

**Gait, mobility, and falls in older people**

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Dedicated to my mother, father and sister.

“Pain is temporary. Quitting lasts forever.”

Lance Armstrong

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### III. Summary

My doctoral thesis contributes to the understanding of gait, mobility, and falls in older people. All presented projects investigated the most prominent and sensitive markers for fall-related gait changes, that is gait velocity and gait variability. Based on the measurement of these spatio-temporal gait parameters, particularly when using a change-sensitive dual task paradigm, it is possible to make conclusions regarding walking, balance, activities of daily living, and falls in older people. The research summarized in my doctoral thesis will help in the detection of early fall risk and modulation of therapeutic interventions to improve gait and consequently reduce fall risk in older people.

To identify modifiable fall risk factors, such as gait disorders, the GAITRite electronic walkway system was used for objective spatio-temporal gait analysis. The simplicity and feasibility of the administration of single and dual task gait analysis make it a desirable clinical and research measurement tool. Gait analysis with walking as a single task condition alone is often insufficient to reveal underlying gait disorders present during everyday activities. However, measuring gait with a dual task paradigm can detect subtle gait deficits. Dual-tasking, walking while simultaneously performing an additional task, was used to assess the effects of divided attention on motor performance and gait control.

The presented publications in this doctoral thesis investigated the association between gait parameters and several hypothesized fall-related modalities: (a) Our first review article highlighted the association between gait disorders and falls, and how related motor and cognitive impairments can be detected by measuring gait while dual-tasking. (b) A second review looked at how the dual task paradigm can be used for gait assessment in older people and how spatio-temporal gait parameters are associated with increased fall risk. (c) Our systematic literature review provided evidence about effective fall prevention interventions (exercise, home modifications, footwear, and walking aids) to reduce the risk of falls in vulnerable older people. (d) To evaluate which exercise modalities are effective in modifying risk factors for falls, we conducted an eight-week salsa intervention trial and measured the effect of dancing on static and dynamic balance, and leg muscle power in older people. (e) Besides exercise, inadequate nutritional intake is another modifiable risk factor for falls in older people, and therefore our most recent cross-sectional study examined how serum 25-hydroxyvitamin D levels are associated with functional mobility in older people assessed in a memory clinic. (f) Walking aids are commonly prescribed for older people with a high risk of falls which is why we examined the influence of walking aids on spatio-temporal gait parameters in older people who used a cane, a crutch or a walker. (g) Finally, besides predominantly investigating fall risk factors for motor abilities, our prolonged and ongoing randomized, double-blind, and placebo-controlled intervention trial explores the potential influence of ginkgo biloba on the cognitive domain relevant for dual-tasking in older people with mild cognitive impairment.

## IV. Introduction

### 1.1 The aging population

Aging is not a clearly defined single entity, but the result of a combination of anatomical, biochemical, and physiological changes that occur over time.<sup>1</sup> These changes can either be functional or pathological, modifying the individual's health status.<sup>2</sup> Successful aging does not only reaching a very old age, but also being able to live independently.<sup>3</sup> Older people, mostly defined as people aged 65 years and older,<sup>1</sup> have the goal to "age gracefully"<sup>3</sup> which includes living in their own homes, remaining independent and active, and contributing to social life of relatives and the community.<sup>4</sup>

In the past, life expectancy increased steadily by about two years per decade showing little sign of change.<sup>4-6</sup> Higher life expectancy and declining birth rates are a worldwide phenomenon, including industrial<sup>3,7,8</sup> and developing countries.<sup>9</sup> Worldwide, the number of people over 60 years is growing faster than any other age group and expected to grow from 688 million in 2006 to almost 2 billion by 2050.<sup>10</sup> In Switzerland, the proportion of people over the age of 65 years increased from 13.9% in 1980 to 16.6% in 2008, representing about one-sixth (1,276,400 persons) of the general population (57.6% female).<sup>9</sup> This increase will continue, at least partially, due to the generation of baby boomers from 1955 to 1964 who will reach retirement age between 2015 and 2035.<sup>9,11</sup> Within the population of older people, the sector of people aged 85 years and older is rapidly increasing (15.4% in 1970 to 28.4% in 2008).<sup>6,9</sup>

Although population aging is one of humanity's greatest triumphs, it presents today's societies with major challenges for the health and aged care systems.<sup>7,10</sup> The future increase of the proportion of older people is important for public health,<sup>12</sup> because aging is generally associated with progressive decline in physiological health.<sup>13,14</sup> Aging is further associated with an increased risk of disability and dependency,<sup>13</sup> as well as an increase in the number of comorbidities.<sup>15</sup> The research presented in this doctoral thesis helps to understand several of these detrimental outcomes of age-related changes in health and functionality (e.g. gait),<sup>4</sup> and investigates new intervention strategies.

### 1.2 Gait in older people

Gait is defined as any method of bipedal locomotion in humans.<sup>16</sup> The most frequently used gait in humans is walking.<sup>17,18</sup> Walking requires synchronization of more than 1,000 muscles over 200 bones and 100 moveable joints (Clark JE in Prince et al., 1997),<sup>19</sup> and is used to move the body forward while

maintaining postural stability. In this doctoral thesis the terms gait and walking are used interchangeably.

### **1.2.1 Walking is a complex motor skill**

Walking is the primary human movement for means of transportation<sup>20,21</sup> and physical activity<sup>22-24</sup> across ground level, uphill, or downhill.<sup>19</sup> The average person takes between 5,000 and 15,000 steps per day.<sup>18</sup> Walking often happens effortlessly and subconsciously, and therefore it is difficult to appreciate the immense complexities involved.<sup>18</sup> An important aspect of walking is the constant adaptation to the changing environment. The ability to walk results from coordinated processes involving sensory, respiratory, circulatory, cognitive, neuromuscular, musculoskeletal, and biomechanical systems<sup>25-28</sup> sending nerve signals via the spinal cord and peripheral nerves to the muscles which in turn move joints and limbs.<sup>16,29</sup> Thereby, walking constantly integrates numerous sensory, conscious, and competing inputs from all modalities of perception<sup>30,31</sup> to control the center of mass in relationship to the constantly changing base of support and achieve gait stability.<sup>32</sup>

### **1.2.2 Safe gait in older people**

A safe and efficient gait is not only integral to functional mobility and independence,<sup>33</sup> but also as a protective factor for falls.<sup>10</sup> Older people's gait is mainly influenced by age and the effect of pathological conditions.<sup>16</sup> Typical age-related gait changes start taking place between 60 and 70 years of age,<sup>16</sup> and are believed to increase gait stability while walking.<sup>16,34</sup> To date, there are no clearly accepted definitions for "normal" gait in older people.<sup>35</sup> Many older people adopt a stiffer, less coordinated, more conservative and precautious gait,<sup>25,36</sup> characterized by a slower walking speed, widened base of support, decreased stride length, increased double support time, increased stride time, and increased gait variability.<sup>16,26,35,37-39</sup> However, it is still unknown if these changes represent either a loss of stability or a compensatory strategy to stabilize gait<sup>39</sup> and avoid falls.<sup>38,40</sup>

## **1.3 Skeletal muscles and physical function in older people**

Skeletal muscles, also known as striated or as voluntary muscles, are responsible for the movement of the limbs.<sup>16</sup> A certain minimal amount of muscle strength is needed for human movement throughout life.<sup>41,42</sup> However, strength eventually declines to the point where activities of daily living (ADL), such as walking, become challenging.<sup>42,43</sup>

### **1.3.1 Aging and inactivity cause loss of skeletal muscle mass**

General causes of age-related skeletal muscle mass loss are manifold (i.e. cellular, neural, metabolic, hormonal contributors),<sup>14,44,45</sup> including sedentary lifestyle, inadequate exercise, decreased functional

capacity, decreased basal metabolic rate, inadequate nutrition, reduced levels of trophic hormones (e.g. growth hormones), decreased protein metabolism (i.e. reduced rate of muscle protein synthesis, protein degradation exceeds synthesis),<sup>14,42,46</sup> neurodegenerative processes (e.g. decrease in motor units),<sup>44</sup> and muscle fiber atrophy.<sup>46-48</sup> Humans lose approximately 20% to 30% of their skeletal muscle mass between young adulthood and 80 years of age.<sup>47</sup> The term used to describe this age-associated loss of skeletal muscle is sarcopenia (“sarx” is Greek for flesh and “penia” for deficiency)<sup>49, 42,45</sup> but to date there is no consensus on the definition of sarcopenia.<sup>50,51</sup> Operationally, sarcopenia is defined as a height-adjusted appendicular skeletal muscle mass of more than two standard deviations (SD) below the young normal mean.<sup>46,49</sup> The prevalence of sarcopenia increases from about 20% in people under the age of 70 years to over 50% in people over 80 years.<sup>49,52</sup> Sarcopenia is a multifactorial<sup>15</sup> condition that is associated with functional decline,<sup>53</sup> impaired physical function,<sup>54</sup> and frailty,<sup>55,56</sup> eventually leading to disability, dependence, and death in older people.<sup>49,51</sup>

### **1.3.2 Loss of muscle strength and muscle power decrease postural stability**

The aforementioned loss of skeletal muscle mass leads to an age-related muscle strength (ability of the neuromuscular system to generate tension)<sup>57</sup> loss.<sup>42,45</sup> Despite the direct correlation between the two measurements, muscle strength decline is faster than the concomitant loss of muscle mass,<sup>58</sup> and therefore may be more crucial for muscular function in older people. Beginning at age 30 to 40 years muscle strength declines at a rate of 3% to 5% per decade.<sup>59</sup> By the sixth or seventh life decade the decline in muscle strength increases up to 20%.<sup>42,59,60</sup> Age-related strength loss mainly depends on type II (fast twitch) muscle fibers<sup>15</sup> which are used for brief bursts of powerful contractions generating high forces (e.g. lift grocery bags).<sup>16,18</sup> The precise cause of the loss of type II muscle fibers is unclear, but it has been suggested that the number of type II muscle fiber motor neurons decreases during aging, eliminating innervation of these muscle fibers.<sup>42</sup> This predominant loss of type II muscle fibers supports recent research which shows that muscle power is more rapidly decreasing than overall muscle strength.<sup>61</sup> Muscle power reflects the maximal rate of rapid force production (generation of muscular work per unit of time)<sup>62,63</sup> which is important in walking, because sometimes quick postural reactions are needed in response to perturbations<sup>62</sup> to maintain balance and avoid falls.<sup>64</sup> Older people often try to maintain balance by increasing the size of the base of support using the step strategy (fall avoidance via a rapid step) rather than the hip strategy (fall avoidance through weight shifts at the hip) when the center of mass is moved toward the stability limits.<sup>25,26</sup> A decrease in muscle power would delay such postural reactions to external perturbations (e.g. correction step),<sup>65,66</sup> probably leading to loss of balance<sup>67</sup> and falls.<sup>25</sup>

### **1.3.3 Muscle power and mobility in older people**

Decreased muscle strength and power mostly stems from disease and inactivity rather than aging per se,<sup>25,36,52</sup> and can therefore be counteracted. Traditional strength training usually consists of progressive resistance training (PRT) which is defined as work in form of muscle contractions against

an external force that is increased as muscle strength increases.<sup>68,69</sup> PRT is required for acute and long-term adaptations in skeletal muscle mass and neuromuscular systems.<sup>45,46</sup> A standard protocol of PRT (e.g. 80% of one repetition maximum, three times per week, for a duration of eight weeks) primarily results in morphological adaptations through an increase in contractile proteins which in turn leads to an increased skeletal muscle mass (e.g. from 11.4% to 33.5%) and muscle strength (e.g. from 107% to 227%).<sup>68</sup> More recently, power training has shown to cause rather neuromuscular adaptations than skeletal muscle mass hypertrophy compared to PRT.<sup>61,62</sup> For example, eight weeks of power training elicited significant gains in muscle strength (e.g. 82% for leg curls) and muscle power (e.g.  $17.2 \pm 18.3\%$ , mean  $\pm$  SD, for knee extension at 60°/s), leading to increased physical performance (e.g. 10.4% reduction in chair rise time).<sup>62</sup> A recent study by Reid et al. (2008)<sup>61</sup> compared a 12-week muscle power training with traditional PRT in older people. The results showed that both training modes significantly increased muscle strength (49% vs. 41%), but muscle power training lead to higher gains in leg power (55% vs. 44%).<sup>61</sup> It can be concluded that power training may be superior in improving measures of physical performance and ADL in older people compared to traditional PRT.<sup>13,62,69-72</sup> However, both muscle power and muscle strength training are currently recommended to improve physical performance and prolonged functional independence in older people.<sup>5,62,68,73-76</sup>

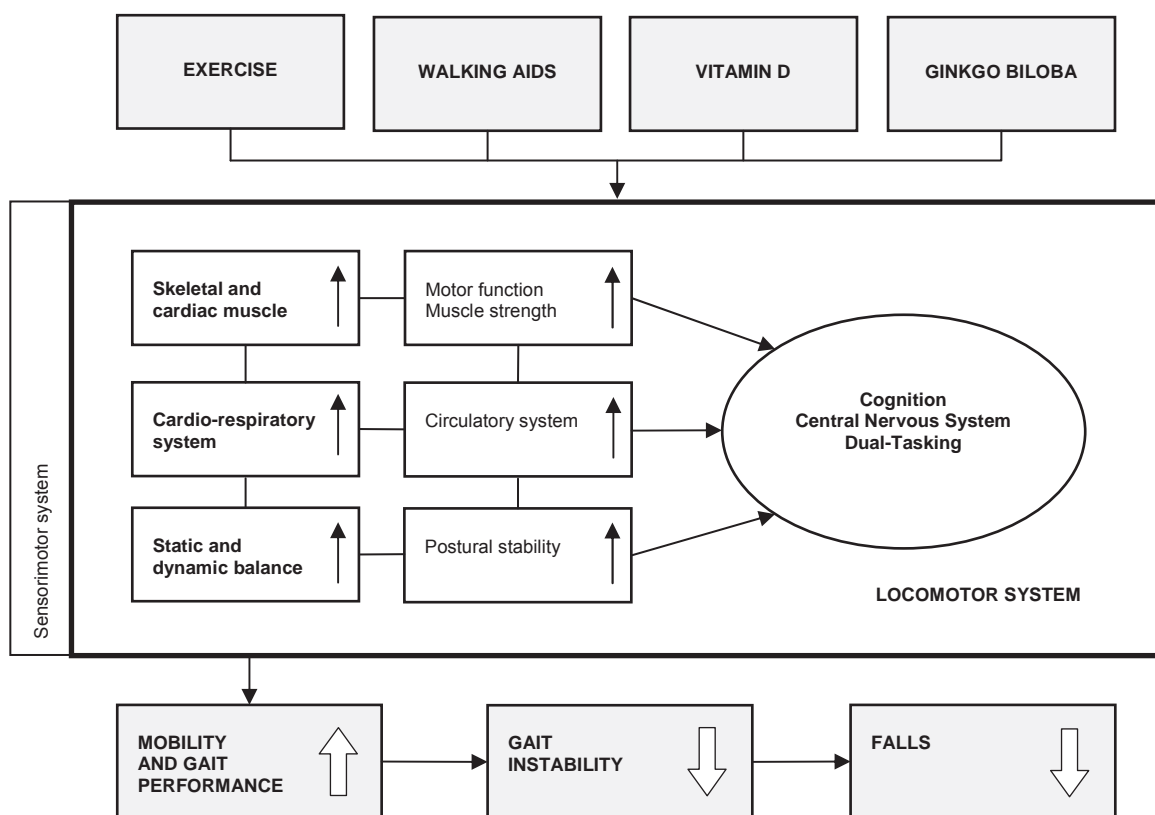
## 1.4 Falls in older people

Falls are among the most common and serious public health problems<sup>77-83</sup> facing the growing population of older people,<sup>84,85</sup> and will increase to epidemic proportions in all parts of the world over the next few decades.<sup>10</sup> The consequences of falls in older people can be devastating, contributing to a considerable increase in mortality and morbidity<sup>25,36,82,86-88</sup> negatively impacting autonomy, health care systems and the community.<sup>12,89</sup> In many societies, falls in older people are perceived as “an inevitable natural part of aging” or “unavoidable accidents”, but most often they are predictable and preventable.<sup>10,40</sup>

### 1.4.1 Epidemiology of falls

Falls among older people often result in decreased physical activity, injury, and loss of autonomy which frequently require medical attention.<sup>10,12,90</sup> A fall due to a sudden or unexpected event, such as tripping, slipping, stumbling, hitting obstacles, or by falling from stairs<sup>25,36,88,91-94</sup> may also imply that an older person is not able to walk safely anymore.<sup>40</sup> The majority of older people over the age of 65 years falls during level-ground walking<sup>95,96</sup> as a consequence of irregular gait,<sup>97</sup> unstable balance, as well as reduced postural control, reflexes, muscle strength, and stepping height (Figure 1).<sup>25,36</sup>

The prevalence of falls in community-dwelling older people increases with age.<sup>98</sup> A fall is commonly defined as “an unexpected event in which the person comes to a rest on the ground, floor or lower level.”<sup>10,99-101</sup> Between 33% and 40% of community-dwelling people aged over 65 years fall at least once a year, and of those 50% will have repeated falls.<sup>25,78</sup> In people aged over 75 years the rate of falls and fall-related complications can increase up to 60%.<sup>25,36</sup> Falls and fall-related injuries in older people generate costs of about CHF 1.4 billion per year (average in Switzerland from 2003 to 2007).<sup>102</sup> Complications can be rather expensive, with a single fall-related hip fracture causing direct costs of about CHF 63,000.<sup>83,103</sup> As a result, healthcare impacts of direct (i.e. health care) and indirect (i.e. societal productivity) costs of falls in older people are significantly high.<sup>10</sup>



**Figure 1.** Exercise, walking aids, vitamin D and ginkgo biloba possibly influence the locomotor system, gait and fall risk. Adapted from de Bruin ED (2012),<sup>104</sup> Hausdorff et al. (2005),<sup>24</sup> and Hausdorff et al. (2001).<sup>105</sup>

### 1.4.2 Fall-related injuries

Although young children and athletes fall more often than older people, older fallers sustain more fall-related injuries due to comorbid diseases and age-related physiological decline.<sup>25,36,85</sup> Additionally, recovery from a fall injury is often delayed in older people, which in turn increases the risk of subsequent falls through deconditioning.<sup>25</sup> Overall, 10% to 20% of all falls in older people result in injury, hospitalization, or death.<sup>25</sup>

Although the relative proportion of falls resulting in a fracture is low, the absolute number of older people suffering fall-related fractures is considerably high.<sup>106</sup> One in ten falls causes serious injuries<sup>107</sup> of which 5% are a hip, pelvic, wrist, forearm, arm, or collar bone fracture.<sup>25,107,108</sup> In terms of morbidity and mortality, one of the most devastating fall-related injuries for older people is the hip fracture.<sup>1,103,109</sup> When older people lose their balance in the mediolateral plane,<sup>110,111</sup> they tend to fall to the side which can lead to a femoral neck fracture.<sup>110</sup> In Switzerland, accidental hip fractures have a rate of 7.7 per 1000 persons (3.9/1000 men, 10.3/1000 women).<sup>112</sup> Older people are prone to post-operative complications which often result in partial immobility, reduced ADL, and death.<sup>1,113</sup> As a consequence, hip fractures often affect functional ability and the potential for independent living.<sup>103</sup> Overall mortality of older people who sustained a hip fracture ranges from 11% to 23% at six months, 22% to 29% after one year, and up to 47% at five years after injury.<sup>109,114</sup> In survivors, 40% of older people are able to ambulate independently one year after hip fracture compared to 79% before fracture.<sup>109</sup> In this context, 27% of older people require more walking aids one year after a hip fracture surgery.<sup>113</sup> This hip fracture associated decline in functionality and mobility has a detrimental effect on living independently in the community and quality of life of older people.<sup>115</sup> Despite participation in multidisciplinary rehabilitation programs after a hip fracture, many individuals do not regain the level of functional performance they had before the fracture, which often prevents them from returning to their homes.<sup>103</sup> Hence, it is of uttermost importance to prevent a fall and possible consequent injuries in first place.

### 1.4.3 Fall risk factors in older people

Early, simple and effective detection of modifiable fall risk factors is important in geriatric medicine.<sup>110</sup> The detection of fall risk factors is integral to implement effective fall prevention strategies, as well as to prevent falls and its serious consequences.<sup>92,116,117</sup> This is a difficult endeavor, because falls in older people are often multifactorial,<sup>78,98</sup> and attributed to complex interactions between several intrinsic and extrinsic risk factors, as well as exposure to fall risk (e.g. due to a high activity level).<sup>10,106,110,112</sup> Fall risk assessment involves either the use of multifactorial assessments or functional mobility assessments. Multifactorial assessments identify possible fall risk factors and consequently implement appropriate interventions adjusted for the identified fall risk factors.<sup>36,117,118</sup> Functional mobility assessments identify possible fall risk factors in the physiological and functional domains of postural stability including strength, gait, and balance.<sup>96</sup> Some risk factors are irreversible while others are potentially modifiable with appropriate interventions.<sup>1,85</sup> The major focus of the projects in this doctoral thesis lies on three of the most common modifiable intrinsic fall risk factors: muscle strength (relative

risk ratio/odds ratio 4.4), gait (relative risk ratio/odds ratio 2.9), and balance (relative risk ratio/odds ratio 2.9) which are further discussed in chapters 1.3, 1.6 and 1.12 (Table 1).<sup>36,72,85</sup> A description of modifiable fall risk factors within the home (home falls hazards) or outdoors (public falls hazards)<sup>118</sup> was recently reviewed by Pighills et al. (2011)<sup>119</sup> and Gschwind et al. (2011) (Table 2).<sup>120</sup>

#### **1.4.4 Somatosensory decline and fall risk**

Over 400 risk factors for falls have been identified.<sup>98</sup> Many of those risk factors also contribute to immobility and functional decline in older people.<sup>121</sup> Risk factors for falls can be attributed to biological, medical, behavioral, environmental, and socioeconomic factors.<sup>10</sup> Particularly, structural and functional declines in the somatosensory system seem to increase the risk of falling due to their association with postural instability.<sup>26,65,92</sup> The affected sensorimotor functions are: vision and contrast sensitivity necessary to navigate safely through the environment,<sup>26</sup> and avoid tripping over obstacles (i.e. steps, curbs, tree roots);<sup>26</sup> hearing and vestibular function;<sup>26,122</sup> tactile information from the soles of the feet important for walking and balance control;<sup>26</sup> and sensory information from receptors in the muscles, tendons and joints providing feedback regarding joint position and body movement.<sup>26,106</sup> Intake of prescription and over the counter drugs are important as fall risk factors,<sup>123</sup> because their possible side effects or sedative effects may influence the somatosensory functions,<sup>36,81,117</sup> and thus improve or impair physical functioning.<sup>22</sup> It is important to critically review drug dosage and the possibility of drug reduction or drug withdrawal for fall risk reduction in older people.<sup>118,123,124</sup> Furthermore, falls can also have psychological and social consequences. In this context, fear of falling is a well-recognized concept.<sup>85</sup> Older people who fall can develop fear of falling even if the fall does not cause an injury.<sup>27</sup> The prevalence of fear of falling (54%) and consequent avoidance of activities (38%) is considerably high in community-dwelling older people.<sup>10,125,126</sup> As a result, ADL, mobility and social participation are decreased leading to weakness, isolation, and risk of future falls.<sup>10,27</sup>

#### **1.4.5 Walking aids and fall risk**

For older people with gait and balance problems specific assistive devices may provide a safer gait.<sup>25</sup> Walking aids, such as canes and crutches are used to support part of the body weight through the arms rather than the legs to increase stability and generate moment.<sup>16</sup> The use of walking aids may stabilize gait in older people with an increased fall risk, but such aids also require considerable attention and energy for handling,<sup>91,127</sup> which may paradoxically increase fall risk (see publication (f)). Instead of improving walking ability, improper use or tripping over the walking aid may be responsible for developing a cautious gait pattern<sup>128</sup> (slower walking speed, smaller steps, increased stance time, and decreased swing time)<sup>129</sup> or falling.



#### 1.4.6 Low vitamin D levels and fall risk

In the past, vitamin D studies predominantly focused on bone health<sup>130</sup> and calcium homeostasis<sup>131</sup> (e.g. rickets in children, osteomalacia, and osteoporosis in older people).<sup>132</sup> Vitamin D levels may decrease as a result of poor nutrition, missing supplementation,<sup>133</sup> and lack of sunlight in combination with age-related skin structure modifications.<sup>132,134-136</sup> Serum 25-hydroxyvitamin D [25(OH)D] represents the best clinical measure of systemic vitamin D status.<sup>137</sup> In older people, 25(OH)D levels often lie between 50 nmol/L and 75 nmol/L (to convert to nanograms per liter divide by 2.496),<sup>138</sup> which is markedly below healthy levels between 75 nmol/L and 190 nmol/L.<sup>137</sup> Low 25(OH)D is defined as less than 50 nmol/L<sup>139</sup> while the optimal upper level ranges over 100 nmol/L.<sup>131,138</sup> In terms of improved physical, muscle, or lower limb function in older people, several lower 25(OH)D thresholds exist: 40 nmol/L,<sup>131</sup> 50 nmol/L,<sup>140</sup> 60 nmol/L,<sup>141</sup> and 75 nmol/L<sup>130</sup> Further, low 25(OH)D levels (<75 nmol/L) are associated with lower muscle mass, greater visceral fat,<sup>142</sup> decreased distance vision (<25 nmol/L),<sup>143</sup> cognitive impairment (<25 nmol/L),<sup>144</sup> dementia (<25 nmol/L),<sup>145</sup> and fall risk.<sup>146</sup>

In community-dwelling older people low 25(OH)D (<50 nmol/L) is associated with poorer physical performance,<sup>140</sup> lower muscle strength,<sup>133</sup> decreased mobility, ADL disability,<sup>135</sup> and frailty.<sup>139,147</sup> Previous research showed that gait may be affected by low 25(OH)D concentrations adversely affecting different subsystems involved in gait control including muscular<sup>135,144</sup> and neuronal components.<sup>148</sup> In older people, vitamin D seems to improve muscle properties, postural and dynamic balance, and also executive functions which are all needed for walking.<sup>144,149</sup> A recent study by Annweiler et al. (2010)<sup>144</sup> highlighted the association between 25(OH)D and spatio-temporal gait parameters. Particularly, gait velocity has been linked to vitamin D by mechanisms involving skeletal muscles and the nervous system.<sup>144,150</sup> In older women, slow walking speed is associated with low 25(OH)D concentrations,<sup>144</sup> suggesting a higher risk for disability, institutionalization, and mortality in older people (see publication (e)).<sup>35</sup>

Falls may be reduced by oral vitamin D supplements in older people who have low 25(OH)D levels (risk ratio 0.96, 95%CI 0.92 to 1.01),<sup>151</sup> and in malnourished older people (hazard ratio 0.41, P = .02).<sup>87</sup> A meta-analysis by Michael et al. (2010)<sup>89</sup> showed that vitamin D supplementation (median, 800 IU/d) with or without calcium is associated with a 17% (95%CI 0.77 to 0.89) reduced risk for falling during 6 to 36 months of follow-up. In another meta-analysis of eight randomized controlled trials (RCT) in older people, the pooled relative risk for any dose of vitamin D preventing a fall was 0.87 (95%CI 0.77 to 0.99), whereas daily vitamin D doses in the range of 700 IU to 1,000 IU reduced fall risk by 19% (pooled relative risk 0.81, 95%CI 0.71 to 0.92).<sup>152</sup> Additionally, a meta-analysis of 12 RCTs in older people, vitamin D doses of more than 400 IU/d showed a pooled relative risk of 0.80 (95%CI 0.72-0.89) for non-vertebral fractures and 0.82 (95%CI 0.69 to 0.97) for hip fractures.<sup>153</sup> The importance of 25(OH)D for gait velocity and fall risk is further discussed in publication (e).

