

## REVIEW ARTICLE

# The Fall in Older Adults: Physical and Cognitive Problems

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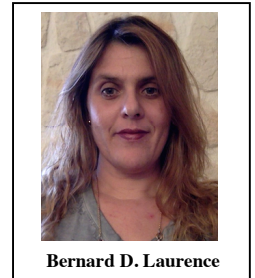
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**Abstract: Background:** The aging of posture and balance function alters the quality of life in older people and causes serious problems in terms of public health and socio-economic costs for our modern societies.

**Methods:** This article reviews the various causes of imbalance and dizziness in the elderly, and considers how to prevent falls, and how to rehabilitate a faller subject in order to regain a good quality of life. Two effective ways of intervention are discussed, emphasizing the crucial role of physical activity and cognitive stimulation, classic or using the latest technical advances in virtual reality and video games.

**Results:** Fall in the elderly result from aging mechanisms acting on both the sensorimotor and cognitive spheres. The structural and functional integrity of the peripheral sensory receptors and the musculoskeletal system deteriorate with age. The brain ages and the executive functions, memory, learning, cortical processing of information, sharing of attentional resources and concentration, are modified in the elderly. Psychological affective factors such as depression, anxiety and stress contribute also to speed up the sensorimotor and cognitive decline. The rehabilitation of the postural balance in the elderly must take into account all of these components.

**Conclusion:** The aging of the population and the increased of lifespan are a challenge for our modern societies regarding the major health and socio-economic questions they raise. The fall in the elderly being one of the dramatic consequences of the aging equilibration function, it is therefore imperative to develop rehabilitation procedures of balance.



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**ARTICLE HISTORY**

Received: March 14, 2016  
Revised: May 16, 2016  
Accepted: June 27, 2016

DOI: 10.2174/1874609809666160630124552

**Keywords:** Postural control, sensorimotor aging, cognitive aging, psychological affective factors, fall, fall prevention.

**INTRODUCTION**

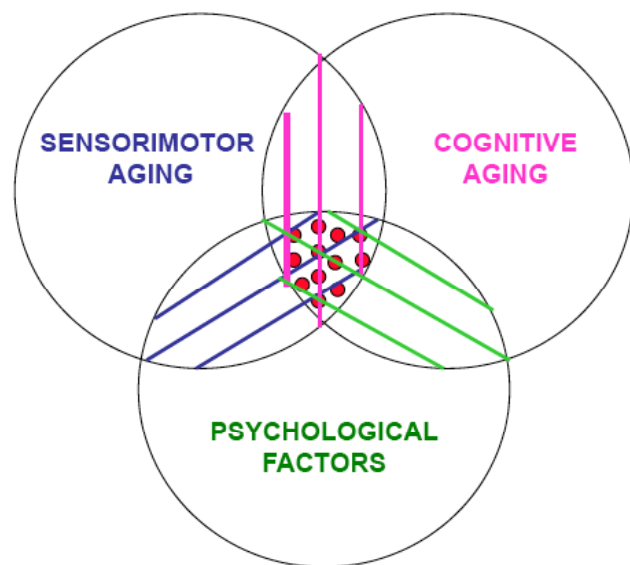
In humans, the balance function ensures the maintaining of erect posture at rest (static postural control), and during daily activities such as walking, running, jumping... (dynamic posture control). We have reported in a previous article how the control of posture and balance is performed, and what was the role of the genetic and cognitive models in the regulation of static and dynamic balance [1]. It has been mentioned that balance function is based essentially on the central integration of sensory information from the three main reference frames: the allocentric (vision), egocentric (somesthesia), and geocentric (vestibular system) frames, involving both rapid (musculo-articular proprioceptive feedback, vestibular and cutaneous foot afferents) and slower (visual feedback) sensory loops. The balance control is based in a non-pathological adult subject on automatic processes involving various neural networks (spinal cord, brain stem). In addition, the environmental context where the regulation of balance takes place plays a crucial role in the choice of the best-adapted behavioral strategy, which can differ for the

same task between the individuals (vicarious idiosyncratic strategies, sensory preferences). Moreover, feed-forward mechanisms modify the spatial and temporal patterns of balance control by taking into account the expected postural consequences of the action (anticipation). And the internal representation of the task (fear of height, for instance) induces also changes in balance strategy. Anticipation, internal representation, environmental context and attention load are key elements highlighted in the cognitive models. They put forward the concept of plasticity in the regulation of balance and the crucial role of the cortical control, which oversees the more automatic processes described by the genetic models at the spinal level. The deterioration of the balance function with age originates from changes at these different levels, from the periphery (sensory receptors, muscles) to the central nervous system. Aging reduces the sensitivity and the discriminatory power of the sensory receptors, and affects the central integration of the sensory information. Reducing the force of the effectors with age also contributes to the deterioration in the performance of the balance function. And the cognitive decline observed in the elderly modifies deeply the anticipatory and attention capacities required to perform both simple posture-locomotor tasks and more complex day life performances with dual tasking. Taken together, the risk of fall is

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dramatically increased with aging. In addition, the sensorimotor and cognitive impairments observed in the elderly have significant psychological repercussions such as loss of interest, sadness and depression, stress and anxiety, which further contribute to increase the risk of falling and to degrade the quality of life (Fig. 1). The mean age of the world population is increasing year by year, and demographic studies show that this phenomenon will increase over the future decades [2]. Deterioration of balance and quality of life with advancing age is therefore a major socio-economic challenge for our modern societies. How to prevent falls and how to rehabilitate the balance function, should be the questions regarding the control of health care costs. Indeed, it was estimated that 30% to 40% of the elderly fall at least once a year in the situations of everyday life, and that their probability to fall was 90% higher compared to younger subjects [3]. Falling costs represent 1.5 % of the total health care costs in Europe [4].

The objective of this article is to analyse the main neurophysiological mechanisms of aging and cognitive aging, causing falls in the elderly. We have grouped these mechanisms into three sections shown schematically in Fig. 1: aging of the sensorimotor functions, aging of the brain and cognitive processes, and the role of psychological affective factors.



**Fig. (1).** Interrelationships between sensorimotor aging, aging of the brain and cognitive processes, and psychological affective factors.

The hatched areas indicate an increased risk of fall and, the area containing both hatched and points correspond to the highest risk of fall (adapted from [196]).

## EFFECT OF AGING ON THE SENSORY SYSTEMS

Postural control is no longer considered simply as the interplay of static reflexes, but rather as a complex skill based on the dynamic interaction of sensorimotor mechanisms supervised by high-level cognitive processes. The two main functional goals of posture control are postural

orientation and postural stabilization [5]. Among the many functions of the posture control system is its ability to integrate the various sensory inputs for the purpose of orientating our body in the three-dimensional space, to coordinate our motor activities (standing, walking, jumping...), and to ensure that we can have a clear vision during self-motion or motion of the visual environment [6]. It is well established now that the sensory systems implicated in the orientation and the stabilization of the body in space are altered by aging [7].

The peripheral retina is a motion detector that interacts actively with posture control in the low range of motion velocity and motion frequency. Organic damages (macular degeneration) or functional alterations (amblyopia, reduced visual acuity) of vision are often associated with falls [8]. Evolving atrophic macular degeneration represents at least 80% of all macular degenerations and is currently without a standardized care [9]. Similarly, postural control impairments were observed in subjects with ocular convergence defects like heterophoria [10] and strabismus [11], or with capsular thickening (cataract) that reduces the vision of colours and contrasts. In general, any age-related involution process that alters the perception of space (visual field reduction) increases the risk of fall. Adults with visual impairments experience a loss of balance and mobility, which represents a barrier to independent life and enhances the fear of falling [12-14]. Ray *et al.* [15] indicated that women with profound vision loss showed a greater decline in postural control than men did.

