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Does the postural variable affect the determination of balance compensation level in vestibular schwannoma patients?

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Abstract

Previous sensory organization test (SOT) outcomes provided evidences that the vestibular schwannoma (VS) removal led to acute and slow changes in the ability to use vestibular cues for balance control. However, the assumptions behind the equilibrium score (ES) are somewhat controversial within the literature. Therefore, we compared the time-course of balance control in eighteen VS patients across different postural variables. Analyses of variance and unsupervised clustering (k-means) were used to compare the whole dataset of four postural variables: ES, a modified ES which factored in the time before a fall (cES), the mean amplitude (MA) and the mean velocity (MV) of center of pressure displacements. Early after surgery, postural performances significantly decreased ($p < 0.01$), especially when vestibular cues are predominant, with lower ES ($12.5 \pm 22.8\%$) and cES ($26.6 \pm 16.7\%$) and higher MA (27.7 ± 7.1 mm) and MV (95.2 ± 53.2 mm.s⁻¹) than before or three months after surgery. For each postural variable, the k-means clustering divided the whole dataset into two clusters: cluster #1 corresponded to a SOT with low sway amplitude and cluster #2 with high sway amplitude and falls. Overall, whatever the selected postural variable, the main recovery profile of VS patients was highlighted, thus surpassing the ambiguities inherent of the ES calculation.

Keywords: Balance control; Centre of pressure fluctuations; Sensory Organization Test; Unilateral vestibular deafferentation.

INTRODUCTION

The slow growth of vestibular schwannoma (VS) leads to a progressive vestibular dysfunction which is compensated by central adaptive mechanisms to minimize the alteration of the gaze and balance control [1,2]. The total unilateral vestibular deafferentation (uVD) consecutive to the VS surgical removal leads to a decompensation of this previously compensated situation. Early after uVD, the balance control has been found to be severely

altered and then progressively restored due to *de novo* implementation of central adaptive mechanisms which could be of vestibular origin [3,4] and from learning mechanisms implying neural structures and pathways beyond the vestibular nuclei [5-7].

Performing a Sensory Organization Test (SOT) was thoroughly appropriate to assess the relative contribution of visual, vestibular and somatosensory afferences in the balance control of VS patients [2-7]. However, the main calculated variable, called equilibrium score (ES), is not without limitations. Indeed, ES is an estimate of postural stability based on peak-to-peak

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anteroposterior sway relative to theoretical sway limits of stability. In their review, Chaudhry et al. [8] summarized multiple ambiguities/disadvantages of the ES. Among other issues, the ES computation is based on the anteroposterior sway angle of the centre of mass (CoM) itself computed from the anteroposterior trajectory of the CoM's orthogonal projection on the balance platforms. However, this anteroposterior CoM trajectory is derived from a low-pass filtering of the anteroposterior centre of pressure (CoP) trajectory [9] assuming that the subject behaves like an inverted pendulum around the ankle joint. Nevertheless, when the balance condition is challenging (e.g., sway-referenced support), upward projection of the CoP did not provide an accurate measure of body sway angle [10]. Therefore, errors in estimates of postural stability based on ES may occur in several conditions of the SOT, especially in condition 5 (i.e., eyes closed and sway-referenced support) which appeared to be of particular interest in characterizing the ability to use vestibular cues for balance control of VS patients prior to and after surgery [2,3].

As VS patients underwent large changes in their ability to use vestibular cues, a bias might come from the ES calculation to assess balance control for such a population. Consequently, we assessed the time-course (pre- and post-uVD) of balance control of VS patients performing the SOT across different postural variables. In comparison with ES, we used

the continuous ES (cES) which takes into account the time spent during a given trial allowing to discriminate trials in which a fall occurred instead of assigning a unique score of 0 [9]. In addition, the mean amplitude (MA) and mean velocity (MV) were selected as they took into account the full history of CoP displacements in both directions (mediolateral and anteroposterior) and were reported to distinguish stable balance control from reduced stability [11].