**Table 1.** Potential intrinsic fall risk factors in older people.

Domain	Fall risk factor	Domain	Fall risk factor
Mobility / Gait	Physiological impairments <sup>27</sup> Low activity level <sup>78</sup> Activities of daily living <sup>78</sup> Functional impairment <sup>85</sup> Poor mobility <sup>110,154</sup> Gait deficit / instability / impairment / disorder <sup>27,36,78,85,89,98,110,123,154-157</sup> Reduced walking speed <sup>154</sup>	Muscle strength	Sarcopenia <sup>123</sup> Frailty <sup>89</sup> Muscle function <sup>26,98</sup> Muscle weakness <sup>36,85,98,156</sup> Decreased muscle strength <sup>72,123,155</sup> Lower extremity impairments / weakness <sup>1,78,85,154</sup> Reduced muscle power <sup>1</sup> Poor grip strength <sup>85</sup>
Balance / Posture	Balance deficit / impairment <sup>36,78,82,85,89,110,123,155-157</sup> Reduced static and dynamic balance <sup>154</sup> Reduced postural stability <sup>154</sup> Deficits in postural control <sup>72</sup>	Cognition	Disordered central nervous system <sup>25,36,98</sup> Cognitive deficit / impairment / disorder <sup>25,36,85,98,110,154,155</sup> Dementia <sup>110,123,154,157</sup> Executive function (i.e. attention) <sup>158</sup>
Mental	Mental status <sup>78,82</sup> Psychic disorders <sup>110</sup> Depression <sup>78,98,110,123</sup> Fear of falling <sup>98,110</sup> Dizziness <sup>78,107,123,155</sup> Vertigo <sup>155</sup> Delirium <sup>98</sup> Confusion <sup>155</sup>	Vision	Poor vision <sup>25,26,36,78,82,89,110,123,154</sup> Visual deficit / impairment / disorder <sup>78,85,87,98,155</sup> Decreased / loss of contrast sensitivity <sup>1,26,155</sup> Decreased depth perception <sup>1,154,155</sup> Visual field dependence <sup>1</sup> Reduced peripheral vision <sup>154</sup> Poorer visual construction ability <sup>158</sup> Cataracts <sup>155</sup>
Bone	Unstable joints <sup>25,36</sup> Degenerative joint disease <sup>123</sup> Osteoporosis <sup>25,36,82</sup> Arthritis <sup>98</sup> Kyphosis <sup>98</sup> Foot problems <sup>25,36</sup> Foot deformity <sup>98</sup> Toe deformities (e.g. hallux valgus) <sup>159</sup>	Cardiovascular	Loss of consciousness Syncope <sup>98,107,110,155</sup> Hypoglycemia <sup>110</sup> Orthostasis <sup>78,98,110,123,155</sup> Drop attack <sup>107,155</sup> Transischemic attack <sup>110</sup> Stroke <sup>89,157</sup> Epilepsy <sup>98,110</sup> Cardiac arrhythmia <sup>110,155</sup> Cerebrovascular disease <sup>98</sup> Anemia <sup>25,36</sup> Cardiorespiratory insufficiency <sup>98</sup> Reduced endurance <sup>1</sup>
Incontinence	Urinary tract infections <sup>98</sup> Urinary incontinence <sup>36,78,110,123</sup> Nocturia <sup>123</sup>	Parkinson	Parkinson's disease <sup>89,98,107,123,154</sup> Cerebellar syndromes <sup>98</sup> Cervical myelopathy <sup>107</sup>
Sensation	Impaired sensory input <sup>98</sup> Neuropathy <sup>1,26,98,107,154</sup> Impaired proprioception <sup>26,155</sup>	Hearing / Vestibular	Hearing impairment <sup>78,110</sup> Vestibular impairment / dysfunction <sup>1,26,98,154</sup>
Medical	Chronic diseases <sup>82,154</sup> Acute illness <sup>25,36,154</sup> Recent hospitalization <sup>89</sup> Hypothyroidism <sup>25,36</sup> Insomnia <sup>123</sup> Reduced reaction time <sup>1,26,154</sup> Normal pressure hydrocephalus <sup>107</sup>	Others	Age <sup>27,82</sup> (>75 years) <sup>123</sup> Sex <sup>82</sup> (female gender) <sup>123</sup> Obesity <sup>160</sup> History of falls / fall history / previous falls <sup>89,110,123,155</sup> Malnutrition <sup>123</sup> Low 25-hydroxyvitamin D <sup>146</sup> Alcohol use <sup>25,36,82,98</sup>

**Table 2.** Potential extrinsic fall risk factors in older people.

Domain	Fall risk factor	Domain	Fall risk factor
Drug	Medication use <sup>27,81,82,89,98,110,155</sup> Cardiovascular drugs <sup>78,98,110,123,155</sup> Psychotropic drugs <sup>78,110</sup> Antiepileptic drugs <sup>117,155</sup> Neuroleptics <sup>155</sup> Sedatives <sup>81</sup> Hypnotics <sup>81,98,155</sup> Antidepressants <sup>81,155</sup>	Drug	Benzodiazepines <sup>81,155</sup> Analgesics <sup>78</sup> Diuretics <sup>110</sup> Adverse drug effects <sup>25,36,123</sup> Combination of drugs <sup>78,123</sup> Polypharmacy (use of 4 or more prescription drugs) <sup>85,87,98,154,155</sup>
Environment	Environmental hazards <sup>78,85,98</sup> Streets <sup>82</sup> Walkway cracks and ridges <sup>82,154</sup> Ice and snow <sup>154</sup> Home hazards <sup>89,155</sup> Accidents <sup>155</sup> Bedroom size in hospitals <sup>161</sup>	Stairs	Stairs <sup>82</sup> Steep stairs <sup>110</sup> Missing stair railing / lack of handrails on stairs <sup>27,154</sup> Missing handrails <sup>110</sup> Bedrails <sup>36</sup> Lack of grab bars around toilet <sup>154</sup>
Floor	Unsafe floor conditions <sup>82,98,123</sup> Slippery floors <sup>110</sup> Wet floors (caused by spills) <sup>36</sup> Polished or waxed floors <sup>154</sup> Cords and wires on the floor <sup>154</sup> Tripping hazards <sup>27,98,123</sup> Loose carpets / rugs <sup>27,82,85,110,154</sup>	Furniture	Low and instable furniture <sup>98,154</sup> Bed height <sup>36</sup> Low toilet seat <sup>154</sup> Shelving <sup>82</sup> Lack of bathroom safety equipment <sup>85</sup> Bathtubs <sup>82</sup> Lack of grab bars around bathtub <sup>154</sup>
Walking aids	Use of walking aid <sup>78,110,123,157</sup> Walker use <sup>154</sup>	Footwear	Inappropriate footwear <sup>82,98,110,123</sup>
Lighting	Inadequate lighting <sup>27,36,82,85,98,110,123,154</sup> Brightness <sup>154</sup> Placement of switches and fixtures <sup>154</sup>	Other	Pets <sup>110</sup> Inappropriate clothing <sup>110</sup>

## 1.5 Gait analysis

The assessment of physical functioning and mobility in older people is a crucial component in many clinical and research settings.<sup>162</sup> Measures of physical performance allow the quantification of therapeutic treatment of older people with disability, functional decline, and gait disorders at an early stage.<sup>39,163,164</sup>

### 1.5.1 Gait analysis in older people

Gait analysis is the systematic study of human walking<sup>16</sup> used to improve our understanding of gait, and the quantification of benefit of a treatment in older people.<sup>16</sup> As a vital sign, such as body weight or blood pressure, gait analysis may offer a powerful mechanism to understand and act on the health

of older people.<sup>165</sup> Many gait changes are common with aging,<sup>26,33</sup> but when gait becomes impaired (see chapter 1.7) this is associated with postural instability leading to falls.<sup>25,79</sup> Gait problems adversely affect function in 20% to 40% of people over 65 years and 40% to 50% of people aged over 85 years.<sup>25</sup>

Standardized performance-based measures are used to assess the contribution of gait and balance impairment to outcomes such as fall risk.<sup>166,167</sup> For example, a health professional could screen older people using a gait assessment to identify underlying treatable medical and fall risk factors, and consequently attempt to intervene to prevent adverse outcomes.<sup>16,25,40,79,164</sup> A gait assessment includes the synthesis of data from gait analysis, information about the older person obtained from the medical history and physical examination, combined with the experience of the observer.<sup>16</sup> In general, a gait assessment forms a basis of clinical decision making, helps with the diagnosis of disordered gait, or documents a patient's health condition.<sup>16</sup> Quantitative gait markers may improve the aforementioned diagnoses and help set intervention targets in older people.<sup>29,35</sup>

### **1.5.2 Limitations of observing gait**

Measures of gait are not constant but rather fluctuate with time and change from one stride to the next, even when environmental and external conditions are fixed.<sup>24</sup> Visual observation is the most common method of assessing gait disorders, but it lacks objectivity, validity and reliability. The eye has a limited ability to discern rapid motion,<sup>18</sup> gives no permanent record, cannot measure forces, and depends entirely on the skill of the individual observer.<sup>16</sup> Although some gait disorders can be identified by eye, others can only be detected with appropriate measurement systems.<sup>16</sup>

### **1.5.3 History of measuring gait**

The first movement recording systems were complex, expensive, required highly trained staff, took a long time to administer, and were not sensitive to detect clinically significant changes.<sup>154,168,169</sup> Gait was measured by measuring tape, stopwatch, and adhesive felt pads with soluble dye or talcum powder attached to the foot.<sup>169</sup> One of the major disadvantages of these approaches was the need to attach equipment to the subject's foot or footwear, thereby inhibiting natural gait, and the time needed to obtain a single measurement.<sup>169</sup> Currently a variety of clinical and laboratory measurement tools are commercially available for the assessment of complex neuromuscular functions of gait, balance, and postural control, change over time, baseline status, and the effect of interventions.<sup>82,154</sup> Motion analysis systems started with cine photography, before marker systems including television screens<sup>16</sup> were introduced.<sup>169</sup> Passive marker systems with light reflecting material are still in use today:<sup>16</sup> Vicon (Oxford Metrics Ltd., Oxford, UK), Elite (Bioengineering Tech & Systems, Milan, IT), Coda MPX 30 (Charnwood Dynamics Ltd., Loughborough, UK)<sup>18</sup>, or Expertvision (Motion Analysis Corp., Santa Rosa, CA, US). Active marker systems, typically with light emitting diodes (LED)<sup>16</sup> include: Selspot (Selspot AB, Molndal, SE) or Watsmart (Northern Digital Inc., Waterloo, CA, US).<sup>169</sup> A major

disadvantage of these marker systems is the difficulty in appropriately placing the markers on the skin and digitizing the position of markers.<sup>18</sup>

In the past decades, technologies such as computer or direct video recording to a digital versatile disc (DVD) allowed extensive gait examination on computer or television (TV) monitor.<sup>16</sup> A more modern gait analysis system is the Clinical Stride Analyzer (B&L Engineering, Tustin, CA, US) which consists of footswitches placed inside the shoes (e.g. instrumented insoles),<sup>17</sup> and is attached to a portable data logger worn at the subject's waist.<sup>170</sup> Another wireless wearable system to collect quantitative gait data is called GaitShoe.<sup>138</sup> The GaitShoe has the advantage that it can be worn in any shoe, is designed to collect data over long periods, and can be applied even outside the traditional gait laboratory.<sup>138</sup> Recently, instrumented walkways are becoming increasingly popular for measuring the timing of foot contact, the position of the foot on the ground, or both:<sup>16</sup> GaitMat II (E.Q. Inc., Cahlfont, PA, US) or GAITRite (CIR Sytems Inc., Havertown, PA, US).<sup>18</sup> These user-friendly portable gait analysis systems allow a simpler measurement of spatio-temporal gait parameters, for both the examiner and the subject. These various gait analysis systems are often combined with measurements of further devices such as balance platforms (GKS 1000, IMM, Mittweide, DE),<sup>171</sup> force platforms (Kistler Corp., Winterthur, SUI), accelerometers (DynaPort MiniMod, Mc Roberts Moving Technology, The Hague, NL), electrogoniometers (Gait Analysis System, MIE Medical Research Ltd., Leeds, UK), or angular velocity transducers (Swaystar, Balance International Innovations Ltd., SUI).<sup>39</sup> Additionally, pedometers and gyro sensors can be put into small pods attached to the shoe and used via a wristwatch to measure steps and monitor activity: FitSense FS-1 (FitSense Technology Inc., Southborough, MA, US), or Nike sdm[triax 100] (Nike, Portland, OR, US).<sup>18</sup>

## **1.6 Quantifying gait with the GAITRite walkway system**

Electronic walkways have been developed to simplify gait analysis by eliminating the need to apply any instrumentation to the individual.<sup>17</sup> A commonly used tool to collect gait data, in the form of footfalls representing the interface between body and floor,<sup>18</sup> is the GAITRite instrumented walkway (Table 3).<sup>172</sup> The GAITRite system is a simple, efficient<sup>173</sup> and fast clinical tool for objective automated measurement of spatio-temporal gait parameters, both for the subjects and the test administrator.<sup>39,170</sup> Quantitative gait analysis with the GAITRite system was shown to be feasible, reliable, having strong concurrent validity and test retest variability.<sup>170,174</sup> GAITRite is sensitive to relevant gait changes in older people (e.g. detection of early signs of falls risk),<sup>174</sup> even in vulnerable older people with mild cognitive impairment (MCI) or dementia.<sup>170,174,175</sup> In addition, assessment of quantitative gait data using the GAITRite system is highly reliable under single and dual task conditions.<sup>174,176</sup>

**Table 3.** Specifications of the GAITRite Platinum walkway model.

Length	972 cm
Width	61 cm
Number of pressure sensors	29,952
Sample rate	60, 80, 100, 120,180, 240 Hz
Spatial resolution	±1.27 cm
Walkway top cover	Flame retardant, anti-slip vinyl
Walkway bottom cover	Open cell neoprene rubber
Internal materials	Uncoated polyesters
Electronic boxes (on the right-hand side of the walkway)	6 mm high

Note: cm = centimeters; mm = millimeters; Hz = hertz.

Adapted from Bridenbaugh and Kressig (2011).<sup>39</sup>

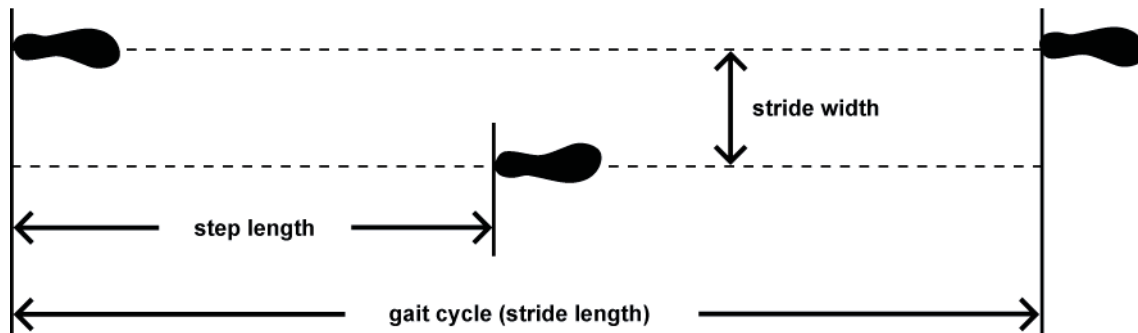
### 1.6.1 Standardization of the test environment for gait analyses

Gait analyses require sophisticated methodology and equipment to reduce the potential for systematic error.<sup>18</sup> They should be performed in a standardized, quiet, closed, and well-lit room with indirect lighting.<sup>177</sup> Subjects should wear comfortable and non-restricting clothing, footwear, glasses and hearing aids if needed, as well as a safety-belt around the waist for easy support by the examiner in case of loss of balance.<sup>177</sup> Furthermore, when using the GAITRite system, the test environment should be spacious while subjects can wear their own clothes, their own shoes and use their own walking aid.<sup>39</sup> Although wearing shoes may reduce standardization of the measurements, they should be worn to closely match normal, everyday walking.<sup>18</sup> The beginning and end of the walkway should be fixed to the floor to avoid tripping while an acceleration and deceleration phase of at least two meters ensures measurement of steady-state walking.<sup>177</sup> It is generally recommended that walking is measured under steady-state conditions to exclude measurements from phases of acceleration and deceleration.<sup>18</sup> The author Whittle MW (2008)<sup>16</sup> states that a preferable length for a gait analysis walkway is 10 m to 12 m, while Kressig et al. (2005)<sup>177</sup> recommend the measurement of six gait cycles, and Lord et al. (2011)<sup>172</sup> suggest analyzing 12 steps from continuous walking. The instructions should be standardized and all walks conducted in the same direction.<sup>177</sup> It is further not recommended to constrain walking by urging an older person to walk in time with a metronome or to step on particular places on the ground.<sup>16</sup>

### 1.6.2 Phases of the gait cycle

Each time a leg goes forward, it makes a step.<sup>18</sup> A step comprises the distance between sequential initial floor contacts by the ipsi- and contralateral leg. A stride, also referred to as one gait cycle,<sup>48</sup> consists of two steps (Figure 2). Broadly described, the gait cycle starts with the initial contact (0%) of one foot, and ends with the next contact (100%) of the same foot.<sup>18</sup> The gait cycle is further divided into stance phase (approx. 60%) which designates the entire period during which the foot is on the ground, and swing phase (approximately 40%) which refers to the time the foot is in the air.<sup>17,178</sup> Both

the start and end of the stance phase involve bilateral foot contact (double support), while during middle proportion of stance only one foot has contact.<sup>17</sup> The described phase of double support is the basic characteristic of walking<sup>17</sup> comprising about 20% of the gait cycle.<sup>18</sup> If double support were missing, a person would be running.<sup>18</sup>



**Figure 2.** Right and left footfalls indicating spatial gait parameters. Adapted from Bridenbaugh and Kressig (2011).<sup>39</sup>

The gait cycle consists of an initial contact (0% to 2%, right leg colored in black in Figure 3)<sup>17</sup> which marks the beginning of the loading response equal to the first period of the stance phase.<sup>16</sup> After the loading response (2% to 12%)<sup>17</sup> the double support period between initial contact and opposite toe off follows.<sup>16</sup> Toe off with the opposite foot is the end of the double support period known as loading response and the beginning of mid-stance (12% to 31%).<sup>16,17</sup> Mid-stance is the period of the gait cycle between toe off and heel rise, reflecting the first period of single support.<sup>16</sup> The time at which the heel begins to lift from the walking surface (heel rise) marks the transition from mid-stance to terminal stance (31% to 50%).<sup>16,17</sup> Opposite initial contact occurs roughly at 50% of the gait cycle marking the end of single support and the beginning of pre-swing (50% to 62%),<sup>17</sup> the second period of double support.<sup>16</sup> The part of stance phase between the double support phases, when only one foot is on the ground, is also referred to as single support.<sup>18</sup> Toe off (terminal contact) generally occurs at about 60% of the gait cycle separating pre-swing from initial swing (62% to 75%),<sup>17</sup> indicating the point when the stance phase (foot is on the ground) ends and the swing phase (foot is in the air) begins.<sup>16</sup> The time when the swinging leg passes the stance phase leg and the two feet are side by side is called feed adjacent, separating initial swing from mid-swing (75% to 87%).<sup>16,17</sup> When the tibia of the swinging leg becomes vertical at about 86% of the gait cycle, the terminal swing (87% to 100%)<sup>17</sup> begins.<sup>16</sup> The gait cycle ends at the next initial contact of the same foot (also known as terminal foot contact).<sup>16</sup>

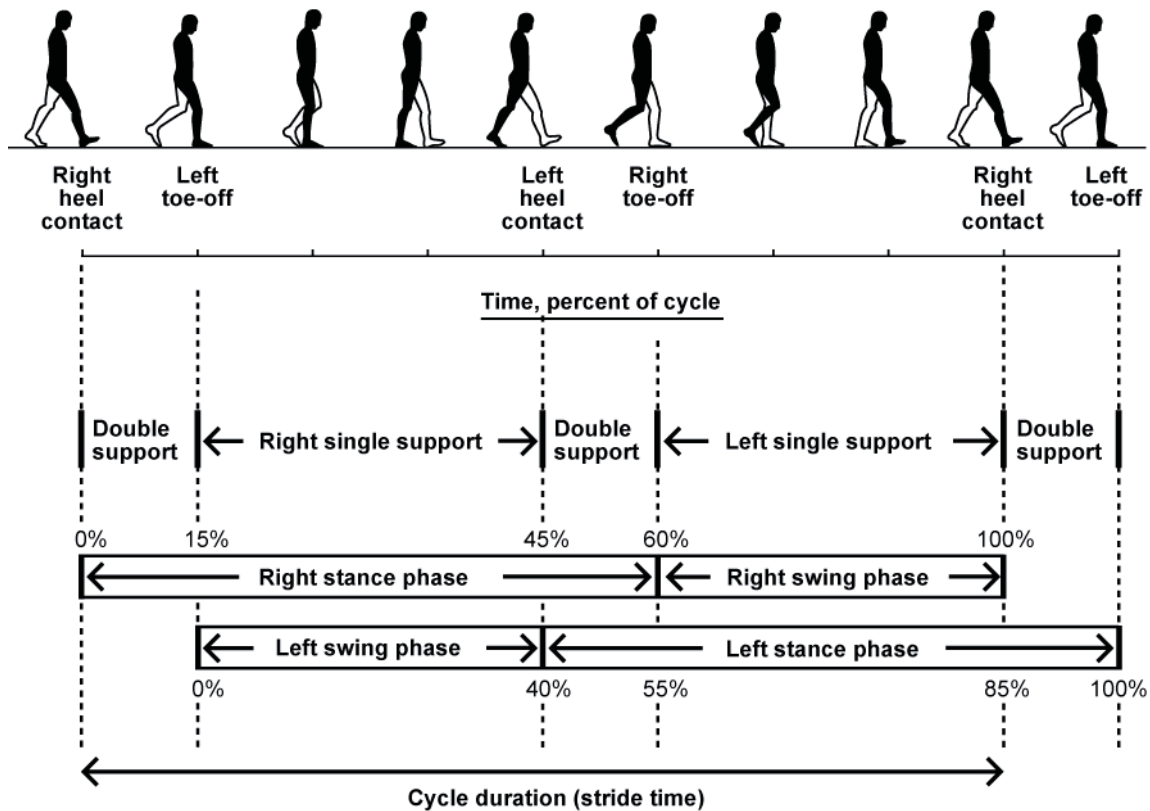


Figure 3. Temporal gait parameters of one gait cycle. Adapted from Bridenbaugh and Kressig (2011).<sup>39</sup>

### 1.6.3 Gait velocity is a vital sign for global health and functional status

The terms gait velocity and walking speed are used interchangeably in this doctoral thesis.<sup>179</sup> Gait velocity represents a simple, practical and informative “vital” clinical marker for global health (i.e. disability, chronic disease, physiological decline, cognitive impairment, falls, mortality)<sup>163,180,181</sup> and functional status (ADL)<sup>180</sup> in older people.<sup>18,182,183</sup> Changes in gait velocity may occur up to six years before clinical manifestation.<sup>167,180</sup> These changes in gait velocity are useful for understanding the risk and causes of falls,<sup>164,166,182</sup> and when monitored over time they may also indicate a new health problem that requires evaluation.<sup>28</sup>

Gait velocity decreases with age in healthy older people.<sup>184</sup> In community-dwelling older people gait velocity ranges from 40 cm/s to more than 140 cm/s,<sup>28,185</sup> whereas at least 100 cm/s seem to be required for unimpaired walking, and greater than 120 cm/s suggests exceptional life expectancy.<sup>28,186</sup> A walking speed of less than 100 cm/s is associated with an increased risk for limitations in gait and ADL.<sup>183</sup> Higher risk for adverse outcomes (i.e. functional and/or cognitive decline) is associated with a walking speed of less than 80 cm/s.<sup>181</sup> Severely impaired walking can be defined as walking slower than 60 cm/s<sup>186</sup> and is a sign for increased risk of early mortality.<sup>28</sup> In a group of older people with



various medical conditions, 4 cm/s to 6 cm/s was calculated as a small but meaningful improvement in physical performance, however, for moderate effects, 10 cm/s to 14 cm/s change were needed.<sup>165</sup> Furthermore, meta-analytic statistics showed that the overall hazard ratio for survival for each 10 cm/s increase in walking speed was 0.88 (95%CI 0.87 to 0.90) in community-dwelling older people, especially after the age of 75 years.<sup>28</sup> Improvement in gait velocity over time might indicate improved physiological health due to medical interventions or change in health behaviors such as exercise.<sup>182</sup> Significant improvement in usual gait velocity one year after baseline is associated with a 17.7% reduction in absolute mortality risk through the subsequent eight years in people aged 65 and older.<sup>182</sup>

#### **1.6.4 The association between quantitative gait parameters and gait stability**

Robust evidence supports the routine use of quantitative gait analysis<sup>182</sup> to enhance the understanding of movement control in older people and to better target preventive interventions.<sup>187</sup> The current literature reports several quantitative spatio-temporal gait parameters that offer important insight in normal and pathological walking patterns,<sup>169</sup> to make diagnoses (e.g. identifying older people at risk for falling),<sup>29</sup> determine appropriate therapy, and monitor patient progress.<sup>170</sup> Gait analysis usually comprises measurements of temporal (time) and spatial (distance) parameters.<sup>169</sup> In the literature, gait velocity, cadence, cycle time and stride length are common spatio-temporal gait parameters used for screening, performance measure, or monitoring a therapy (Table 4).<sup>18</sup> Today the major limitation is not to collect gait data, but identifying changes in spatio-temporal parameters associated with significant clinical change.<sup>16</sup> While established reference values for gait velocity exist, many spatio-temporal gait parameters, particularly those quantifying variability, are lacking.<sup>188</sup> To date, there is no good consensus about normative ranges for spatio-temporal gait parameters, however, Table 5 and Table 6 offer an overview of selected published data.<sup>18</sup>

#### **1.6.5 Gait velocity and fall risk**

Gait velocity is a simple and quick option for measuring fall risk.<sup>35</sup> There is a U-shaped relationship between gait velocity and falls with both extremes of walking speed showing higher rates of falls.<sup>189</sup> Older people with faster ( $\geq 130$  cm/s, incident rate ratio 2.12, 95%CI 1.48 to 3.04) and slower ( $< 60$  cm/s, incident rate ratio 1.60, 95%CI 1.06 to 2.42) walking speed had more falls compared to those with normal walking speed (100 cm/s to  $< 130$  cm/s).<sup>189</sup> Fallers often walk slower than non-fallers<sup>33</sup> with walking speeds below 70 cm/s having a 1.5-fold increased risk for falls.<sup>35</sup> Under a dual task condition the fall risk is already increased if gait velocity is below a threshold of a 100 cm/s.<sup>190</sup> Any decrease in gait velocity of 10 cm/s is associated with a 7% increased risk for falls (risk ratio 1.07, 95%CI 1.00 to 1.14),<sup>191</sup> while a decline in gait velocity (relative risk 5.9, 95%CI 1.9 to 8.5), requirement of a caregiver (relative risk 9.5, 95%CI 1.3 to 2.5), and new falls (relative risk 5.4, 95%CI 2.0 to 4.3).<sup>180</sup> However, other spatio-temporal gait parameters should be taken into account when looking at gait velocity, because walking is a complex functional activity and many variables influence gait velocity,<sup>179</sup> especially cadence (steps taken per minute),<sup>16,18,178</sup> stride length, or both.<sup>16,18</sup> There is a relationship

between cadence and leg length: those with shorter legs usually have a higher cadence.<sup>18</sup> Because cadence hardly changes with age (range of 100 steps/min to 130 steps/min),<sup>18,34</sup> stride length is more likely to be the source of decreased walking speed.<sup>18</sup> In addition, older people who fall may also walk with pronounced gait variability (see chapter 1.6.6 and 1.6.7).<sup>35,192</sup>

**Table 4.** Definitions of selected spatio-temporal gait parameters.

Gait parameter	Definition
Temporal parameters	
Cadence (steps/min)	Number of steps per minute
Step time (s)	Time elapsed from first contact of one foot to first contact of the opposite foot
Stride time (s)	Time elapsed between the first contacts of two consecutive footfalls of the same foot
Stance time (s)	Starts with heel contact and ends with toe off of the same foot and is equal to the weight bearing portion of each gait cycle: time elapsed between the first contact and the last contact of two consecutive footfalls of the same foot
Swing time (s)	Starts with toe off and ends with heel strike: time elapsed between the last contact of the current footfall to the first contact of the next footfall of the same foot Swing time is equal to the single support time of the opposite foot
Single support time (s)	One foot is on the ground: time elapsed between the last contact of the current footfall to the first contact of the next footfall of the same foot Single support time is equal to the swing time of the opposite foot
Double support time (s)	Both feet are on the ground simultaneously: consists of two periods called initial double support and terminal double support; initial double support occurs from the first contact of one footfall to the last contact of the opposite footfall; terminal double support occurs from the first contact of the opposite footfall to the last contact of the support footfall; total double support is the sum of the initial double support added to the terminal double support
Ambulation time (s)	Time elapsed between first contact of the first and the last footfalls
Velocity (cm/s)	Distance walked divided by the ambulation time
Stride velocity (cm/s)	Stride length divided by stride time
Spatial parameters	
Step length (cm)	Measured from the heel center of the current footprint to the heel center of the previous footprint on the opposite foot
Stride length (cm)	Measured between the heel points of two consecutive footprints of the same foot (left to left, right to right) Two steps comprise one stride or one gait cycle
Base of support (cm)	Vertical distance from heel center of one footprint to the line of progression formed by two footprints of the opposite foot
Step width (cm)	Measured from the midline midpoint of the current footprint to the midline midpoint of the previous footprint on the opposite foot
Stride width (cm)	Vertical distance from midline midpoint of one footprint to the line formed by midline midpoints of two footprints of the opposite foot
Gait variability	
Stride-to-stride fluctuations (%)	The CV is calculated by dividing the SD across all strides by the mean times a 100 [CV = (SD / mean) x 100]

Note: cm = centimeters; CV = coefficient of variation; min = minutes; s = seconds; SD = standard deviation.

