SENSORY IMPAIRMENTS IN QUIET STANDING IN SUBJECTS WITH MULTIPLE SCLEROSIS

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ABSTRACT

Balance disorders and falls are frequently observed in subjects with multiple sclerosis. Along with motor impairment sensory disorders and integration deficits of sensory inputs lead to inadequate motor responses. The assessment of these sensory disorders in an every day tasks, such as upright stance, increases our knowledge of postural control in this pathology thus promoting more effective treatments. The aim of the study was to describe sensory impairments and sensory strategies in different sensory conditions.

A stabilometric assessment was carried out in a consecutive convenience sample of 53 subjects. The age of the sample was 52.7 (21.1) years; the onset of pathology was 27.20 (14.5) years before the assessment. Balance was assessed in six sensory conditions. The impact of pathology on balance control was shown by the high percentage of abnormal scores: 75% of subjects with MS showed abnormal scores even in the eyes open condition. The alteration of a single sensory input led to an increase of abnormal scores in up to 82% of subjects. Almost all subjects showed abnormal scores in the vestibular conditions where 22% of them fell. The pattern of the subjects' performance in the six sensory conditions suggests that balance control may be more correlated to the number of reliable sensory inputs than the nature of the sensory input itself.

INTRODUCTION

Disturbance of balance and falls are commonly observed in subjects with multiple sclerosis (MS). Balance disorders are reported as one of the initial symptoms of the disease [i]. Epidemiological studies have found that 23% of subjects with MS show evidence of cerebellar and brainstem involvement already at disease onset and that this figure increases to 82% after longstanding illness [i]. About 70% of subjects show ataxia and sensory system involvement [ii]. Moreover, balance impairments and falls are frequent in this population of subjects [iii, iv].

Adequate balance relies on accurate perception of physical input from the visual, somatosensory and vestibular systems [v, vi] as well as their integration. A deficit in these two steps leads to inadequate motor responses [vii] which are frequently observed in subjects with MS [viii]. The ability of the central nervous system (CNS) to use the three sensory inputs and to weigh them has to be assessed in order to plan efficacious rehabilitation strategies.

The most commonly used technique to assess balance is to record displacement of the center of pressure on a force-measuring platform (stabilometry). Classical testing compares subject's body sway in eyes open and eyes closed conditions. Sensory integration deficits have also been investigated by stabilometry. An approach to study these deficits has been described by Nashner and colleagues [ix]; Shumway-Cook adapted the test to assess subjects without the use of a stabilometric platform [x]. This study used the protocol adapted by Shumway-Cook with a stabilometric platform. The subjects are required to stand still in upright position for 30 seconds in six sensory conditions. The first three conditions are: C1. eyes open, C2. eyes closed and C3. Sway reference visual enclosure was obtained by a surrounding visual device swaying consensually with subject's body sway. The other three sensory conditions (C4-6) are the same but with the addition of foam pads placed under subject's feet.

Stabilometry has been used to investigate balance disorders in subjects with MS. In general these studies reported just antero-posterior sways. Daley and Swank [xi] assessed 113 subjects in the eyes open / eyes closed conditions. Of the subjects categorized as actively ambulant but with moderate impairment of function 30 and 40% showed abnormal body sway in the eyes open and eyes closed conditions respectively. The percentages of subjects still ambulant but severely impaired with abnormal body sway were 69 and 100% respectively for the eyes open and eyes closed conditions. Moreover, they found a correlation between body sway and a neurological examination.

Ramdharry et al [xii] assessed balance impairments in the eyes open and eyes closed conditions with feet together and apart. MS subjects swayed more than controls under all conditions. Statistically significant increase of sway was also observed in eyes closed vs. eyes open and feet together vs. feet apart conditions.

Nelson et al [xiii] assessed MS subjects using the approach developed by Nashner. The paper reported just antero-posterior sway. Considering a global composite score of the six sensory conditions they found differences between subjects with a high and low functional status. 30% of subjects (7 subjects) with high functional status showed abnormal scores. Of these 7 subjects, four showed broad sensory integration deficits, two subjects had a vestibular deficit (impaired performance in condition 5 and/or 6), 1 subject showed somatosensory and vestibular deficits (abnormal scores in conditions 2, 3, 5 and 6). 58% of subjects (7 subjects) with low functional status showed abnormal scores. Four subjects showed vestibular impairments and two subjects had vestibular plus visual or somatosensory dysfunction, one subjects showed broad sensory deficits. Group comparison showed that the high functional group had abnormal sway just in the eyes closed condition and performed within the normal scores for the other sensory conditions. In contrast, the low performance group performed below normal scores in all conditions except in conditions C4 and C6.

