Neurologic aspects and falls

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Summary

Falls are widely recognized as a social problem due to the related economic burden on public health budgets. Following the growing body of evidences on the physiopathology of postural control in humans, many factors leading to falls are already well established in the literature. Given the high prevalence of falls among elderly people, the present review focuses on parkinsonism and those "mild parkinsonian signs" frequently presented by elderly subjects. Parkinsonism is a good paradigm for the understanding of the pathophysiology of falling. Specifically, parkinsonian patients display specific features related to falls, such as axial motor symptoms, the impairment of executive functions and of the interplay between motion and cognition, as revealed by the disruption of automaticity.

KEY WORDS: parkinsonism; falls; freezing of gait.

Introduction

Falls are the leading cause of injury related admissions to hospital in people of 65 years and over, accounting for about 14% of emergency admissions and 4% of all hospital admissions in this age group (1). Given its association with fractures, immobilization, poor quality of life and life-span reduction, falling is recognized worldwide as a major medical, social and economical problem (2, 3).
Unraveling the pathophysiology of falls is critical with respect to fall prevention, which would ideally be the best therapy available. A recent evidence-based review of the American Academy of Neurology concluded that stroke, dementia and gait/postural instability impairment are level-A risk factors for falling. Parkinson's disease (PD), neuropathies, lower limbs weakness and poor visual acuity are level-B (4). The present mini-review deals with those specific neurological aspects shared by fallers with PD, parkinsonism or "mild parkinsonian signs" (5, 6) (MPS).

Motor impairment: the role of parkinsonism

Falls are much more frequent among patients with PD as compared to elderly subjects (7) (Figure 1). One of the most important risk factor for falls is the postural instability gait disturbance (PIGD) complex (8), also known as "axial impairment". Albeit the term PIGD has been traditionally employed in PD, it is well known that ageing processes unrelated to the dopaminergic deficit play the major role in its pathogenesis. On the other hand, the interest on MPS in elderly subjects without PD is steadily increasing in recent years (5, 6). Interestingly, parkinsonian signs in subjects without PD involve almost exclusively gait and postural stability (5, 6) and are linked to specific cognitive features, also relevant to the pathogenesis of falling (9, 10). Moreover, the occurrence and severity of MPS have been linked to high mortality (10, 11). It is yet to be determined if falls are implicated with the high mortality among subjects with MPS.
Perhaps a broader association between MPS, falls and potential pathogenesis of falls can be drawn from the fact that the emergence of MPS is related to brain vascular pathology mainly involving the integrity of the periventricular frontal regions (12, 13). The same correlation has been already well documented by the leukoaraiosis and disability (LADIS) study that examined the impact of age-related brain white matter changes on transition to disability in the elderly (14). One of the findings of the study was an association between the risk of falling and vascular lesions within the frontal lobe.
Recurrent falls are exclusively related to the "intrinsic" features of a given individual and, more specifically, these can be related to a disorder of either the base of support (BOS) or the center of body mass (COM) (15). The most common disorder of BOS is freezing of gait (FOG), defined as the episodic inability (lasting seconds) to generate effective stepping (16). It occurs most frequently during turning and step initiation and may be worsened by additional factors like spatial constraints, stress, and mental distraction (16). FOG affects more than 50% of parkinsonian patients (16, 17) and represents a major cause of falls during walking (18) among the subjects who suffer from the symptom. Accordingly, recent studies identified FOG as one of the most relevant contributors to the worsening of quality of life in PD patients (19). The pathophysiology of FOG is not yet fully understood but it has been demonstrated that patients with FOG have a pathological gait pattern even in-between freezing episodes (20). Particularly, impairment in rhythmicity (21), symmetry (22), bilateral coordination (23), step scaling (24) and dynamic postural control (25) have been implicated with FOG episodes [see below, and for review see (20)]. The typical disorder of COM is postural instability, which typically leads to a backward body sway. Directionality deserves some comments: patients with FOG usually fall forward also because the typically stopped posture of these patients mechanically favors such direction (26).

Cognitive impairment: the role of executive functions

The cognitive profile of patients with parkinsonism and FOG is cha-

Figure 1 - Two parkinsonian patients captured while falling during turning (top) and backward walking (down). *Courtesy of Dr. Francesca Morgante, Department of Neurosciences, Psychiatry, and Anaesthesiological Science, University of Messina, Messina, Italy.*