Modified from Hollman et al. (2011)<sup>188</sup> and GAITRite Electronic Walkway Technical Reference (2012).<sup>193</sup>

### 1.6.6 Gait variability and gait instability

Research on the variability of walking began in 1960,<sup>16</sup> but the fluctuations in gait were largely ignored, or erroneously viewed as instrumental and physiological noise.<sup>24,172</sup> To date, gait variability (stride-to-stride fluctuations) seems to be a more sensitive marker of gait performance than conventional spatio-temporal measures such as gait velocity, step time, or cadence.<sup>172,192</sup> Measures of gait variability provide a clinical index of gait instability,<sup>24,194</sup> whereby increased variability represents a more unstable walking pattern<sup>174</sup> characterized by reduced postural control and stability which probably makes older people more susceptible to falls.<sup>27,176,188,195</sup> Gait variability may therefore serve as a sensitive and clinically relevant marker for impaired mobility,<sup>196</sup> fall risk,<sup>24</sup> and falls.<sup>197</sup> Further, gait variability has been used as an outcome measure for frailty,<sup>198</sup> cognitive decline, and the response to therapeutic interventions.<sup>24</sup> In healthy people gait variability remains fairly stable throughout the lifespan<sup>184</sup> which is why changes in gait variability seem to reflect underlying disease processes rather than age-related changes.<sup>199</sup>

Stride-to-stride variability is measured by the coefficient of variation (CV) and is a marker for the control of leg movements when walking.<sup>200,201</sup> The CV is calculated by dividing the SD across all strides<sup>176</sup> by the mean times a 100 [ $CV = (SD / \text{mean}) \times 100$ ].<sup>202,203</sup> The SD reflects the dispersion around the average value, and CV quantifies the magnitude of the deviations of the gait parameter with respect to each subject's mean value.<sup>203</sup> Using CV for expression of gait variability has the advantage of being a dimensionless unit, facilitating comparability with other studies,<sup>172</sup> and being more accurate than solely reporting SD.<sup>178</sup> The latter is often largely due to biological and instrumental variability making normative ranges based on SD rather wide, indicating that too many measurements would be considered normal (a false negative result).<sup>18</sup>

### 1.6.7 Stride time and stride length variability are associated with fall risk

Stride time variability, the magnitude of the stride-to-stride fluctuations in the gait cycle duration,<sup>203</sup> is considered the neural control for maintenance of a steady walking rhythm.<sup>204</sup> The CV of stride time variability is a good marker of higher-level subcortical and cortical involvement in gait control.<sup>202,205,206</sup> Significantly low and high stride time variability provide objective information for the diagnosis of gait unsteadiness and instability,<sup>194,205,206</sup> and serve as a fall predictor in older people.<sup>197,201,203</sup> Generally, lower stride time variability is associated with a safe gait,<sup>201,207</sup> because older people with a history of falling have a higher, up to twice or more, stride time variability compared to older people who had no fall.<sup>192,199</sup> The CV of stride time variability is usually below 3% among young healthy adults<sup>20</sup> with higher values being associated with decreased muscle strength, balance, walking speed, functional status, health status, and physical performance.<sup>199</sup> A stride time variability threshold of CV >4% for walking alone and CV >10% for walking during backward counting is proclaimed for older people at risk for falls and subsequent admission to an acute care geriatric department.<sup>173</sup> Furthermore, high stride length variability is a fall predictor,<sup>197</sup> whereas low stride length variability is associated with a safe gait.<sup>201,207</sup> Stride length variability under dual task conditions is significantly greater in older

people compared to younger adults,<sup>208</sup> whereas already a small increase of 1.7 cm in stride length variability doubles the likelihood of falling in the upcoming six months.<sup>197</sup>

Other spatio-temporal gait parameters are not covered by this doctoral thesis, because the literature may only provide limited evidence for their interpretation, or they are not relevant for the presented publications: swing time,<sup>24,178,196,209</sup> stride width,<sup>16,18,33,126,197,210</sup> stride width variability,<sup>196,210,211</sup> and stride velocity variability.<sup>188,197,212</sup>

**Table 5.** Selected spatio-temporal gait parameters in older people under a normal walking condition.\*

Author	Population	Age (years) <sup>†</sup>	n (male/female)	System	Gait velocity (cm/s)	Cadence (steps/min)	Step length (cm)	Stride length (cm)	Step width (cm)	Step time (s)	Stride time (s)	Stride length (%CV)	Stride time (%CV)	Stride width (%CV)	Stride velocity (%CV)	Swing time (%CV)
Beauchet et al. (2009) <sup>206</sup>	healthy	74.4 ± 7.1	33 (2/31)	GAITRite	NA	NA	NA	NA	NA	NA	NA	NA	2.1 ± 1.3	21.9 ± 10.3	NA	4.3 ± 3.2
Beauchet et al. (2005) <sup>202</sup>	transitionally frail	72.2 ± 6.3	16 (4/12)	Physilog	NA	NA	NA	NA	NA	1.10 ± 0.10	NA	NA	3.6 ± 1.8	NA	NA	NA
Beauchet et al. (2003) <sup>20</sup>	healthy	83.4 ± 7.7	12 (1/11)	Physilog	NA	NA	NA	NA	NA	NA	3.9 ± 1.6	NA	NA	NA	5.6 ± 2.2	NA
Dubost et al. (2006) <sup>201</sup>	healthy	65.3 ± 3.2	45 (21/24)	Physilog	135 ± 16	NA	NA	NA	NA	1.06 ± 0.10	NA	1.6 ± 0.6	NA	NA	NA	NA
Granacher et al. (2010) <sup>208</sup>	healthy pretest	71.9 ± 5.5	16	GAITRite	124 ± 15	NA	NA	139 ± 10	NA	NA	2.0 ± 0.7	NA	NA	NA	NA	NA
Brach et al. (2010) <sup>196</sup>	community-dwelling	80.3	241 (104/137)	GAITRite	96 ± 21	NA	57 ± 9	NA	9.9 ± 3.8	NA	NA	NA	NA	NA	NA	NA
Hardy et al. (2007) <sup>182</sup>	community-dwelling	73.9 ± 5.6	439 (244/195)	4 m course	88 ± 24	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Hausdorff et al. (2005) <sup>31</sup>	healthy	71.9 ± 6.4	43 (21/22)	25 m hallway	111 ± 28	NA	NA	NA	NA	1.09 ± 0.09	NA	2.0 ± 0.6	NA	NA	NA	NA
Hausdorff et al. (2001) <sup>198</sup>	community-dwelling non-fallers	80.3 ± 5.9	52 (16/36)	footswitches	91 ± 24	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Hollman et al. (2011) <sup>§212</sup>	community-dwelling	67-91	44 (20/24)	GAITRite	127 ± 24 125 ± 23	NA	NA	NA	NA	NA	NA	NA	NA	NA	4.7 ± 2.2 4.9 ± 1.9	NA
Hollmann et al. (2011) <sup>§198</sup>	community-dwelling	75-79	107 (30/77)	GAITRite	122 ± 15 112 ± 17	106 ± 10 114 ± 13	68 ± 7 59 ± 7	137 ± 12 118 ± 15	8.9 ± 5.2 7.7 ± 4.0	0.56 ± 0.05 0.53 ± 0.06	1.13 ± 0.09 1.06 ± 0.12	4.2 ± 4.6 4.7 ± 5.6	3.8 ± 4.4 5.2 ± 6.9	NA	5.5 ± 4.4 5.5 ± 2.7	4.5 ± 7.8 8.5 ± 9.5
Hollman et al. (2007) <sup>27</sup>	community-dwelling	>70	20	GAITRite	122 ± 23	NA	NA	NA	NA	NA	NA	NA	NA	NA	6.1 ± 2.0	NA
Ijmker and Lamoth (2012) <sup>37</sup>	demented	81.7 ± 6.3	15 (13/2)	DynaPort	67 ± 21	NA	NA	NA	NA	1.19 ± 0.12	NA	9.9 ± 5.3	NA	NA	NA	NA
Ijmker and Lamoth (2012) <sup>37</sup>	healthy	76.9 ± 4.1	14 (12/2)	DynaPort	114 ± 11	NA	NA	NA	NA	1.07 ± 0.04	NA	3.5 ± 0.9	NA	NA	NA	NA

**Table 5. (continued)** Selected spatio-temporal gait parameters in older people under a normal walking condition.\*

Author	Population	Age (years) <sup>†</sup>	n (male/female)	System	Gait velocity (cm/s)	Cadence (steps/min)	Step length (cm)	Stride length (cm)	Step width (cm)	Step time (s)	Stride time (s)	Stride length (%CV)	Stride time (%CV)	Stride width (%CV)	Stride velocity (%CV)	Swing time (%CV)
Kressig et al. (2008) <sup>173</sup>	inpatients non-fallers	84.0	47 (10/37)	GAITRite	NA	NA	NA	NA	NA	NA	NA	NA	5.3 ± 4.6	NA	NA	NA
Kressig et al. (2008) <sup>173</sup>	inpatients fallers	84.0	47 (10/37)	GAITRite	NA	NA	NA	NA	NA	NA	NA	NA	7.8 ± 5.6	NA	NA	NA
Kressig et al. (2004) <sup>187</sup>	transitionally frail	79.6 ± 5.8	50 (5/45)	Peak Motus	97 ± 23	106 ± 13	NA	111 ± 18	NA	NA	NA	NA	NA	NA	NA	NA
Maki BE (1997) <sup>197</sup>	healthy non-fallers fearless (n = 19)	82.0 ± 6.0	75 (14/61)	footswitches	NA	NA	14.0 ± 4.0	101 ± 23	NA	NA	1.27 ± 0.16	NA	NA	NA	NA	NA
Maki BE (1997) <sup>197</sup>	healthy fallers fearless (n = 17)	82.0 ± 6.0	75 (14/61)	footswitches	NA	NA	15.0 ± 3.0	89 ± 19	NA	NA	1.23 ± 0.16	NA	NA	NA	NA	NA
Montero-Odasso et al. (2011) <sup>198</sup>	community-dwelling non-frail (n = 25)	82.0 ± 5.4	100 (22/78)	GAITRite	124 ± 13	118 ± 7	64 ± 7	127 ± 14	NA	NA	1.02 ± 0.06	4.0 ± 1.5	2.3 ± 1.1	NA	NA	NA
Montero-Odasso et al. (2011) <sup>198</sup>	community-dwelling pre-frail (n = 55)	82.0 ± 5.4	100 (22/78)	GAITRite	95 ± 21	106 ± 9	59 ± 8	109 ± 18	NA	NA	1.14 ± 0.11	5.1 ± 2.8	3.0 ± 1.4	NA	NA	NA
Montero-Odasso et al. (2011) <sup>198</sup>	community-dwelling frail (n = 20)	82.0 ± 5.4	100 (22/78)	GAITRite	80 ± 19	101 ± 21	56 ± 8	99 ± 16	NA	NA	1.21 ± 0.14	5.7 ± 2.2	3.8 ± 2.0	NA	NA	NA
Montero-Odasso et al. (2009) <sup>174</sup>	MCI patients baseline	76.6 ± 7.3	11 (5/6)	GAITRite	119 ± 20	NA	66 ± 12	132 ± 24	NA	0.55 ± 0.04	1.10 ± 0.07	NA	NA	NA	NA	NA
Öberg et al. (1993) <sup>82,13</sup>	healthy	70-79	29 (14/15)	photocells	118 ± 15 111 ± 13	115 ± 8 122 ± 8	62 ± 5 54 ± 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sterke et al. (2012) <sup>214</sup>	nursing home	81.7 ± 7.0	176 (72/104)	GAITRite	63 ± 25	99 ± 16	NA	76 ± 26	10.7 ± 4.0	NA	1.30 ± 0.4	9.3 ± 5.4	9.6 ± 32.7	19.1 ± 11.7	NA	NA
Van Iersel et al. (2007) <sup>175</sup>	inpatients no dementia (n = 46)	78.3	85 (38/47)	GAITRite	65 ± 31	NA	NA	NA	NA	NA	NA	4.5 ± 2.4	3.9 ± 2.9	NA	NA	NA
Van Iersel et al. (2007) <sup>175</sup>	inpatients demented (n = 39)	78.3	85 (38/47)	GAITRite	61 ± 30	NA	NA	NA	NA	NA	NA	6.5 ± 2.2	5.0 ± 2.3	NA	NA	NA
Verghese et al. (2007) <sup>178</sup>	healthy	78.9 ± 4.7	366 (160/206)	GAITRite	94 ± 24	102 ± 12	NA	111 ± 21	NA	NA	NA	NA	NA	NA	NA	NA

**Table 5. (continued)** Selected spatio-temporal gait parameters in older people under a normal walking condition.\*

Author	Population	Age (years) <sup>†</sup>	n (male/female)	System	Gait velocity (cm/s)	Cadence (steps/min)	Step length (cm)	Stride length (cm)	Step width (cm)	Step time (s)	Stride time (s)	Stride length (%CV)	Stride time (%CV)	Stride width (%CV)	Stride velocity (%CV)	Swing time (%CV)
Whittle MW (2008) <sup>‡16</sup>	healthy	65-80	female	NA	116.0	116	NA	120	NA	NA	1.07	NA	NA	NA	NA	NA
Whittle MW (2008) <sup>‡16</sup>	healthy	65-80	male	NA	121.0	103	NA	141	NA	NA	1.22	NA	NA	NA	NA	NA

\* mean ± standard deviation; <sup>†</sup> mean ± standard deviation or range; <sup>‡</sup> mean values of 95% confidence interval range; <sup>§</sup> upper values men, lower values women.

Note: cm = centimeters; MCI = mild cognitive impairment; min = minutes; NA = non-applicable; s = seconds; CV = coefficient of variation.

**Table 6.** Selected spatio-temporal gait parameters in older people under a dual task walking condition.\*

Author	Population Dual task	Age (years) <sup>†</sup>	n (male/ female)	System	Gait velocity (cm/s)	Cadence (steps/ min)	Step length (cm)	Stride length (cm)	Step width (cm)	Step time (s)	Stride length (%CV)	Stride time (%CV)	Stride width (%CV)	Stride velocity (%CV)	Swing time (%CV)
Beauchet et al. (2005) <sup>202</sup>	transitionally frail subtraction	72.2 ± 6.3	16 (4/12)	Physilog	NA	NA	NA	NA	NA	1.20 ± 0.10	NA	10.1 ± 8.9	NA	NA	NA
Beauchet et al. (2005) <sup>202</sup>	transitionally frail naming animals	72.2 ± 6.3	16 (4/12)	Physilog	NA	NA	NA	NA	NA	1.20 ± 0.10	NA	5.8 ± 7.2	NA	NA	NA
Beauchet et al. (2003) <sup>20</sup>	healthy subtraction	83.4 ± 7.7	12 (1/11)	Physilog	NA	NA	NA	NA	NA	NA	10.2 ± 9.3	NA	NA	12.5 ± 9.2	NA
Granacher et al. (2010) <sup>208</sup>	healthy subtraction, pretest	71.9 ± 5.5	16	GAITRite	106 ± 18	NA	128 ± 12	NA	NA	NA	4.0 ± 2.8	NA	NA	NA	NA
Dubost et al. (2006) <sup>201</sup>	healthy naming animals	65.3 ± 3.2	45 (21/24)	Physilog	121 ± 17	NA	NA	NA	NA	1.15 ± 0.14	NA	2.9 ± 1.5	NA	NA	NA
Hollman et al. (2011) <sup>§212</sup>	community-dwelling spelling	67-91	44 (20/24)	GAITRite	96 ± 23 105 ± 17	NA	NA	NA	NA	NA	NA	NA	NA	10.2 ± 6.5 7.1 ± 3.5	NA
Hollman et al. (2007) <sup>27</sup>	community-dwelling spelling	>70	20	GAITRite	97 ± 22	NA	NA	NA	NA	NA	NA	NA	NA	9.0 ± 6.5	NA
Ijmker and Lamoth (2012) <sup>37</sup>	demented letter fluency	81.7 ± 6.3	15 (13/2)	DynaPort	51 ± 18	NA	NA	NA	NA	1.19 ± 0.11	NA	12.9 ± 6.8	NA	NA	NA
Ijmker and Lamoth (2012) <sup>37</sup>	healthy letter fluency	76.9 ± 4.1	14 (12/2)	DynaPort	98 ± 10	NA	NA	NA	NA	1.10 ± 0.05	NA	4.3 ± 1.0	NA	NA	NA
Kressig et al. (2008) <sup>173</sup>	inpatients, non-fallers subtraction	84.0	47 (10/37)	GAITRite	NA	NA	NA	NA	NA	NA	NA	7.4 ± 7.0	NA	NA	NA
Kressig et al. (2008) <sup>173</sup>	inpatients, fallers subtraction	84.0	47 (10/37)	GAITRite	NA	NA	NA	NA	NA	NA	NA	17.2 ± 14.7	NA	NA	NA
Montero-Odasso et al. (2009) <sup>174</sup>	MCI patients subtraction, baseline	76.6 ± 7.3	11 (5/6)	GAITRite	111 ± 20	NA	65 ± 13	132 ± 25	NA	0.59 ± 0.07	1.18 ± 0.13	NA	NA	NA	NA

\* mean ± standard deviation; <sup>†</sup> mean ± standard deviation or range; <sup>§</sup> upper values men, lower values women.  
 Note: cm = centimeters; min = minutes; NA = non-applicable; s = seconds; CV = coefficient of variation.



## 1.7 Gait control and disorders

A gait disorder is, at best, an inconvenience, and at worst, a major risk factor for falls and injury (see publication (a)).<sup>40</sup> Gait problems have many etiologies<sup>25</sup> resulting from specific dysfunctions of the locomotor system including the nervous, muscular, skeletal, circulatory, and respiratory system.<sup>16,25,36</sup> A gait disorder may indicate a systemic decompensation in an older person<sup>35</sup> due to health problems such as stroke, different forms of arthritis, cerebral palsy, spinal cord injuries, multiple sclerosis, amputation, traumatic brain injuries, systemic diseases, foot deformities, and falls.<sup>18</sup> Further contributing factors to gait disorders are metabolic disorders, urinary disorders, cognitive decline, subdural hematoma, depression, anxiety, psychotropic medication, vitamin B12 and folic acid deficiency.<sup>35,128</sup> Often these problems stem from age-related changes and fall into five functional categories: deformity (e.g. contracture), decreased muscle strength (e.g. muscle atrophy), sensory loss (e.g. impaired proprioception), pain (e.g. excessive tissue tension), and impaired motor control (e.g. central neurological lesion in the brain or spinal cord).<sup>17,25,36</sup>

### 1.7.1 The generation of walking

Human movement is controlled and monitored by the nervous system consisting of the central nervous system (CNS) (brain and spinal cord) and the peripheral nervous system (all branches of nerves outside the spinal cord).<sup>41</sup> Three areas in the brain are particularly involved in the regulation of gait: the basal ganglia which learn and reproduce basic movement patterns,<sup>24</sup> the motor cortex which calls into action the necessary muscles for movement, and the cerebellum which monitors activity and provides feedback about the performance.<sup>16,40,215</sup> The central pattern generator which produces the nerve impulses initially causing walking is not located in a single place, but consists of networks of neurons in various parts of the brain and spinal cord.<sup>16</sup> On the spinal level, the central pattern generator provides cadence and rhythm for walking.<sup>215</sup>

Walking begins with incoming afferent sensory information from the periphery which is processed by the hippocampus and related regions to plan walking.<sup>30</sup> The plan of walking is then transferred to the primary cortex with simultaneous processing in the basal ganglia (long-term storage of motor programs) and cerebellum (control of timing).<sup>30</sup> On the efferent pathway from the brain to the periphery, spinal cord interneurons pass muscle firing patterns to motor neurons which activate skeletal muscles.<sup>30</sup> Lastly, the skeletal muscles will be activated to perform the movement of walking.<sup>41</sup>

### 1.7.2 Three levels of gait control

Gait disorders are often classified according to the location in the nervous system of the sensorimotor deficit.<sup>35</sup> The low sensorimotor level classifies gait disorders into peripheral sensory impairment, commonly caused by vestibular disorders, peripheral neuropathy, proprioceptive deficits, or visual ataxia.<sup>35</sup> Older people usually can compensate to such gait disorders and learn to overcome issues including Trendelenburg, antalgic and steppage gait characteristics.<sup>35</sup> The middle sensorimotor level

classifies gait disorders in lower switching structures of the CNS (i.e. cerebellum, brain stem).<sup>40</sup> Such middle-level deficits result from spasticity, hemiparesis, paraplegia, Parkinsonism, and cerebellar ataxia.<sup>35</sup> In these middle-level disorders, posture and locomotion are also impaired, resulting in impaired stepping patterns such as shuffling steps, reduced arm swing, and increased trunk sway due to disrupted sensory and motor modulation of gait.<sup>35</sup> High sensorimotor level gait disorders are due to disrupted or altered cortical control of gait.<sup>40</sup> Such disorders can impair the generation of gait impulse<sup>40</sup> which often results in walking patterns that are not suitable for safe ambulation.<sup>185</sup> High level sensorimotor deficits are characterized by deficits in planning, intention, and executive functions,<sup>117</sup> and are prominent in older people with frontal-related white matter lesions, normal pressure hydrocephalus, cognitive decline, cognitive dysfunction, slowed cognitive processing, or depression (see publication (a)).<sup>35</sup>

### **1.7.3 Frontal brain areas are associated with motor control**

The prefrontal cortex which plays a prominent role in cognitive aging, cognitive flexibility, attention division, executive function, dual-tasking and multi-tasking,<sup>174,216-219</sup> provides the stimulus to reach a destination and avoid obstacles while walking.<sup>215</sup> In dementia, particularly with impaired executive function,<sup>203,204,220</sup> dysfunction of the frontal lobe and its motor circuits may be related to balance disturbances, gait disorders, gait instability, and increased risk of falls.<sup>203,204,220,221</sup> Hence, in line with the cognitive theory of falling, aging of the frontal cortex may alter executive function, attention domains, and motor responses, prior to the generalized changes seen in normal cognitive aging,<sup>92</sup> and thus plays a key role in the regulation of routine walking.<sup>174</sup>

## **1.8 Walking while performing an attention-demanding task**

Daily life offers countless situations where locomotion requires coordination of multiple sensory stimuli for concurrent performance of motor and cognitive functions, such as carrying a cup of tea.<sup>219,222</sup> Such multi-tasking, performing several activities simultaneously, or dual-tasking, doing two tasks concurrently (often a cognitive and a motor task),<sup>223</sup> are omnipresent in daily life.<sup>31,219,223,224</sup>

### **1.8.1 Walking is not an automated motor activity**

Gait has been traditionally considered as an automated motor activity not involving cognition in form of executive control.<sup>27,225-227</sup> However, as described in chapter 1.9, current evidence shows a close relationship between gait and cognition.<sup>228</sup> Even in older people who have intact locomotor and cognitive function, routine walking requires executive function (e.g. attention)<sup>229</sup> for motor control.<sup>31,37,203,230</sup> This is particularly evident in frail older people who stop walking when they have to start a conversation with or answer a question to a walking companion.<sup>231</sup> Older people who “stop walking when talking” have more future falls, impaired gait, and difficulties with ADL compared to

those who continue walking.<sup>231</sup> Once they have fallen, older people may pay more active attention and consciously monitor their movements in an attempt to ensure safety.<sup>226</sup> Ironically, conscious movement control may be another factor that contributes to disruption of automaticity of walking, increasing the likelihood of subsequent falls.<sup>226</sup>

### **1.8.2 Multi-tasking**

Young adults do not have much difficulty performing several activities at the same time,<sup>232</sup> and therefore the performance of additional tasks during walking, dual-tasking per se,<sup>233</sup> does not represent a threat to stability. When the postural system is quite stressed, and young adults are required to perform a fairly complex additional task,<sup>91</sup> only minor changes in spatio-temporal gait parameters can be observed, implying that minimal attention is needed.<sup>207,209</sup> In contrast, in older people many concurrently performed simple cognitive and motor tasks drastically interfere with each other due to divided attention (see chapter 1.8.4), and have deleterious effects on mobility and safety.<sup>31,39,166,224,232,234-239</sup> This interference is often evident by a decrease in gait velocity<sup>233</sup> and an increase in gait variability compared to normal walking.<sup>27,32,212</sup> A resultant decrease in walking speed can be interpreted as an implicit strategy to avoid loss of balance and gait stability<sup>201</sup> while an increase in gait variability is viewed as a reflection of the inconsistency in the central neuromuscular control system's ability to regulate gait and maintain a steady walking pattern.<sup>24,32</sup>

### **1.8.3 The dual task paradigm**

In recent years, dual-tasking became the most popular method for testing the relationship between gait stability, executive functions and attention in older people.<sup>91,209,218,220,229</sup> Dual task paradigms are used to examine impaired attention function, attention allocation between two simultaneously performed (cognitive challenging)<sup>27</sup> tasks,<sup>220</sup> and involvement of cortical control in older people.<sup>30,202,203</sup> Instead of focusing on either motor or cognitive impairment, dual-tasking allows to assess the ability of an individual to pay with some attention resources for maintaining cognition, and vice versa.<sup>240</sup> The use of the dual task paradigm in gait assessment consists of walking and simultaneously executing an attention-demanding task,<sup>232</sup> and permits early detection of gait and cognitive impairments due to a central overload, which under a single task condition of walking may otherwise go unnoticed.<sup>39,240</sup> Such deficits in dual task performance are often due to difficulties performing the attention-demanding task<sup>27</sup> and predict clinically significant impairment in motor or cognitive function<sup>230</sup> which increases the risk and occurrence of falls in older people.<sup>32,116,201,237</sup>

### **1.8.4 The attention-demanding task in dual-tasking**

Older people attempt to compensate for disrupted attention allocation between two simultaneously performed tasks<sup>207</sup> by either slowing their gait to improve the cognitive output,<sup>241</sup> or by sacrificing the performance of the attention-demanding task to avoid gait instability.<sup>224</sup> In this context the

unconscious, healthy posture first or safety first strategy<sup>84</sup> suggests that older people tend to protect their motor functioning at the expense of cognitive performance when their balance is threatened during walking<sup>3</sup> in order to avoid hazards and falls.<sup>229</sup>