Similar age-related impairments have been reported for the somatosensory and the vestibular systems. Recently, Lopez [16] showed that vestibular signals contribute to bodily perceptions ranging from low level bodily perceptions, such as touch, pain, and the processing of the body's metric properties, to higher level bodily perceptions, such as the sense of body owning, the sense of being located within this body (embodiment), and the anchoring of the visuo-spatial perspective to this body. Aging of the sensorimotor systems plays a major role in the deterioration of balance in old age (see [17] for a review). Hasselkus and Shambes [18] investigated the effects of aging on postural sway in upright and forward lean stance, in two age groups of female subjects (20 to 30 years, and 70 to 80 years old). The older adults demonstrated significantly larger sway areas than the young adults in both stance positions. Baloh *et al.* [19] have demonstrated that the velocity of sway is higher in older subjects compared with younger subjects, and the difference between young and older is greater with dynamic posturography than with static posturography. The number of muscle spindles in the soleus muscles - an important proprioceptive input for posture regulation - decreases with aging [20]. The effects of fatigue on postural control are more important when proprioceptive information at the ankle is altered. In particular, older adults have more difficulty and need more attention to stand quietly, compared with young adults [21]. In the same way, the number of mechanoreceptors in the foot sole is reduced, and this reduction is accompanied by a decrease in the plantar sensitivity that plays a critical role in the maintenance of the upright stance [22]. Indeed, Meyer *et al.* [23] reported that a plantar sensation was an important contributor to dynamic balance,

and the risk of fall was increased when this sensation was altered. In line with this, Patel *et al.* [24] found that torque variance was markedly larger in the elderly, and that both tactile sensitivity and vibration perception thresholds were considerably higher. The sense of position is also altered, presumably because of similar morphological and functional changes at the joint receptors level. The sense of touch tends to decline with aging, but this decline is not uniform across individuals and is more noticeable for spatial discrimination than for object recognition. Aging alters mostly the peripheral receptors and the central integration of the somatosensory inputs [25], but mechanical changes in the skin properties, like elasticity, seem also to play a role.

The otolith system plays a major role in the perception of verticality and of body orientation in space [26]. It is composed of the saccule and utricle located in the inner ear in the vertical and horizontal planes, respectively. The number and the morphology of the otoliths change with aging. While the calcite crystals have a 3-19  $\mu\text{m}$  long cylindrical body taking a 3 facets shape at their extremity in the younger subjects, they show demineralized pictures and are even fewer in the older adults. This degenerative process predominates in the saccule after 60-70 years. It alters the sensitivity of the mechano-electrical transduction at the peripheral level and the neural coding of the head movements. Otoconial debris can flow into the semicircular canals, and cause benign paroxysmal positional vertigo (BPPV) when they accumulate in the canals (canalolithiasis) or are deposited on the ampullary crests (cupulolithiasis). With aging, there is also a reduction in the number of the sensory hair cells, in the number of the afferent nerve fibers, and of the primary vestibular neurons located in the Scarpa's ganglion. These age-related morphofunctional changes are accompanied by a concomitant deterioration of the postural control (Fig. 2).

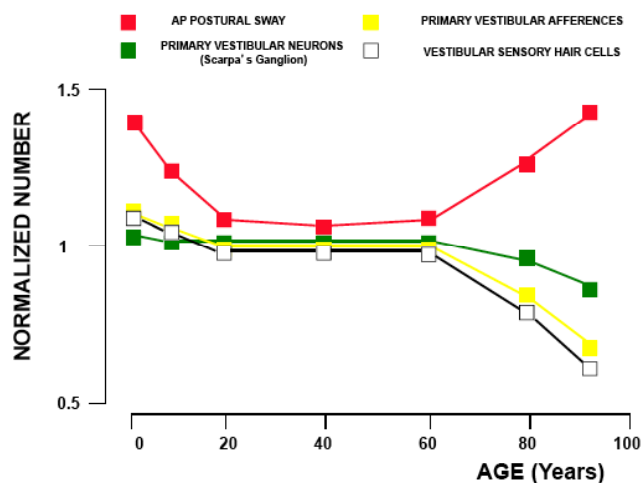


Fig. (2). Aging of the vestibular system.

Normalized representation (abscissae) of the development of the number of sensory hair cells in the vestibular epithelium (otolith system: open squares), the number of the primary vestibular afferences (grey squares), and the number of the primary vestibular neurons in the Scarpa's ganglion (grey squares) as a function of age (ordinates, in years). Postural sway in the sagittal plane (black squares) is reported for comparison with the histologic data. It is

shown that improvement of posture control from childhood to adulthood, and its deterioration after 60 years, are correlated to maturation and aging of the peripheral vestibular system (adapted from [196]).

Age-related hearing loss is characterized by a more or less symmetric sensorineural hearing loss more pronounced in the high frequency range. Age of onset, progression, and severity of hearing impairment show great variations in the population, but with a demonstrable increased prevalence in males [27]. Viljanen *et al.* [28] reported that old people with poor hearing acuity have a higher risk of fall. But the same result was observed in students with sensorineural hearing loss who showed greater instability in their postural control compared to normal hearing students of the same gender and age [29]. Auditory information may thus be important for tasks requiring sound localization, which can help for body orientation, of course for speech comprehension in noisy environments [30], and for safe mobility [31].

### EFFECT OF AGING ON THE MOTOR SYSTEM

Age-related skeletal muscle changes do not affect all muscles equally and modify the muscle fibers differently according to their type [32, 33]. It has been reported that aging is also accompanied by structural changes in the spinal networks that alter their functionality and the motor command. In the older adult, there is a 37% decline of the unmyelinated fiber density and a 38% loss of the myelinated fiber density [34]. It was estimated that the net loss of myelinated fibers together with those showing demyelination pictures is responsible for 10 to 20% reduction of the nerve conduction velocity in the elderly [35]. The degeneration of the efferent pathways is stronger in the anterior tibialis muscle, a dorsal foot flexor. It would reach 39% of the estimated number of motor units in adults aged 66 years and 61% at 82 years [36]. However, the isometric muscular strength does not seem reduced before 80 years, probably due to the collateral re-innervation of the muscles by intact nerve endings, which increase the size of the functional remaining motor units [36, 37]. It is also well known that the center of foot pressure (CoP) displacements correlates negatively with the maximal isometric torque (MIT) of the ankle muscles. Cattagni *et al.* [38] have suggested that measuring ankle torque could be used in routine clinical practice to identify potential fallers.

The loss of the muscle mass with aging (sarcopenia) is mainly due to the reduction in the size of the fast muscle fibers (type II), so that the elderly patients have a higher proportion of slow muscle fibers (type I). The force-generating capacity of the muscles and their contractile properties are more homogeneous therefore in the older subjects compared with younger subjects. Indeed, the aged muscles show a reduced functional working range and remain unable to contract at high velocities and to produce different levels of muscle force. A study of Laughton *et al.* [39] suggested that high levels of muscle activity are characteristics of age-related declines in postural stability, and that such activity is correlated with short-term postural sway. These structural and functional changes can be interpreted in the light of the aging model based on the two concepts of dedifferentiation and loss of functional

complexity of the systems [7]. Although sarcopenia is a highly significant problem in a public health perspective, clinical cut scores for specific populations are needed before this age-related muscle change can be diagnosed and treated [40]. Alexandre *et al.* [41] found that both sarcopenia and dynapenia were associated with mortality in older people, independently of socio-demographic, behavioural and clinical characteristics. Bone loss, more typical in post-menopausal women, further enhances this deficient peripheral musculoskeletal picture.