racterized by the impairment of executive and attentive functions (27-29), thus representing another link between movement control and cognition. Though gait and postural stability are mostly automatic motor behavior, cognitive (i.e. cortical) functions control the strategies employed for navigation and management of perturbations and obstacle avoidance (30). Preserving stability seems the primary function of these cortical functions (31). In doing so, they integrate multi sensorial information and act on the motor system by selecting the strategies that guarantee dynamic stability minimizing energy expenditure. The role of attention and cognition in postural control can be inferred also form the side benefits seen after the use of drugs for enhancing cognition. For example, a recent study on the effect of donepezil (a central cholinesterase inhibitor used for Alzheimer disease) on fall prevention has disclosed a significant frequency reduction of falls rather than near-falls (32), thus indicating that the drug did not lead to more stability but rather more efficient selection of the appropriate rescue reactions. Similarly, it has been shown that the protective arm response (i.e. the safety actions performed by upper limbs once the fall cannot be avoided) is impaired in parkinsonian subject. To this regard, it is difficult to isolate the relative role of the motor impairments vs. the cognitive deficits related with the syndrome, in leading to the inability to generate a well organized protective response. Thus, as a consequence, in subjects with parkinsonism higher rate of injurious falls are seen in comparison with elderly healthy subjects (33).

The failure to maintain a conversation while walking ("stop walking while talking") has been found to be a strong predictor of future falls (34). This observation drove the research on dual-task (DT), i.e. the abilities to perform a secondary task simultaneous to walking. In elderly people (35) and in patients with overt disease, such as stroke or PD (36-39), DT abilities deteriorate due to the decline of automaticity and attention secondary to subclinical disease processes or medication. This DT cost, i.e., the related decrease in motor performance, makes gait less secure and increases the risk of falling. The involvement of cognitive control in normal gait could explain why falls are so common in patients with dementia and why demented patients are so vulnerable to DT performance while walking (40, 41).

The interplay between motion and cognition: the role of automaticity

Gait is essentially rhythmic and gait variability is used to assess its rhythmicity, i.e. the more variable is the gait the less rhythmic it is. While gait variability represents the rhythmicity in walking, gait asymmetry (GA) and bilateral coordination of gait are features that address the automaticity of gait in the level of the relative timing of stepping between the two sides of the body, in particular the legs. GA has been traditionally measured in terms of spatial features (e.g., step length), in more recent years the timing properties of gait have been considered as a better index of neural and coordination control. Human gait is considered to be symmetric (42) with the relative timing of left-right stepping in anti-phase (43, 44). With ageing both features deteriorate, and even further deteriorate in subjects with PD (45). DT has been implicated with further deterioration in GA, more profoundly among PD patients and elderly subjects considered idiopathic fallers as compared to healthy elderly subjects (46). Moreover, reduction in the ability to

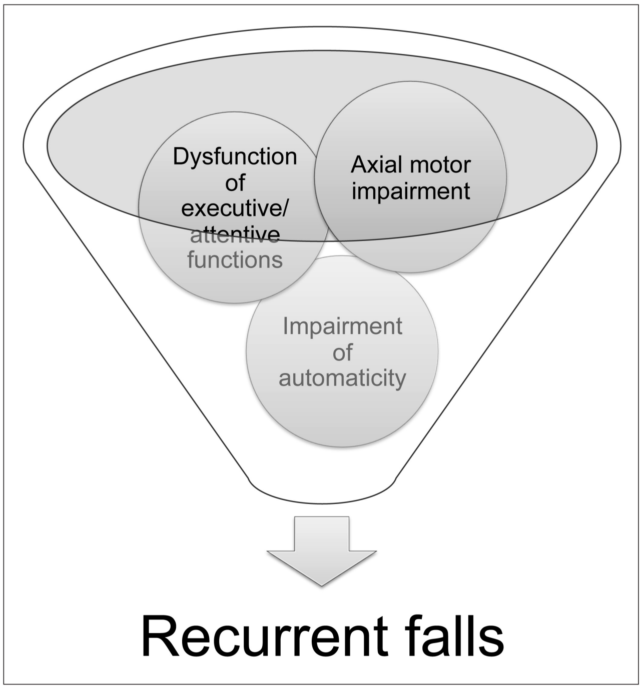

Figure 2 - The complex interplay between motor and cognitive features and their interaction in patients with parkinsonisms susceptible to recurrent falls.

maintain left-right stepping anti-phasing was seen in PD patients in DT paradigms (47). A recent study found that bilateral coordination of gait, GA, gait variability and gait speed were worse in the PD fallers in either usual-walking or DT as compared to the PD non-fallers; the DT effects on gait variability and bilateral coordination were larger in the fallers (39).

Conclusions

Parkinsonism is a good paradigm for the understanding of the pathophysiology of falling. Parkinsonian patients display specific features related to falls, such as axial motor symptoms, the impairment of executive functions and of the interplay between motion and cognition, as revealed by the disruption of automaticity (Figure 2). The recognition of this complex process is the first step towards the definition of specific therapies, which are currently under evaluation (32, 48-50).

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