The choice of the attention-demanding task in dual task gait assessment has to be made carefully.<sup>92</sup> How attention is divided between two simultaneously performed tasks depends on the efficiency of executive functions and the attention load of each task.<sup>91,200,202,203,207</sup> The amount of attention needed for a task depends on the type and difficulty of the task,<sup>224</sup> as well as the priority given to one or both tasks.<sup>91,225,229,232</sup> Relatively simple tasks can already reveal much about the underlying limitations on people's ability to perform different tasks at the same time.<sup>232</sup> Compared to walking alone, gait becomes instable when walking and forward counting and even more when walking and simultaneously backward counting<sup>202,220</sup> or naming animals.<sup>190,229</sup> A verbal fluency task relies on semantic memory which is not directly associated with executive functions while an arithmetic task, like backward counting, depends on working memory which is a system for temporary storage and processing of information related to executive functions.<sup>92</sup> An arithmetic task may provoke higher gait instability compared to a verbal fluency task,<sup>92</sup> because counting has a strong rhythmic component which can influence the walking pattern when performed simultaneously ("magnet effect").<sup>235</sup> In this context it is interesting, that older people who counted fewer numbers while subtracting aloud starting from 50 when seated compared to when walking, had a higher risk of falling and more falls.<sup>235</sup>

### **1.8.5 Motor-cognitive interference**

When older people are required to divide attention among two simultaneously performed tasks performance in one or both tasks may decline.<sup>30</sup> The resultant deterioration in performance is known as dual task decrement or dual task interference.<sup>30,242</sup> The most widely accepted concept of dual task interference is the capacity sharing theory which assumes that older people share processing capacity among tasks.<sup>232</sup> If more than one task is performed at the same time, there is less capacity for each individual task, and performance is impaired.<sup>232</sup> In terms of gait this assumes that walking, or the execution of the concurrent task, or both are altered.<sup>229</sup> The bottleneck theory suggests parallel processing for certain mental operations.<sup>232</sup> If two or more tasks need the processing capacity at the same time, then a bottleneck results, and one or more tasks will be delayed or impaired.<sup>232</sup> In terms of gait, this results in slower walking speed or delayed performance of the concurrent task, because the neuronal networks involved in the two processes overlap.<sup>229</sup> Another concept of dual task interference is the cross-talk model. It depends on the information being processed, suggesting that it may be easier to perform two tasks at the same time when they involve similar inputs and need similar processing machinery.<sup>232</sup> Detection of dual task-related interference is relevant for fall prevention in older people, because a safe locomotion depends on efficient gait control.<sup>92</sup> Further, dual task-related interference may show the need of therapeutic interventions,<sup>239</sup> such as exercise or drugs, to improve attentional resources or make a particular task (e.g. walking) more routine.<sup>219</sup>

### 1.8.6 Gait and executive function

Executive function consists of initiation, planning, execution, response, inhibition, and attention associated with the prefrontal cortex and related brain networks.<sup>92,199,229</sup> They are required for the timing and sequencing in motor control and walking,<sup>30,195,203,229</sup> and ensure that the appropriate amount of attention is allocated to gait in dual-tasking and other multi-task situations.<sup>209,232</sup> Attention is a complex cognitive function that describes the information processing central capacity of an individual.<sup>91,239</sup>

Older people often have difficulties maintaining a stable gait pattern while dual-tasking<sup>209,228</sup> which can be related to executive dysfunction.<sup>219</sup> With aging and pathological conditions, especially when a gait disorder is present or under a dual task condition, executive functions become even more important for the performance of gait.<sup>204,229</sup> Impairment in executive function, especially in the ability to divide<sup>209</sup> and rapidly switch attention from one task to another<sup>219</sup> may impair mobility and gait stability<sup>194</sup> required to overcome hazardous situations (e.g. obstacles, uneven path),<sup>229,243</sup> and avoid falls.<sup>2,209,229,233</sup> This is particularly evident in older people with impaired cognitive function due to cognitive decline (e.g. dementia).<sup>194,203,225</sup>

Gait variability is sensitive to the ability to divide attention under a dual task walking condition, because executive function input is needed to allocate attention among simultaneously performed tasks.<sup>203</sup> Generally, irregular gait (e.g. CV of stride time)<sup>31,194</sup> is associated with impaired executive functions in older people.<sup>205,220,230</sup> The latter possibly causes a disturbance of the automatic stepping mechanism due to abnormal higher cortical levels of gait control.<sup>198</sup> Consequently, the detection of impaired executive function in older people emphasizes the importance of clinical gait analysis in the evaluation of walking,<sup>91</sup> and the suitability of spatio-temporal gait parameters as markers in the early diagnosis of dementia.<sup>194,203,220,225</sup>

## 1.9 The association between cognitive decline and gait

Recent findings suggest that cognition is essential for maintaining gait and balance, and that impaired cognition is associated with the risk of falls and fractures.<sup>30,92,117,118,203,216</sup> Hence, one of the major aims of dementia research is, or at least should be, to improve or maintain not only cognitive but also physical functioning.<sup>218</sup>

### 1.9.1 Gait analysis for detection of cognitive decline

Older people with cognitive disorders are one of the most vulnerable populations of our society and are more likely to experience mobility decline and falls.<sup>215</sup> Recent evidence shows that gait disorders can be found in early stages of cognitive decline and dementia.<sup>37,185</sup> Compared to older people with healthy cognition, those with Alzheimer's disease (AD) have slower and more irregular gait,<sup>203</sup> more

falls (a first clinical symptom of cognitive decline),<sup>107</sup> and more fall-related injuries.<sup>30,118</sup> Research is currently uncovering the associations between dementia subtypes and gait characteristics, although the value of gait analysis in the diagnostic process has yet to be fully recognized.<sup>29</sup> Identifying early quantitative gait markers of dementia may help detecting high risk older patients for further evaluation and intervention.<sup>178</sup> Spatio-temporal parameters collected during gait analysis represent such early markers and may be as sensitive as traditional tests of cognitive function.<sup>30</sup> Gait depends on and is a marker of executive function<sup>229</sup> which allows prediction of future risk of cognitive decline and dementia in initially non-demented older people.<sup>178</sup> Hence, gait analysis can help postponing or attenuating the diminishing components of cognitive decline.<sup>244</sup>

### **1.9.2 Mild cognitive impairment**

A wide range of cognitive functions decline in older people (e.g. attention and executive functions),<sup>245</sup> leading to MCI, a transitional zone between normal and pathological cognitive function.<sup>245,246</sup> Early detection of MCI is critical in order to begin therapeutic treatment as early as possible,<sup>247</sup> because older people with MCI appear to be at an increased risk of developing AD at a rate of 10% to 12% per year.<sup>248</sup> There are neither generally accepted criteria nor major classification systems providing consensus diagnostic criteria for MCI.<sup>249</sup> MCI is characterized by subjective and/or objective complaints of deterioration in cognitive performance, but no evidence of dementia.<sup>249</sup> In addition, ADL are preserved and complex instrumental functions are either intact or only minimally impaired.<sup>245</sup> Cognitive impairment can be in the memory (amnesic) or non-memory (non-amnesic) domain.<sup>245</sup> Either single or multiple cognitive domains can be affected.<sup>245</sup> Older people with MCI would greatly benefit from therapeutic interventions to prevent the progression towards dementia.<sup>248</sup> However, there is a lack of treatment options for MCI patients,<sup>246</sup> and the efficiency of drug interventions in older people with MCI is still unclear.<sup>250</sup> Besides brain atrophy, older people with MCI show deficits in regional cerebral blood flow,<sup>245</sup> for which ginkgo biloba with its microcirculation-increasing modalities offers a promising therapeutic option (see publication (g)). Furthermore, exercise may substantially reduce the odds for developing MCI,<sup>251</sup> but the effective characteristics of such interventions are not yet defined.

### **1.9.3 Dementia**

Dementia is widely recognized as a global public health problem,<sup>178</sup> and its prevalence is steadily increasing due to an increase in longevity.<sup>252</sup> An estimated 30 million people in the world are affected by dementia, and there are about 4.6 million new cases every year (one new case every 7 s).<sup>247</sup> Dementia is a syndrome caused by a great variety of diseases and progressively affects cognitive functioning in older people.<sup>247</sup> AD represents the most common form of dementia, leads to death within 3 to 9 years after diagnosis,<sup>253</sup> and accounts for over 50% of cases at autopsies and clinical studies.<sup>254</sup> The pathology of dementia and AD is mainly characterized by cerebral lesions and loss of neuronal cells<sup>97</sup> causing cognitive decline and memory deterioration in older people.<sup>254,255</sup> Brain

changes in AD are marked by severe neurodegenerative alterations, such as the loss of synapses and neurons, atrophy, and the selective depletion of neurotransmitter systems (e.g. acetylcholine) in the hippocampus and cerebral cortex.<sup>256</sup> AD is characterized by an accumulation of misfolded proteins in the aging brain which results in oxidative and inflammatory damage and consequently to energy failure and synaptic dysfunction.<sup>254</sup> Vascular injuries from strokes and white matter lesions also promote to the cycle of protein aggregation and oxidation in the brain contributing greatly to cognitive decline.<sup>254</sup> Two pathological hallmarks of AD are amyloid plaques and neurofibrillary tangles.<sup>253</sup> The deposition of amyloid  $\beta$  seems to trigger neuronal dysfunction and death in the brain while changes in tau, an insoluble microtubule-associated protein and major constituent of neurofibrillary tangles, may disrupt the structure and function of neurons.<sup>253</sup> Amyloid plaques correlate with subtle deficits in cognitive functioning and suggest early disease processes leading to AD.<sup>257</sup> Expensive and time-consuming tools such as computer tomography (CT), magnetic resonance imaging (MRI), single-photon emission computer tomography (SPECT), positron emission tomography (PET), and cerebrospinal fluid (CSF) are used for detection of these AD markers. However, AD can only be definitely diagnosed post mortem,<sup>253</sup> and gait analysis increasingly qualifies as a simple, cost-effective supportive diagnostic tool in the contribution to set a diagnosis for AD in vivo.<sup>253</sup> To date, the focus in treating cognitive decline lies on pharmaceutical therapy (see chapter 1.10) to enhance both cognitive and motor function (i.e. acetylcholine esterase inhibitors (AChEI) and memantine).<sup>30,253</sup> However, dementia does not appear to be contraindicated for exercise.<sup>218</sup> Exercise may help to reduce the prevalence of the disease and the high rate of falls,<sup>253</sup> as well as decrease associated morbidity (see chapter 1.11).<sup>30</sup> Efficient exercise strategies in older people with AD include training of complex over-learned motor activities, such as gait or dancing which prevent or improve higher level gait disorders.<sup>244</sup>

#### **1.9.4 Brain plasticity may improve cognitive function**

Traditionally, it was believed that anatomical structures of the human brain only change in morphology due to aging or pathological conditions.<sup>258</sup> However, recent research suggests that the brain maintains its ability to change in function and structure in response to environmental stimuli throughout life.<sup>259</sup> Theoretically based concepts suggest that structural brain plasticity plays a crucial role in coping and adaptation to environmental changes and disease.<sup>259,260</sup> It has been shown that learning-induced brain plasticity is also reflected at structural level,<sup>258</sup> allowing the acquisition of new skills.<sup>259</sup> As a consequence, age-related functional decline in large brain systems seems to be an evitable process of aging and can be reduced and possibly reversed in a stimulus-response specific manner.<sup>217,261</sup> It has been shown that even in older people the brain remains plastic and responsive to changes due to exercising.<sup>217</sup> Exercising modulates those features of the brain anatomy specifically associated with the demands of the exercise,<sup>262</sup> and therefore repetitive learning of a new skill is more critical for the brain to change its structure compared to continued training of an already mastered skill.<sup>260</sup> This implies that exercise should consist of long-term performance of several different motor tasks combined with changing sensory inputs to have the greatest effect on brain plasticity and related functional improvement.<sup>263,264</sup> With proficiency, lower activity in cortical motor control areas suggests

more efficiency in the control of movements<sup>265</sup> and a reduction in neural effort to perform a motor task.<sup>266</sup> As an example, gray matter (contains many cell bodies and nerve endings)<sup>16,267</sup> brain plasticity on a structural level is specific and fast adjusting to an exercise stimulus.<sup>258-260</sup> An increase in gray matter may be partially due to changes in blood flow<sup>259</sup> while the effect of increased sensory, cognitive, and motor activity must be induced via enhanced synaptic and neuronal activity.<sup>268</sup> In general, brains which have received increased stimulation through enhanced mental and physical activity are better protected from neurodegenerative processes, traumatic insults, or other forms of neural dysfunction.<sup>268</sup>

## **1.10 Cognitive enhancers and their effect on gait**

The preservation of cognitive function is important in older people to maintain independence and to prevent institutionalization.<sup>269</sup> Pharmaceutical therapy with AChEI and ginkgo biloba helps to diminish the negative effects of cognitive decline in older people with MCI and dementia.

### **1.10.1 Acetylcholine esterase inhibitors and memantine**

Usually AChEI, such as donepezil, galantamine, rivastigmine, and tacrine are used in the symptomatic treatment of cognitive decline in dementia.<sup>270</sup> The molecular mechanism of action of AChEI is through increased cortical and hippocampal acetylcholine, an important neurotransmitter for memory regulation and neural plasticity.<sup>215</sup> These drug-associated cognitive enhancements in neurotransmission<sup>254</sup> may also be important for gait performance<sup>203</sup> as shown by a study of Assal et al. (2008)<sup>270</sup> which reported a significant increase of stride time under dual task conditions in the control group compared to a galantamine group. Memantine is another drug used to treat symptoms of moderate to severe AD showing similar effects on gait. It is hypothesized that combined effects on the glutamatergic and dopaminergic systems improve high level sensorimotor deficits.<sup>271</sup> A recent study by Beauchet et al. (2011)<sup>271</sup> showed that after 16 months of treatment with memantine 20 mg once daily, the CV of stride time in patients with AD was significantly lower ( $3.6 \pm 1.3\%$ ) than at baseline ( $6.3 \pm 6.1\%$ ). The effect of memantine on CV of stride time was attributed to changes in higher-level gait control including prefrontal cortex whose atrophy is partly responsible for cognitive decline.<sup>271</sup>

### **1.10.2 Ginkgo biloba**

It is expected that in older people with MCI, gait and balance performance can be improved and fall risk reduced by treatment with cognitive enhancers due to an improvement in attention and executive function.<sup>215</sup> The approach to target cognition with an outcome to improve mobility, gait, and balance offers a new way to improve the autonomy and quality of life in older people suffering from cognitive decline.<sup>215</sup>



Ginkgo biloba derived from the Chinese “Yin-Kuo”, meaning silver apricot and “biloba” referring to its two-lobed, fan-shaped leaves.<sup>272</sup> Ginkgo biloba contains of 24% flavonoids (quercetin, kaempferol, and isorhamnetin) and 6% terpenens (ginkgolides A, B, C, J, M, and bilobalide).<sup>256</sup> It is gained from a dry extract of ginkgo biloba leaves.<sup>273</sup> The herbal preparation is prescribed for deficits in memory, concentration, and depression stemming from organic brain disease.<sup>272</sup> The costs for ginkgo biloba are low, ranging from USD 0.31 to 1.17 for 120 mg depending on the brand.<sup>272</sup> In human and animal studies ginkgo biloba shows peripheral and central effects, including vasomodulatory (e.g. increase in cerebral blood flow and dilatory effects on blood vessels), metabolic (e.g. increase in glucose and glycogen synthesis), antiplatelet (e.g. inhibition of platelet aggregation), and receptor as well as transmitter (e.g. receptor density modulation) modulating properties.<sup>272</sup> Particularly, the vasomodulatory properties may increase decreased regional cerebral blood flow in older people with cognitive decline and improve associated postural and gait disturbances (i.e. postural sway, decreased stride length, and increased stride length variability) (supposed mode of action in publication (g)).<sup>255</sup> In vitro and in vivo, ginkgo biloba may also have neuroprotective, antioxidant, and anti-apoptotic properties including protection against amyloid  $\beta$  aggregation, and decreased reduction of age-related acetylcholine receptors.<sup>256,273,274</sup> Ginkgo biloba is widely taken by older people with normal cognition or MCI for its potential effects to improve or maintain cognitive performance<sup>269,275</sup> A recent study by Yoshitake et al. (2010)<sup>276</sup> reported that, in a dose-dependent manner, ginkgo biloba positively affected the prefrontal cortex, the brain area that is neuroanatomically relevant to cognitive function and gait (see chapter 1.7.3). Once daily 240 mg ginkgo biloba for 12 weeks can improve aspects of quality of life in addition to cognitive functioning in older people with very mild cognitive impairment.<sup>249,277</sup> Demented patients treated with ginkgo biloba improved in cognitive test performance, neuropsychiatric symptoms, and ADL (Syndrome Short Test scores, a neuropsychological test for attention and memory, and Neuropsychiatric Inventory scores, an assessment of behavioral disturbances).<sup>252,277</sup>

However, the neurochemical correlates of the positive effects of ginkgo biloba on cognitive function are not yet fully clarified.<sup>276</sup> There is little evidence of the effectiveness of ginkgo biloba in the primary prevention or delay of dementia compared with placebo (3.3/100 person-years vs. 2.9/100 person-years,  $P = .21$ ).<sup>269</sup> Additionally, a large RCT ( $n = 1,545$ ) showed that intake of 120 mg ginkgo biloba twice daily had no effect on cognitive decline in older people with normal cognition or with MCI compared to placebo.<sup>275</sup> A possible effect of ginkgo biloba may take years to manifest,<sup>269</sup> and despite showing no effect on the conversion rate from MCI to dementia, it appears that ginkgo biloba at doses of 120 mg to 240 mg per day may have a relevant clinical impact on specific phases of cognitive decline.<sup>273</sup> Preliminary findings of a place-controlled study with ginkgo biloba showed that patients treated for at least four years had lower rates of developing AD compared to those who took ginkgo biloba for less time.<sup>278</sup> However, long-term intake of ginkgo biloba is safe and tolerable, and the rare side effects mainly include gastrointestinal symptoms.<sup>249,277</sup>

## **1.11 Physical activity for improving cognitive function, mobility and gait**

Physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure,<sup>279</sup> such as exercise, activities of daily living, occupation, and leisure.<sup>280</sup> Living organisms tend to decrease their physical activity as they grow older.<sup>42</sup> In humans, the consequences of reduced physical activity such as exercise are manifold and include obesity, osteoarthritis, cardiovascular disease, osteoporosis, type II diabetes,<sup>259</sup> and hypertension.<sup>22</sup>

### **1.11.1 Physical activity and exercise are important for health**

Physical activities such as walking are the most feasible, safe, and accessible mode of exercise for older people.<sup>10,22</sup> Regular physical activity can maintain or improve exercise capacity in all domains (strength, endurance, balance, flexibility), retard the biologic aging process, modify risk factors for chronic diseases, alter the expression or consequences of present diseases, affect psychosocial functioning, and lead to a higher quality of life and independence.<sup>22,42,44</sup> The Physical Activity Guidelines Advisory Committee report (2008)<sup>281</sup> shows that physical activity and exercise reduce the risk of mortality by approximately 30% in older people by improving cardiovascular health outcomes (i.e. coronary heart disease, stroke, control of blood pressure, dyslipidemia, and cardiorespiratory fitness), weight stability (i.e. preventing and treating metabolic syndrome and type II diabetes), bone mass density (i.e. decrease in hip and spine fractures), skeletal muscle mass (i.e. strength, power, neuromuscular activation), and mental health (i.e. cognitive decline, onset of dementia, depression). Maintenance of physical activity with aging may also partially prevent gait changes, balance decrease,<sup>279,282,283</sup> falls, and fall-related injuries.<sup>68,74,284</sup>

### **1.11.2 Exercise for fall prevention in older people**

The ideal exercise program for older people is a combination of walking, dancing (see publication (d)), resistance training, and balance training.<sup>59</sup> Effective exercise programs for older people generally consist of mainly two components performed on a regular schedule:<sup>52</sup> strength and balance.<sup>285,286</sup> Exercises to improve strength and balance are also one of the most feasible and cost-effective strategies in falls prevention among older people.<sup>10</sup> The recommended exercise interventions of the Panel on Prevention of Falls in Older Persons (2011)<sup>118</sup> and the current Cochrane Review (2012)<sup>146</sup> for community-dwelling older people consist of progressive balance, gait, and strength training in the form of tai chi group exercise, group exercise containing multi-components, individually prescribed multiple-component home-based muscle strengthening and balance training.<sup>287,288</sup> Of particular importance for fall prevention in community-dwelling older people seem to be lower limb muscle strength, gait and balance.<sup>5,106</sup> Previous research shows that especially multicomponent and multifactorial interventions are capable of reducing falls in older people.<sup>100</sup> On the one hand, multicomponent interventions refer to a set of interventions offered to all participants in a program that addresses more than one intervention category.<sup>118</sup> On the other hand, multifactorial interventions (strategies using several interventions together)<sup>106</sup> offer only the adjusted subset of interventions that target the risk factors that

have been identified through a fall risk factor assessment.<sup>118</sup> However, it is not yet known which components of successful multicomponent or multifactorial interventions are essential.<sup>100</sup> For detailed information about recommend exercise type, intensity, frequency, duration, and further components of exercise in fall prevention it is referred to a systematic review by Gschwind et al. (2011) (see publication (c)).<sup>120</sup>

### **1.11.3 Exercise-induced brain changes may improve walking**

The human brain maintains the capacity to change its structure and function according to exercise demands at old age.<sup>289</sup> The effects of physical activity and exercise on neurodegenerative diseases are not well understood, but modern medicine supports the importance of regular exercise<sup>218</sup> to affect the underlying causes of a neurodegenerative disease,<sup>290</sup> delay onset of cognitive impairment,<sup>291</sup> and slow neurodegenerative disease progression.<sup>290</sup> Aerobic exercise programs in older people are, for example, associated with increased neurogenesis, angiogenesis and synaptogenesis in the brain.<sup>218</sup> Besides improving physical performance, these adaptations lead to improvements in cognition,<sup>3</sup> and functional connectivity, both relevant for executive function.<sup>217</sup> Gait control in prefrontal brain regions depends highly on executive functioning and may therefore be improved by exercise.<sup>3,292</sup> Furthermore, exercise coupled with cognitive interventions may also make brain activity more efficient<sup>242</sup> due to possible crossover effects between the motor and cognitive modalities.<sup>218,243</sup> These crossover effects may help improve motor and cognitive dual-tasking performance in older people in regard to maintaining gait stability and reduce fall risk (see chapter 1.9.4).

## **1.12 Balance exercises improve stability**

Balance requires coordinated neuromuscular, musculoskeletal, and sensory systems<sup>107</sup> which make it a complex component that describes the ability to maintain equilibrium while standing or moving.<sup>29,279</sup> Maintaining balance is fundamental to many independent ADL (e.g. transitional movements like standing up from a toilet seat).<sup>129,293</sup> Walking is inherently a very challenging task to balance, because of the rather instable single support phase.<sup>1</sup> Despite this thread to balance, dynamic stability during walking can be preserved during short periods in which the body is unsupported.<sup>18</sup> In this context, compensatory strategies for recovering balance by keeping the center of mass between the base of support play an important functional role in preventing falls.<sup>72</sup>

### **1.12.1 Balance is important for safe walking and prevention of falls**

If individuals have poor static balance, then it can be inferred that their dynamic balance will be compromised as well which will affect their walking ability and/or increase their risk of falling.<sup>33</sup> Impaired gait and balance are associated with a sedentary lifestyle, chronic diseases, and physiological changes due to aging,<sup>18,129</sup> most of which are modifiable by exercise.<sup>22</sup> Specific balance

training can affect postural control, force production, and gait stability reducing the risk of falls and fall rates in older people.<sup>5,8,26,86</sup> Exercises that challenge postural stability such as ice-skating may also counteract age-related changes in balance.<sup>294</sup> However, walking interventions do not generally show an enhancement of balance.<sup>22</sup>

Previous research shows that balance exercises are recommended for all older people who had a fall.<sup>78</sup> However, standardization of balance training, for example as part of a dance intervention, is difficult due to various exercise modalities.<sup>22</sup> Balance is usually challenged by reducing the base of support, moving the center of gravity to the limits of tolerance, or reducing the need for upper limb support.<sup>12</sup> Stressors such as perturbation of ground support, a decrease in proprioception, vision, or vestibular system input, and increased compliance of the support surface may additionally challenge balance.<sup>22</sup> The application of balance training has been increasingly postulated in the geriatric population, but hardly any evidence-based guidelines concerning contents, optimal duration and intensity of balance training are available.<sup>72</sup> However, static and dynamic measures of postural control should be trained complementary<sup>171</sup> with a core of exercises on stable and unstable surfaces during bipedal or monopodal stance with eyes open or closed.<sup>72</sup>

### **1.13 Association between dancing and balance**

Balance involves anticipatory and ongoing postural adjustments and is thus a coordination task.<sup>5</sup> As dancing requires coordination of torso and limbs according to the perceived rhythmic component of music,<sup>262</sup> its practice is likely to be beneficial in maintaining balance abilities in older people.<sup>5</sup> In this context, a cross-sectional study showed that older social dancers had better balance and gait patterns (i.e. increased gait velocity and stride length) compared to normal older non-dancers.<sup>295</sup>

#### **1.13.1 Salsa dancing affects postural control**

Dance provides a vehicle for adequate exercises in a number of cultures.<sup>10</sup> Salsa dance, as one of many dance styles, may improve static and dynamic postural control which is important for walking, balance, and fall prevention in older people.<sup>171</sup> Dancing seems to be specifically suited for the promotion of balance due to frequent changes in direction, and because dance steps are performed on toes of the feet.<sup>171</sup> After dancing, older people might be able to imagine the steps just learned.<sup>244</sup> This in turn may improve locomotion, because motor imagery of gait is sensitive to the same brain areas as actual walking.<sup>296</sup> Additionally, the rhythmic component of salsa dance may resemble a stable walking pattern, possibly improving spatio-temporal gait parameters.<sup>171</sup> A recent study by Granacher et al. (2011)<sup>171</sup> showed that eight weeks of salsa training increased stride velocity and stride length, and concomitantly decreased stride time (see publication (d)). Thus, salsa dance may be a feasible exercise program for older people to improve static and particularly dynamic postural control.<sup>171</sup>

### 1.13.2 Jaques Dalcroze eurhythmics improves gait stability and reduces falls

In the early 20<sup>th</sup> century in Geneva, Switzerland, the composer Emile Jaques-Dalcroze (1865 to 1960) developed a program to improve rhythm in children known as Jaques-Dalcroze eurhythmics (JDR).<sup>283</sup> JDR consists of progressive multi-task exercises depending on movement coordination, attention, imagination, memory, musicality, and balance, performed to the rhythm of improved piano music.<sup>177,297</sup> The chosen music and its rhythm may play an essential role in recalling memories, especially memories of body sense and motor skills.<sup>298</sup> It has been shown that older people tend to synchronize their cadence to the rhythmic sound from a metronome or piano (frequency modulation)<sup>18</sup> making rhythmicity a key feature of walking.<sup>31</sup> Older people need to maintain a steady walking rhythm despite numerous sensory inputs and competing objectives<sup>31</sup> to adapt to any perturbations and postural challenges, and prevent falling.<sup>230</sup>

Repetitive motor training of complex skills from an early age on and for long periods of time<sup>263</sup> can induce anatomical differences in several brain areas that are involved in motor and auditory processing.<sup>265</sup> Through JDR, such automatic movement patterns may be relearned and integrated to a highly automated level of motor control.<sup>177</sup> A study by Kressig et al. (2005)<sup>177</sup> showed that women aged over 70 years who had practiced JDR for over 40 years had lower gait variability (CV of stride time,  $2.1 \pm 1.4\%$ ) compared to older women with no particular exercise routine ( $3.9 \pm 0.9\%$ ). In novice older exercisers the positive effect on gait variability under a dual task condition could be reproduced with a six months once per week JDR intervention.<sup>283</sup> Additionally, a remarkable 54% reduction in falls was observed in the same trial.<sup>283</sup> Further, a major advantage of such interventions, like JDR or salsa dance, are high attendance rates of 78%<sup>283</sup> and 92.5%, respectively,<sup>171</sup> which are a key factor for effective long-term exercising. In summary, dance and eurhythmic programs should include improvised movements to the rhythm of music and power-specific elements to optimally target various components of gait and postural stability.<sup>171</sup>

## V. Research objectives

This doctoral thesis investigates the association between gait, mobility, and falls in older people. Fall-related gait parameters (e.g. gait velocity and gait variability), and several aspects related to fall prevention are highlighted in a total of seven studies.