METHODS

Participants

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee. Eighteen patients (10 women and 8 men, mean age: 53.0 ± 11.7 years, mean height: 1.69 ± 0.11 m, mean weight: 74.6 ± 15.8 kg) gave their written informed consent to participate voluntarily in the study and followed the experimental requirements. All were scheduled for a surgical ablation of a unilateral VS by the same surgeon using the translabyrinthine approach. Tumor characteristics and vestibular patterns are detailed in Table 1. Each patient was submitted to posturographic evaluations three days before surgery (BS) and three times after surgery: eight (AS₈), thirty (AS₃₀) and ninety days (AS₉₀).

Posturographic evaluation

During a SOT (Equitest®, NeuroCom®, Pleasanton, CA, USA), the patients were instructed to maintain an upright stance, as stable as possible, during three 20 s trials in six conditions. During the first three conditions, the support was fixed and the patient's eyes were open (Condition 1, C1), closed (C2) and open within a sway-referenced visual surround (C3). For conditions 4–6, somatosensory information was disrupted by a sway-referenced support and the patient's eyes were open (C4), closed (C5) and open within a sway-referenced visual surround (C6). To protect against falls, an operator stood within touching distance of the patient and all wore a safety harness.

Table 1. Distributions of patients' characteristics within the sample.

	<i>n</i>	%
Tumor size		
Small*	9	50.0
Large**	9	50.0
Tumor location		
Right ear	5	27.8
Left ear	13	72.2
Vestibular reflectivity†		
Areflexy	1	5.6
Hyporeflexy	14	77.8
Normoreflexy	3	16.6

Note: *: tumor size is less than 20 mm, penetrating the cerebello-pontine angle without contact with the brainstem; **: tumor size is greater than 20 mm, filling in the cerebello-pontine angle and in contact with the brainstem (with or without compression); †: vestibular reflectivity determined through bithermal caloric testing.

Table 2. Calculations of the four postural dependent variables and their interpretation.

Postural variable	Equation	data	Understanding
Equilibrium score (ES, %)	$ES = \left[1 - \frac{(\max \theta - \min \theta)}{12.5} \right] \times 100$	θ : anteroposterior sway angle (in degree) 12.5: theoretical range of sway limit (in degree).	An ES value of 100 represented no sway, while 0 indicated sway that exceeded the limits of stability, resulting in a fall.
Continuous equilibrium score (cES, %)	$cES = \left[1 - \frac{(\max \theta - \min \theta)}{12.5} \right] \times \frac{\alpha}{20} \times 100$	θ : anteroposterior sway angle (in degree); 12.5: theoretical range of sway limit (in degree); α : trial time (in second, if no fall occurred $\alpha=20$); 20: maximal trial time (in second).	cES took into account the time spent during a given trial allowing to discriminate trials in which a fall occurred instead of assigning a unique score of 0. Without fall, the cES did not differ to the ES [9].
Mean amplitude (MA, mm)	$MA = \frac{1}{n} \sum_{i=1}^n \sqrt{(\bar{x} - x_i)^2 + (\bar{y} - y_i)^2}$	n : number of time samples ($n=2000$ if no fall occurred during a trial); x_i and y_i : i^{th} mediolateral and anteroposterior CoP coordinate, respectively;	MA and MV took into account the full history of CoP displacements in both directions (mediolateral and anteroposterior) and were reported to distinguish stable balance control from reduced stability [11]. Lower values of MA or MV indicated a higher postural steadiness.
Mean velocity (MV, mm.s ⁻¹)	$MV = \frac{1}{n-1} \sum_{i=1}^{n-1} \frac{\sqrt{(x_i - x_{i+1})^2 + (y_i - y_{i+1})^2}}{\Delta t}$	n : number of time samples ($n=2000$ if no fall occurred during a given trial); x_i and y_i : i^{th} mediolateral and anteroposterior CoP coordinate, respectively; Δt : time period of 0.01 s.	