#### **EFFECT OF AGING ON THE INFORMATION PROCESSING**

It is now well established that the cerebral cortex contributes to postural control of both quiet standing and dynamic equilibrium. The morpho-functional changes earlier described at the peripheral sensorimotor and spinal levels are concomitant of morphological changes that occur at the brain level, in cortical areas known to regulate the postural control system. Modifications of both the gray and white matters have been reported. A reduction of the gray matter volume has been observed in magnetic resonance imaging investigations [42], which concerns both the neurons and the glial cells. The gray matter loss ranged from 4 to 16%, depending on age, in cortical regions including the somatosensory and motor areas, the prefrontal and the inferior parietal cortices [43, 44]. This volume reduction could characterize a loss of complexity of the neuronal connections (synaptic density, size of the neurons, presynaptic afferent terminals) rather than a loss of nerve cells *per se* [43], and it was correlated to the decline of the motor performance in the elderly [45]. Recently, Boisgontier [46] proposed that the early cell loss observed in older adults could prevent the cerebellum from outputting accurate estimates of intrinsic and extrinsic forces acting on the body, thereby increasing the computational load required to perform a motor task at the same level as in young adults. As age-related neuron death appears to prominently affect the cerebellum, the resulting impairment of predictive motor control is likely to have a major role in motor aging. In the white matter, composed mainly of myelinated axons interconnecting different brain areas, the volume reduction would start later, but this process would accelerate thereafter [47]. The volumetric loss of the white matter concerns primarily the corpus callosum; it would reach about 2.5% per decade, and would be partly responsible for the slower motor performances observed in tasks that require inter-hemispheric transfers [48].

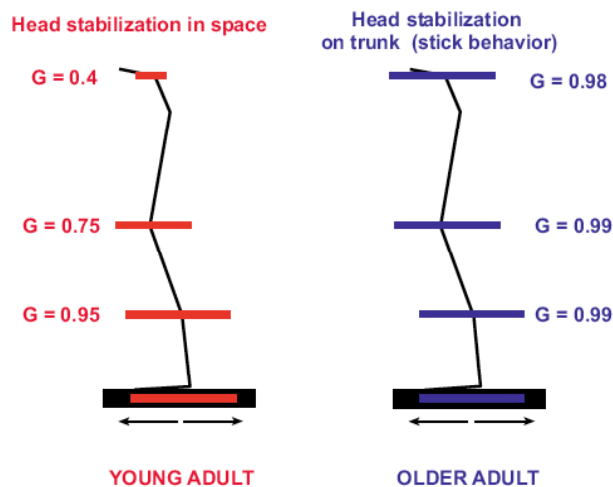
These age-related structural changes found at the spinal and cortical levels, reported so far mainly in conjunction with simple manual motor tasks, affect also the mechanisms that control complex motor tasks, including posture control and equilibrium [49, 50]. Correlations were made between these degenerative processes and the center of foot pressure (CoP) displacements observed in posturography studies [48, 51]. Diminished adaptive capacity with human aging may be reflected by a loss of the fractal-like, multiscale complexity within the dynamics of standing postural sway (*i.e.* CoP). Indeed, the study of Zhou *et al.* [52] indicate that an age-related loss of CoP complexity of magnitude series may reflect a clinically important reduction in postural control

system functionality as a new biomarker. The slower speed in the sensory data processing required for postural control would be due in part to the reduction of the white and gray matter volumes, and could explain the slower walk typical of the elderly [53]. Similarly, the increased onset of the short and long latency muscle responses recorded in elderly subjects in dynamic posturography investigations would be due to the changes reported previously at the spinal and cortical levels. Increased latencies of the muscle responses disrupt the postural adjustments necessary to maintain body equilibrium in dynamic conditions [54].

However, the age-related alterations of the neuromotor system do not lead to damage of the sensorimotor performance in all cases, because neuronal plasticity exists at any age and that compensatory mechanisms are observed in the old people [50]. For example, elderly subjects increase the cortical motor command to produce a strong voluntary isometric plantar flexion, while young subjects preferentially reduce the presynaptic inhibition at the spinal level. Compensation of age-related deficits has been investigated by functional magnetic resonance imaging and positron emission tomography techniques. These studies have shown a reorganization of the activation and inhibition patterns associated with the motor control in old subjects. Greater brain activation was described with advance in age in the motor and premotor areas and in the frontal cortex [55, 56]. With respect to balance function, brain activation was found mainly in subjects tested in quiet standing position in comparison with more dynamic activities such as walking or running. The lower efficiency of sensory inputs that contribute to postural control, such as vision, can be compensated in the older people by increased activities in brain areas where the cortical representation of other sensory modalities is increased [57]. There would be a reduction of the reciprocal inhibitory interaction between the sensory modalities with age, in contrast to what is observed in young adults. The level of agonist/ antagonist co-activations is mediated by an increased supraspinal mechanisms (increased cortical activity pattern and decreased reciprocal inhibitory interaction). Muscle co-activations cause postural stiffening of the whole body, that is, a detrimental strategy for maintenance of both static and dynamic balance, and much more costly in terms of energy [58-61] (see Fig. 3). Moreover, such compensatory processes suggest that larger neuronal resources are allocated to the realization of a motor task in the elderly compared with young adults. This can have negative consequences for the realization of difficult postural tasks, or when postural tasks are performed simultaneously with cognitive tasks, that is, in most of the day life conditions (see § cognitive aging).

#### **EFFECT OF AGING ON THE MEMORY, THE COGNITIVE PROCESSES AND THE SPATIAL NAVIGATION**

Besides impairment of the sensorimotor functions, aging is generally accompanied by a deterioration of higher-level brain functions [62]. Together with the reduced capacity of the brain to integrate and process the sensory inputs, the cognitive functions are altered with life span [63, 64]. Attention and memory seem the most affected by age among



**Fig. (3).** Posture control strategies and aging.

Schematic representation of the two strategies of head stabilization in space and head stabilization on trunk recorded in young adults and older adult subjects, respectively, when they were asked to keep balance on a moving platform (AP displacement). The gain was calculated for the head, hip and ankle body segments as the ratio between body segments displacements and platform displacement. It decreased from the ankle to the head (0.95, 0.75, and 0.4 for the ankle, hip and head, respectively) in the young adult, attesting of a good head stabilization in space, whereas it remained stable at all body segments and close to unity (0.99 and 0.95 for the ankle, hip and head, respectively) in the older adult, indicating that those subjects swayed “in block” with the platform displacement (stiffening body strategy).

the basic cognitive functions that may impair posture control [65]. The brain executive functions, which include motor plan, decision-making and attention resources sharing have been reported to be strongly altered with age and at the origin of fall in the elderly. It was estimated that old subjects with both sensorimotor and cognitive deficits fell twice more than old people without any cognitive impairment [66, 67]. Recently, Coxon *et al.* [68] suggested that inhibitory control deficits are associated with less effective recruitment of task-specific cortical and subcortical regions in some older adults, and that maintenance of brain structure may have positive implications for brain function.

Ageing in humans is accompanied by stereotypical structural and neurophysiological changes in the brain [69]. The morphological and biochemical changes described in the frontal and prefrontal cortices [70] could be responsible for the alteration of the attention processes. A lower capability to give attention to the environment decreases the access to the sensory inputs regulating posture and equilibrium, and thus increases the risk of fall [50, 71, 72]. Li and Lindenberger [73] suggested that an alteration of the cortical areas responsible for sensory-treatment process could involve greater attentional resources in postural control in the older adults. Shumway-Cook and Woollacott [74] suggested also that with aging, attentional demands for postural control increase as sensory information decreases. Conversely, changes in brain concentration on a particular

task can explain the walking behaviour of the elderly, characterized by a reduced speed and a shortened length step [75]. It was suggested that outside falls, in non-familiar environments, are mainly due to impairment of concentration and attention, while those occurring at home reflect more clearly the physical weakness of the old people [76].

Decrease of the data processing speed and of the working memory can result from the loss of white matter in the anterior brain areas [77]. Salthouse and Meinz [78] investigated the failures of inhibition contribution to working memory in adults of different ages. Using the Stroop task as measure of inhibition, they have concluded that that speed of cognitive processing was altered with aging, and that age-related deficits in working memory and other cognitive functions can be explained in terms of a general slowing of information processing. Ferreira *et al.* [79] found that subtle executive dysfunctions can occur before the age of 50 years, while slower processing speed appears later in the transition to the old age. Because of an increased time for analysing the sensory inflow and to produce the adequate motor output, the reaction times are much longer and the risk of fall is increased [80]. It was assumed that among the markers of fall prediction, the speed of mental processing is one of the best parameters [81]. Age-related differences between young and older subjects regarding the cognitive abilities were encountered also in the medial temporal area and in the parietal cortex [82]. Representation of the body in space is elaborated in the parietal cortex [83] and plays a major role in the top-down processes that control posture and equilibrium.