(a) Walking disorders can stem from motor as well as cognitive impairments. Using a dual task paradigm, walking while performing an attention-demanding additional task, helps to reveal gait problems and cognitive impairments. Deficiencies in these domains often lead to motor-cognitive interference which is thought to be an important contributor to falls in older people. Hence, our research objective was to highlight the current evidence in terms of walking disorders and falls including the association with attentional resources and dual-tasking.

(b) In the past decade, gait analysis became a routine clinical measurement and research tool. It is now possible to objectively quantify gait rather than relying on observation. This allows early detection of gait disorders before clinical symptoms become manifest which is important for early detection of fall risk factors and the implementation of primary fall prevention. Our research objective was to highlight the importance of gait analysis as part of fall risk assessments.

(c) Once an older person's gait is instable and prone to falls, fall prevention interventions should be implemented to reduce the risk of falling. Hence, the goal of our systematic literature review was to summarize current research about fall prevention in order to detect effective exercise, home modifications, footwear, and walking aids to form a basis for the implementation of evidence-based fall prevention in Switzerland.

(d) Jacques-Dalcroze eurhythmics improves walking stability and reduces fall rates in older people. Salsa dancing consists of comparable movements and therefore is expected to elicit similar effects on gait and falls. The objective of our dance intervention was to show that, in addition to walking stability, static postural control and muscular power are affected by salsa dancing. Our hypothesis stated that salsa dancing improves static and dynamic postural control and leg extensor power in older people.

(e) Vitamin D supplementation is a simple and cost-effective treatment for 25(OH)D deficiency. Epidemiologic studies showed that sufficient 25(OH)D levels are required for efficient fall prevention in older people. Despite associations between 25(OH)D, muscle and neuronal function, the exact mechanism of how vitamin D affects muscle strength and mobility remains unknown. The aim of our study was to examine the association between spatio-temporal gait parameters and 25(OH)D concentrations under a normal and fast walking condition in older patients referred to a memory clinic

using the GAITRite walkway system. It was hypothesized that higher 25(OH)D levels are associated with faster gait velocity during normal and fast walking in older patients assessed at a memory clinic.

(f) Walking aids such as cane or walker are used by many older people to improve static and dynamic postural stability. However, in the literature limited quantitative gait data is available on older people who use walking aids. Hence, the aim of our recent cross-sectional study was to improve the understanding of how spatio-temporal gait parameters are affected by walking aid use in community-dwelling older people. We hypothesized that older people walk faster and more stable when using a walking aid compared to unaided walking, and that older people who use canes walk faster than those who use crutches or a walker.

(g) Ginkgo biloba is prescribed to improve cognition in older people who suffer from mild cognitive impairment. It is thought that ginkgo biloba increases cognition, particular attention capacity, by improving cerebral blood flow. Higher attentional resources could further be used to increase walking stability, particularly under a challenging motor-cognitive dual task situation. Our hypothesis states that ginkgo biloba improves spatio-temporal gait parameters under dual task conditions in older people with mild cognitive impairment.

## **VI. Original research**

In this chapter all publications which have been considered for this doctoral thesis are presented:

**(a) Gait Disorders and Falls**

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**(b) Gait Changes and Fall Risk**

Page 62 ff.

**(c) Basis for a Swiss Perspective on Fall Prevention in Vulnerable Older People**

Page 70 ff.

**(d) Effects of a Salsa Dance Training on Balance and Strength Performance in Older Adults**

Page 81 ff.

**(e) Association between Serum Vitamin D Status and Functional Mobility in Memory Clinic Patients Age 65 and Older**

Page 90 ff.

**(f) The Effect of Three Different Types of Walking Aids on Spatio-Temporal Gait Parameters in Community-Dwelling Older Adults**

Page 115 ff.

**(g) Effect of Ginkgo Biloba Special Extract LI 1370 on Dual-Tasking in Patients with MCI: a Randomized, Double-Blind, Placebo-Controlled Exploratory Study**

Page 139 ff.



**Publication (a)**

**Gait Disorders and Falls**

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## Short Review

## Gait Disorders and Falls

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**Abstract.** Since approximately 30% of persons over the age of 65 fall each year, prevention of falls is a very important topic. Gait disorders and diminished ability to walk safely are associated with an increased risk of falling. In older adults, falls commonly lead to injuries, institutionalization, and early death. The resultant decline in activities of daily living further contributes to loss of mobility and independence. Gait analysis using the dual-task paradigm (e.g., walking and carrying a cup of tea) offers a sensible tool for detecting older persons prone to falling. Changes in gait patterns due to simultaneously performing a secondary attention-demanding task are interpreted as interference by competing demands for attentional resources in gait control. Exercise interventions such as Jaques-Dalcroze eurhythmics address these attentional properties and aim to decrease such interference. To fully stress physical capacities in older adults, not only does automaticity of walking have to be trained, but also simultaneous performance of additional tasks. Exercise interventions for fall prevention should focus on developing basic skeletal muscle strength as a prerequisite to training gait automaticity in dual or multiple task situations. Recommendations for further research center on new approaches to combine exercises with additional tasks to improve gait and functionality in older adults.

**Keywords:** older persons, gait disorders, falls, dual task, exercise

## Gait Disorders and Falls

Falls are a prevalent and serious clinical problem faced by older adults, often leading to morbidity, mortality, and the use of health care services (Rubenstein, 2006). Almost all fall incidents due to extrinsic factors, intrinsic factors, idiopathic mechanisms, exposure to risk, and risk-taking behaviors have one factor in common: They happen while walking (Rynänen, Kivelä, & Honkanen, 1991; Scott, Votova, Scanlan, & Close, 2007; Todd & Skelton, 2004). Although walking may seem to be a simple task, it is actually a complex motor skill that takes years for humans to learn and master (Woolacott & Shumway-Cook, 1990) and whose automaticity is often diminished in older adults (Wong, Masters, Maxwell, & Abernethy, 2008). Thus, simultaneously performing a cognitive or motor task while walking may cause gait disturbances and an increased fall risk, particularly in older adults (Kelly, Schrage, Price, Ferrucci, & Shumway-Cook, 2008). The following review focuses on gait and falls in older persons. Further, the age-related reduction of muscle strength in association with mobility and functionality is highlighted. Conventional exercise interventions are presented and compared to recent approaches aimed at decreasing fall risk.

## The Epidemiology of Falls

In 2005, the Prevention of Falls Network Europe defined a fall as “an unexpected event in which the participants come

to rest on the ground, floor, or lower level” (Lamb, Jøstad-Stein, Hauer, & Becker, 2005; see also Gibson, Andres, Isaac, Radenbaugh, & Worm-Petersen, 1987). Falls are one of the most significant preventable health problems facing older people (Duxbury, 2000). Approximately one-third of the population over the age of 65 years falls at least once a year. While half of those fallers suffer recurrent falls, retirement, and nursing home residents, as well as women in general are even more prone to falls (Campbell, Borrie, & Spears, 1989; Rao, 2005). The rates of falls and their associated complications are correlated with increasing age (Lord, Sherrington, Menz, & Close, 2007). As a consequence, falls are the leading cause of older adults’ developing a fear of falling, becoming institutionalized or disabled (Nikolaus, 2005).

Falls are often caused by environment-related accidents, gait and balance disorders, weakness and several forms of dizziness, drop attacks, or syncope. Other specific causes include neurological disorders, cognitive deficits, poor vision, drug side effects, alcohol intake, anemia, hyperthyroidism, unstable joints, foot problems, osteoporosis and chronic illness (American Geriatrics Society, British Geriatrics Society, & American Academy of Orthopedic Surgeons Panel on Falls Prevention, 2001; Fuller, 2000; Todd & Skelton, 2004). Consequently, since most older adults have multiple identifiable risk factors, it is difficult to determine one specific cause for falling.

A report by Beer, Minder, Hubacher, and Abelin (2000) revealed that in Switzerland falls are the most common type of accident sustained by older people (40.8/1000 men, 77.0/1000 women). In particular, tripping and slipping

cause many falls in older persons (Woollacott & Shumway-Cook, 2002). Falls are responsible for many severe injuries such as hip fractures and head injuries (Sattin, 1992). In fact, one out of ten falls causes severe injuries. The highest incidence of fall-related mortality occurs after hip fractures (3.9/1000 men, 10.3/1000 women) (Beer et al., 2000). Mortality following hip fracture is approximately 22–29% at one year from injury (Haleem, Lutchman, Mayahi, Grice, & Parker, 2008). As a consequence of falling, older adults often have to be institutionalized. Hospitalization after a fall has a considerable detrimental effect on independence and quality of life (Salkeld et al., 2000), and only about half of those seniors admitted are alive a year later (Dowling & Finch, 2009; Nikolaus, 2005; Rubenstein, 2006). It is noteworthy that underlying gait disorders are likely to increase falls (Dunn, Rudberg, Furner, & Cassel, 1992). Fallers as well as nonfallers who suffer from a fear of falling decrease their activities of daily living (ADL) (Nikolaus, 2005). Hence, if gait disorders are combined with a fear of falling (e.g., postfall anxiety syndrome), an older person may decrease their ADL even more drastically (Zijlstra et al., 2007). A vicious cycle is established that decreases not only social activities, but also physical functioning and may lead to frailty (Bauer & Sieber, 2008; Clark & Manini, 2008).

Many falls may not be reported to a health professional, particularly those in which no injuries were sustained. While most inpatient falls can be recorded by medical staff, there is still no adequate fall assessment tool available for outpatients. In most studies, falls are self-reported using questionnaires. Thus, accurate self-reporting of falls remains questionable: Do older adults define a fall the same way as health professionals? Does a fall “count” to the person if no injuries occurred? And can older adults remember the timing and details of the fall incident? Until more accurate assessments are developed and broadly available, data about falls must be regarded with caution.

## Fall Risk Factors in Relation to Functionality and Gait

Falls are seldom the result of a single cause, but rather often represent a multifactorial occurrence including intrinsic and extrinsic factors. Individuals with gait and muscle dysfunctions demonstrate a substantially increased risk of falls and fractures compared to healthy older adults (Rubenstein, 2006). Many falls are caused by accidents, environmental hazards, gait problems, and muscular weakness. The four most common risk factors for falls are muscle weakness (OR = 4.4), history of falls (OR = 3.0), and gait and balance deficits (OR = 2.9) (AGS, 2001; Rubenstein & Josephson, 2002). Individuals with a history of falls also often have an inferior static balance and sway more than those who do not fall (Overstall, Exton-Smith, Imms, &

Johnson, 1977). Since increased postural sway is associated with increased postural instability, this may pose another potential risk factor for future falling (Rogers, Rogers, Takeshima, & Islam, 2003). Further factors related to falls of older adults include aging, disease, reduced postural stability, decreased dynamic balance, gait disorders, strength deficits, difficulty standing from a chair as well as other fall contributors such as medication and environmental factors (Modreker & von Renteln-Kruse, 2009). Except for history of falls, all major risk factors for falls (muscle weakness, gait and balance deficits) are at least partially related to decreased skeletal muscular strength, decreased ADL, little exercise, and malnutrition. Hence, to retain mobility, functionality and independence in old age, modification of these risk factors is necessary (Rogers et al., 2003).

## Gait Disorders Causing Falls

Normal walking depends on several components including muscle strength, peripheral sensibility, free mobility of joints, neuromuscular and motor control, as well as normal sensory input (Lord et al., 2007). Gait and balance disorders have many etiologies and numerous therapeutic approaches exist. Gait problems adversely affect up to approximately 40% of older persons while half of the problems are severe (Rubenstein, 2006). Often, the first symptom of a gait disorder is an injurious fall (Sattin, 1992).

In the past, disordered gait was defined as gait that was slowed, esthetically abnormal or both; not necessarily an inevitable consequence of aging, but rather often a reflection of the increased prevalence and severity of age-associated diseases (Alexander & Goldberg, 2005). Gait disorders in older adults can be an inconvenience, albeit underreported, because they may not cause pain or discomfort (Duxbury, 2000). However, gait disorders can also be a major risk factor for falls and are often a sign of specific dysfunctions of the nervous, muscular, skeletal, circulatory, or respiratory system (Rubenstein, 2006). Often a gait disorder represents the combined effect of more than one coexisting condition, so that differentiating between disordered and normal gait can be difficult (Alexander & Goldenberg, 2005).

Gait disorders can be due to underlying diseases such as normal pressure hydrocephalus, sensory disorders, myelopathy, Parkinson syndromes, and cerebellar diseases.

Other contributors to gait disorders include metabolic disorders, tumors of the central nervous system (CNS), subdural hematoma, hyperthyroidism, depression, and deficiency of vitamin B12 and folate (Alexander & Goldberg, 2005).

Overviews by Alexander and Goldberg (2005) and Duxbury (2000) offer a classification of gait disorders based on the level of sensorimotor nervous system deficits. Low sen-

Table 1. Gait parameters in older adults

Gait parameters	<i>M</i> ± <i>SD</i>	Age	Sex	Reference
Velocity [m/s]	1.4			Götz-Neumann (2003)
(healthy)	1.25 ± 0.18	80.1 ± 16.0	m < f	Nelson et al. (1999)
	1.15 ± 0.20	70–79	m/f	Öberg et al. (1993)
	1.11 ± 0.19	71.1 ± 5.2	f	Lord et al. (1996)
Velocity [m/s]	< 1.0			Götz-Neumann (2003)
(impaired)	0.97 ± 0.23	79.6 ± 5.8	m < f	Kressig et al. (2004b)
	0.82 ± 0.26	79.4 ± 8.7	m < f	Nelson et al. (1999)
	0.66 ± 0.19	82 ± 6	m < f	Maki (1997)
Cadence [steps/min]	100–130			Götz-Neumann (2003)
(healthy)	118.2 ± 11.9	70–79	m/f	Öberg et al. (1993)
	115.4 ± 11.2	71.1 ± 5.2	f	Lord et al. (1996)
	108.0 ± 8.2	79.0 ± 3.0	m < f	Menz et al. (2003)
Cadence [steps/min]	105.7 ± 12.7	79.6 ± 5.8	m < f	Kressig et al. (2004B)
(impaired)	78.9 ± 14.3	84.4	m < f	Liu et al. (2009)
Stride length [m]	1.4			Götz-Neumann (2003)
(healthy)	1.30 ± 0.14	79.0 ± 3.0	m < f	Menz et al. (2003)
	1.15 ± 0.13	71.1 ± 5.2	f	Lord et al. (1996)
	1.15 ± 0.12	70–79	m/f	Öberg et al. (1993)
Stride length [m]	1.11 ± 0.18	79.6 ± 5.8	m < f	Kressig et al. (2004b)
(impaired)	0.83 ± 0.16	82 ± 6	m < f	Maki (1997)

Note. Average data of men and women calculated for Öberg et al. (1993). Stride length was calculated by multiplying step length by a factor of two.

sensorimotor diseases include peripheral sensory and peripheral motor impairments. Hence, CNS processing is not affected, though execution through the peripheral structures may be hindered. On this level, the patient can adapt well to the gait disorder and can compensate with an assistive device or altered environmental conditions. Mid-level sensorimotor diseases involve lower CNS structures of cerebellum, midbrain, brain stem and spinal cord. As a consequence, proper postural and locomotor responses may be prevented and the motor modulation of gait is disrupted. Consequently, the stepping pattern is abnormal, while gait initiation might remain normal. High sensorimotor diseases of the cerebral cortex may interfere with higher-order information processing. Cognitive dysfunction, for example, due to dementia, affects gait initiation and ambulation. This level of frontal lobe-related gait disorders often has a cerebrovascular component that may lead to frontal disequilibrium or gait apraxia, especially when distracted by other stimuli. However, most older patients have several comorbidities and therefore gait disorders are likely to represent deficits at more than one sensorimotor level.

## Gait Disorders and Cognitive Impairment

As mentioned earlier, gait disorders are common in subpopulations with cognitive impairments. Locomotor function depends on executive function, which can be affected in cerebral diseases such as mild cognitive impairment (MCI) or

dementia (Sheridan, Solomont, Kowall, & Hausdorff, 2003). In addition, deficits in language and visual spatial skills are dependent on executive functioning (e.g., attention) and are also common in cognitively impaired patients (Hulette et al., 1998). Hence, executive dysfunctions may be associated with the same brain networks responsible for the timing and sequencing of motor activity (Sheridan et al., 2003). As a consequence, patients with dementia have a twofold increased risk of falling compared to cognitive healthy older individuals. Further, patients with Alzheimer's disease often develop considerable difficulties with gait and postural stability (Sheridan et al., 2003). In this context, an increased risk of falling may be the first clinical symptom of cognitive decline or dementia progression (Nikolaus, 2005). In the Einstein Cohort Aging Study by Verghese et al. (2006), gait changes (irregular gait) were identified that preceded dementia by 5 years as diagnosed by neuropsychological and cerebral imaging assessments. Consequently, gait analyses may valuably contribute to the assessment of fall risk and aid in early detection of cognitive decline.

## Gait Parameters as Fall Predictors

A safe and efficient gait is important for mobility and independence in older persons (Nelson et al., 1999). Studying gait among older adults enhances our understanding of elders' movement control and is useful in quantifying out-

Table 2. Gait parameters as fall predictors

Gait Parameters	Change in fallers	Reference
Stride width	↑	Maki (1997)
Stride length variability	↑	Maki (1997)
Stride velocity variability	↑	Maki (1997)
Stride time variability	↑	Hausdorff et al. (1997)
Swing time variability	↑	Hausdorff et al. (2001)

comes of therapeutic interventions (Kressig & Beauchet, 2004). In addition, the ability to adapt gait patterns to different situations plays a central role in the safety of gait. Older adults with an increased risk of falling adopt a behavior pattern that often results in cautious gait (Nikolaus, 2005). Such a conservative gait pattern is characterized by reduced velocity, shorter step length, and increased step time variability (Menz, Lord, & Fitzpatrick, 2003).

Early detection of gait changes or deficits allows preventive measures to be implemented to stabilize gait, reduce fall risk, and thus maintain mobility and functional independence. Objective spatio-temporal gait analysis is particularly important in older persons because certain gait parameters have been identified as fall predictors. A number of studies revealed that frail older persons and fallers walk significantly slower, which is related to reduced cadence and shorter step length (see Table 1). A study by Studenski et al. (2003) showed that slow walkers (< 0.6 m/s) are admitted to the hospital significantly more often than fast walkers (> 1.0 m/s). Gait variability is a quantifiable feature of walking that is often altered (in terms of both magnitude and dynamics) in fallers (Sheridan et al., 2003). Maki (1997) showed that increased gait variability represents impaired motor control, which may reflect errors in foot placement, as well as an increased fall risk (see Table 2). The most important gait parameter for postural stability in older walking adults today is stride-to-stride variability, seen as a marker for gait regularity. If gait from one stride to the next is completely regular, there is no variability: The more irregular the gait, the higher the variability (Hausdorff, Rios, & Edelberg, 2001). In other words, stride-time variability represents the quantified magnitude of stride-to-stride fluctuations in the gait cycle duration (Hausdorff, 2005). Stride-to-stride variability is measured by the coefficient of variation ( $CV = [SD/mean] \times 100$ ), which is used as a clinical index of gait steadiness and has been found to be a sensitive predictor of falls in older persons (Allali et al., 2007; Hausdorff et al., 2001; Maki, 1997; Priest, Salamon, & Hollman, 2008). In fact, an increase in stride length of just 1.7 cm from one stride to the next nearly doubles the likelihood of falling in the next 6 months (Maki, 1997).

Under normal walking conditions (self-chosen pace) and specifically under dual-task conditions (walking while simultaneously performing another task, either motor or cognitive; see “Dual-Task Paradigm for Falls Assess-

ment”), high stride-time variability is strongly associated with impaired executive function and a high risk of falling in older people (Hausdorff, Edelberg, Mitchell, Goldberger, & Wei, 1997; Kressig, Hermann, Grandjean, Michel, & Beauchet, 2008; Sheridan et al., 2003;). Further, frail older adults suffering from recurrent falls without any known organic reason may present an increase of gait variability under dual-task walking conditions which are not detectable during walking alone (Springer et al., 2006).

## Clinical Application of Gait Analysis

In the past, most movement recording systems were complex, expensive, and required highly trained operators. Basic equipment such as tape, stopwatch, adhesive felt pads impregnated with dye attached to the foot, or the use of talcum powder dusted on the plantar surface of the foot, were used to measure temporal and spatial gait parameters. These research tools were not only time-consuming, but also had substantial disadvantages such as attaching equipment to the heels of patient’s footwear which consequently influenced natural gait (Begg, Wytch, & Major, 1989). More recent assessment tools facilitate gait analyses and offer a simple way to collect objective, valid, and reliable data (Menz, Latt, Tiedemann, Mun San Kwan, & Lord, 2004). To appropriately assess human gait, it is essential to evaluate temporospatial parameters as well as kinetic and kinematic gait data (Begg et al., 1989). Several systems are available to measure gait, ranging from optoelectronic systems (e.g., Vicon Motion Systems, LA, USA), force platforms (e.g., Kistler Corp., Winterthur, Switzerland), and shoe-integrated wireless sensor systems (“GaitShoe,” Bamberg, Germany; Benbasat, Scarborough, Krebs, & Paradiso, 2008), to electronic walkways with integrated pressure sensors (e.g., GAITRite® Gold, CIR Systems, PA, USA). All of these motion analysis systems have individual potential as a research tool and may be also combined with other external devices (e.g., accelerometers or surface EMG) in order to obtain more complete locomotion data. In general, newer assessment tools require substantially less time to collect data about gait, less human and financial resources to administer gait analysis, and are less prone to investigator-induced errors. Regardless of which system is used, it is important that standardized procedures for that system of gait analysis be implemented.

## Dual-Task Paradigm and Falls

Rarely do we just walk without doing anything else simultaneously. Everyday life offers numerous situations in which multiple sensory stimuli have to be coordinated to perform motor tasks while a simultaneous cognitive task is added (e.g., walking while talking on a cell phone). In the

past, gait has been described as an automated motor behavior. In a study by Poldrack et al. (2005) automaticity was defined as performance of a primary task which is minimally affected by other ongoing tasks. However, there is some evidence that gait in older persons is only partially automatic, implying that even highly automated gait requires some attentional resources (Beauchet & Berrut, 2006). Using a simple dual-task paradigm of walking and talking, Lundin-Olsson, Nyberg, and Gustafson (1997) showed that older patients who stopped walking in order to answer a question had a much higher fall incidence in the ensuing 6 months than those who could walk and talk at the same time. Changes in gait while simultaneously performing a secondary attention-demanding task are interpreted as dual-task interference and may play an important role in prediction of falls (Beauchet & Berrut, 2006).

Increasing evidence links executive function to motor skills (Yogev-Seligmann, Hausdorff, & Giladi, 2008). Impairment in one of the components of executive function (volition, self-awareness, planning, response inhibition, response monitoring, attention/dual tasking) may impact an individual's ability to walk efficiently and safely. Deficits in executive function, particularly in attention, are associated with typical gait disorders such as decreased walking speed and increased gait variability. The more difficult and challenging a combined task becomes under dual-task conditions (walking and simultaneously performing another difficult task), the more walking seems to rely on executive function (Yogev-Seligmann et al., 2008).

Dual-task paradigms are now widely used to examine attentional requirements for walking while performing a secondary task. Woollacott and Shumway-Cook (2002) defined attention as the information processing capacity of an individual. It is hypothesized that when attentional demands of a dual-task situation exceed the attentional capacity of an individual, performance of one or both tasks is impaired (capacity-sharing theory) (Lehle & Hübner, 2009). The bottleneck model is another theoretical approach to dual-task interference, which suggests that mental operations may compete for a single mechanism at the same time resulting in a bottleneck, whereby the performance of one or both tasks is delayed or impaired. Caused dual-task interference by concurrent tasks involving similar sensory inputs and sharing processing capacities is referred to as the cross-talk model (Pashler, 1994). In terms of fall prevention, this implies that interventions aiming to decrease the attentional demands for either walking or an additional task, for example, by increasing gait automaticity, may likely be beneficial.

Yogev-Seligmann et al. (2008) showed that dual task-related gait performance often deteriorated in older persons, while younger persons showed no change in gait parameters while performing a secondary cognitive task unless the postural control system was stressed by a very complex additional task, such as serial subtraction by 7 out loud from 500. The example of counting backwards depends on working memory, which is directly related to executive

functions. It seems that combining an arithmetic task with walking creates a competitive demand for executive functions, which may result in a decrease of lateral stability in older persons (Beauchet, Dubost, Gonthier, & Kressig, 2005). Other external influences such as acoustic perturbations also seem to have a greater negative effect on gait parameters in older versus younger adults. Because of high prevalence of vision and hearing impairments in older persons, cognitive tasks seem more appropriate than sensory stimulation (e.g., visual or auditory stimulation) for testing dual-task-related gait performance; however, spoken cognitive tasks may also interfere with gait performance due to their articulomotor and rhythmic component (Beauchet, Dubost, Aminian, Gonthier, & Kressig, 2005).

Nevertheless, reaction times to acoustic signals while sitting were faster in both older and younger persons than while walking, and thus indicate a possible attention interference between walking and reaction task (Lajoie, Teasdale, Bard, & Fleury, 1993). It is important to consider these differences to elicit interference for testing older adults under dual-task conditions, because the type of walking-associated task seems to matter. When using dual-task paradigms in gait analysis, one has to choose appropriate secondary walking-associated tasks to sufficiently stress the attentional resources and thus to quantify deterioration in either task.

Dual tasking is the most widely used approach to determine to what extent walking requires attention in an older subject. A review by Yogev-Seligmann et al. (2008) showed that a secondary task (e.g., holding a cup filled with water) negatively influenced gait in healthy older adults who had intact locomotor and cognitive function; however, as mentioned earlier, in older adults even walking alone is often not an automated behavior and needs some amount of attention. Consequently, there seems to be a walking-related attentional component while dual tasking which can be quantified.

Measuring the interference between gait and a simultaneously performed additional task can provide such quantitative measures. It is hypothesized that more of the total available attentional resources are allocated to walking in older than younger persons in order to compensate for age-related deficits such as decreased vision or skeletal muscle strength (Anstey, Lord, & Williams, 1997). Hence, dual task-related gait changes that occur with an additional task reflect competition for attentional resources and may provide an indicator of change in gait control (Beauchet & Berrut, 2006). In this context, a study by Chen et al. (1996) demonstrated that contact time while stepping over a virtual obstacle on a walkway was significantly higher in older adults when a secondary task was performed at the same time. The authors suggested that attention was divided under the dual-task condition, which resulted in decreased physical abilities to respond to environmental hazards. Recently, other studies also revealed that cognitive activity while walking, such as mental calculation may reduce gait velocity (Beauchet, Dubost, Hermann, & Kressig, 2005; Priest et al., 2008). In certain older adults, the required attentional demands for walking and si-

multaneously counting backwards may overload available central resources and explain major dual task-related gait changes as well as competitive interaction with executive function (Allali et al., 2007; Beauchet, Dubost, Gonthier et al., 2005b; Dubost et al., 2006). In summary, dual-task performance may be explained by the concept of limited individual attentional resources. Hence, it is evident that conducting two tasks at the same time will exceed available attentional resources limits more so than a single task (Krampe, Rapp, Bondar, & Baltes, 2003). This concept is important for the occurrence of falls, because locomotion needs sufficient attentional resources for a safe gait control (Beauchet, Dubost, Gonthier et al., 2005).

Furthermore, dual tasking-induced gait changes are also used to explore the cortical involvement in gait control (Allali et al., 2007). There is growing evidence that gait changes are associated with the incidence of dementia and cognitive decline (Beauchet & Berrut, 2006). Recently, Beauchet, Dubost, Aminian et al. (2005) reported decreased gait speed and increased stride time variability when older subjects with a broad range of cognitive function disabilities (i.e., mild dementia) performed the dual task of walking while counting backwards. These findings suggest that dual-task interference on gait is based on the cerebral capacity to divide attentional resources between gait and an additional task (Beauchet, Najafi, Dubost, & Mourey, 2003, see also Sheridan et al., 2003).