The effects of pathology on the balance system have also been investigated with dynamic platforms. In this experimental set-up the platform is rotated and/or translated. Jackson [xiv] found longer latencies of muscular responses during platform displacements with respect to healthy subjects and less ability to minimize antero-posterior sway after unexpected support surface rotation.

The aim of this study was to describe sensory impairment in a sample of subjects suffering from MS. Along with AP sway we investigated sway in the medio-lateral (ML) direction, length of the path, and velocity of sways in both planes. These variables may be more useful than AP sway alone to describe sensory impairment in this population of subjects.

MATERIALS AND METHODS

A consecutive convenience sample of subjects with multiple sclerosis was assessed. To reduce selection bias we recruited both inpatient and outpatients subjects referred for a rehabilitation program or for a periodical assessment to the Department of Multiple Sclerosis or the rehabilitation unit of the XXXXXX. Subjects who met the following inclusion criteria were enrolled in the study: clinically or laboratory definite relapsing–remitting, primary or secondary progressive multiple sclerosis [[xv]], ability to stand independently in the upright position for 30 seconds, ability to walk for 6m even with an assistive device. The sample consisted of 53 subjects, 13 males. The age was (mean and (SD)) 52.7 (21.1) years; the onset of pathology was 15.20 (6.53) years before the assessment. Fifteen subjects were dependent on assistive devices (cane or walker). The percentages of subjects with primary progressive, secondary progressive and relapsing remitting type of MS were: 11.1, 51.8, 37.0 respectively . Sixteen healthy subjects (HS) were tested to provide normative data. Subjects were selected among the employees of XXXX, six were men, mean age was 45.8 (11.8) years. No subjects reported any musculoskeletal or neurological conditions that precluded their participation in the study.

The assessment was carried out between April 2004 and March 2007.

Clinical Assessment

To describe the functional characteristics of the sample a clinical assessment was carried out at the beginning of the study. After informed consent was obtained one test of static balance and one test of dynamic balance were administered along with a self-administered scale on balance confidence. Berg Balance Scale (BBS); this scale rates balance skills from 0 (cannot perform) to 4 (normal performance) on 14 items with a maximum total score of 56 [[xvi]]. Dynamic Gait Index (DGI); this scale measures the mobility function and the dynamic balance [[xvii]]. The performance is rated on a 4-point scale. The score ranges from 0 to 24 (best score). Activities-specific Balance Confidence scale (ABC); this is a scale in which the subject rates his or her perceived level of confidence while performing 16 daily living activities [[xviii]]. Scores range from 0 to 100, where 100 means high level of confidence in balance skills. The psychometric properties of the scales have been assessed in people with multiple sclerosis [[xix],[xx]]. The functional level of subjects with respect to balance disorders is shown in Table 1.

Table 1. ABOUT HERE

Instrumental Assessment

The stabilometric assessment was carried out with a monoaxial platform. The Technoboby© platform[1] consists of three strain gauges placed under a circular surface of 50 cm of diameter at 120 degrees to each other (Figure 1) and has a 20 Hz sampling frequency. Subjects were tested wearing their normal shoes and clothes. The position of the feet on the platform was standardised using a V shaped frame. The subjects had to place the medial borders of the feet against the frame, the malleolus were aligned to vertical bars (White dots in FIGURE 1) . The distance between one malleolus and the other was 3cm. The medial borders of the feet were extrarotated 12 degrees with respect to the antero-posterior axis. The subjects were tested sequentially from condition C1 to C6 for 30 seconds in each condition as described above. The surrounding visual device used for condition C3 and C6 consisted in a “dome”. It is a spherical structure constructed from a paper lantern that is positioned on the subject's head. The subject can just see a cross added on the inside of the dome. The cross is about 30 cm from the subject's eyes. When properly fitted peripheral vision is restricted completely and the dome moves in phase with the subject's head movements. Outpatient subjects were recruited during periodical assessments. Given the limited amount of available time for outpatient subjects a shorter evaluation was carried out: condition C3 and C6 were not carried out.