Although there are clear generalities and common principles that can be demonstrated in cognitive aging, what is perhaps most compelling is the variability of the age-related cognitive changes (see [65]). Inter-individual variability is likely attributable to a wide range of factors including biological, psychological, health-related factors, environmental conditions, and lifestyle [84]. Three hypotheses have been proposed to explain this variability: a) presence or not of compensatory mechanisms at the origin of increased brain activation underlying some reorganization of the aging brain [85, 86]; b) inefficient or less selective cognitive strategies [87]; and c) differential decline of the sensory and cognitive abilities among the older subjects [88] as well as the ways to compensate the deficits [89]. Correlates of cognitive functioning of older adults visiting an emergency department after a minor injury were explored [90]. The results revealed that gender, age  $\geq 85$  years, higher depression scores, slower walking speed, and self-reported memory problems were significantly associated with lower baseline in the Montreal Cognitive Assessment score. Falls and concomitant instability can be markers of poor health and declining function. Risk factors for falls in the elderly include increasing age, medication use, sensory deficits and cognitive impairments [91]. The risk factors responsible for a fall can be intrinsic (*i.e.*, age-related physiologic changes, diseases and medications) or also extrinsic (*i.e.*, environmental hazards: poor lighting, unsafe stairways and irregular floor surfaces). Fuller [91] proposed five behaviours: 1) Patients with accidental falls and no intrinsic or extrinsic risk factors; 2) patients with acute illness; 3) patients with moderate illness, loss of mobility and some medications who fall

because of extrinsic factors; 4) severely ill patients with many medications who falls even without extrinsic factors; 5) and elderly patients with numerous age-related changes who fall because of extrinsic factors. Hsu *et al.* [92] have examined recently whether there were volumetric differences in gray and white matter in subcortical and cortical regions between older fallers and non-fallers. In addition, they investigated whether the baseline volumetric differences were associated with changes in cognitive function. The data suggested that falls may indicate subclinical alterations in regional brain volume that are associated with subsequent decline in executive functions.

It is well known that the hippocampus and the temporal lobe are implicated in the cognitive processes. Recent studies using functional brain imaging in humans and neuropsychological analyses of humans and animals with hippocampal damage have revealed some of the elemental cognitive processes mediated by the hippocampus [93-96]. A study of Kaye *et al.* [97] has reported that the volume loss of the hippocampus and the temporal lobe in healthy elderly persons marked the beginning of the disease process within six years prior to dementia onset. Middle cognitive impairment (MCI) has been characterized as a translational stage between normal ageing and dementia [98]. There is general consensus regarding the criteria used to diagnose MCI and the classification of MCI into two main broad types, amnesic and non-amnesic, depending on whether memory is deteriorated or not [99]. The National Institute on Aging-Alzheimer's Association workgroup on diagnostic guidelines for Alzheimer's disease recently proposed use of the term MCI due to "Alzheimer's disease (AD)" to refer to amnesic subtypes as pre-clinical forms of AD. The minimal mental Parkinson (MMP) examination is a cognitive screening tool designed in French specifically for Parkinson's disease [100]. Both dementia and fall-related injury pose an international health challenge. Individuals with dementia fall twice as often as cognitively intact people and are more likely to have injurious falls [101]. Several categories of fall risk factors emerged in older people with dementia or cognitive impairment: disease-specific motor impairments, impaired vision, type and severity of dementia, behavioural disturbances, functional impairments, fall history, neuroleptics and low bone mineral density [102]. The cognitive impairment is an established fall risk factor; however, it is unclear whether a disease-specific diagnosis (*i.e.* dementia), measures of global cognition, or impairment in specific cognitive domains (*i.e.* executive function), have the greatest association with fall risk. The systematic review and meta-analysis of Muir *et al.* [103] confirmed that cognitive deficits detected on clinical assessment are associated with an increased fall risk in community and institution-dwelling older adults. Importantly, their findings strongly suggested that how cognitive impairment is defined and assessed is essential in identifying individuals at risk of falls, and is paramount to facilitate knowledge translation into clinical practice.

Spatial navigation is a complex cognitive process that is essential for our everyday life. Spatial navigation a) is a multimodal process, the spatial information relevant for navigation being usually derived in parallel from a variety of sensory cues [90], including cues provided by the

environment and body-based self-motion cues [91]; b) involves numerous parallel computations, the incoming spatial information being not only used to extract various primitives such as position, facing direction, and the position of external objects, but also computed in multiple reference frames [91]; and c) recruits multiple memory systems, the online representations of position and facing direction interacting with long-term memory representations of local views and the overall structure of an environment [91]. Spatial navigation is a skill used for determining and maintaining a trajectory, for moving from one place to another. Mild progressive decline of spatial navigation develops gradually during the course of physiological ageing. A study of Gazova *et al.* [92] demonstrated that navigation deficits in older age seem limited to allocentric navigation, whereas egocentric navigation and learning would be preserved. Altered spatial representation and information processing in the hippocampal-striatal circuitry was observed with advanced age, which may contribute to the reported spatial and memory deficits associated with normal and pathological aging.

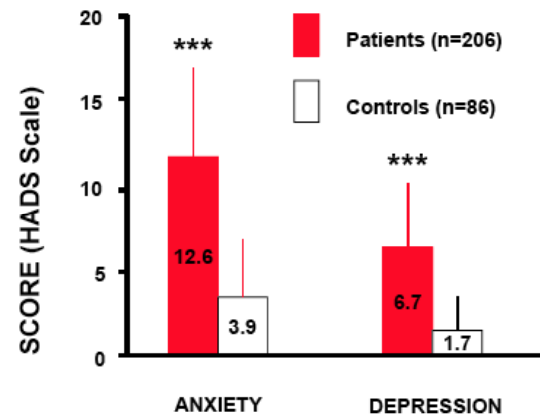
#### **EFFECT OF AGING ON THE POSTURE CONTROL DURING DUAL TASKING**

Ageing is a major factor affecting the cross-talk between postural and cognitive tasks, that is, when two tasks must be performed simultaneously – a very frequent task in most of the day life conditions. In the literature, the dual-task paradigm is made generally of two tasks, one being the primary task (the postural task), and the other being the secondary task (cognitive task like count down, or the Stroop task).

A reduction of the stride length and of the speed of walking has been reported when a disturbing signal was provided to aged subjects instructed to walk normally [75]. The perturbation of the walking pattern can be so high that subjects stopped walking. Indeed, the "stop walking when talking" was described in old people who could not perform simultaneously the behavioural (walking) and the cognitive (talking) tasks, and it was proposed as a predictor of fall in the elderly [107]. In this study, some frail elderly patients stopped walking when they started a conversation with a walking companion, presumably because they could not share their attentional resources required to perform the two tasks. In unstable elderly subjects, when attention was alternately directed from one task to another, deleterious effects were observed on balance control [108]. Taken together, this indicates that low attentional capacity is correlated in the elderly with an increased risk of fall and with an increased recurrence of falling. The inability to allocate sufficient attention resources to postural control under multitask conditions could be a contributing factor to imbalance and fall in old adults. Hamel and Lajoie [109] have shown that mental imagery is an effective technique, not only to reduce the antero-posterior postural oscillations, but also to render the postural control tasks more automatic. It should be incorporated in the rehabilitation of posture control in the elderly population in order to improve their balance, to prevent falls, and to regain a good quality of life.