Gait analysis using a dual task seems a valuable measurement tool to assess older adults at risk for falling comparable to other established screening methods, e.g., the Timed Up & Go Test (TUG) (Shumway-Cook, Brauer, & Woollacott, 2000). Underlying gait disorders due to attentional capacity problems could be detected and used to tailor preventive exercise interventions. New exercise programs including secondary or multiple tasks have to be implemented to entirely stimulate bodily functions in order to maintain or improve mobility, functionality and independence in older adults.

## Exercise Interventions to Improve Gait and Prevent Falls

On an individual basis, regular physical activity is able to reduce functional limitations and extend years of active independent life (American College of Sports Medicine [ACSM], 2004). However, in terms of improving gait, targeted exercise programs to improve strength, walking and balance have been among the most promising interventions to reduce fall risk (Gillespie et al., 2009; Rubenstein, 2006; Sherrington et al., 2009).

Postural control, reflexes, muscle strength, and height of stepping decline with increasing age (Rubenstein, 2006). In addition, the presence of a physical handicap prior to a fall-related accident seems rather common and mainly con-

cerns walking and mobility (Beer et al., 2000). Hence, primary prevention of falls should focus on improving physical conditioning through exercise to decrease detrimental fall incidents. Sufficient exercise capacity and functional reserve is not only needed to primarily improve fall-related risk factors (e.g., muscle weakness), but also to quicken recovery in older adults who are more likely to fall due to deconditioning (Rubenstein, 2006). In this context, lower extremity strength gain is particularly important to maintain or improve gait performance and should therefore play a central role in exercise prescription (Chandler, Duncan, Kochersberger, & Studenski, 1998; Guralnik, Ferrucci, Simonsick, Salive, & Wallace, 1995).

## Gait and Exercise-Related Determinants of General Physical Functioning

The age-related loss of skeletal muscle mass is approximately 1–2% per year after the fifth decade (Hughes, Frontera, Rubenoff, Evans, & Fiatarone Singh, 2002). This decline in skeletal muscle mass is associated with reduced muscle strength, which in turn is responsible for sarcopenia, functional decline, and frailty (Kressig & Proust, 1998). Other factors are also important determinants of elders' physical performance such as neuronal muscle recruitment in terms of intramuscular coordination, cardiac output, total number of erythrocytes, and maximal oxygen consumption (VO<sub>2</sub> max). Nevertheless, when muscle strength in older adults is insufficient to rise from a chair or stand upright safely, it is inappropriate to immediately train endurance, balance, or flexibility. The major conditioning component in older persons is the capacity of skeletal muscle to produce strength, depending on contractions of actin and myosin filaments within the skeletal muscle. This process is energetically dependent on the number of adenosine triphosphate (ATP) producing mitochondria within the muscle cells. Consequently, an exercise program should primarily intend to increase the number of mitochondria within skeletal muscle in order to create the base for further physical functional improvement. In general, an increase in mitochondria density is achieved, independent of age, by repeated muscle stimuli through exercises that lead to muscle hypertrophy and increased muscle strength (Carmeli, Coleman, & Reznick, 2002). Adequate nutritional status is a prerequisite for eliciting such muscular adaptations, particularly because energy expenditure at rest and during exercise is reduced in older persons (Hunter, McCarthy, & Bamman, 2004).

## Progressive Resistance Training

Progressive resistance training (PRT) is among the most popular exercises involved in anabolic growth of skeletal muscle and therefore suitable to counteract muscular weakness in older people. PRT, which may be defined as the act

of moving forward or advancing toward a specific goal over time until the target goal has been achieved (ACSM, 2009), improves walking performance such as gait speed, climbing steps, or standing up from a chair more quickly. However, although these improvements are significant, the impact on physical ability and falls seems only small (Liu & Latham, 2009), and inappropriate training prescriptions may even result in nonsignificant or possibly adverse outcomes (Latham et al., 2003; Latham, Bennett, Stretton, & Anderson, 2004). Several trials have demonstrated that PRT, particularly in combination with nutritional supplementation, improves muscle strength in healthy and frail older people (Wieser & Haber, 2007). In a study by Fiatarone et al. (1994) high-resistance exercise training increased muscle strength of very old people ( $87.1 \pm 0.6$  years) by 113% ( $\pm 8\%$ ) in the exercise group. Even greater results were obtained by the group that, in addition to exercise, received a nutritional supplement containing carbohydrates, protein, and fats. Their muscle strength significantly increased to 150% above the baseline measure indicating the importance of nutrition in eliciting maximal strength gains due to exercise. Recently, studies reported positive associations between decreased levels of vitamin D and decreased muscle function (Annweiler, Bridenbaugh et al., 2009) as well as quadriceps weakness (Annweiler, Schott-Petelaz et al., 2009). Consequently, for optimal exercise performance and muscular adaptations in responses to PRT nutrition always has to be taken into consideration.

### Power Training

In recent years, another form of resistance training has been implemented that may prove to be more beneficial in increasing physical performance than ordinary strength training (Hazell, Kenno, & Jakobi, 2007; Porter, 2006). High-velocity power training has shown similar increases of strength compared to traditional slow-velocity strength training in older adults (Reid, Callahan, Carabello, Phillips, Frontera, & Fielding, 2008). Muscle power (force  $\times$  velocity) decreases faster than “raw” muscle strength in older adults and therefore may also be an additional, early predictor for fall risk, gait-related balance disorder, and functional decline (de Vos et al., 2005, 2008). In fact, successful recovery after losing balance while walking is dependent on quick corrective limb movements and therefore muscular power. In this context, Orr et al. (2006) were able to show that power training using a low load and high-velocity regimen significantly improved balance in community-dwelling healthy older adults.

Although there is some indication that PRT can increase functional outcomes such as gait velocity (Lord et al., 1996), further research will still have to confirm whether sole strength or power gains are equivalent to clinical improvements in functionality. In this context, research tools such as the physical functional performance (PFP) test or the short physical performance battery (SPPB) may be

helpful for transferring muscular changes into a more practical daily measure (Cress et al., 1996; Guralnik et al., 2000). While the SPPB focuses on lower extremity function (standing balance, walking speed, and ability to rise from a chair), the PFP-10 test consists of ten daily activities including upper and lower extremity function (i.e., carrying groceries, floor sweeping, or putting on a jacket). Both tests are designed to quantify measures of functionality in older adults by a score (Cress, Petrella, Moore, & Schenkman, 2005). The achieved scores allow quantitative descriptions of functional limitations in older persons. Functional limitations assessed by the PFP are based on measures of peak oxygen consumption and isokinetic knee extensor torque, which are associated with predicting dependency in living status (Cress & Meyer, 2003). On the other hand, the SPPB performance measures show a gradient of risk among a population allowing identification of subgroups at very low and high risk of disability (Guralnik et al., 1995). As a consequence, strength gains could be assessed in a clinical context and assessed as functional improvements.

### Multidimensional Exercise Programs

Although strength training alone can provide benefits to seniors, a multidimensional activity program tailored to the individual that includes endurance, strength, balance, and flexibility is considered to be optimal for older adults (ACSM, 2004). An early study by Shumway-Cook, Gruber, Baldwin, and Liao (1997) showed that a multifaceted exercise program addressing impairments and functional disabilities improves gait, balance, and mobility in community-dwelling older adults with a history of falls. Another study by Delbaere et al. (2006) suggested that a home-based, individualized, multidimensional exercise program reduces several physical factors associated with falls in community-dwelling older people with moderate physical impairment. In addition, a recent review by Baker, Atlantis, and Fiatarone Singh (2007) highlights the efficiency of a multidimensional approach and emphasizes the positive effect on falls prevention in older persons. In this context, supervised home-exercise programs and group exercises both seem beneficial in falls prevention in older community dwellers (Sherrington, Lord, & Finch, 2004), yet changes may be small and short-lived (van der Bij, Laurant, & Wensing, 2002). In addition, intensive rather than low-intensity multidimensional exercise programs seem capable of improving physical performance in sedentary older adults (Binder et al., 2002), whereas the former type of exercise has been associated with greater negative effects like injury and nonadherence (Latham et al., 2003).

Tai Chi, with its slow, low-impact movements requiring multidirectional weight shifting, single and double support, and awareness of alignment, proved to be another type of exercise to challenge functional limitations related to falls in older adults (i.e., impaired gait, poor balance, and muscular weakness) (Harmer & Li, 2008). A landmark paper



by Wolf et al. (2003) showed that a moderate Tai Chi intervention improved fear of falling and reduced fall risk by 47.5% in older adults. In addition, Tai Chi also seems to improve postural stability, which is an important attribute of safe gait (Kressig, Beauchet, & Tharicharu, 2003). Hence, Tai Chi has the potential to reduce falls or fall risk among older persons (Low, Ang, Goh, & Chew, 2009). Nevertheless, the number of randomized controlled Tai Chi trials is low and further research is needed to warrant the preventive effect of this particular type of exercise.

## New Gait-Related Exercise Approaches to Reduce Falls

The findings in relation to dual-task-related gait problems may offer a promising approach for future exercise interventions. Based on the correlation between cognitive function and gait stability (Scherder et al., 2007; Sheridan & Hausdorff, 2007), combining cognitive and motor exercises might add additional functional improvements compared to exclusive strength training. In particular, combined cognitive and motor training may be particularly promising because of the omnipresence of multitask situations in daily life and their relevance to falls. There are different approaches to improve dual-task performance. Interventions can focus on one or both of the tasks conducted. In terms of gait, dual-task interventions may either target to improve automaticity of gait or to improve the secondary task or even a combination of both. On the one hand, it seems plausible to focus on automating gait because of its direct relation to falls before trying to improve a secondary cognitive task. On the other hand, a holistic approach including training of both tasks (e.g., gait and cognition) at the same time may be also favorable because of its inclusion of all physiological and psychological dual-task variables comparable to real life situations.

Recently, interventions using functional, physiological, and psychological components received more attention on the basis of the dual-task paradigm. Exemplarily, approaches with rhythmical exercises seem promising to reduce fall risk. The eurhythmics method of Jaques-Dalcroze, originally created for the musical education of children and increasingly used with seniors, comprises multitask exercises performed to the rhythm of improvised piano music (Winkelmann, Gianadda, Beauchet, & Kressig, 2005). In a study by Kressig, Allali, and Beauchet (2005), older women who had practiced Jaques-Dalcroze eurhythmics for over 40 years showed gait regularity under dual-task conditions similar to that of younger adults. It was assumed that the high expertise in the use of attentional skills required to multitask while walking to changing rhythmic patterns may have resulted in highly automated gait patterns, minimizing the effect of dual tasking on gait regularity in the studied older Dalcroze practitioners. As a consequence, a Jaques-Dalcroze intervention may stimulate motor brain areas and

facilitate movements through a combination of music, rhythm, and exercise in older adults (Allali et al., 2004).

Higher-dosed exercise programs that contain two or more components of strength, balance, flexibility, or endurance can reduce the number of people falling (Gillespie et al., 2009; Sherrington et al., 2008). Exercising in supervised groups, participating in Tai Chi, and carrying out individually prescribed exercise programs at home are all effective for preventing falls, though comparison between various studies can be difficult. Overall, a wide range of exercise programs is applied to improve gait parameters and prevent falls. In addition, baseline levels, power and outcome measures as well as intervention time frames differ largely between trials (Lord et al., 2007). Thus, especially in terms of fall risk reduction, the most efficient type of exercise or a combination thereof still remains unclear. Nonetheless, for all types of exercise intervention it remains a challenge to ensure safety and long-term adherence. In addition, it is suggested that physical activity interventions include established principles of behavioral changes to maximize recruitment, motivation and progression (ACSM, 2004).

## Discussion and Conclusion

Aging is associated with several changes in gait, including diminished gait automaticity, which increases the likelihood of falling. Spatio-temporal gait analysis under dual-task conditions offers insight into decreased gait automaticity and thus the allocation of attentional resources by quantifying gait changes during simultaneous performance of a secondary task. Analysis of gait parameters, such as stride-to-stride variability, may provide a sensitive marker of gait disturbances associated with future falling. However, the extent to which postural responses and gait make demands on attentional resources still has to be defined. It also remains unclear how individual gait parameters can be optimally and clinically significantly improved, and how they are related to the movement of other body segments (e.g., trunk and head).

In a demographically aging population, progressive resistance training and exercises including cerebral motor control (Jaques-Dalcroze or Tai Chi) are important to maintain a stable gait or improve disordered gait. In fall prevention, exercises should be combined with a balanced diet, sufficient protein (Koopman & van Loon, 2009), and vitamin D intake (Annweiler, Allali et al., 2009; Bischoff-Ferrari et al., 2009) to maximize physiological adaptations. In terms of exercise prescription, not only sociocultural and economic factors, but also the enjoyment, socializing, and attractiveness of the exercise programs are important. In addition, family support and integration of the general practitioner are key determinants of a long-term exercise adherence.

## Conclusion

This review shows that gait disorders and falls are closely related in the older population. Various types of exercise programs are able to improve a range of fall risk factors and consequently reduce fall risk. The basis of functional exercise (e.g., dual or multiple tasks) for older adults involves development of skeletal muscle strength. In particular, interventions aiming at improving gait (e.g., by muscle power training or practice of Jaques-Dalcroze eurhythmics) seem promising. However, the inclusion of new models such as the gait-related dual-task paradigm may even further improve the impact of exercise interventions on falls. Future research is needed to assess the effect and efficacy of such programs to increase gait stability and automaticity and thus reduce falls.

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**Publication (b)**

**Gait Changes and Fall Risk**

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## Gangveränderungen und Sturzrisiko

Gait Changes and Fall Risk

### Zusammenfassung

Gehen ist eine komplexe motorische Aufgabe, die bei vielen älteren Menschen nicht mehr automatisch funktioniert. Die Folge können Stürze mit und ohne schwerwiegenden Konsequenzen wie Frakturen oder Sturzangst sein. Ganganalysen zeigen, dass schon kleine Schritt-zu-Schritt-Veränderungen das Sturzrisiko deutlich erhöhen. Diese Gangveränderungen sind oftmals beim normalen Gehen nicht zu erkennen, sondern äussern sich erst in Kombination mit einer zusätzlichen Aufgabe, dem sogenannten Dual-Tasking. Ein unregelmässiger Gang ist jedoch keine Fatalität des Alters, sondern kann durch gezielte Interventionen wieder verbessert werden.

**Schlüsselwörter:** Sturzrisiko – Gangvariabilität – Dual-Task – ältere Menschen

### Einleitung

Im Alter wird dem Sturz eine ganz andere Bedeutung zugeschrieben als in jungen Jahren. In der Altersgruppe der über 65-Jährigen zählen Stürze zu den häufigsten gesundheitlichen Problemen mit ernsthaften Folgen. Epidemiologische Daten zeigen, dass etwa 30% der über 65-Jährigen im Laufe eines Jahres stürzen, bei hochaltrigen Personen ist es sogar jeder Zweite [1]. Das Problem der Stürze ist nicht nur in der hohen Inzi-

denz verankert, sondern vielmehr in der Kombination mit der Verletzungsanfälligkeit älterer Menschen, beispielsweise aufgrund chronischer Erkrankungen wie Osteoporose [2]. Etwa 10–15% der älteren Menschen erleiden schwere Verletzungen aufgrund eines Sturzes, die zu dauerhaften Gehproblemen, Verlust der Selbständigkeit oder gar zum Tod führen können [3]. Auch wenn nicht jeder Sturz zwangsläufig gravierende Verletzungen nach sich zieht, kann die Angst vor erneuten Stürzen zu selbst auferlegten Einschränkungen körperlicher Aktivität führen [4,5], was wiederum das Risiko für zukünftige Stürze erhöhen kann.

Die Forschung hat sich in den letzten Jahren intensiv mit der Bestimmung verlässlicher Sturzrisikofaktoren befasst (Tab. 1). Unter den vielen sturzverursachenden Faktoren im Alter sind insbesondere die muskuläre Schwäche sowie Gang- und Gleichgewichtsprobleme zu nennen [2]. Unter anderem bedingt durch diese Risikofaktoren stellt sicheres Gehen und Stehen für ältere Menschen

eine zunehmende Herausforderung dar. Daher erstaunt es nicht, dass sich die meisten Sturzunfälle von über 65-Jährigen während dem Gehen [6] oder bei der zeitgleichen Ausführung anderer Tätigkeiten ereignen [7]. Von grossem Interesse ist dabei die frühzeitige Erkennung von Risikofaktoren und damit sturzgefährdeter Personen, um rechtzeitig Massnahmen einzuleiten, die im besten Fall das Auftreten von Stürzen zu verhindern vermögen. Der folgende Bericht soll aufzeigen, wie anhand spezifischer sturz-assoziiierter Gangveränderungen ein erhöhtes Sturzrisiko erkannt und die Gangsicherheit durch geeignete Massnahmen wieder verbessert werden kann.

### Normales Gehen bei älteren Menschen

Das Gangbild älterer Menschen kann durch alters-assoziierte Veränderungen beeinträchtigt werden. Beispielsweise nehmen im Alter wichtige Körperfunk-

Tab. 1: Risikofaktoren für einen Sturz.

Intrinsische Faktoren	Extrinsische Faktoren
<ul style="list-style-type: none"> <li>• Muskelschwäche</li> <li>• Gang- und Gleichgewichtsstörungen</li> <li>• Seh- und Hörstörungen</li> <li>• Kognitive Störungen</li> <li>• Synkopen</li> <li>• Inkontinenz</li> <li>• Frühere Stürze</li> </ul>	<ul style="list-style-type: none"> <li>• Umgebungsgefahren wie Bodenbeschaffenheit, schlechte Lichtverhältnisse usw.</li> <li>• Ungeeignetes Schuhwerk</li> <li>• Ungeeignete Gehhilfe</li> <li>• Ungeeignete Sehhilfe</li> <li>• Medikamente, v.a. Psychopharmaka, Antiarrhythmika, Diuretika</li> </ul>
<p>Intrinsische Faktoren betreffen den Gesundheitszustand einer Person, extrinsische Faktoren die Einflüsse aus Umwelt und Umgebung.</p>	

**Tab. 2:** Definition räumlich-zeitlicher Gangparameter.

Gangparameter	Einheit	Definition
Gehgeschwindigkeit	cm/sek	Distanz dividiert durch die Gehzeit
Kadenz	Schritte/min	Anzahl Schritte pro Minute
Spurbreite	cm	Distanz zwischen dem Fersenzentrum des einen Fussabdrucks zur Fortbewegungslinie des anderen Fusses
Gangzykluslänge	cm	Distanz zwischen zwei aufeinander folgenden initialen Bodenkontakten desselben Fusses
Gangzyklusdauer	sek	Zeit zwischen zwei aufeinander folgenden initialen Bodenkontakten desselben Fusses
Doppelstandphase	sek	Summe der Zeit von zwei Perioden im Gangzyklus, in der beide Füße gleichzeitig im Kontakt mit dem Boden sind.

tionen wie Muskelkraft, Koordination, Gleichgewichtsreaktion und Sinneswahrnehmungen ab [8], wodurch sich das Gangbild ändern kann. Andererseits führen Krankheiten, die mit zunehmendem Alter häufiger auftreten, wie z.B. Arthritis oder Parkinson-Erkrankung, zu Gangveränderungen. Bleiben die krankhaften Veränderungen unberücksichtigt, ist das normale Gangbild gesunder älterer Menschen im Vergleich zu jüngeren durch eine reduzierte Gehgeschwindigkeit, eine verkürzte Gangzykluslänge und eine Zunahme der Doppelstandphase gekennzeichnet (Tab. 2) [9]. Ein Gangparameter, der bis ins hohe Alter unverändert bleibt, ist die Kadenz [9].

Gerade die Gehgeschwindigkeit ist eine massgebliche Grösse zur Bestimmung der Gehfähigkeit einer Person, die mit einfachen Mitteln gemessen werden kann. Eine reduzierte Gehgeschwindigkeit ist ein Vorbote für die Einschränkung bei Alltagsaktivitäten. Auch kann die Teilnahme als Fussgänger am öffentlichen Verkehr in der Schweiz zu einem Problem werden, wenn die Gehgeschwindigkeit weniger als 120 cm/sek beträgt. Folglich ist nicht mehr gewährleistet, die Strasse innerhalb einer Grünphase überqueren zu können. Die Abnahme der Gehgeschwindigkeit nach dem 63. Lebensjahr beträgt etwa 12–16% pro Dekade und verstärkt sich nach dem 75. Lebensjahr [10]. Liegt die Gehgeschwindigkeit unter 100 cm/sek,

kann davon ausgegangen werden, dass gesundheitliche Probleme vorliegen [11].

## Abklärung der Sturzgefährdung

### Mobilitätsassessments in der Praxis

Gangprobleme beeinträchtigen bis zu 40% der älteren Menschen über 65 Jahre, wovon die Hälfte der Probleme schwerwiegend sind [2]. Oftmals werden Gangprobleme erst wahrgenommen, wenn ein Sturz Verletzungen zur Folge hat. In der Praxis ist es daher wichtig, Patienten mit Gangproblemen frühzeitig zu erkennen, bevor es zu einem Sturz kommt. Zunächst ist ein Screening der Risikofaktoren zur Feststellung eines generellen Sturzrisikos indiziert. Dazu zählen unter anderem die Befragung zur Sturzanamnese und Sturzangst, der Ausschluss akuter medizinischer Störungen sowie die Überprüfung von Medikamenten.

Für die Untersuchung der Funktionalität und Mobilität älterer Menschen bietet sich dem Allgemeinpraktiker eine Fülle von validierten, standardisierten Screening-Tests an. Diese erfassen jeweils unterschiedliche Aspekte der Mobilität, wie beispielsweise Gleichgewicht oder Beinmuskulatur. Weil zurzeit kein umfassender Screening-Test vorhanden ist, der in Kürze die Notwendigkeit für eine weiterführende Sturzrisikoabklärung in

der Klinik eruiert, ist die Kombination einzelner Tests ratsam. Ein Nachteil solcher Tests ist oftmals, dass sich erst bei gebrechlicheren älteren Menschen auffällige Resultate ergeben.

Zwei Möglichkeiten, die sich in der Praxis anbieten, um einen Mobilitätsabbau bei älteren Menschen rechtzeitig zu erkennen, sind der *Timed Up and Go Test* [12] und der Geh- und Sprechtest [13]. Der *Timed Up and Go Test* ist ein schneller, einfacher und globaler Mobilitätstest. Dieser misst die Zeit, die benötigt wird, um von einem Stuhl aufzustehen, drei Meter in selbstgewähltem normalem Tempo hin und zurück zu gehen und sich wieder hinzusetzen. Liegt die dafür benötigte Zeit über 14 Sekunden, ist von einer Mobilitätseinschränkung auszugehen. Der Geh- und Sprechtest beruht auf der Beobachtung, dass sturzgefährdete Personen stehenbleiben, wenn sie gleichzeitig eine einfache Frage beantworten sollen. Ergibt sich in einem dieser Tests ein auffälliger Befund, ist eine Zuweisung in eine Klinik für eine detaillierte Ganganalyse in Erwägung zu ziehen.

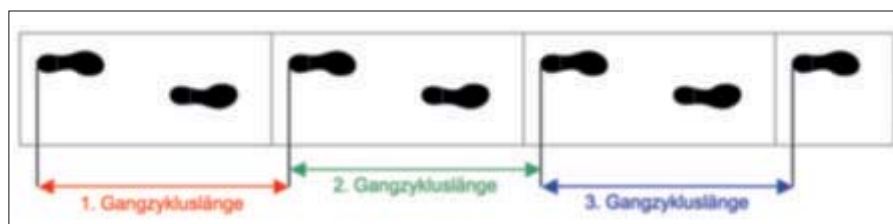
### Ganganalyse in der Klinik

Erhärtet sich bei einem allgemeinen Mobilitätstest der Verdacht einer vorliegenden Gehproblematik, kann mittels einer spezifischen Ganganalyse das Ausmass des Sturzrisikos genauer bestimmt werden. Verschiedene Ganganalyse-Systeme wie beispielsweise elektronische Schuheinlagen, reflektierende Marker an den Füßen oder unteren Extremitäten, Kraftmessplatten oder ein elektronischer Teppich mit integrierten Druckrezeptoren (Abb. 1), ermöglichen heute die einfache, schnelle und objektive Beurteilung des menschlichen Gangbildes. Diese Systeme erlauben sowohl die Quantifizierung räumlich-zeitlicher Gangparameter als auch kinetischer und kinematischer Gangdaten unter standardisierten Bedingungen. Der Nutzen des jeweiligen Systems hängt von der klinischen Fragestellung ab. Ganganalyse





**Abb. 1:** Ganganalyse mittels elektronischem Gangteppich (GAITrite® System) im Basel Mobility Center.



**Abb. 2:** Die Gangvariabilität widerspiegelt die Veränderungen von einem Gangzyklus zum nächsten. Beispiel: Schritt-zu-Schritt-Veränderung der Gangzykluslänge links.

lysen ermöglichen zudem die Überprüfung von Behandlungen und tragen im Rahmen wissenschaftlicher Untersuchungen zum Verständnis von Gangstörungen bei.

## Gangvariabilität als Sturzprädiaktor

Während einige Gangparameter sich mit dem Älterwerden ändern können (z.B. die Gehgeschwindigkeit), bleibt die Gangregelmässigkeit bei gesunden älteren Menschen weitgehend unverändert. Das heisst, dass die Abweichungen von einem Schritt zum nächsten relativ klein sind und die sogenannte Gangvariabilität von vielen Gangparametern (z.B. der Gangzykluslänge) in der Grössenordnung von wenigen Prozenten liegt (Abb. 2). In anderen Worten ausgedrückt, je unregelmässiger der Gang, desto höher die Gangvariabilität. Verschiedene Studien ermittelten Verän-

derungen in bestimmten räumlichen und zeitlichen Gangparametern als unabhängige Prädiktoren für zukünftige Stürze. Maki [14] beobachtete, dass eine Variation der Schrittlänge von 1.7 cm von einem Schritt zum nächsten, das Sturzrisiko für ältere Menschen in den nächsten sechs Monaten verdoppelt. Eine hohe Variabilität der Gangzyklusdauer wurde ebenfalls als potenter Sturzprädiaktor für ein Beobachtungsintervall von zwölf Monaten ermittelt [15]. Die Autoren berichteten auch, dass die quantitative Bestimmung der Gangvariabilität möglicherweise ein sensitiverer Marker zur Erueierung des Sturzrisikos darstellt als ein konventioneller Gangparameter wie die Gehgeschwindigkeit oder die Kadenz. Diese Annahme wurde in den letzten Jahren wiederholt bestätigt [16,17]. Da diesbezüglich eine Gangbeurteilung von blossen Auge vielfach unzureichend ist, ist die Quantifizierung des Gangbildes mittels instrumentierter Ganganalyse unabdingbar.

## Gangveränderungen unter Dual-Task

Obschon Gehen eine einfache Aufgabe zu sein scheint, ist es in Wahrheit eine komplexe motorische Aufgabe, die Jahre benötigt, um sie zu lernen und zu festigen [8]. Bedingt durch Faktoren wie körperliche Inaktivität, Sehstörungen, Sensibilitätsstörungen oder Sturzangst müssen ältere Menschen mehr Aufmerksamkeitsressourcen investieren, um selbst eine weitgehend automatisierte Aufgabe wie das Gehen durchzuführen [18,19]. Oftmals sind Gangveränderungen beim normalen Gehen nicht erkennbar, sondern äussern sich erst in Kombination mit einer zusätzlichen Aufgabe, wie z.B. Gehen und gleichzeitig Sprechen. Sogenannte Dual-Task-Paradigmen (Gehen während der gleichzeitigen Ausführung einer entweder motorischen oder kognitiven Aufgabe) finden heute eine breite Anwendung bei der Untersuchung des Gangbildes älterer Menschen. Ist nun die Aufmerksamkeit für das Gehen und eine zeitgleiche Tätigkeit gefordert, können Interferenzen zwischen diesen konkurrierenden und auf gleiche Hirnareale zurückgreifenden Aufgaben auftreten, so dass die Ausführung in einer oder beiden Aufgaben beeinträchtigt ist [20]. Dieser Wettbewerb zwischen den Anforderungen der Aufmerksamkeit während dem Gehen und der konkurrierenden zweiten Tätigkeit kann zu einer Veränderung des Gangbildes führen [21].