During the testing the subjects were told to stay still and not talk, an operator stood behind the subject to prevent falls.

FIGURE 1. ABOUT HERE

The instant positions of the CoP was used to calculate the following variables:

Sway AP (or ML) [mm]: mean CoP excursion in the antero-posterior (AP) or medio-lateral (ML) axes; calculated as the standard deviation of raw AP (or ML) CoP position.

Length [mm]: length of CoP trajectory. Computed as sum of the displacements of CoP on the platform surface for each frame.

Velocity AP (or ML) [mm/s]: velocity of CoP along the AP (ML) axes. Computed as the first time derivative of the CoP displacements.

Clinical and instrumental assessments were carried out in one session.

Data analysis

The Technobody platform measures vertical ground reaction forces and is routinely used in clinical practice in our institution. The validity of the measures was assessed comparing data obtained with the Technobody© platform with a gold standard. The platform under study was placed upon a Kistler© platform. The Kistler platform sensors are four triaxial piezoelectric transducers, its analogue output is usually sampled at 996 Hz. Any load applied to the upper platform was

[1] http://www.tecnobody.it/

measured also by the lower one. The CoPs measured by the two platforms were transformed into one unique reference system to compare them. A static standing test with eyes open was administered.

The following indexes were computed considering the two COP measurements: Root Mean Square (RMS) of the difference between signals and the Pearson's correlation coefficient.

To assess the impact of the time length of the test we compared two consecutive assessments respectively of 30 and 60 seconds in a sample of 12 subjects with MS; two minutes rest was allowed between assessments. Intraclass Correlation Coefficient[xxi] ($ICC_{2,1}$) and the Bland Altman method[xxii] were used to assess reliability. Level of significance was set at 0.01.

The objective of the study was to characterize the sensory impairments of subjects with MS, for that reason and also to reduce the number of statistical tests no statistical comparisons between groups (HS and MS) were done except for the frequencies of abnormal scores; the same was true for the comparisons within the HS group.

The analysis was hampered by the frequent falls observed in conditions C5 and C6. To take into account those falls a transformation of data was done taking the reciprocal of the actual values and setting a zero in case of a fall. This approach, frequently used with other stabilometric systems, may lead to a distortion in the assessment; to verify this potential distortion transformed and not transformed data were compared. Friedman test was used to assess the differences among conditions. Cochrane's Q test was used to compare the percentages of falls among conditions. Level of significance was set at 0.01 for all tests.

RESULTS

We compared the instant position of the COPs of the two platforms during the standing task. The Pearson's correlation coefficients were 1 and 0.98 respectively for the AP and ML axes. The RMSs of the differences of the signals from the two platforms were 0.3 and 0.5mm for the ML and the AP axes.

The comparisons of two consecutive 30 and 60s trials yielded similar results for four variables (Table 2). Conversely Sway ML showed a 21.5% increase of sway. Intraclass correlation coefficients were satisfactory (>0.90) for Vel AP and Vel ML and acceptable for the rest of the variables - (0.77 to 0.79). A visual evaluation of the Bland-Altman scatter plots did not reveal bias, outliers or relationships between the variances in measures with the size of the mean.

Table 2. ABOUT HERE

Frequencies of falls and sub-group analysis.

The frequencies of falls in the six sensory conditions were: C1: 0%; C2: 6%; C3: 3%; C4: 6%; C5: 22%; C6: 13%. The overall effect for conditions was highly statistically significant (Q test, $p<0.004$). Among all comparisons, statistically significant differences were found using the Q test between condition C5 and all the other conditions except C6: C1 and C5 ($p<0.002$), C2 and C5 ($p<0.01$), C3 and C5 ($p<0.01$) C4 and C5 ($p<0.008$). Almost statistically significant differences were found between C1 and C6 ($p<0.04$).

The percentages of subjects who scored higher than two standard deviations with respect to healthy subjects or fell are reported in **Table 3**.