Data processing and dependent variables

The support surface consisted of a dual force platform supported by four strain gauges sampled at 100 Hz to measure the distribution of vertical forces. The mediolateral and anteroposterior positions of the CoP and CoM were obtained directly from the Equitest® software and data were processed offline with custom scripts (Matlab®, The MathWorks Inc.™, Natick, MA, USA).

From the CoM trajectory, the anteroposterior sway angle (θ , in degree) was computed as follows:

$$\theta = \sin^{-1} \left(\frac{CoM_y}{0.5527 \cdot BH} \right) - 2.3, \quad (1)$$

where CoM_y was the anteroposterior CoM trajectory, BH was the body height and 2.3 was the angle (in degree) between the upright body and its CoM position in front of it. From these θ values, ES and cES were calculated (Table 2) for each trial. In addition, after the filtering (20 Hz, Butterworth

filter, 4th order) both mediolateral and anteroposterior CoP positions, MA and MV were calculated (Table 2) for each trial. For each SOT condition, a mean value of each variable (ES, cES, MA, MV) was calculated from the three respective trials of the given condition (C1 to C6).

Statistical analysis

To explore the effect of time (BS, AS₈, AS₃₀, and AS₉₀) and conditions (C1 to C6) on postural variables (ES, cES, MA, or MV), a two-way repeated measures ANOVA was conducted for each postural variable. When appropriate, Scheffé's tests were used to detect paired differences. Measures of effect size in ANOVA were provided with partial Eta squared values (η_p^2). The significance level was set at $p < 0.05$. In addition, the standard k-means method was used to summarize the whole dataset of each postural variable into a limited set of

homogeneous groups called clusters (see supplementary materials).

RESULTS

Fig. 1 depicted the changes of each postural variable according to the six SOT conditions and evaluation stages. Similar main and interaction effects were found among the four postural variables. A main effect of SOT condition (C1 to C6) appeared to be significant ($p < 0.001$) for each of the postural variable [$F_{(5,85)} = 116.59$, $\eta_p^2 = 0.87$ for ES; $F_{(5,85)} = 146.27$, $\eta_p^2 = 0.90$ for cES; $F_{(5,85)} = 197.58$, $\eta_p^2 = 0.92$ for MA; $F_{(5,85)} = 81.15$, $\eta_p^2 = 0.83$ for MV]. Also, a main effect of evaluation stage (BS, AS₈, AS₃₀, and AS₉₀) was significant ($p < 0.01$) for each of the postural variable [$F_{(3,51)} = 30.50$, $\eta_p^2 = 0.64$ for ES; $F_{(3,51)} = 25.74$, $\eta_p^2 = 0.60$ for cES; $F_{(3,51)} = 9.52$, $\eta_p^2 = 0.36$ for MA; $F_{(3,51)} = 6.47$, $\eta_p^2 = 0.28$ for MV]. Finally, an interaction effect (SOT's condition \times evaluation stage) was found to be significant ($p < 0.01$) for each of the postural variable [$F_{(15,255)} = 14.10$, $\eta_p^2 = 0.45$ for ES; $F_{(15,255)} = 12.33$,

$\eta_p^2 = 0.42$ for cES; $F_{(15,255)} = 4.14$, $\eta_p^2 = 0.20$ for MA; $F_{(15,255)} = 4.23$, $\eta_p^2 = 0.20$ for MV].

Pairwise differences among the six SOT conditions are depicted in the Figure 1 and mainly showed that C5 and C6 differed from the four other SOT conditions. Pairwise difference among the four evaluation stages were found to be significant for all the postural variables between BS and AS₈ ($p < 0.05$) and between AS₈ and AS₉₀ ($p < 0.01$). A significant difference between AS₈ and AS₃₀ was found for ES, cES and MA (all $p < 0.01$), while solely ES and cES were significantly higher at AS₉₀ in comparison with BS ($p < 0.01$). Regarding the significant interaction effect of all the postural variables, it appeared that C5 and C6 were the most sensitive conditions to reveal significant changes in balance control of VS patients pre- and post-surgery. In other words, the postural stability was the most challenged in these two conditions of the SOT and significant balance compensation (at least up to three months) was quantified whatever the postural variable used.

