. 80% of the participants were female and 20% were male. Tandem eyes open/eyes closed tests were used to evaluate balance and statistical significance was found. VAS was applied for the severity of dizziness and improvement was observed.

They stated that the head is inclined towards the side with impaired otolith function [18]. Liu et al. To measure the perception of horizontality and verticality in their study in patients with UVH; They suggested that SVH and SVV tests are useful [19]. In our study, SVV and SVH tests were used and improvements were found in the perception of verticality and horizontality after exercise.

In the pathophysiology of vestibular hypofunction; There is a decrease in the tone of the vestibular nuclei and a decrease in the VOR gain. When the VOR decreases, dynamic visual acuity deteriorates [10]. VHIT and dynamic visual acuity testing have been suggested in a study in the literature to measure the loss in VOR [20]. In our study, dynamic visual acuity was used among the evaluation methods and statistical significance was found.

The quality of life of patients is adversely affected due to the symptoms occurring in individuals with vestibular

**Table 1** Results of Tandem Stance Test, SVV and SVH Tests, Dizziness Severity and Dynamic Visual Acuity Parameters

		Pre- (n = 30)		Post-(n = 30)		Z	p
		Mean ± SD	Median (min–max)	Mean ± SD	Median (min–max)		
Tandem Stance Test	Eyes Open	25.70 ± 8.84	30.00 (2.36–30.00)	30.00 ± 0.00	30.00 (30.00– 30.00)	– 2.366	0.018*
	Eyes Closed	10.99 ± 11.10	6.36 (0.00–30.00)	27.66 ± 5.20	30.00 (11.35–30.00)	– 4.458	0.000*
SVV and SVH Tests	SVV Sitting Down	0.67 ± 0.76	1.00 (0.00–3.00)	0.13 ± 0.346	0.00 (0.00–1.00)	– 2.782	0.005*
	SVH Sitting Down	0.77 ± 1.04	0.00 (0.00–3.00)	0.13 ± 0.43	0.00 (0.00–2.00)	– 3.094	0.002*
	SVV Hard Floor	1.03 ± 0.85	1.00 (0.00–3.00)	0.23 ± 0.43	0.00 (0.00–1.00)	– 3.621	0.000*
	SVH Hard Floor	1.00 ± 1.17	1.00 (0.00–4.00)	0.27 ± 0.52	0.00 (0.00–2.00)	– 3.027	0.002*
	SVV Soft Floor	1.37 ± 0.89	1.00 (0.00–3.00)	0.13 ± 0.35	0.00 (0.00–1.00)	– 4.210	0.000*
	SVH Soft Floor	1.53 ± 1.17	2.00 (0.00–4.00)	0.20 ± 0.61	0.00 (0.00–2.00)	– 3.895	0.000*
Dizziness Severity		7.15 ± 1.36	7.30 (4.20–9.30)	1.06 ± 2.02	0.000 (0.00–9.30)	– 4.763	0.000*
Dynamic Visual Acuity		0.49 ± 0.31	0.50 (0.00–0.90)	0.14 ± 0.20	0.10 (0.00–0.80)	– 3.924	0.000*

Wilcoxon Test; SVV: Subjective Visual Vertically; SVH: Subjective Visual Horizontally; SD: Standard Deviation; n: Number of Persons; min: minimum; max: maximum; \*( $p \leq 0.05$ )

**Table 2** Results of Quality of Life and Kinesiophobia Parameters

		Pre- (n = 30)	Post-(n = 30)	t	p
		Mean ± SD	Mean ± SD		
WHOQOL-BREF-TR	WHOQOL-BREF-TR (General health status)	43.33 ± 22.92	72.92 ± 14.34	– 9.091	0.000*
	WHOQOL-BREF-TR (Physical health)	54.73 ± 18.75	76.12 ± 11.80	– 8.846	0.000*
	WHOQOL-BREF-TR (Psychological)	55.68 ± 16.61	69.84 ± 13.78	– 9.039	0.000*
	WHOQOL-BREF-TR (Social relations)	68.57 ± 15.73	74.69 ± 14.75	– 3.960	0.000*
	WHOQOL-BREF-TR (Environment)	68.99 ± 11.96	74.37 ± 10.81	– 4.173	0.000*
Tampa Kinesiophobia Scale		49.60 ± 7.71	43.77 ± 4.39	4.575	0.000*

T test; WHOQOL-BREF-TR: World Health Organization Quality of Life Scale Turkish Version; SD: Standard Deviation; n: Number of Persons; \*( $p \leq 0.05$ )

disorders [21]. In their review, McDonnell and Hillier stated that the positive effect of VR on the quality of life of individuals with unilateral VH was better than other treatments [22]. In our study, quality of life was evaluated with the WHOQOL-BREF-TR and a significance was found in the post-exercise scores. Improvement in quality of life; This can be attributed to the fact that patients have progressed in dizziness and loss of balance after exercise.