Table 3 ABOUT HERE

The rate of abnormal scores in the eyes open condition ranged from 16.7% to 75.0% across variables. The highest rate of abnormal scores was observed for condition C6 for Vel ML, Vel AP and Length. The conditions C5 and C6 also showed the highest means of abnormal scores across variables: the mean of the row for condition C5 was 84.8% of abnormal scores, the mean for condition C6 was 89.9%. With respect to variables the highest mean of abnormal scores across conditions were observed for Length (78,5%), followed by Vel ML (77.4%).

For C1 (eyes open condition) 75% of patients had an abnormal performance in Length, a variable that describes the amount of excursion of the CoP in 30s and consequently the energy expenditure. With respect to the same variable the highest percentages of abnormal scores was observed in condition C6 (97.0%). The percentage of subjects who showed abnormal scores in all six sensory conditions was 41.0%.

Of those patients that completed the test under all six conditions (38) an overall statistically significant difference was found among conditions ($p<0.002$). Statistically significant differences were found between C1 and C6 ($p<0.002$), C2 and C6 ($p<0.001$), C3 and C6 ($p<0.01$), C4 and C6 ($p<0.003$). An almost statistically significant difference was found between C5 and C6 ($p<0.02$).

Figure 2. panel A depicts the antero-posterior and medio-lateral sways in the six sensory conditions for the MS and HS group. With respect to the antero-posterior axis three main levels of sway performances were observed for the MS group: the first level was the eyes open condition (C1), the second level was formed by conditions in which one sensory input was altered (C2-C3-C4) and the third level was formed by conditions in which two sensory inputs were altered (C5 and C6).

In Figure 2. panel B the variables depicted in panel A above are shown after transformation (x^{-1}). The pattern was the same as above for Sway AP but the transformation affected the range of variability within each sensory condition due to the number of 0s in conditions C5 and C6.

A pattern similar to that observed in panel A was found for Vel AP and Length (Figure 2. Panel C and D), with a slight increase of values in the eyes closed condition and a reduced length of sway in C5 with respect to C6 probably due to the reduction of sway amplitude on the ML axis.

To verify if there was a statistically significant difference between the three levels of performance, and not among the conditions forming the level, we computed the Friedman's test for the variable Length after reciprocal transformation. We found an overall highly statistically significant difference ($p<0.0001$) among the six conditions. Post hoc analysis revealed statistically significant differences between the first level (C1) and the other levels ($p<0.0001$), between the second level (C2, C3 and C4) compared to third (C5 and C6, $p<0.0001$). No statistically significant differences were found comparing C2, C3 and C4. The same was true for the comparison between C5 and C6.

Figure 2. ABOUT HERE

Out of the whole group of 53 subjects with MS, 15 subjects (28%) showed a paradoxical effect, this occurred when subjects had an abnormal score in C1 and a normal score in one or more other sensory conditions. Considering only the 15 subjects above the paradoxical effect was mainly observed in condition C4 (69%), followed by condition C2 (30%) and C5 (30%); surprisingly, in conditions C3 and C6 a paradoxical effect was observed only in one case.

Finally the correlations between instrumental and clinical measures were computed. We found only a moderate, statistically significant correlation between Sway AP and the BBS scale and just for condition C4 ($r=0.47$; $P<0.004$).

DISCUSSION

The aim of the study was to describe the effect of sensory impairment on balance in a sample of subjects suffering from MS. The results show the effects of the pathology on balance control.

Balance disorders are evident considering the high percentages of subjects that had abnormal scores in condition C1,probably due to both motor and sensory impairments. The impact of the impairment of sensory reweighing on balance was also observed, the alteration of a single sensory input led to an increase in the frequency of abnormal scores for 82% of the individuals. The alteration of two sensory inputs led to a sharp increase of abnormal scores for almost all (97%) of the individuals and many of them fell during the test.

With respect to validity of measures the comparison between a monoaxial platform and a triaxial platform used as gold standard showed good concurrent validity, with correlation coefficients close to 1. The mean differences between the signals of the two platforms were small (0.3 and 0.5mm respectively for ML and AP axis) compared with the mean sway amplitude observed in subjects with MS (about 4 and 8 mm, see Figure 2).
The comparison between 30 and 60s of assessment time showed in general a slight increase of values between the two trials, the percentages of increment were low (range 1-10%) except for Sway ML that showed a relevant increment of 21%.

The variables that best distinguished between healthy subjects and individuals with MS were Length and velocity of CoP in ML and AP directions. The ability of these variables to differentiate between groups was best observed in conditions C5 and C6 where subjects were primarily required to use vestibular input.