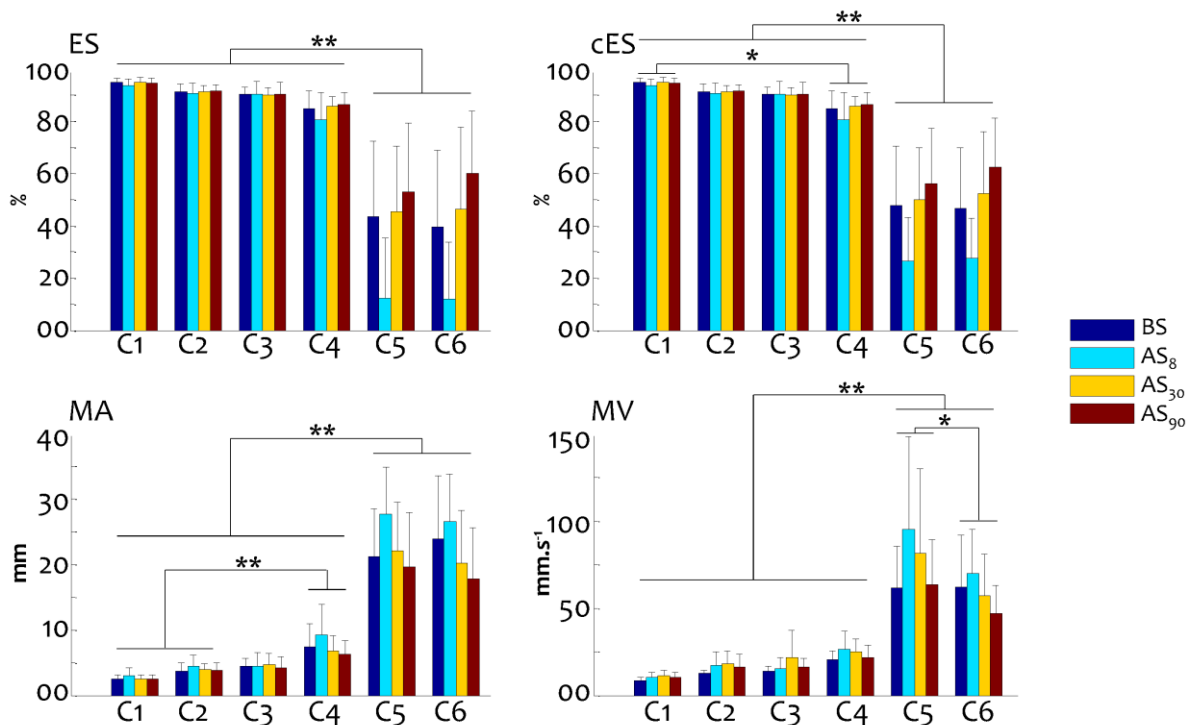


Fig. 1. Mean values (+ SD) of the equilibrium scores (ES), the continuous ES (cES), the mean amplitude (MA) and the mean velocity (MV) of the six conditions of the sensory organization test (C1 to C6) observed before (BS), eight (AS₈), thirty (AS₃₀) and ninety (AS₉₀) days after surgery. *: statistically significant, $p < 0.05$; **: statistically significant, $p < 0.01$.

DISCUSSION

We assessed herein the time-course (pre- and post-uVD) of balance control of VS patients performing a SOT among four postural variables and found similar balance compensation, especially for C5 and C6, whatever the postural variable used. Moreover, the results of the unsupervised clustering analysis (*see supplementary materials*) showed that each whole dataset behaved quite similarly in distinguishing two main SOT outcomes, although the classification was of different level among the postural variables.