The dual-task paradigm is commonly used to test the executive functions involved in posture control [110]. In a dual-task paradigm, the attentional resources mobilized for the postural control depend on several factors. One is the voluntary attentional focus on the control of posture [111]. It has been shown that the antero-posterior sway velocity decreased in healthy young adults in a dual-task paradigm with a simple reaction time task when the focus was on balance [112]. Polskaia *et al.* [113] suggested that a cognitive task withdraws attention from the postural task, thereby facilitating a more automatic control of posture. A second factor is the sensory information available [74], a third is the nature and the complexity of the postural task [114, 115], and supplementary factors are the level of expertise [116, 117], the disability of the subjects [118, 119], and the age [120]. In healthy adults, Li *et al.* [121] showed a decrement in postural performance during dual tasking compared to single postural-task performance, and they suggested this was very likely due to cognitive load and competition for attentional resources [122]. Remaud *et al.* [112] indicated that in daily activities such as walking, increased attentional demands would reduce the resources available for other concurrent tasks. Demanding gait tasks (walking in darkness, or with competing distractions) could alter the gait performance and increase the risk of fall. Furthermore, navigation precision is affected by age, presumably because a secondary task interferes with path estimation [123]. In a study comparing young and older subjects in a dual-task paradigm using a crossed design, including both a static- (quiet standing) and a more challenging dynamic- (keeping balance on a translational platform) postural task, and cognitive tasks with low- (silent mental arithmetic) and with higher (spatial memory task) attention loads, we found that the postural performance in the young subjects was improved during dual tasking while it was deteriorated in the elderly [60]. The amplitude of the effects was dependent of the postural and cognitive tasks complexity. Postural performance improvement in the younger adults seems to be due to the lack of resource competition, all attentional resources being allocated to the cognitive task as a result of posture control automatization. In contrast, postural performance decrement among older adults likely reflects a cross-domain attentional resource competition. Older adults focus more strongly on their postural control under conditions of postural threat. They affect all their attentional resources to the postural task to avoid fall. Consequently, their cognitive performance was also altered (see also [124]). It has been suggested that when the complexity of the postural task is increased, the performance on the concurrent task, or both, is more degraded in older as compared to young adults [125]. These results show an age-related increase in the recruitment of generic neural resources indicative of cognitive (controlled) processing of posture, that is, an age-related penetration of cognition into the processing of quiet standing in the elderly. Lion *et al.* [126] have shown that the limits in human cognitive processing can lead to difficulties in performing two tasks simultaneously. Their results indicate that cognitive load alters balance control even in simple postural tasks. We had previously demonstrated that age-related changes during dual-tasking could be detected with very easy postural tasks such as standing quietly on a stable

support, especially if the traditional descriptors of posture control were replaced by more functional descriptors based on nonlinear analyses of posture (Fig. 4).



**Fig. (4).** Anxiety and depression in patients with postural instability.

The score to the Hospital Anxiety and Depression Scale (HADS) is illustrated for each parameter (anxiety and depression) in patients ( $n = 206$ ) with instability and vertigo and in healthy matched subjects ( $n=86$ ). Anxiety and depression scores were significantly increased in patients with instability. \*\*\* Significant differences ( $p<0.001$ ) (adapted from [149]).

Several models have been elaborated to explain what happens in older subjects during dual-task conditions (see [59]). Posture control and cognitive activity compete for attentional resources, and the postural performance in dual tasking is generally altered compared to the single postural-task performance. However, this cross-domain competition model is not univocal, no change or even improvement of posture being reported in the literature, depending on the difficulty of the postural task and on the complexity of the cognitive task [122, 127]. A U-shaped nonlinear interaction has been proposed to describe this more complex interaction between age and task characteristics [128]. However, the U-shaped relationship between physical activity and falling has been not confirmed [129]. More recently, Wollesen *et al.* [130] introduced the supra postural task model [131-133] that offers an alternative approach to the U-shaped model, with balance performance integrated into a cognitive task and not considered as a pure sensorimotor task. The limited capacities of the aging brain explain why decreased cognitive resources correspond to decreased dual-task performance, because doing two things at once becomes more difficult (see Lundin-Olsson *et al.* [107]: “stop walking when talking”). A task prioritization is required with advanced age, as illustrated by the “posture first” principle proposed as an explanation for cognitive-task deterioration as a consequence of balance prioritization in dual-task conditions in the elderly. Another illustration is the description by Nashner [134] and McCollum and Nashner [135] of distinct ankle and hip strategies in humans when standing on a force platform suddenly moved forward or backward. These strategies are underpinned by different spatio-temporal patterns of muscular activation, and it was observed that most of the old people shift from the ankle (bottom-up pattern) to the hip (top-down pattern) strategy,

more safe for balance control. Taken together, the results confirm the prioritization of posture control in old subjects – the “posture first” principle described in the literature – [136], particularly in challenging conditions. Prioritization of posture control leads also to alternative strategies. Older people shift from the head to space stabilization to head on trunk stabilization, with muscular co-contractions, body stiffening and more rigid stance. In threatening postural contexts, older subjects demonstrate more frequent postural adjustments [137], and equilibrium maintenance can be realized either by a shift from the ankle to the hip strategy or by step initiation [138].

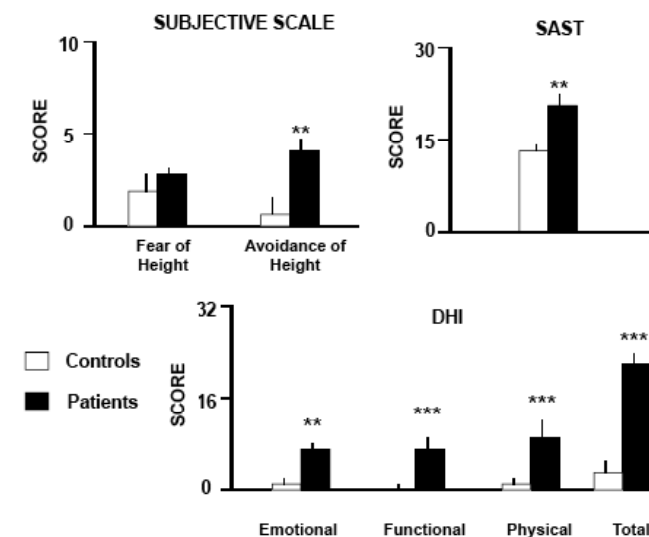
### IMPACT OF THE PSYCHOLOGICAL AFFECTIVE FACTORS

Retrospective studies showed that the subjects' neuropsychological profile affects posture control and balance in the elderly [139]. Stress, anxiety, feeling of fear and depression are different factors growing to the emotional sphere, which increase the risk and the incidence of falling. Anxiety differs from the feeling of fear by its non-specificity (absence of exogenous conscious object) and by its cognitive bias (waiting negative events of endogenous origin). According to the Diagnostic and Statistical Manual of Mental Disorders [140], depression is characterized by a lack of interest, sadness, lack of concentration, loss of appetite and sleep, and fatigue. A correlation with the incidence of fall has been clearly established in depressed patients [141], a result that should be considered to prevent falling in such patients. Depression and falls seem to share the same base of risk factors: poor health, poor cognitive status, slower walking and several hospital visits in a close period before onset of the symptoms [142]. The functional capacity seems to be independently associated with depressive symptoms in older people living in community and residential care facilities, whereas overall activities of daily living performance may not be associated [143]. Poorer life-space mobility interrelates also with higher probability for depressive symptoms, thus compromising older adult's mental wellbeing [144]. Recently, the study of Iaboni *et al.* [145] examined the correlation between improvement in depressive symptoms and reduction of falls, which raises the question whether a cognitive-behavioral intervention that simultaneously targets both depression and falls would be a useful component in a fall prevention program. The authors found a high frequency of depressive disorders among persons attending such a program, but depression did not impede improvement in fear of falling.