The condition C1 allows the analysis of performance in quiet standing in the eyes open, firm surface condition. In agreement with Daley et al [xi] we found a high percentage of subjects with abnormal scores. The high frequency of abnormal scores in this condition reflects the difficulty of subjects with MS in maintaining balance even with all the sensory inputs available. In this condition the CNS appears to control better AP and ML sways with respect to the other variables.

The increased velocity of excursion of the CoP in both planes in more than half of the subjects confirmed the difficulty of postural control. Moreover, the increase of CoP velocity in both planes increases the energy expenditure as demonstrated by an increase of the length of the CoP path (see Figure 2, Panel D).

The analysis of the next three sensory conditions allowed us to study subjects' performance with one sensory input removed or altered. We would predict that subjects with MS were visually dependent [xi]. The sample actually showed a decrease of performances in eyes closed condition (C2) but similar performances were obtained also in conditions C3 and C4 both for frequencies of abnormal scores (**Table 3**) and magnitude of considered variables (see Figure 2). The reduction of performances with respect to C1 were also observed in a published study by Baloh et al [xxix]. They found a decrease in performance in conditions with eyes closed and on the foam with respect to condition C1 in subjects with vestibular disorders and subjects with cerebellar atrophy.
With respect to healthy subjects the subjects with MS had difficulty in controlling posture with just two sensory systems available. While healthy subjects maintained the same level of performances from C1 to C2, C3 and C4, subjects with MS showed a statistically relevant decrement of performance with respect to the eyes open condition. These results indicate two issues: The first one concerns the difficulty in controlling the CoP with only two sensory inputs available. The second is the ability of the CNS to use sensory strategies to keep the same level of performance irrespective of the sensory input available.
One possible explanation for these results could be the quality of information that arrives to the CNS. Neural signals are inherently noisy thus limiting the reliability of information [[xxiii]]. Reliability is further limited by the precision of the sensory receptors [[xxiv]]. In healthy subjects the small range of sway movements may not trigger receptors beyond their physiological thresholds. In fact, it appears that physiological levels of sway are close to the thresholds of vestibular, joint, and muscle receptors [[xxv]]. In individuals with MS the noise in the sensory system may be increased and

level of accuracy may be decreased. This may be due to the demyelination of tracts carrying information from the periphery to the CNS and/or systems that integrate the information. This unreliability of sensory signals translates into uncertainty and variability at higher levels where the inputs are weighed and used to plan correct motor responses. The increase of noise may decrease the ability of the CNS to have spatial information about the relative position of body segments and the relative position of body segments with respect to the gravity vector and base of support. This may cause difficulty for the CNS in using the gravity vector and information about the base of support as a frame of reference in defining the body schema. This uncertainty leads to noise in motor commands resulting in inaccuracy of forces controlling the CoM. Finally, correct estimation of the position of body segments relies on the comparison of sensory inputs with the afferent copy sent by CNS to the motoneuron pool. Muscle weakness and fatigability impose an increased motor output further increasing the mismatch between sensory inputs and the efferent copy [[xxvi]].

The second concern is the ability of the CNS to use sensory strategies to integrate redundant sensory inputs. Sensory strategies allow the selection and the integration of the relevant incoming inputs thus allowing the balance system to adapt its output to a variety of environmental contexts and tasks. In the administered protocol when subjects changed the sensory environment, they needed to re-weigh their relative dependence on each of the senses. The ability of healthy subjects to adjust the relative weight of sensory inputs was demonstrated by the stability of performances in conditions C2-C4. Also individuals with MS were able to maintain the same level of performance in different sensory conditions. It appears that individuals with MS are able to effectively use sensory strategies to maintain the same level of performance irrespective of the available sensory inputs.

Even though performances were the same across conditions with only one sensory input altered this does not mean that there should not be an emphasis on one sensory system over another in rehabilitation. The precedence for the rehabilitation of one sensory system over another should be given considering spared function of the individual's sensory system, its possibility to recover and the importance of the sensory input in activities of daily living.