This study confirmed that the balance compensation in VS patients induced large changes in their ability to use vestibular cues to maintain balance since significant differences among the evaluation stages, especially for C5 and C6, were found whatever the postural variable used [2,7]. As already addressed [8,9], similar ES (and in a lesser extent cES) values could be obtained from different combinations of postural strategies, which potentially might biased the characterization of the balance compensation of VS patients. Nevertheless, MA and (in a lesser extent) MV allowed to characterize similar changes in balance control, while they were based on different assumptions than ES (and cES) to represent the overall postural stability. Therefore, despite the different assumptions of each postural variable, the central adaptive mechanisms allowing a recovery in the ability to manage vestibular cues for balance control, called balance compensation, could be quantified based on the most challenging conditions of the SOT. In addition, a higher peak-to-peak sway (lower ES or cES) was accompanied by an increase in CoP trajectories amplitude (higher MA) over the whole trials at a higher velocity (higher MV) suggesting that patients needed a broader amount of information to compensate for the altered vestibular function.

In conclusion, the four postural variables used herein allowed estimating similar balance compensation of VS patients who underwent an uVD, especially during challenging postural tasks which necessitate a substantial contribution of vestibular inputs in maintaining balance. Nevertheless, due to some shortcomings in its computation, it appeared that ES might lead to

overestimation in the time-course of postural recovery of such patients (*see supplementary materials*). In line with previous reports [9,10,12], it could be recommended to provide a new definition of ES that would represent a measured physical parameter instead of CoM estimates.

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CONFLICT OF INTEREST

The authors have no conflicts of interest that are directly relevant to the content of this study.

ETHICAL APPROVAL

SOT outcomes of human patients used in this study were gathered as part of the clinical trial number NCT01743248 (ClinicalTrials.gov). Our study was approved by an appropriate Human Ethics Committee (*Comité de Protection des Personnes de Lorraine*; Approval Number: 12.06.01).

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Does the postural variable affect the determination of balance compensation level in vestibular schwannoma patients?

The unsupervised clustering analysis (Supplementary materials)

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METHODS

To summarize the whole dataset of each postural variable into a limited set of homogeneous groups called clusters, the standard k-means method (*kmeans* Matlab® function) was used, in which the distance measure for k-means was the squared Euclidean distance. To determine the correct *k* value to use for each postural variable, a silhouette analysis was conducted [1]. The k-means cluster analysis was iterated by varying the *k* value between 2 to 6 and the appropriate *k* value was considered from the highest average silhouette width. To determine if there was an influence of the postural variable and of the evaluation stage on the distributions of patients of each cluster, Chi-squared tests of independence were used. Measures of effect size in Chi-squared tests were provided with Cramer's V values (Φ_{Cramer}). The significance level was set at $p < 0.05$.

RESULTS

For each postural variable, the whole dataset behaved similarly with the highest averaged

silhouette width corresponded to a value of $k=2$. Therefore, the k-means algorithm defined two clusters (clusters #1 and #2). The centroid of each cluster represented an averaged SOT outcome (Fig. S1). For each postural variable, the scores in C1 to C4 did not differ between the two clusters. Nevertheless, the centroid of cluster #1 had higher / lower scores (ES and cES / MA and MV, respectively) in C5 and C6 in comparison with the centroid of the cluster #2. These two centroids could represent, even if not restricted to, typical SOT outcomes of VS patients at BS, AS₃₀ and AS₉₀ for cluster #1 and at AS₈ for cluster #2 (Table S1). This was especially true for ES, cES and MA, while for MV, solely few cases were identified as belonging to the cluster #2 in each evaluation stages. The calculated Chi-squared tests of independence confirmed that the distributions of patients belonging to the cluster #1 and #2 were related to the evaluation stages for ES [$\chi^2_{(3, N=72)}=24.4$, $p < 0.001$, $\Phi_{\text{Cramer}}=0.58$], for cES [$\chi^2_{(3, N=72)}=23.1$, $p < 0.001$, $\Phi_{\text{Cramer}}=0.57$], for MA [$\chi^2_{(3, N=72)}=8.6$, $p=0.04$, $\Phi_{\text{Cramer}}=0.35$], but not for MV [$\chi^2_{(3, N=72)}=5.5$, $p=0.14$, $\Phi_{\text{Cramer}}=0.28$].