Many studies in animal models and humans suggested the existence of a link between the sense of balance and the emotional feeling [146, 147]. Anxious subjects would be less able to solve sensory mismatches and sensory conflicts compared to non-anxious subjects, that is, they would be less able to produce appropriate responses when uncorrelated or contradictory sensory inputs feed the brain. Visual motion cues of the visual environment not associated with vestibular inputs relative to own body displacement (ex: the so-called train illusory self motion) constitutes a sensory decorrelation, and creates a conflict in the internal representation of body motion in space, based on a learned pattern of expected sensory cues. In such cases, the lived experience causes

anxiety, and besides the generated autonomic signs are concomitant postural effects. The postural destabilization and the loss of balance observed in anxious subjects would result from a deficit in the integration of the different sensory modalities. The brain would remain unable to solve the inter-sensory conflicts. It should also be the case for people with motion sickness, who do not adapt to unusual patterns of sensory cues. Similarly, agoraphobic (phobia of open spaces or crowds) or acrophobic (phobia of heights) subjects exhibit the whole range of anxiety symptoms. The loss of gray matter volume reported in the elderly in the parietal and medial prefrontal cortices could be involved in such deficient multisensory integration processes [148]. Other studies suggested however a different explanation not based on a multisensory integration deficit, but on an increased or wider time window for the multisensory integration process in older subjects compared to young adults [149]. The reason could be a bad filtering of the sensory noise and/or a lower capacity to concentrate.

The Hospital Anxiety and Depression Scale (HADS) showed that these two parameters are significantly increased in patients with vertigo and instability [150] (Fig. 5). Approximately 50% of subjects with postural instability report psychological problems, and 25% exhibit symptoms of both panic and agoraphobia. In a telephone survey of 1003 patients with severe or moderate dizziness and instability, 80% highlighted the need to consult and to stop their professional work [151]. Emotional factors and dizziness are extremely invalidating and increase the risk of fall, especially in the older people. And they negatively impact their quality of life [97].

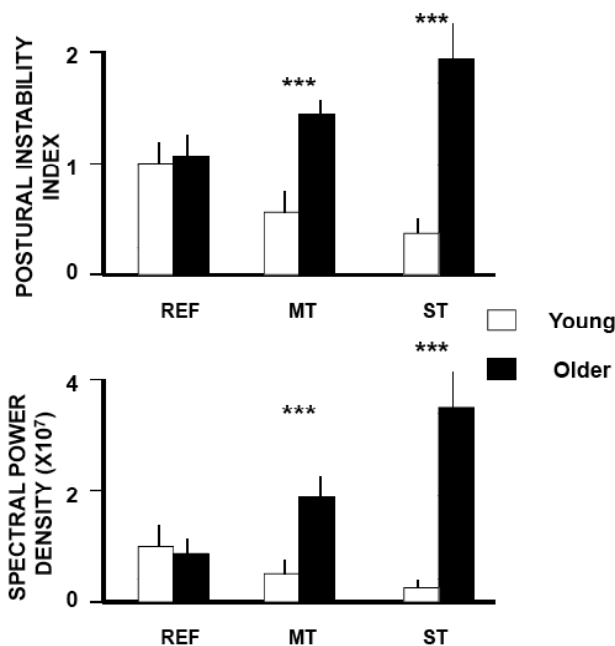


**Fig. (5).** Role of the psychological and emotional factors in posture control.

The scores to the fear and avoidance of height scales, the Short Anxiety Screening Test (SAST), and the Dizziness Handicap Inventory (DHI) are illustrated in healthy subjects (open symbols) and patients with postural instability (closed symbols). The scores to the avoidance of height scale, the SAST, and the DHI are increased in patients with postural instability. For the DHI, the scores for the emotional, physical and functional items are also increased in the patients. (\*\*, \*\*\*) Significant differences  $p < 0.01$  and  $p < 0.001$ , respectively (adapted from [152]).



Stress usually accompanies subjects with sensorimotor or cognitive disability. Older people with visual impairment, osteoarthritis, vestibular decline or with developed sarcopenia degrading their locomotion are generally stressed when they have to move, especially in crowd environments or spaces with visual overstimulation. Similarly, elderly with mild cognitive impairment will show fear to navigate in unusual environments. These psychological profiles explain why the elderly are stressed by the fear of falling, particularly if they have already fallen, because the risk of fracture and loss of independence are important [152]. In a study conducted in unstable patients, we have used two questionnaires (DHI: Dizziness Handicap Inventory; SAST: Short Anxiety Screening Test) together with a subjective scale of fear and avoidance of height to test the stress and anxiety levels of those patients compared to healthy adults [153]. The results showed significant differences between the two populations, with higher values for all items in the three tests (Fig. 6). In a recent study [154], the ability to maintain balance was challenged by manipulating the level of postural threat while walking. As a rule, increasing postural threat by constraining or elevating the walking path was associated with increased anxiety levels and emotional states, as evidenced with galvanic skin conductance recordings [155-157].



**Fig. (6).** Comparison of postural control between young and older subjects during dual tasking. Mean result recorded in the two groups of age (younger, older adults) with the nonlinear analysis of the center of pressure (CoP) displacements using the wavelet transform. The data show the effects of dual-tasking with a mental arithmetic task (MT) or a spatial memory task (ST) on the single-postural task performance without concurrent cognitive task (REF). Group mean for two parameters elaborated from the wavelet transform: the postural instability index (PII) and the spectral power density calculated in the 0.5 to 1.5 Hz range. Significant differences between experimental conditions are indicated by asterisks (\*\*\*) $p < 0.001$ .

### CLINICAL AND INSTRUMENTAL TESTS TO PREDICT THE FALL

Falls are the most common cause of injury in old age [158] and prognostic clinical or instrumental tools to identify individuals with an increased risk of fall must be defined [74,159-161]. The Tinetti balance scale is a simple clinical test with good performance on interrater reliability and concurrent validity [162-164]. Frequently used is the Timed Up-and-Go Test (TUG), recommended by the American Geriatrics Society, the British Geriatric Society and Nordic Geriatricians to screen the risk of fall [165]. It is a timed performance in which subjects must get up from a chair, walk 3 m, turn around, walk back and sit down [166]. The origin of this test was the Get-Up-and-Go Test (GUG), an observational rating of fall risk using a score from 1 to 5 [167], but further studies are required to assess its predictive ability to identify fallers. Nordin *et al.* [168] have evaluated and compared the prognostic validity relative to fall of the TUG at normal speed, of a modified Get-Up-and-Go Test (GUG-m), of a rating of fall risk scored from 1 (no risk) to 5 (very high risk), of staff's judgement of global rating of fall risk as « high » or « low », and of fall history in a previous 6 months among frail older people. The occurrence of falls during the follow-up period was compared to the following assessments at baseline. These assessment tools were evaluated using sensitivity, specificity, and positive and negative likelihood ratios. 53% of the participants had felt at least once. In this population of frail older people, staff judgement of their residents' fall risk as well as previous falls both appear superior to the performance-based measures of TUG and GUG-m in ruling in a high fall risk. A TUG score of less than 15 s gives guidance in ruling out a high fall risk but insufficient information in ruling in such a risk. The grading of fall risk by GUG-m appeared of very limited value.