Kinesiophobia was evaluated and treated in pain-related disease groups. Archer et al. applied cognitive-behavioral therapy-based exercise to 102 patients with pain after lumbar spine surgery and found that it had a positive effect on kinesiophobia [23]. In a large-scale review of patients with chronic fatigue syndrome and fibromyalgia, pain neuroscience education was found to be effective in improving patients' pain-induced kinesiophobia [24]. Our study focused on kinesiophobia caused by dizziness. The patients were evaluated using the TKS, and statistical

significance was observed in the patients' fear of movement after vestibular rehabilitation. The result was significant, and the exercise program had positive effects on dizziness and balance.

According to some of the studies; The exercises used in vestibular rehabilitation and the diseases in which the rehabilitation is applied vary. The exercises used in vestibular rehabilitation and the diseases in which the rehabilitation is applied vary. Whitney et al. examined the developments related to vestibular rehabilitation and rehabilitation; they said that gaze stabilization exercises, habituation exercises, virtual reality, and biofeedback were used [25]. In a review made in 2019, they found that gaze stabilization exercises positively affected VOR gain, improved dynamic visual acuity, and reduced dizziness [26]. In our study, a significant improvement was achieved with vestibular rehabilitation exercise training in our

patients by providing balance training with adaptation, habituation, and replacement exercises.

It was observed that there were significant improvements in balance parameters after vestibular rehabilitation treatment in patients diagnosed with vestibular hypofunction, resulting in improvements in the perception of verticality and horizontality. It has been determined that vestibular rehabilitation increases VOR gain, reduces the discomfort of patients from crowds, and this results in an increase in their quality of life. At the same time, it was observed that there was a decrease in the severity of dizziness, thus leading to improvements in kinesiophobia scores.

The limitations of our study, the relationship between kinesiophobia, balance, dynamic visual acuity, and quality of life could not be examined due to the insufficient number of samples, vestibular hypofunction patients were followed for 2 months, but especially BVH patients need long-term follow-up and rehabilitation. The reason for not being able to follow long-term; patients have compliance problems and our study was carried out during the Covid-19 pandemic.

**Funding** The authors did not receive support from any organization for the submitted work.

#### Declarations

**Conflicts of interest** Employment: No employment by any organization. Financial interests: The authors have no financial interests. Non-Financial interests: The authors have no non-financial interests.

**Consent for Publication** Patients signed informed consent regarding publishing their data.

**Ethics Approval** This study was performed in line with the principles of the Declaration of Helsinki. The ethics committee approval dated 07/08/2020 and numbered E-10840098-772.02-34270 of Istanbul Medipol University Non-Interventional Clinical Research Ethics Committee was received.