Typische Gangveränderungen, wie eine reduzierte Gehgeschwindigkeit oder eine zunehmende Gangvariabilität unter Dual-Task, werden mit einem erhöhten Sturzrisiko in Verbindung gebracht. Hierzu zeigte Lundin et al. [13] mit Hilfe eines einfachen Dual-Task-Paradigmas erstmals, dass ältere Personen, die nicht gleichzeitig Gehen und eine einfache Frage beantworten konnten («stops walking when talking»), ein erhöhtes Risiko für Stürze in den kommenden sechs Monaten aufweisen. Ein erst kürzlich erschienener Übersichtsartikel von Beauchet et al. [22] bestätigt,

dass ein signifikant erhöhtes Sturzrisiko besteht, wenn ältere Menschen Veränderungen im Gang oder in der kognitiven Aufgabe unter Dual-Task aufweisen. Speziell die Gangvariabilität hat sich auch unter Dual-Task-Bedingungen als sensitiver Marker für die Gangsicherheit etabliert, wobei beispielsweise ein Anstieg des Variationskoeffizienten der Gangzyklusdauer mit einer Abnahme der Gangstabilität und einem Anstieg des Sturzrisikos einhergeht [17].

Im Alltag werden oftmals Aktivitäten durchgeführt, die den zeitgleichen Vollzug mehrerer Aufgaben erfordern. Dual-Task-bezogene Gangveränderungen geben einen Anhaltspunkt, um festzustellen, inwieweit die gleichzeitige Durchführung von zwei Aufgaben die zur Verfügung stehenden Aufmerksamkeitsressourcen übersteigt. Darüber hinaus ist das Konzept des Dual-Tasking für das Auftreten von Stürzen im fortgeschrittenen Alter von wesentlicher Bedeutung, da die Fortbewegung genügend Aufmerksamkeitsressourcen für die sichere Gangkontrolle benötigt. Eine Ganganalyse ermöglicht die frühzeitige Erkennung von Gangveränderungen und erlaubt eine gezielte Vorgehensweise bei der Planung von geeigneten therapeutischen Massnahmen.

## Was kann ich tun – gezielte Interventionen

Ältere Menschen, die über Gangunsicherheit und Stürze berichten, sehen dies oftmals als Fatalität des Alters an. Stürze, bedingt durch Veränderungen der Gangregelmässigkeit, müssen nicht sein, sondern können durch gezielte präventive Interventionen positiv beeinflusst werden.

Grundsätzlich sind alle Interventionen empfehlenswert, die auf eine verbesserte Körperkontrolle und eine Reautomatisierung der Gehbewegung abzielen. Gehhilfen können dazu beitragen, die Gehfähigkeit zu verbessern und das Sturzpotential zu vermindern. Da die



Abb. 3: Jaques-Dalcroze-Rhythmik in einem Atelier.

Indikation für eine Gehhilfe oftmals aufgrund verminderter Muskelkraft und/oder Kontrolle in den Beinen, Ganginstabilität oder verminderte Propriozeption der Füße gegeben ist [3], dient die Verwendung einer Gehhilfe lediglich als Kompensation der zugrundeliegenden Probleme. Daher sollten andere Strategien wie z.B. Bewegungsprogramme für die Verbesserung der Gangstabilität in Betracht gezogen werden.

Im Rahmen der Sturzprävention erwiesen sich multimodale Bewegungsprogramme, die Kraft-, Gleichgewichts-, Gang- und Koordinationstraining kombinierten, als am wirksamsten [23]. Ob das Training eines einzelnen Konditionsfaktors, beispielsweise das muskuläre Krafttraining, ein Sturzereignis zu verhindern vermag, wird in der Literatur kontrovers diskutiert. Krafttraining wirkt sich primär auf die Muskelmorphologie aus, nicht aber auf sturzverursachende Risikofaktoren wie Gang- oder Gleichgewichtsprobleme [24]. Hinsichtlich der Bewältigung des Alltags wirkt sich ein Gleichgewichtstraining mit kognitiven oder motorischen Zusatzaufgaben positiv auf das Gangbild älterer Menschen aus [25]. Dies lässt vermuten, dass möglicher-

weise Trainingsformen, die mehr Aufmerksamkeitsressourcen mobilisieren, für die Verbesserung der Gehfähigkeit wirksamer sind.

Ein erfolgversprechendes Trainingsprogramm ist die Jaques-Dalcroze-Rhythmik (Abb. 3). Dabei handelt es sich um motorische und kognitive Übungen zum Rhythmus improvisierter Klaviermusik. Ältere Menschen, die zeitlebens Jaques-Dalcroze-Rhythmik praktizierten, zeigten im Gegensatz zur Kontrollgruppe (keine regelmässige körperliche Aktivität) auch unter Dual-Task eine gute Gangvariabilität [26]. Eine kürzlich erschienene Studie untersuchte den Einfluss dieses Trainingprogramms auf das Gangbild bei zu Hause lebenden älteren Menschen ohne vorhergehende Erfahrung mit Jaques-Dalcroze-Rhythmik. Die Resultate zeigten, dass eine sechsmonatige Rhythmik-Intervention nach Jaques-Dalcroze die Gangvariabilität unter Dual-Task verbesserte und die Sturzrate um 54% reduzierte [27]. Die beobachteten Verbesserungen führen vermutlich zu einer Reduktion der Interferenzanfälligkeit, wodurch die freigegebenen Aufmerksamkeitsressourcen nunmehr für die Gangkontrolle genutzt werden können.

Eine weitere Trainingsform, die die Sturzrate positiv zu beeinflussen vermag, ist Tai Chi. Die langsamen, fließenden und präzisen Bewegungen beanspruchen Konzentration und fördern das Gleichgewicht. Wissenschaftliche Erkenntnisse zeigen, dass eine regelmässige Teilnahme an Tai Chi die Sturzrate um beinahe die Hälfte reduzieren, die Sturzangst vermindern und das Selbstvertrauen fördern kann [28]. Inwieweit Tai Chi die Gangregelmässigkeit beeinflusst, ist Gegenstand laufender Forschungen. Die besten therapeutischen Massnahmen nützen jedoch nichts, wenn sie von den betroffenen Personen nicht befolgt werden. Neben der Freude an der Aktivität selbst spielen soziale Aspekte, wie die Gelegenheit neue Kontakte zu knüpfen, ebenso eine wichtige Rolle. Jaques-Dalcroze-Rhythmik und Tai Chi erwiesen sich in dieser Hinsicht als geeignete Trainingsformen für ältere Menschen. Nach Studienabschluss fuhren rund 56 resp. 35% der Teilnehmer mit der Jaques-Dalcroze-Rhythmik resp. dem Tai Chi-Training fort [27,28]. Wenn das Gehen bei älteren Menschen nicht mehr automatisch funktioniert, können Gangprobleme und sogar Stürze auftreten. Das frühzeitige Erkennen von Gangveränderungen erlaubt die rechtzeitige Planung sturzpräventiver Massnahmen. Interventionen, die auf die Reautomatisierung der Gehbewegung und die Verbesserung der Koordination motorisch-kognitiver Aufgaben abzielen, sind zur Reduktion der Sturzrate bzw. des Sturzrisikos am geeignetsten. Für ältere Menschen ist das Erhalten bzw. Wiedererlangen eines regelmässigen Ganges und damit der Gangsicherheit massgebend für ein autonomes Leben zuhause.

## Abstract

Walking is a complex motor task generally performed automatically by older

## Key messages

- Sicheres Gehen ist Voraussetzung für die funktionelle Unabhängigkeit, Selbstständigkeit und gute Lebensqualität im Alltag.
- Stürze kommen mit steigendem Alter häufiger vor und können gravierende Folgen haben.
- Bestimmte Gangparameter, wie die Gangvariabilität, erweisen sich als aussagekräftige Sturzprädiktoren. Eine einfache räumlich-zeitliche Ganganalyse kann diese Parameter quantifizieren und dadurch ein Sturzrisiko frühzeitig erkennen.
- Normales Gehen allein ist oftmals unzureichend, um diskrete Gangstörungen zu erkennen. Dabei können Ganganalysen unter Dual-Task-Bedingungen (Gehen und gleichzeitig eine zusätzliche Aufgabe lösen) helfen, sturzgefährdete ältere Menschen zu identifizieren.
- Regelmässige Teilnahme an Jaques-Dalcroze-Rhythmik kann die Gangregelmässigkeit verbessern und das Sturzrisiko senken.

## Lernfragen

1. Welches ist kein intrinsischer Risikofaktor für Stürze? (Einfachauswahl, 1 richtige Antwort)
  - a) Muskelschwäche
  - b) Gangdefizite
  - c) Sturzangst
  - d) Osteoporose
  - e) Sehbeeinträchtigung
2. Was sind die Indikationen für eine räumlich-zeitliche Ganganalyse? (Mehrfachauswahl, mehrere richtige Antworten)
  - a) Früherkennung des Sturzrisikos
  - b) Zur Überprüfung von therapeutischen Massnahmen
  - c) Laufstilanalyse
  - d) Gangunsicherheit
  - e) Schuhberatung
3. Welcher Gangparameter erweist sich als sensitiver Marker zur Einschätzung des Sturzrisikos? (Einfachauswahl, 1 richtige Antwort)
  - a) Schrittlänge
  - b) Spurbreite
  - c) Gangzyklusdauervariabilität
  - d) Gehgeschwindigkeit
  - e) Kadenz

adults. Falls with or without serious consequences such as fractures or fear of falling can be the result. Gait analysis shows that even minor stride-to-stride variations increase the risk for falls. These gait changes are often too small to be detected during normal walking alone, but rather appear in

combination with an additional task, the so-called dual tasking. Irregular gait is not an inevitability of older age, but can be improved by targeted interventions.

**Key words:** fall risk – gait variability – dual-task – older people

## Résumé

Marcher est une tâche motrice complexe qui ne fonctionne souvent plus automatiquement chez beaucoup de personnes âgées. Des chutes, avec ou sans conséquences graves telles que des fractures ou une peur de tomber, peuvent en être le résultat. L'analyse de la marche montre que déjà de petites modifications de durée ou de longueur d'un pas à l'autre augmentent clairement le risque de chute. Ces modifications de marche ne sont souvent pas reconnues lors de la marche seule, mais se manifestent plutôt en combinaison avec une tâche supplémentaire (double-tâche). La marche irrégulière n'est toutefois pas une fatalité liée à l'âge, mais peut être améliorée par des interventions spécifiques.

**Mots-clés:** risque de chute – variabilité de la marche – double tâche – personnes âgées

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**Publication (c)**

**Basis for a Swiss Perspective on Fall Prevention in Vulnerable Older People**

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# Basis for a Swiss perspective on fall prevention in vulnerable older people<sup>1</sup>

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<sup>1</sup> The work presented here is a summary of our work for the Swiss Best Practice Health Promotion [54]. We provided the current evidence for fall prevention, one of five subgroups of the Best Practice project ([www.gesundheitsfoerderung.ch/bpgfa](http://www.gesundheitsfoerderung.ch/bpgfa)). These consolidated scientific findings are intended to provide a basis for new national recommendations for the implementation of fall intervention measures for vulnerable older people. Additionally, over the next two years, with the help of an expert working group, these findings are to be translated into hands-on practical tools, such as brochures, guidelines and training programmes.

## Summary

During the 20<sup>th</sup> century Switzerland, like many other Western countries, experienced significant ageing of the population over the age of 65. As the lifespan of the Swiss population increases, so does the prevalence of falls. A multiplicity of fall prevention programmes are available, but extracting their most effective components remains a challenge. This article summarises the results of current studies on fall prevention, with a particular focus on methodological quality and successful reduction of fall incidence in vulnerable older people. Characteristics of effective fall prevention programmes in the fields of exercise, home modifications, appropriate footwear and walking aids are assessed. We then briefly discuss how these study results can be adapted to the Swiss context. This knowledge emphasises an interdisciplinary approach in the prevention of falls, the objective being to reinforce autonomy, promote health and enhance quality of life in vulnerable older people.

**Key words:** falls; fall prevention programmes; older adults; fall risk factors; Swiss health promotion

## Introduction

Switzerland, like most other Western countries, experienced rapid growth of the population over the age of 65 during the 20<sup>th</sup> century [1]. Currently, persons aged 65 years and over account for 16.6% of the permanent resident population. According to projections of the Swiss Federal Stat-

istical Office [1], in about 40 years almost every third person will belong to this age group. This development is the result of a declining birth rate and a continuously increasing lifespan. As the lifespan of the Swiss population continues to rise, so does the prevalence of falls.

Approximately one third of individuals over the age of 65 fall at least once during a one-year period [2, 3]. This increases to nearly half in people over the age of 80 [3]. In addition to the heavy financial burden on the public health care system, falls and fall-related injuries affect the quality of life of older people due to restricted mobility and functional decline [4, 5]. Hip fractures in particular, with a one-year mortality of 22%, create a significant and increasing burden of illness for older persons in Switzerland [6]. In addition to physical injury, falls can have major psychological and social consequences, such as fear of falling [7, 8]. The majority of falls in older people are not usually the result of a single cause, but rather a combination of interacting factors [9, 10]. Numerous studies with either prospective or retrospective designs have identified a multitude of risk factors for falling [2, 11–14]. These factors have been broadly classified into intrinsic (e.g. poor balance, muscle weakness, impaired gait, low vision) or extrinsic factors (e.g. environmental hazards, inappropriate footwear). Understanding these risk factors is an important step in planning fall prevention strategies.

A variety of fall prevention programmes targeting older persons have been established in recent years. These prevention programmes have used either a single intervention strategy such as exercise, home hazard assessment with modifications, vision assessment with correction and medication management, or a combination of single interventions in a multifactorial approach. However, it is not yet clear which interventions are the most beneficial for vulnerable older people.

In this systematic literature review we summarise the results of current studies on fall prevention, with a particular focus on methodological quality and successful reduction of fall incidence in vulnerable older people. We focused on single intervention studies to be able to isolate possible effects of one component of these intervention programmes. We limited our review to fall prevention interventions specifically targeting vulnerable older people, since they are

likely to benefit most. We then discuss how these study results can be interpreted in the Swiss context.

## Literature search

### Search strategy

Studies were identified by conducting a computer-based literature search using PubMed, MEDLINE, CINAHL and EMBASE electronic databases. References from current fall prevention guidelines and books were also examined [12, 15–17]. Papers recommended by experts in the field of fall prevention and scientific colleagues were also considered. The search included papers and abstracts from January 1990 to August 2010. Inclusion criteria for this review were as follows: randomised controlled trials of single interventions and non-experimental studies published in English, German or French. We included multifactorial fall prevention programmes if either exercise, home modifications, appropriate footwear or walking aids were individually assessed in separate intervention arms. The targeted populations were vulnerable older people, described by terms often used to describe pre-frail older people, such as risk of falling, history of falls or transitioning to frailty. However, given the heterogeneity of the population enrolled in some of the studies reviewed, and inconsistent methodologies regarding the definition of pre-frail older people (e.g. the Fried [18] criteria), we refrained from describing the study populations as pre-frail and instead used the term vulnerable.

Older people of both genders living alone were included. We also included one study [19] in which the participants were living in senior housing communities that included a continuum of care, because they displayed the physical capabilities (e.g. ADL and functional independence) of a vulnerable population. Participants in one study [20] lived in a residential care facility with no details provided on care status. In view of their ability to participate in a 12-week exercise programme, we considered this population appropriate for inclusion. Study participants were aged 65 or over. Only trials designed to assess fall prevention which

documented the number of falls (i.e. by falls calendars) were examined.

### Article selection

Two research authors screened title, key words and abstracts of identified studies for possible inclusion (YJG, IW). From the full text, those authors independently assessed potential eligibility for inclusion of papers concerning exercise, plus home modifications, appropriate footwear and walking aids. Any disagreement was resolved by discussion between the two authors or by a decision of a third author. Due to time, personnel and financial constraints, additional risk factors could not be included in the scope of this article.

The results were summarised qualitatively in a table and stratified according to type of intervention (exercise, home assessment and modifications, footwear and walking aids). We view this table of summarised studies as a valuable reference tool for those planning fall prevention programmes or studies (for further details see tables S1 - S3 published as separate PDF files: [table S1](#) - [table S2](#) - [table S3](#)).

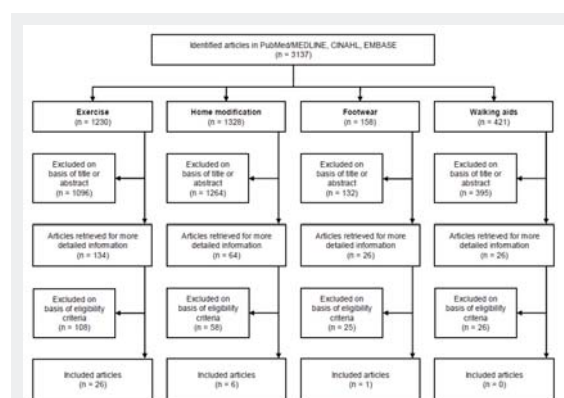
### Quality assessment

Quality assessment of the articles included was based on the Physiotherapy Evidence Database (PEDro) methodological quality score (table 1) [21]. Randomised controlled trials indexed on PEDro are rated according to an 11-item scale [22]. Ten of the 11 scale items, excluding one item pertaining to external validity, contribute to the total PEDro score (range 0–10 points). The higher the score, the better the methodological quality [23].

A multidisciplinary group of health professionals met at a network congress of the Swiss Health Promotion institution ([www.gesundheitsfoerderung.ch/bpgfa](http://www.gesundheitsfoerderung.ch/bpgfa)) to discuss the results of this systematic literature review. The feedback was included in the discussion section of this paper.

### Interventions to prevent falls

Our initial literature search identified 3137 articles. Removal of duplicates and unsuitable papers based on information in the title or abstract resulted in 250 relevant articles. After thorough review of the full text of these articles, 33 of them fulfilled our eligibility criteria and were included in this review (fig. 1).



**Figure 1**

Flowchart for illustration of literature search and selection. In this paper we will first present the information summary regarding intrinsic factors (exercise as a single intervention approach to reduce falls) followed by extrinsic factors (home assessment and modifications, footwear and walking aids, each as a single intervention approach to reduce falls).

## Exercise as a single intervention approach

This section summarises the characteristics of 26 exercise trials which were compared with each other to distinguish substantive characteristics for prospective exercise interventions in Swiss fall prevention. Overall the exercise trials showed a 14–47.5% reduction of fall rate for the intervention groups. The duration of the exercise trials ranged from five weeks to two years.

### Population characteristics of the exercise trials identified

The 26 exercise trials were conducted in eight countries (n refers to the number of trials): Australia (n = 4), England (n = 1), Finland (n = 1), Japan (n = 3), Korea (n = 1),



the Netherlands (n = 3), New Zealand (n = 4), Taiwan (n = 1) and the USA (n = 8). Most of these exercise trials were carried out in an urban setting (n = 20). In total, 7707 participants were recruited from emergency wards, fracture clinics, hospitals, physiotherapists' practices, primary care providers, general practitioners, nurses, receptionists, researchers and others. Most of the exercise trials used patient files, plus population, resident and electoral registers for recruitment.

The study populations consisted of older community-dwellers living independently at home, in congregate housing, living facilities, self- and intermediate-care retirement villages, long-term care centres, senior housing communities and residential care facilities. Most of the exercise trials included more women than men (n = 20) with a range of 51.0% to 94.5% women. The mean age of study populations was between  $69.0 \pm 6.5$  and  $88.0 \pm 3.0$  years, and the size of the intervention groups ranged from 31 to 472 persons. The populations were heterogeneous in terms of physical health, for example, number of prescribed medications, cardiovascular complications and the presence of vision or hearing impairments.

#### Intervention characteristics of the exercise trials identified

Exercise frequency ranged from one to six sessions per week (n = 23 consisted of one to three sessions weekly) with a session duration of 30 to 120 min. The exercise sessions often consisted of a warm-up phase which lasted from five to 15 minutes (n = 8) and a cool-down phase which lasted five to ten minutes (n = 8). Common sites for the exercise sessions were ambulatory care centres, community or facility rooms, medical centres and at home. Exercise trials were with groups (n = 14), individuals (n = 3) or both individual and in groups (n = 5). The size of the exercising groups ranged from five to 20 participants.

Interventions took place in the following major categories: balance (e.g. one-leg stance), skeletal muscle strength (e.g. squats), gait (e.g. trail walking exercises), mobility (e.g. walking over doorsteps), coordination (e.g. dance steps), flexibility (e.g. stretching), endurance (e.g. on a treadmill) and functionality (e.g. sit to stand). A variety of exercise equipment was used such as strengthening machines, bicycle ergometers, balance boards, chairs, balls, elastic bands, as well as foot, hip and ankle weights. The trials analysed reported exercise supervision by qualified exercise instructors, licensed physiotherapists, nurses, occupational therapists, health therapists and tai chi masters.

The reported dropouts in the exercise trials were due to health problems (n = 15), death (n = 11), moving away (n = 7), institutionalisation in long-term care or hospitals (n = 7), conflicting schedules (n = 6), loss of interest (n = 4), transportation problems (n = 2), falls (n = 2), family commitments (n = 2), cognitive decline (n = 1), depression (n = 1), surgery (n = 1) and other reasons (n = 6). Only a few trials reported means of achieving long-term adherence by, for example, integrating musical (n = 4) or social components (n = 2). Music from the past of the participants was used to stimulate memories [19] and for accompaniment [24]. Social components consisted of recreational tea breaks [25] or sitting together over a drink [26].

#### Effective components of exercise interventions

Of the 26 total exercise intervention trials in this review, these six are focused on separately because of their high methodological quality (>5 of 10 points on the PEDro scale), large sample size (n >35 in the intervention group) and large fall prevention effect (>30% fewer falls during intervention period) (table 2). Compared to the other 20 exercise interventions, these six exercise interventions not only consisted of one to three supervised exercise sessions per week, but also at least two additional individual exercise sessions at home. On average, the weekly, usually supervised group exercise duration was higher at 60–180 minutes, whereas additional individual exercises at home were conducted for 15–35 minutes. Exercise interventions lasted from at least five weeks to one year and were held in smaller groups of nine to 12 participants. The exercise intensity was similar to the other 20 interventions and often stated to be moderate. Exercise of the six outstanding studies predominantly aimed to increase muscle strength in the lower extremities as well as to improve balance, gait, mobility and functionality.

It was evident from all exercise interventions that monitoring exercise intensity is of the utmost importance to guarantee success. Progress, regular individual review (e.g. based on exercise protocols) and tailored adjustments form the basis of a successful and safe exercise intervention. Including social components in the interventions is important because it seems to improve adherence. A positive example of the integration of several of the above-mentioned components can be found in a recent Swiss study (published after completion of our systematic literature review) which reported a significant reduction in the fall rate of older

**Table 1:** Physiotherapy Evidence Database (PEDro) methodological quality scores of all included studies [21].

PEDro score <sup>1</sup>	Intervention studies
8 / 10	Barnett et al. [55], Campbell et al. [30], Campbell et al. [56], Logghe et al. [57], Robertson et al. [58]
7 / 10	Buchner et al. [59], Lannin et al. [32], Rubenstein et al. [60], Voukelatos et al. [61], Wolf et al. [62], Yamada et al. [63]
6 / 10	Cumming et al. [31], Day et al. [34], Faber et al. [26], Iwamoto et al. [64], Lord et al. [65], Luukinen et al. [66], Skelton et al. [67], Weerdesteyn et al. [68], Wolf et al. [69]
5 / 10	Choi et al. [20], Li et al. [24], Lin et al. [33], McKiernan FE [45], Means et al. [70], Morgan et al. [71], Stevens et al. [35]
4 / 10	Campbell et al. [72], Lin et al. [73], Lord et al. [74], Nowalk et al. [19]
N/A	Inokuchi et al. [25]

<sup>1</sup> Scores range from zero to ten, higher score represents better methodological quality.

Ten of the 11 PEDro scale items of methodological quality are scored: randomisation, concealed allocation of subjects, baseline similarity of groups, blinding of participants, blinding of assessors, adequate follow-up (more than 85% of participants), intention to treat analysis, between-group statistical comparison, point measures and measures of variability; eligibility criteria specified is not scored.

people after their participation in a multi-tasking, rhythmic movement intervention to music [27].

High participation rates also depend on the dedication and motivation of the instructor, group composition and positive reinforcement by family members and general practitioners. Besides advertising or direct contact with older people, general practitioners may also have a pivotal role in recruitment of the targeted population. Additionally, exercise interventions must be feasible for vulnerable older people with respect to accessibility, financial means and personal schedules.

The success of any exercise intervention for fall prevention in vulnerable older people depends on the contents discussed above, but also duly bearing in mind distinct anthropometrical, socioeconomic, civil, ethnical, seasonal and educational data. The beneficial interaction between exercise, nutrition and supplementation (for example, proteins and vitamin D) has also to be considered in regard to functionality and quality of life in vulnerable older people [28, 29]. The latter information is missing throughout most of the trials investigated and highlights the complexity of designing a tailored and targeted exercise trial.

## Home assessment and modifications as a single intervention approach

Six randomised controlled trials of home assessment and modifications were identified as a single intervention for evaluating environmental risk factors with the aim of reducing fall rates. These studies have reported inconsistent findings with only two showing a significant reduction in falls [30, 31]. Campbell et al. [30] found that there were 41% fewer falls in the intervention group compared with those who did not receive the home safety programme. The intervention in the study by Cumming et al. [31] reduced falls by 36% among participants with a history of falls.

The characteristics of the home modification studies included are presented in table 3. Countries of origin were (n refers to the number of trials): Australia (n = 4), New Zealand (n = 1) and Taiwan (n = 1). Participants in these six studies included community-dwelling individuals over the age of 65 [31-33], 70 [34, 35] or 75 [30]. Campbell et al. [30] targeted persons with severe vision impairment. Falls were monitored between a follow-up of three to 18 months.

**Table 2:** Characteristics of six particularly good exercise intervention trials<sup>1</sup>

Study	Participants <sup>1</sup>	Intervention components	Adherence rate	Supervision	Main fall outcome	PEDro Score
Barnett et al. (2003) [55]	n = 163 age >70 years at-risk for falls	Class addressing physical fall risk factors designed by physiotherapist. 1x 60 min/wk for 1 year + home exercises. 5-10 min warm up: stretches, balance, coordination (modified Tai Chi, stepping, dance steps), aerobic capacity, muscle strength (body weight), functional exercise (sit to stand, weight transference, reaching). 10 min cool down. Music used.	Median of attended exercise classes by exercise group was 23 out of 37.	Three accredited and experienced exercise instructors.	The rate of falls in the intervention group was 40% lower than that of the control group (IRR = 0.60, 95% CI 0.36-0.99).	8 / 10
Campbell et al. (1999) [56]	n = 152 age >80 years older women	Individually tailored muscle strengthening and balance. 3x 30 min/wk and walking outdoors ≥3x/wk for 1 year. Moderate strengthening with ankle cuff weights (0.5/1.0 kg): Walking on toes / heels, walking backwards / sideways / turning round, stepping over an object, bending and picking up an object, stair climbing at home, rising from sitting to standing.	44% of the exercise group were exercised at least 3x/wk.	Four home visits by a physiotherapist in the first two months of the study.	The relative hazard for all falls for the exercise group was 0.69 (95% CI 0.49-0.97).	8 / 10
Robertson et al. (2001) [58]	n = 240 age >80 years older people	Exercise programme run from a home health service based in a geriatric assessment and rehabilitation hospital. 3x approx. 30 min/wk and walking 2x/wk for 1 year. Muscle strengthening (ankle cuff weights), balance retraining exercises and walking plan.	43% performed the prescribed exercises ≥3x/wk, 72% at least 2x/wk.	Trained district nurse without previous experience.	A 46% reduction in the number of falls for exercise group (IRR = 0.54, 95% CI 0.32-0.90).	8 / 10
Skelton et al. (2005) [67]	n = 81 age >70 years frequent female fallers	Individually tailored and targeted Falls Management Exercise (FaME) with Otago exercises core. 1x 60 min/wk for 36 wks and 2x 30 min/wk home exercises. Reduction of asymmetry in strength of the lower limbs with Otago exercises core. The exercise classes were balance specific, individually tailored and targeted training for dynamic balance, strength, bone, endurance, flexibility, gait and functional skills.	68% chose to continue exercising after the trial (implying high adherence to the original programme).	Qualified exercise-for-the-older-person instructor with additional FaME training.	A 31% reduction in the number of falls during the whole trial period for the exercise group (IRR = 0.69, 95% CI 0.50-0.96, p = 0.029).	6 / 10
Weerdesteyn et al. (2006) [68]	n = 107 age >70 years with a history of falls	Low intensity Nijmegen Falls Prevention Programme 2x 90 min/wk for 5 wks. Balance, gait (with additional motor and cognitive tasks) coordination in obstacle course with mimics of ADLs and potential fall risk (i.e. walking over doorsteps, stepping stones, uneven pavement, different ground surfaces). Practice of fall techniques.	Attendance rate of 87%.	N/A	The number of falls in the exercise group decreased by 46% (IRR = 0.54, 95% CI 0.34-0.86).	6 / 10
Wolf et al. (2003/1996) [69]	n = 200 age >75 years older people	Tai chi improving movement limitations of older people. 2x individual contact time of 45 min/wk and 2x 15 min/d at home for 15 wks. Synthesis of 108 forms into 10, emphasising components of movement typically limited with ageing.	Attendance in the Tai chi group was 76% (SD 19) (range: 6-100%).	Tai Chi instructors.	The rate of falls/risk of multiple falls was reduced by 47.5% (RR = 0.525, p = 0.01), adjusted.	6 / 10

<sup>1</sup> Age of participants only from intervention groups.