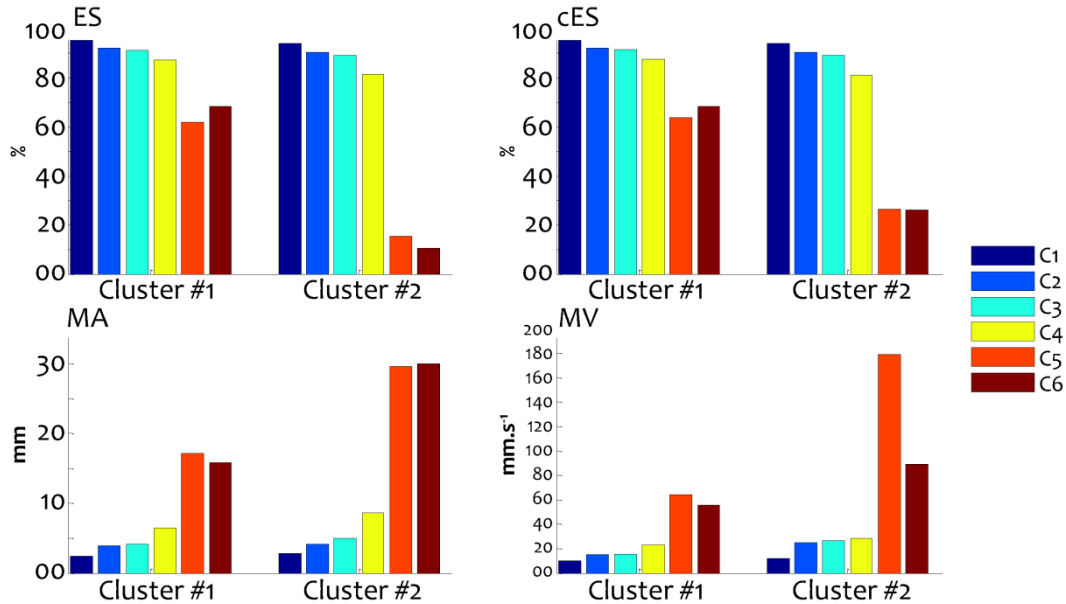


Fig. S1. Centroids of the clusters #1 and #2 determined from the k-means clustering of the whole dataset composed with equilibrium scores (ES), continuous ES (cES), mean amplitude (MA) and mean velocity (MV). Each centroid represents an average of the six conditions of the sensory organization test (C1 to C6) among the four evaluation stages.

Table S1. Distribution of patients (and their corresponding %) within each cluster according to the evaluation stages and the postural variables.

Postural variables	Cluster	Evaluation stages			
		BS	AS ₈	AS ₃₀	AS ₉₀
ES	#1	8 (44)	1 (6)	12 (67)	15 (83)
	#2	10 (56)	17 (94)	6 (33)	3 (17)
cES	#1	9 (50)	1 (6)	11 (61)	15 (83)
	#2	9 (50)	17 (94)	7 (39)	3 (17)
MA	#1	10 (56)	5 (28)	12 (67)	13 (72)
	#2	8 (44)	13 (72)	6 (33)	5 (28)
MV	#1	18 (100)	14 (78)	16 (89)	17 (94)
	#2	0 (0)	4 (22)	2 (11)	1 (6)

Note: ES: equilibrium score (%); cES: continuous equilibrium score (%); MA: mean amplitude of centre of pressure displacement (mm); MV: mean velocity of centre of pressure displacement (mm.s⁻¹); BS: before surgery; AS₈: eight days after surgery; AS₃₀: thirty days after surgery; AS₉₀: Ninety days after surgery.

Also, 60/72 cases (32 and 28 cases for cluster #1 and #2, respectively) were similarly classified between ES, cES and MA, while solely 38/72 cases (33 and 5 cases for cluster #1 and #2, respectively) were similarly classified between ES, cES and MV. Moreover, these distributions of cases across evaluation stages and clusters roughly agreed with the occurrence of falls during the SOT (Table S2).