The analysis of Conditions 5 and 6 highlighted the difficulty in maintaining balance in vestibular conditions. Our results are in agreement with those obtained by Nelson et al [xiii] and Frohman et al [[xxvii]]: we found a high rate of falls and a sharp increase of sways in vestibular conditions. From a signal noise point of view the impairment observed in vestibular conditions reflects the difficulty in keeping the upright stance with just one sensory input. This difficulty is present in the HS group with no vestibular impairment and is further increased in the MS group (see Figure 2), maybe due to demyelination of the VIII cranial nerve, the vestibular nuclei or the vestibular projections to other neural systems. At present there is not the possibility of easily removing the vestibular cue which would allow the assessment of subjects' balance performance with just a visual or a somatosensory cue. However leaving only a visual or only a somatosensory cue would probably result in patterns similar to that observed in C5 or C6 where only the vestibular cue is available. The high values of standard deviations observed for the MS group across all conditions is due to a high variability of performances between individuals and within individuals among the six sensory conditions. Thus a stabilometric evaluation of performance is necessary to assess the unique characteristics of each patient.

With respect to the observed paradoxical effects the relationship between availability of sensory inputs and stability was not clear . Almost one third of subjects with MS who had an abnormal score in the eyes open condition showed an improvement of performance in other, more challenging sensory conditions. Of those presenting with this paradoxical effect in more than two/thirds the events were observed with the inclusion of the foam pad under the feet. The reason for this effect observed is not clear. The paradoxical event might arise because of the difficulty of the CNS in using all three inputs to generate a correct postural response leading to postural over correction (or hypermetria) in response to detection of small displacements of CoM. Hypermetria has been observed in subjects with cerebellar involvement during base of support displacements with larger than normal surface-reactive torque responses and exaggerated and prolonged muscle activity [xxviii]. Hypermetria is a consequence of cerebellar damage and lesions in this area of the brain have been observed in about 80% of the subjects with MS [i]. In condition C1 the cerebellar lesions and the sum of incoming inputs may lead to abnormal response, the foam pad may reduce the gain of somatosensory information leading to a reduction of hypermetric corrections. Moreover, the foam could be viewed as a dumping system able to reduce the high frequency of sway observed in subjects with cerebellar damage [xxix].

In contrast to other studies [xii,xiii] we observed a lack of correlation between clinical and instrumental measures. The stabilometric platform and the clinical scales used in this study appear to assess two different aspects of balance control. It is possible that lower correlation coefficients were due to a lack of sensibility of the clinical scales. Moreover, the Berg Balance Scale assesses balance not only in the quiet upright position but also during turning, bending and other tasks. Subjects with MS have more difficulty during head/body turns with respect to unperturbed stance [xx]. The lack of correlation observed between the Berg Balance Scale and the stabilometric measures may thus be due to different performances in tasks requiring head/body turns with respect to unperturbed stance.

A major limitation of the study is the selection bias. The data collected can only be generalized to other populations of subjects with MS with similar clinical characteristics. The differences observed from other studies may in part reflect the functional differences in the samples.

Another limitation of the study was that the only studied task was quiet standing. Although stabilometric assessment in quiet standing is important to collect information about the state of sensory systems, the instrumental assessment of other clinically significant tasks, such as head turns and forward bending, might better describe sensory and motor impairments in tasks more related to activities of daily living.

In conclusion, subjects with MS have relevant balance disorders observable also when all three sensory systems are available. The decrease of available inputs leads to a sharp increase in sway and frequency of falls. The pattern of the subjects' performance in the six sensory conditions suggests that balance control may be more correlated to the number of reliable sensory inputs than the nature of the sensory input itself. Situations in which individuals with MS have to stand in upright position in the dark and/or on a compliant surface (e.g. a thick mat) increase the likelihood of falls. Other common situations occur when subjects move the head, or the surrounding visual scene is moving. The mismatch caused by these situations challenge the balance systems and can lead to loss of stability.

The high variability and the paradoxical effect observed imposes the necessity of individual assessments of balance skills in subjects with MS. In general our findings suggest that a specific and tailored treatment for sensory disorders has to be considered. The ability of subjects to switch from one sensory input to another may be an indicator of the capability of recovery of function of the CNS.

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Table **Errore. Solo documento principale.**. Functional characteristics of sample.

	Mean	SD
Berg Balance Scale	47.0	6.0
Dynamic Gait Index	15.1	5.5
Activity Balance Confidence	49.8	23.7