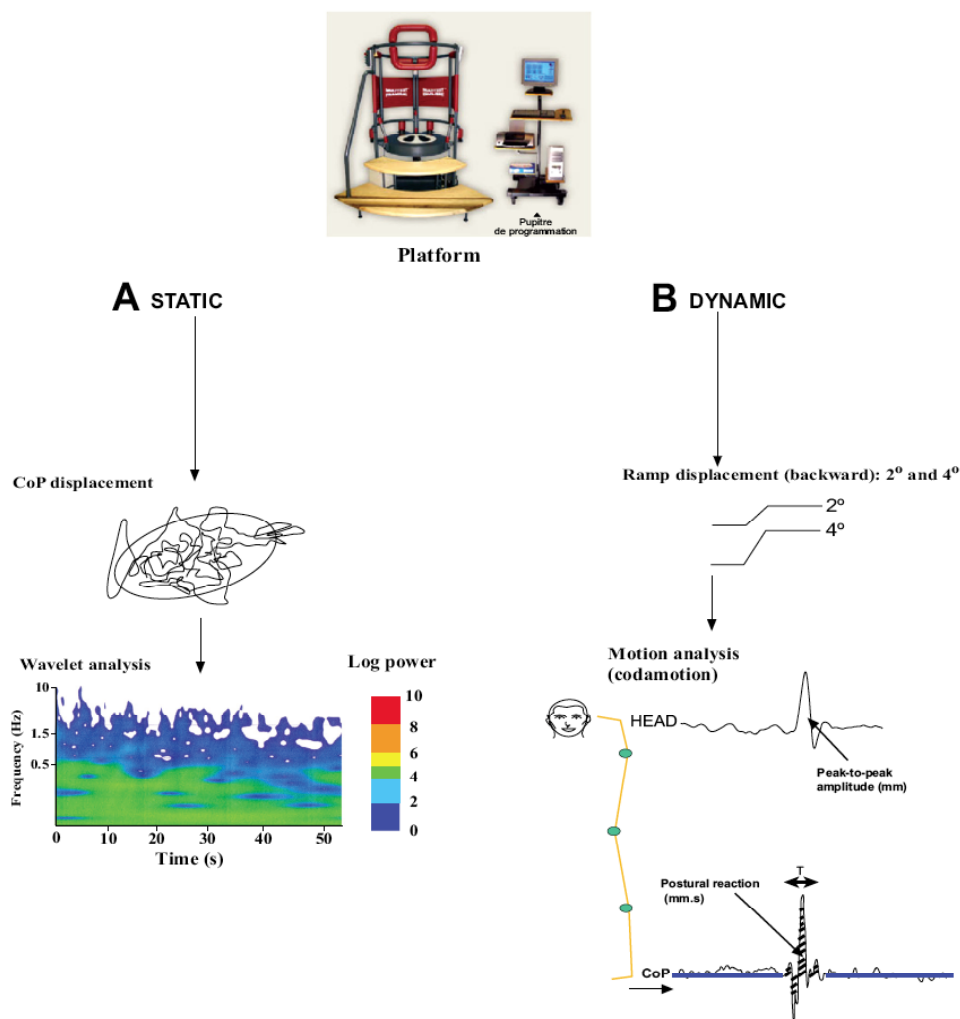
Falling during walking is also a common problem among the older population. Hence, the challenge facing clinicians is to identify who is at risk of falling during walking in order to provide an effective preventive rehabilitation. Tsutsumimoto *et al.* [169] investigated a) the association of the "Ordered Multi-Stepping Over Hoop (OMO)" test with cognitive and physical function among older people; and b) whether the OMO could predict incidents of falling. The OMO time was correlated with cognitive function, physical function, and incidents of falling. This preliminary study indicates that the OMO may help to make a distinction between fallers and non-fallers among older people as effectively as other tests. In an original study, Gimmon *et al.* [170] demonstrated a slower gait speed and more steps during the Narrow Path Walking Test (NPWT) under both single and dual task conditions in fallers. But there was no added value of the dual task over the single task. Recently, the Stroop Stepping Test (STT) device was developed using low-cost computer video game technology able to distinguish fallers from non-fallers, providing a novel way to explore cognitive mechanisms for fall-risk in older people [171].

Static and dynamic posturography seem valuable clinical tools to assess balance disturbances [114, 172]. In 2004, Melzer *et al.* [173] put forward that simple, safe force-plate

measurement of spontaneous postural sway can identify elderly individuals at risk of falls, and can be considered as a preliminary screening tool for the risk of falling. Bernard-Demanze *et al.* [174] have proposed a clinical test to identify elderly individuals at risk of falls using dynamic posturography. The study compared the postural responses of non-fallers elderly subjects (mean age: 77 years  $\pm$  7 years) to young healthy subjects (mean age: 36 years  $\pm$  9 years) during tilts of the platform (amplitude: 2 or 4 degrees; velocity: 2 °/s; see Fig. 7), in the backward direction considered as the more disturbing condition in the elderly. The kinetics of the postural response (CoP displacement) during ramp displacements of the platform (Multitest platform, Framiral, Cannes, France) was recorded, and the time period required for body re-stabilization in the antero-posterior (AP) direction was calculated. Head stabilization in

space was simultaneously recorded using a motion analysis system (Codamotion, Charnwood Dynamics, UK).

The results clearly showed that the elderly and the young subjects used two distinct postural responses to backward displacements (Fig. 8). Most of the young subjects returned to their initial equilibrium (67%), within a short time period, and their head remained stabilized in space. Conversely, most of the elderly moved to a new equilibrium position (71%) in a longer time period, with larger AP sway amplitudes, and their head stabilization in space was very poor. The differences between the two groups were strongly increased without vision. These data show that backward body tilts are very destabilizing in the elderly and causing major perturbations of balance. This simple test could be a good predictor of fall in old people, particularly in the

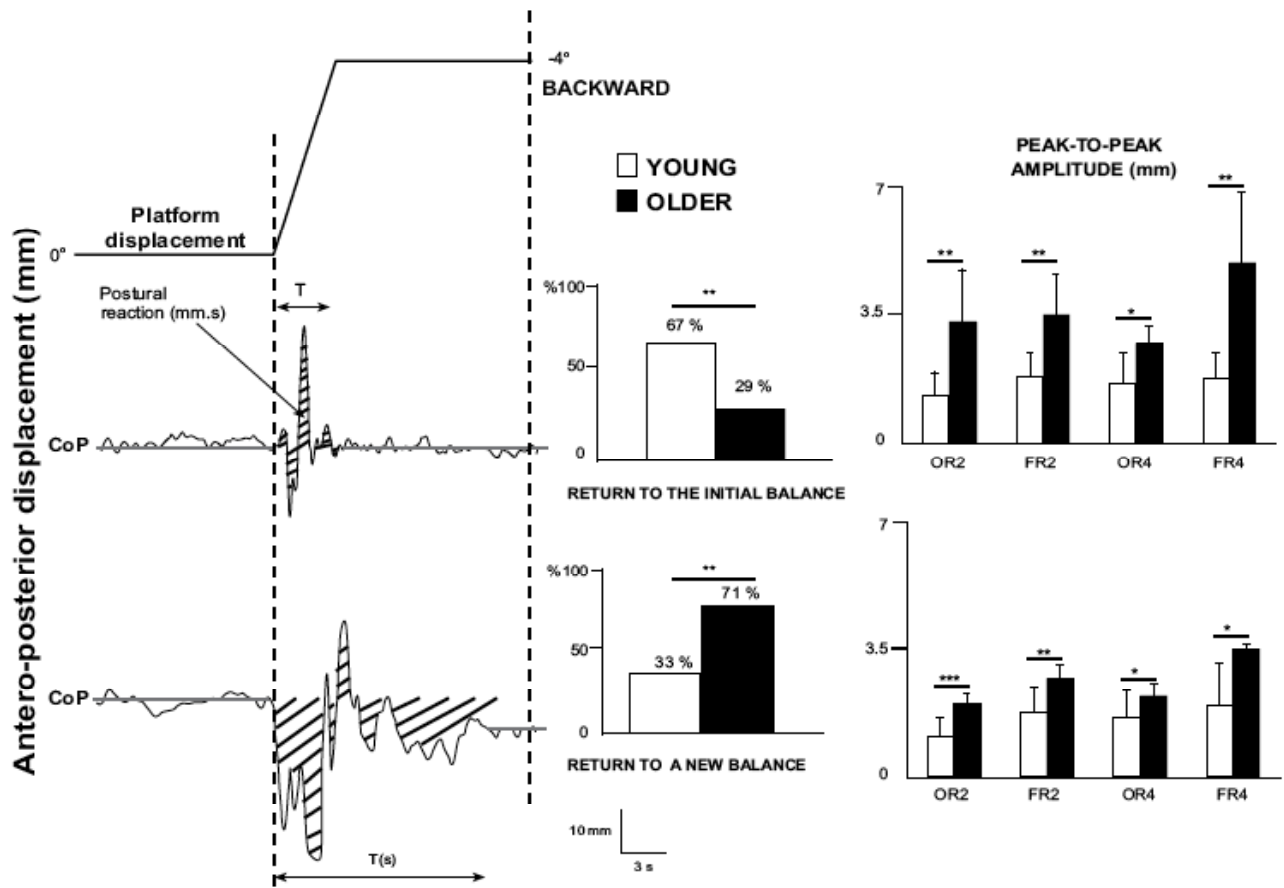


**Fig. (7).** Experimental protocol.

A: Posture investigation under static condition. Subjects stood on a force plate that recorded their center of foot pressure (CoP) displacements. (CoP) displacements were computed through nonlinear analysis (wavelet transform). The Postural Instability Index (PII) and the spectral power density were calculated.