Among all the patients, no fall occurred during all the trials of the first four conditions of the SOT, whatever the evaluation stage. The occurrence of

falls for the two remaining conditions of the SOT showed that patients were unable to maintain posture preferentially during C5 and at AS₈. Falls also occurred in some cases at the three other evaluation stages. The calculated Chi-squared tests of independence confirmed that the distributions of patients who felt at each of the three trials of C5 [$\chi^2(3, N=72)=22.8, p<0.001, \Phi_{\text{Cramer}}=0.56$] and of C6 [$\chi^2(3, N=72)=21.4, p<0.001, \Phi_{\text{Cramer}}=0.55$] were related to the evaluation stages.

Table S2. Occurrence of falling for the last six trials of the sensory organization test (SOT) among the four evaluation stages. Values are the number of falls (and their corresponding %).

SOT		Evaluation stages			
Condition	Trial	BS	AS ₈	AS ₃₀	AS ₉₀
C5	13	5 (28)	15 (83)	5 (28)	4 (22)
	14	5 (28)	14 (78)	5 (28)	4 (22)
	15	4 (22)	13 (72)	2 (11)	3 (17)
	16	7 (39)	15 (83)	5 (28)	2 (11)
C6	17	5 (28)	14 (78)	6 (33)	2 (11)
	18	5 (28)	13 (72)	6 (33)	2 (11)
C5	13-14-15	4 (22)	13 (72)	1 (6)	3 (17)
C6	16-17-18	2 (11)	12 (67)	4 (22)	1 (6)

Note: The two last lines contained the number of cases in which patients were falling for each of the three trials of a given condition of the SOT. BS: before surgery; AS₈: eight days after surgery; AS₃₀: thirty days after surgery; AS₉₀: Ninety days after surgery.

DISCUSSION

The results from the unsupervised clustering analyses allowed us to provide further insights into the key features of each whole dataset. Whatever the postural variable considered, we found two typical SOT outcomes (i.e., cluster's centroids) discriminating all the cases among the four evaluation stages. These two SOT outcomes differed by the values of the postural variable in C5 and C6 relative to the four other conditions: a SOT performed with results in C5 and C6 close to those in C1-C4 (cluster #1) and a SOT performed with distant results in C5 and C6 relative to those in C1-C4 (cluster #2), likely due to several falls in C5 and C6. Nevertheless, the discrepancies in the ability of each postural variable to correctly classify each case might characterize the influence of the postural variable selection on balance compensation estimation. A first hypothesis would be that the ES provided the highest dichotomous dataset in assigning a unique score of "0" when a patient fell. This tended to increase the discrepancy among the evaluation stages, especially in C5 or C6 and might favorably bias the classification. But, when using cES, the classification of the different cases from the whole dataset within the two clusters led to almost the same results than ES. This suggested that assigning a unique score of "0", when a fall occurred, was not the sole computational factor providing a dichotomous dataset. A second hypothesis would therefore be that using two single peaks of the CoM sway itself derived from a low-pass filtering of the anteroposterior CoP positions was the computational factor favoring the dichotomous dataset. Indeed, when taken into

account the full history of a given trial and the mediolateral component of the CoP displacements, the SOT outcomes classification among the evaluation stages differed. Even if using MA still allowed determining a classification dependent to the evaluation stages similarly to ES and cES, the effect size substantially decreased for MA. When using MV, the classification was independent to the evaluation stages and solely few cases were belonging to cluster #2. Therefore, it could be that MA, and even more MV, were more affected by subtle changes in CoP positions during a given trial in the lowest challenging conditions of the SOT (C1 to C4) than ES and cES. This might tend to decrease the discrepancy between the two cluster's centroids for MA and MV variables and thus decrease the ability of such variables to correctly classify all the cases. Finally, the inability of MV to correctly classify cases within the cluster #2 might confirmed that this postural variable seemed to be inappropriate to follow-up the balance control of VS patients [2,3].

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