**Informed Consent** Informed consent was obtained from all individual participants included in the study.

#### References

- Batuk M, Aksoy (2015) Vestibüler rehabilitasyon. *Türkiye Klinikleri J E.N.T. Spec Top* 8:95–98
- Gabilan, Yeda PL (2008) Aquatic physiotherapy for vestibular rehabilitation in patients with unilateral vestibular hypofunction: exploratory prospective study. *J Vestib Res* 18:139–146
- Renga V (2019) Clinical evaluation of patients with vestibular dysfunction. *Neurol Res Int.* <https://doi.org/10.1155/2019/3931548>
- Herdman SJ, Schubert MC, Das VE, ve Tusa RJ (2003) Recovery of dynamic visual acuity in unilateral vestibular hypofunction. *Arch Otolaryngol Neck Surg* 129(8):819–824. <https://doi.org/10.1001/archotol.129.8.819>
- Herdman SJ, Whitney SL (2016) Physical therapy treatment of vestibular hypofunction, vestibular rehabilitation. *J Neurol Phys Ther* 40:394–456
- Gregg CD, McIntosh G, Hall H, Watson H, Williams D, ve C. W. Hoffman, (2015) The relationship between the Tampa Scale of Kinesiophobia and low back pain rehabilitation outcomes, *Spine. J Off J North Am Spine Soc* 15(12):2466–2471. <https://doi.org/10.1016/j.spinee.2015.08.018>
- Larsson C, Ekvall Hansson E, Sundquist K, ve Jakobsson U (2016) Kinesiophobia and its relation to pain characteristics and cognitive affective variables in older adults with chronic pain. *BMC Geriatr* 16:128. <https://doi.org/10.1186/s12877-016-0302-6>
- Kaufmann H (1996) Consensus statement on the definition of orthostatic hypotension, pure autonomic failure and multiple system atrophy. *Clin Auton Res Off J Clin Auton Res Soc* 6(2):125–126. <https://doi.org/10.1007/BF02291236>
- McCaslin DL (2013) *Electronystagmography and videonystagmography*, vol Core. Plural Publishing, Clin. Concepts Audiol. Ser.
- Kaya Ş (2020) Evaluation of utricular function in adults with bucket test. *J Otorhinol Head Neck Surg* 28(2):141–145. <https://doi.org/10.24179/kbbbc.2020-74417>
- Kaur J, Shamanna K (2017) Management of benign paroxysmal positional vertigo: a comparative study between epleys manoeuvre and betahistine. *Int Tinnitus J* 21(1):30–34. <https://doi.org/10.5935/0946-5448.20170007>
- Fidaner H (1999) Measuring quality of life WHOQOL-100 and WHOQOL-bref. *J Psychiatr Psychol Psychopharmacol* 7:23–41
- Yildirim A, Hacıhasanoğlu R (2011) Quality of life and effective variables among health care professionals. *J Psychiatr Nurs* 2(2):61–68
- Strupp M, Długaiczek J, Bettina Ertl-Wagner B, Rujescu D, Westhofen M, Dieterich M (2020) Vestibular disorders. *Dtsch Arztebl Int* 117(17):300–310. <https://doi.org/10.3238/arztebl.2020.0300>
- D. C. Martins E Silva vd. (2016) Effects of vestibular rehabilitation in the elderly: a systematic review. *Aging Clin Exp Res* 28(4):599–606. <https://doi.org/10.1007/s40520-015-0479-0>
- Rine RM (2018) Vestibular rehabilitation for children. *Semin Hear* 39(3):334–344. <https://doi.org/10.1055/s-0038-1666822>
- Koo JW, Chang MY, Woo S, Kim S, ve Y.S. Cho, (2015) Prevalence of vestibular dysfunction and associated factors in South Korea. *BMJ Open* 5:10. <https://doi.org/10.1136/bmjopen-2015-008224>
- Hirvonen TP, Jutila T, Aalto H (2011) Subjective head vertical test reveals subtle head tilt in unilateral peripheral vestibular loss. *Eur Arch Oto-Rhino-Laryngol.* <https://doi.org/10.1007/s00405-011-1560-8>
- Liu R, Chen T, Lin P, Dong H, Lu H, Zhang N (2011) Subjective visual horizontal in peripheral unilateral vestibular dysfunction. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 46(5):382–387
- S M, F K, D M, B T (2016) Bilateral vestibulopathy. *Handb Clin Neurol.* <https://doi.org/10.1016/B978-0-444-63437-5.00017-0>
- Aratani MC, Ricci NA, Caovilla HH, Ganança FF (2020) Benefits of vestibular rehabilitation on patient-reported outcomes in older adults with vestibular disorders: a randomized clinical trial. *Braz J Phys Ther* 24(6):550–559. <https://doi.org/10.1016/j.bjpt.2019.12.003>
- McDonnell MN, Hillier SL (2015) Vestibular rehabilitation for unilateral peripheral vestibular dysfunction. *Cochrane Database Syst Rev.* <https://doi.org/10.1002/14651858.CD005397.pub4>
- K. R. Archer vd. (2016) Cognitive-behavioral based physical therapy for patients with chronic pain undergoing lumbar spine

- surgery: a randomized controlled trial. *J Pain Off J Am Pain Soc* 17(1):76–89. <https://doi.org/10.1016/j.jpain.2015.09.013>
24. A. Malfliet vd. (2017) Kinesiophobia and maladaptive coping strategies prevent improvements in pain catastrophizing following pain neuroscience education in fibromyalgia/chronic fatigue syndrome: An explorative study. *Physiother Theory Pract* 33(8):653–660. <https://doi.org/10.1080/09593985.2017.1331481>
25. Sulway S, Whitney SL (2019) Advances in vestibular rehabilitation. *Adv Otorhinol.* 82:164–169. <https://doi.org/10.1159/000490285>
26. Meldrum D, Jahn K (2019) Gaze stabilisation exercises in vestibular rehabilitation: review of the evidence and recent clinical advances. *J Neurol.* <https://doi.org/10.1007/s00415-019-09459-x>

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.