B: Posture investigation under dynamic condition.

The kinetics of the postural response (CoP displacement) during ramp displacements (amplitude: 2 or 4 degrees; velocity: 2 °/s) of the platform (Multitest platform, Framiral, Cannes, France) was recorded, and the time period required for body re-stabilization in the antero-posterior (AP) direction was calculated. Head stabilization in space was simultaneously recorded using a motion analysis system (Codamotion, Charnwood Dynamics, UK).



**Fig. (8).** Postural response during ramp displacement and head stabilization in space.

A: Center of foot pressure (CoP) displacement during ramp displacement (amplitude: 2 or 4 degrees; velocity: 2 °/s) of the platform (Multitest platform, Framiral, Cannes, France). The kinetics of the postural response and the time period required for body re-stabilization in the antero-posterior (AP) direction were illustrated. Most of the young subjects returned to their initial equilibrium (67%), within a short time period, and their head remained stabilized in space. Conversely, most of the elderly moved to a new equilibrium position (71%) in a longer time period, with larger AP sway amplitudes, and their head stabilization in space was very poor.

B: Head stabilization in space for the young and older subjects in the four experimental conditions: eyes open ramp displacement 2° (OR2), eyes open ramp displacement 4° (OR4), eyes closed ramp displacement 2° (FR2), eyes closed ramp displacement 4° (FR4). Significant differences between experimental conditions are indicated by asterisks (\* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ ).

absence of vision. Indeed, many studies in healthy subjects showed an increased dependency on vision for posture control with aging [175-177].

### THERAPEUTIC IMPLICATIONS AND CONCLUSIONS

The aging of the population and the increased of lifespan are a challenge for our modern societies regarding the major health and socio-economic questions they raise. The fall in the elderly being one of the dramatic consequences of the aging equilibration function, it is therefore imperative to develop rehabilitation procedures of balance.

The aging of the postural balance is multifactorial. It has been shown in this paper that alteration of the sensory systems and muscle effectors implicated in the postural control, morpho-functional changes at the spinal and cortical levels, modifications in multisensory integration and data processing, deterioration of cognitive functions, and intervention of psychological factors (anxiety, stress and

depression) were implicated. The rehabilitation of the postural balance in the elderly must take into account all of these components. Physical exercise, aerobic training and cognitive stimulation are the main procedures to rehabilitate the balance function in the elderly [178].

Physical exercise induces a cascade of cellular and molecular processes promoting synaptogenesis, neurogenesis, angiogenesis and up-regulation of neurotrophins [179]. Neurotrophins in general, and BDNF (Brain-Derived Neurotrophic Factor) in particular, have an important role in the structural and functional maintenance of nerve cells [180]. The reduction in plasma levels of BDNF was correlated with neuronal loss associated with age (and depressive syndrome), and intense physical exercise increases the concentration of BDNF, reduces the loss of brain tissue, increases the volume of the hippocampus, increases cerebral blood flow, and improves cognitive functioning, including the executive functions.

Regular aerobic exercise also improves attention, brain processing speed, memory and learning processes [181, 182]. Ballesteros *et al.* [183] showed that promoting physically active lifestyle throughout adulthood could significantly reduce the decline of effortful executive control functions in old age. In this study, the performance of a group of 20 physically active older adults was compared with that of a group of 20 sedentary healthy older adults while performing a series of cognitive tasks. These tasks were designed to assess the processes that deteriorate most with age, namely the executive control functions and the processing speed, of vital importance for independent living, as evaluated with the Wisconsin Card Sorting Task and simple and choice reaction time tasks, respectively. A repetition priming task that does not decline with age, involving attended and unattended picture outlines at encoding, was also included as a control task. As expected, a physically active lifestyle did not enhance repetition priming for attended stimuli, nor did it produce priming for unattended stimuli at encoding. But physically active lifestyle reduced the decline of effortful executive control functions in old age. These results have practical implications for enhancing the cognitive processes that decline most in old age. Neuroimaging studies showed significant effects in the prefrontal cortex and medial temporal cortex. A volumetric increase (2%) in these brain areas was observed in elderly subjects conducting regular physical exercises [184]. Beneficial anti-inflammatory effects of exercise have been also reported, which slow down cognitive deterioration [185]. At the behavioral level, exercise improves muscle strength, endurance, dynamic balance and fear of falling [186, 187], preserving therefore a good quality of life throughout the life.

As our society becomes more reliant on technology, what is now considered 'healthy' may not be so, for many millions of people [188]. Nevertheless, cognitive stimulation using environmental techniques (memory training, for example) and virtual reality seems also effective in reducing the cognitive decline associated with age [182]. The HERMES Project [189] was developed in Spain to provide assistance and support to healthy older adults, and its aim was to reduce the cognitive decline associated with age, and to reduce also the need for caring. It provides assistance to promote the users' autonomy and independence. This concept was thought a) to have an empirical basis from scientific research, especially on interests and motivations of older adults about computerized gaming; b) to be easy to use since both simple and designed taking into account cognitive changes; c) to promote flow and immersion in users through both concentration and sensation of control; d) to encourage autonomy and sense of independence by stimulating prospective memory, directly addressed to daily events; e) to stimulate prospective memory, using daily-life appointments introduced into the HERMES system as cognitive games stimuli; and f) to stimulate visual attention and bi-manual coordination. Finally, older adults themselves have emphasized that cognitive training support is very much welcomed, in the sense that it enhances their sense to be active and independent.

Data collected in neuroimaging investigations showed an increased volume in different neural structures (CA3 and

CA4 areas of the hippocampus, dentate gyrus, lateral orbitofrontal cortex) involved in memory performance. The use of video games or computer training can help to improve cognition in the elderly [190]. Training with games centred on multi-tasking exercises not only improves the dual task performance, but also the attention and the working memory [191]. Furthermore, studies combining exercise and cognitive stimulation showed synergistic and cumulative effects, of great interest for prevention and rehabilitation of the age-related deficits, including prevention of fall and balance [192].

By characterizing and understanding the effects of cognitive enhancers on fall risk in older adults, and in particular in older patients with cognitive impairments, we will be able to pave the way for a new approach to fall prevention in this population. Brain sensitivity to metabolic disorders is demonstrated by the effect of homocysteine on metabolic pathways, on brain integrity and on the cognitive capacity [193]. Micronutrients (vitamins, trace-elements and also antioxidants) most likely affect brain integrity by normalizing efficient autophagy. A study in animal models focused on the comparative evaluation of ethanolic extracts of *Bacopa monnieri*, *Evolvulus Alsinoides*, *Tinospora Cordifolia* and their combinations on cognitive functions in Rats [194]. From present investigation, it can be concluded that ethanolic extract of *Bacopa monnieri*, *Evolvulus alsinoides* and *Tinospora cordifolia* provides better nootropic effect when used in combination. In Humans, Montero-Odasso *et al.* [195] provided, for the first time, information regarding the effect of a medication (donepezil), designed to augment cognitive function on the risk of fall in older adults with mild cognitive impairment.

## CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

## ACKNOWLEDGEMENTS

Declared none.

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