ADL: activities of daily living; CI: confidence intervals; IRR: incidence rate ratio; min: minutes; N/A: not applicable; RR: rate ratio; SD: standard deviation; wk(s): week(s).

Home assessment is an essential part of this single intervention approach. Four different assessment tools were used throughout the six trials of which two were specifically designed on the basis of published papers and existing checklists [33, 35]. The two successful fall prevention trials used the same validated and reliable home assessment form (table 3).

In four studies a single home visit took place to identify and modify potential fall risk factors [32–35]. These four studies showed no effect in reducing fall rate. The two studies that led to a reduction in fall rates included a follow-up contact to check whether suggested home modifications had been implemented. In one study, a second visit was conducted to check the equipment installed [30]. In the study by Cumming et al. [31] an occupational therapist called all participants two weeks after the assessment to check home modifications and to encourage adherence to recommendations. It thus seems reasonable to verify the recommended modifications after a certain time span. A telephone call may represent a cost-effective option for follow-up contact.

In the four ineffective trials, the intervention was conducted by trained nurses or public health workers. The two effective interventions were done by occupational therapists. The intervention in the study by Cumming et al. [31]

was effective only among participants who reported having had at least one fall in the previous year. However, in this group falls outside the home were also significantly reduced. Similar results were presented by Campbell et al. [30] with no significant difference in the reduction of falls at home compared to those outside the home. This suggests that an effect may not be caused by the home modifications alone but also partly depends on professional advice by the occupational therapist.

Adherence is an important aspect of interventions. It was evaluated in three [30, 31, 35] of the six studies and varied between 13% and 90%. The most commonly recommended home modifications were: removal of obstacles, rugs and mats, installation of grab bars or rails, improvement of poor lighting, use of non-slip bathmat, repair of damaged flooring and fitting of contrast edging to steps. It is known from clinical practice that home assessments and modifications are poorly accepted by older people. Older people's self perception of fall risk is often quite different from that of the health professional. Acceptance of suggested modifications can be facilitated by establishing a good relationship between the target person and the health professional. Help from a health professional or the relatives can also support adherence to home safety recommendations.

**Table 3:** Characteristics of home assessment and modifications studies.

Study	Participants	Intervention	Adherence to recommendations	Main fall outcomes	Comments	PEDro Score
Campbell et al. (2005) [30]	n = 391 age ≥75 years poor vision	Modified version of the Westmead Home Safety Assessment by OT, provision of equipment, payment and supervision (second visit, telephone call).	90% adherence to one or more of the recommendations.	Effective in reducing falls (IRR = 0.59, 95% CI 0.42-0.83).	No significant difference in the reduction of falls at home compared with those away from the home environment.	8 / 10
Cumming et al. (1999) [31]	n = 530 age ≥65 years most were recruited while inpatient at hospital	Westmead Home Safety Assessment by OT, facilitated any necessary home modification, supervision of home modifications (telephone call).	Adherence at 12 months ranged from 19%-75%.	Effective in previous fallers (RR = 0.64, 95% CI 0.50-0.83). Not effective in previous non-fallers (RR = 1.03, 95% CI 0.75-1.41).	Home visit was effective in reducing risk of falling at home and away from home in previous fallers.	6 / 10
Day et al. (2002) [34]	n = 1090 age ≥70 years rated their health as good to excellent	Home assessment by trained assessor, home hazards were removed or modified either by the participants themselves or via the City of Whitehorse's home maintenance programme (provision of materials and labour for providing modifications).	N/A	Not effective in reducing falls (RR = 0.92, 95% CI 0.78-1.08).	Number of hazards was significantly reduced in the intervention group. Effective in combination with exercise (p = 0.02) and in combination with vision (p = 0.07). Strongest effect: all three interventions together (p = 0.004).	6 / 10
Lannin et al. (2007) [32]	n = 10 age ≥65 years recruited while inpatient at rehabilitation	Westmead Home Safety Assessment by OT, advice for home modifications and equipment. Education: focussed on safe performance of activities in and around home.	N/A	One of the intervention participants fell within two weeks of discharge. Two of the control participants fell two weeks and one month post-discharge.	None	7 / 10
Lin et al. (2007) [33]	n = 150 age ≥65 years fall history in the previous 4 weeks	Safety assessment by public health workers, advice for home modifications.	N/A	Not effective in reducing the fall incidence rate per 1000 person years (1.1 in home safety group, 1.6 in exercise group, 2.4 in educational group).	Quality of life (physical and environmental domain), functional reach, ADLs, functional balance and gait improved significantly.	5 / 10
Stevens et al. (2001) [35]	n = 1737 age ≥70 years healthy older people	Home hazard assessment by trained nurse assessor, free installation of safety devices, education about home hazards.	Maintained significant reduction in 4 out of 5 most prevalent home hazards.	Not effective in reducing the rate of falls (falls on environmental hazards inside the home: IRR = 1.11, 95% CI 0.82-1.50).	Covariates significantly associated with an increased rate of falls on environmental hazards were history of falling (RR 2.09) and use of a walking aid inside the home (RR 1.94).	5 / 10

ADL: activities of daily living; CI: confidence intervals; IRR: incidence rate ratio; N/A: not applicable; OT: occupational therapist; RR: rate ratio.

### Effective components of home assessment and modifications

The outcomes of falls in the six studies showed inconsistent findings. The interventions which effectively reduced falls suggest that home assessment and modifications should be offered to people with a previous fall history, severe vision problems or after discharge from hospital. In view of the specific expertise needed in this area, occupational therapists should guide the intervention. Furthermore, the effectiveness of the intervention can be enhanced by follow-up contacts.

It is acknowledged that a home assessment and modifications should be part of a multifactorial approach [36], since the majority of the studies used a multifactorial approach and evidence in fall prevention is strong.

### Footwear as a single intervention approach

The relationship between certain types or characteristics of footwear and the risk of falling is well established in the literature. Walking barefoot or wearing socks has been associated with a higher risk of falling [37–40] than when wearing shoes. Studies which examined footwear characteristics at the time of fall-related hip fractures showed that the most common type of footwear were slippers, walking barefoot or wearing socks [41, 42]. However, walking barefoot or wearing socks or slippers does not necessarily indicate that this type of footwear, or the absence of footwear, caused the fall. Shoes with low heels and a large contact area may help older people to reduce the risk of a fall [43]. Additionally, older people often choose their footwear for comfort and not safety reasons [42]. The difficulty in establishing a relationship between footwear and risk of falls is that the type of shoe worn may change according to the location and activity being undertaken. Furthermore, going shoeless indoors might be more common.

Most falls occur during the winter months [44]. A randomised controlled trial by McKiernan [45] was able to show that an anti-slip device attached to shoes significantly reduced outdoor falls in hazardous winter conditions in older people with a history of previous falls. However, not wearing a gait-stabilising device in hazardous winter conditions does not represent a risk factor for falling.

### Effective components of footwear interventions

Anti-slip devices for shoes may be useful for older people in hazardous winter conditions (e.g. snow and ice). Based on lower quality studies, footwear should be worn indoors and outdoors, have a low heel height, high surface contact area and good fixation. Future research should be made to strengthen the evidence and make recommendations regarding the characteristics of safe shoes for older people.

### Walking aids as a single intervention approach

The use of walking aids is considered a fall-associated risk factor [11, 12]. The study of Rubenstein and Josephson [11] showed that the use of a walking aid is related to a 2.6-fold (confidence interval: 1.2; 4.6) risk of falling. Some older

people fall because of their walking aid, for example by improper use or tripping over the walking aid. A walking aid may also impede the compensatory stepping and grasping mechanism during balance recovery to avoid a fall [46, 47]. However, the increased fall risk associated with the use of a walking aid, as reported by Rubenstein and Josephson [11], probably reflects the functional status of the older people using the walking aids (those with gait disturbance, muscle weakness and increased fall risk are more likely to use a walking aid) rather than the aid itself. When walking aids are appropriately chosen for the clinical condition (for example, a four-points walker instead of a front-wheel walker for people with Parkinsonian gait disturbances), correctly sized (not too high or too low) and properly implemented, they can heighten walking safety by increasing the base of support, enhancing lateral stability and reducing lower-limb load [48], and thus perhaps reduce the risk of falling.

### Important components of walking aid interventions

A suitable walking aid must be appropriate for the individual's abilities and the environment, correctly sized and free of defects [49, 50], and should only be used if necessary. Also, prescription and training in the use of walking aids should be left to a health professional with expertise in the field [12, 51].

### Fall prevention in the Swiss context

Fall prevention in Switzerland needs to overcome specific hurdles and framework conditions. There are many local, regional, cantonal and national peculiarities. It is comprehensible that settings of international studies are often not generally applicable to Swiss settings [52]. Specific geographical, infrastructure, socio-demographic and funding circumstances must be taken into consideration. Besides cultural differences, there are also language barriers to be overcome. In the best case, Swiss fall prevention endeavours are translated into all four of the country's official languages (German, French, Italian and Romansh) to reach as many vulnerable older people as possible. The integration of international scientific findings also faces a unique regional, cantonal and federal legal and political system in Switzerland, which has administrative subdivisions into 26 cantons with considerable autonomy. These cantons are further subdivided into multiple small communities which are often equivalent to the remaining restricted living environment of older people. Gaining the support of local community authorities may be of crucial importance in reaching older people on the subject of fall prevention.

It is necessary to highlight the importance of cooperation and coordination between all health experts in the field of fall prevention. Interdisciplinary cooperation between exercise instructors, physiotherapists, occupational therapists, exercise and health scientists, as well as general practitioners, geriatricians and psychologists, form the foundation for successful fall prevention [53]. Besides professional supervision, different forms of social activity between or after intervention sessions may also improve adherence. In vulnerable older people a high level of motivation must be maintained to guarantee high adherence rates and thus prolong positive health effects of interventions.

## Conclusion

This systematic literature review may serve as a basis for recommendations on the implementation of interventions in vulnerable older people in Switzerland. We identified important features of fall prevention interventions of high methodological quality which successfully showed a reduction in fall incidence rate. However, the rather heterogeneous intervention designs, the potential bias from low quality studies and the inclusion of non-experimental studies prevents us from performing a meta-analysis in the context of our systematic review. The optimal type, intensity, frequency and duration of fall prevention programmes required to significantly lower the rate of falls over the long term are still not known. This is partly due to the varying definitions of falls across studies and the inconsistency with which falls are monitored and reported. In this regard, older people who exercise may become more mobile and therefore more exposed to a greater risk of falling. Hence, apart from simply a change in the number of falls, further outcome measures such as the use of health care services, improvements in the overall level of disability or functionality, and psychosocial measures such as fear of falling and perceived quality of life must be taken into consideration when scrutinising the effectiveness of a fall prevention programme.

Exercise programmes for vulnerable older people should be adjusted to the individual health circumstances, to guarantee safe exercising and prevent health damage or injury. The exercise instructor and the social atmosphere may play a pivotal role in positively affecting adherence rates, sustainability of the programme and general enjoyment of the exercises. It is comprehensible that a multitude of exercise variables and heterogeneous conditions make it difficult to extract, compare and reproduce particular effective exercise components in a real-life setting. Consequently, general statements on exercise content for fall prevention in vulnerable older people in Switzerland remain challenging. Environmental hazards, inadequate footwear and walking aids are implicated as a contributory factor in a large proportion of falls in older people. Considering the small number of published studies, the effectiveness of these fall prevention programmes as a single intervention should be examined in future research. To date, several studies have

included environmental changes, inspection of footwear and walking aids as a component within a multifactorial approach. However, it is very difficult or wholly impossible to extract specific fall-related outcomes from these studies. For a holistic fall prevention approach, further risk factors need to be included, such as visual problems, hearing impairment, syncope, incontinence, fall history, medication, inadequate clothing, cognitive decline, substance abuse and institutionalisation.

In summary, the challenges for a successful transfer of international fall prevention knowledge into the Swiss context are as follows: the efficiency of an intervention, acceptance and motivation of programme providers (e.g., instructors), the quality of the measures implemented and the programmes' sustainability. Finally, it must be noted that not only the provision of fall prevention programmes, but also the demand of the target population itself – the vulnerable older people who are likely to derive the greatest benefit – is crucial for successful fall prevention. Prevention of falls is an active research area and for this reason it is recommended that these results be updated and revised in the near future.

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**Table 4:** Important characteristics of successful interventions.

Domain	Important components of interventions
Exercise	1–3 supervised group exercise sessions per week (60–180 minutes in total) and ≥2 additional individual exercise sessions at home (15–35 minutes per session). Intervention duration of 5–52 weeks. Moderate exercise intensity. 9–12 members per group. Supervision by qualified and trained personnel. Exercises for muscle strength of lower extremities, balance, gait, mobility and functionality.
Home assessment and modifications	For older people with a previous fall history, severe vision problems, after discharge from hospital. Guided by occupational therapists. Implementation of follow-up contacts.
Footwear	Use anti-slip devices in hazardous winter conditions. Footwear should be worn indoors and outdoors, have a low heel height, high contact area and good fixation.
Walking aids	Adapted to individual abilities and environment. Correctly sized and free of defects. Only used if necessary. Training in the use of the walking aid. Recommended by a health professional.

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Figures (large format)

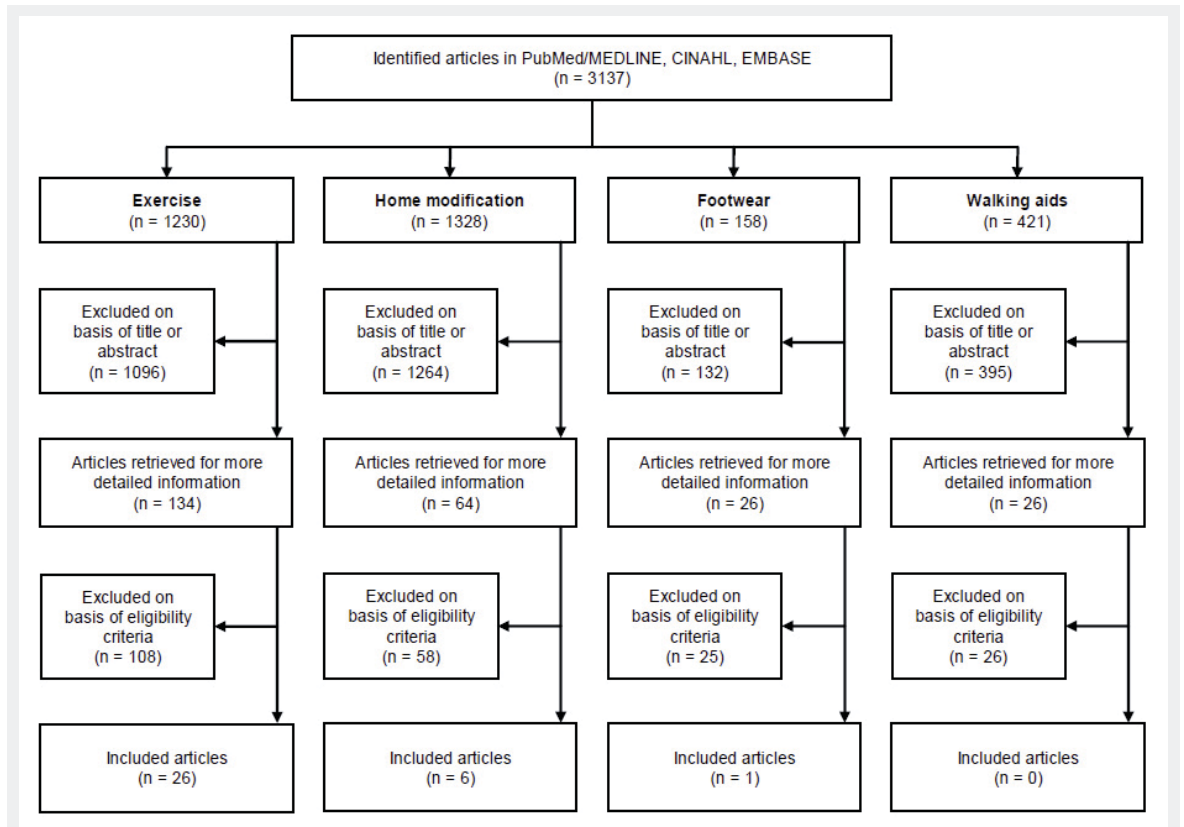


Figure 1

Flowchart for illustration of literature search and selection.

In this paper we will first present the information summary regarding intrinsic factors (exercise as a single intervention approach to reduce falls) followed by extrinsic factors (home assessment and modifications, footwear and walking aids, each as a single intervention approach to reduce falls).



**Publication (d)**

**Effects of a Salsa Dance Training on Balance and Strength Performance in Older Adults**

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Gerontology 2012;58:305-12

# Effects of a Salsa Dance Training on Balance and Strength Performance in Older Adults

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## Key Words

Elderly · Postural sway · Gait · Force production

## Abstract

**Background:** Deficits in static and particularly dynamic postural control and force production have frequently been associated with an increased risk of falling in older adults. **Objective:** The objectives of this study were to investigate the effects of salsa dancing on measures of static/dynamic postural control and leg extensor power in seniors. **Methods:** Twenty-eight healthy older adults were randomly assigned to an intervention group (INT,  $n = 14$ , age  $71.6 \pm 5.3$  years) to conduct an 8-week progressive salsa dancing programme or a control group (CON,  $n = 14$ , age  $68.9 \pm 4.7$  years). Static postural control was measured during one-legged stance on a balance platform and dynamic postural control was obtained while walking on an instrumented walkway. Leg extensor power was assessed during a countermovement jump on a force plate. **Results:** Programme compliance was excellent with participants of the INT group completing 92.5% of the dancing sessions. A tendency towards an improvement in the selected measures of static postural con-

trol was observed in the INT group as compared to the CON group. Significant group  $\times$  test interactions were found for stride velocity, length and time. Post hoc analyses revealed significant increases in stride velocity and length, and concomitant decreases in stride time. However, salsa dancing did not have significant effects on various measures of gait variability and leg extensor power. **Conclusion:** Salsa proved to be a safe and feasible exercise programme for older adults accompanied with a high adherence rate. Age-related deficits in measures of static and particularly dynamic postural control can be mitigated by salsa dancing in older adults. High physical activity and fitness/mobility levels of our participants could be responsible for the nonsignificant findings in gait variability and leg extensor power.

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## Introduction

Continuously greying societies in Western industrialized countries demand intense research efforts in the field of neuromuscular ageing. Specific consequences of neuromuscular ageing are tremendous decreases in different

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**Table 1.** Baseline characteristics by group

	INT (n = 14)	CON (n = 14)
Age, years	71.6 ± 5.3	68.9 ± 4.7
Body height, cm	167.1 ± 10.1	169.1 ± 8.6
Body mass, kg	72.3 ± 13.0	71.9 ± 13.0
BMI, kg/m <sup>2</sup>	25.9 ± 4.2	25.1 ± 4.0
Sex, female/male	9/5	8/6
MMSE	28.5 ± 1.8	28.3 ± 0.8
CDT	all participants were classified as non-pathological	
Physical activity, h/week	11.5 ± 5.3	11.7 ± 8.3

Values are means and SDs. No group baseline differences were detected;  $p > 0.05$ .

components of postural control (e.g. reactive and steady-state balance) and force production (e.g. maximal strength, rate of force development, muscle power) mainly after the age of 60 [1–3]. These deficits are associated with an increased risk of falling in older adults [4, 5]. Thus, the promotion of balance and force production represents two important targets in the field of fall prevention. Traditionally, balance and resistance training have been applied to mitigate age-related processes in the neuromuscular system. However, the effects of resistance training appear to be limited to gains in force production. In fact, a systematic review of randomized controlled trials on the efficacy of resistance training on balance performance could not detect a clear effect on various measures of standing balance in older adults (effect size = 0.11) [6]. Balance training has proven to be effective in increasing measures of postural control and force production in seniors [7, 8]. However, social interaction during balance training is limited which might negatively affect both the motivation of the exercisers and adherence rate during training. Recently, Granacher et al. [9] suggested an intergenerational approach (i.e. seniors exercise together with children) in the promotion of balance in older adults to specifically address the motivation of the exercisers. Another form of enhancing motivation and social interaction during training is to implement dance programmes for the promotion of physical activity in general and balance and force production in particular. Thus, dance may provide a form of exercise that offers both a conditioning stimulus and a socially interactive and motivating activity that older adults would like to perform on a permanent basis [10]. A growing pool of literature indicates that different types of

dance programmes (e.g. Turkish or Greek folklore dance, Latin dance, Tango) are effective in improving measures of postural control [11–15].

Salsa dance appears to be specifically suited for the promotion of balance and force production. In fact, salsa moves are particularly challenging for dynamic postural control and muscle strength/power due to frequent changes in direction and because the dance steps are performed on the toes of the feet. In addition, salsa specifically challenges the performance of movements to the rhythm of the music. Moreover, a stable walking pattern is characterized by low fluctuations of the gait rhythm. Thus, salsa dancing may improve spatiotemporal features of gait because both aesthetic dancing as well as stable walking require some sense of rhythm. Finally, over recent years salsa has become a very popular dance among young and middle-aged adults and might therefore also attract older adults. However, to the authors' knowledge, there is no study available that investigated the effects of salsa dancing alone on measures of postural control and force production in older adults.

Given that deficits in postural control and force production are associated with an increased risk of falling [4, 5], the objectives of this study were to investigate the effects of a progressive salsa dance programme on measures of static/dynamic postural control and leg extensor power in a cohort of older adults. Based on previously published studies [11, 13–15], it is expected that salsa dance improves static and particularly dynamic postural control as well as muscle power of the leg extensors in older adults.

## Methods

### Participants

Twenty-eight community-dwelling older adults between the ages of 63 and 82 gave written informed consent to participate in the study after experimental procedures were explained. The participants' baseline characteristics are presented in table 1. None of the participants had any history of musculoskeletal, neurological or orthopaedic disorders that might have affected their ability to conduct a salsa dance programme or to perform balance and strength tests. The participants were capable of walking independently without any assistive device and they had no prior experience with the applied tests. Participants were randomly assigned into an intervention group (INT) and a control group (CON). The randomization process was done using Research Randomizer, a programme published on a publicly accessible official website ([www.randomizer.org](http://www.randomizer.org)). Local ethical permission was given by the EKBB (Ethikkommission beider Basel) and all experiments were conducted according to the latest version of the declaration of Helsinki.

### *Salsa Dancing*

Participants of the INT group conducted a salsa dance programme over a period of 8 weeks (twice weekly) with a total of 16 sessions. The intervention period was chosen based on a previously published study showing that an 8-week Turkish folklore dance programme was effective in improving balance function in the elderly [15]. Each session lasted 60 min starting with a 10-min warm-up programme mainly consisting of salsa-specific static and dynamic balance exercises and ending with a 5-min cool-down programme (i.e. stretching). The intervention programme was given by a professional dance instructor in 2 separate exercise groups in order to keep the participant-to-instructor ratio small (1 instructor for 6–8 seniors).

Salsa is a partner dance that is characterized by Latin American rhythm and music. The dance programme mainly consisted of basic steps (e.g. 3-step weight change) and simplest movements of salsa in forward, backward, transversal and rotational directions. At the beginning of the programme the 3-step weight change was taught without a partner. This pattern typically uses 3 steps during every 4 beats, 1 beat being skipped. However, this skipped beat is often marked by a tap, a kick or a flick. Exercises like clapping hands, stomping the feet on the dance floor and walking individually to the rhythm of the music were incorporated in the acquisition phase. After the participants were able to accomplish the basic steps individually they were introduced to partner dance. Both men and women practiced leading while dancing salsa. This was accomplished in a first step by asking the lead person to guide their blinded partner over the dance floor. Progression during salsa dancing was realized by increasing the tempo of the music from initially 50 to 70 bpm at the end of the intervention. Of note, salsa can be danced to a count of up to 180 bpm. We further progressed from forward/backward directions to transversal and rotational dancing directions. In addition, salsa-specific moves like knee swings and hip rotations were continuously included in the programme. Finally, the participants learned the technique of toe dancing, which is a typical feature of salsa that demands high dynamic postural control and muscle power while moving with an extremely small base of floor contact.

Due to the small participant-to-instructor ratio, salsa dancing was safe without any intervention-related risk of falling. The participants of the CON group maintained their normal physical activities throughout the experimental period.

### *Testing Procedure*

Upon entering the gait laboratory, all participants were kindly asked to complete two different questionnaires (the 'Freiburg questionnaire for everyday and sports activities'® [16] and the Mini-Mental State Examination, MMSE [17]) and one cognitive test to evaluate executive function (the Clock-Drawing Test, CDT [18]). Thereafter, participants received standardized verbal instructions regarding the test procedure with a visual demonstration of the balance and the power tests. Prior to testing, all participants performed one practice trial on each test instrument to rule out potential learning effects. Measurements of static and dynamic postural control were conducted in a counterbalanced order on a balance platform and a pressure-sensitive walkway. In addition, before- and after-tests included the analysis of jumping power on a force platform.

### *Testing Material*

#### *Balance Platform*

Test circumstances (e.g. room illumination, temperature, noise) were in accordance with recommendations for post-urographic testing [19]. Static postural control was assessed by means of a balance platform (GKS 1000, IMM, Mittweida, Germany). The balance platform consists of four uni-axial sensors measuring displacements of the centre of pressure (CoP) in the mediolateral and anterior-posterior directions. For experimental testing the balance platform was firmly fixed on the floor. Participants were asked to stand on their dominant leg on the platform with their supported leg in 30° flexion, hands placed on hips and gaze fixed on a cross on the nearby wall (the fully extended knee corresponds to 0°). The dominant leg was determined according to the lateral preference inventory [20]. Participants were instructed to remain as stable as possible and to refrain from any voluntary movements during the trials. Data were acquired for 30 s at a sampling rate of 40 Hz [19]. Five parameters were computed from the time series of the CoP displacements. First, the displacements of the CoP in the anterior-posterior direction (CoPap, mm); second, the displacements of the CoP in the mediolateral direction (CoPml, mm); third, the total displacements of the CoP (CoPtot, mm), which represent the summed displacements in the mediolateral and anterior-posterior directions; fourth, the surface area covered by the trajectory of the CoP (CoParea, mm<sup>2</sup>) with a 90% confidence interval, and fifth, the CoP speed (CoPspeed, mm/s), which indicates the total distances covered by the CoP divided by the duration of the sampled period. All of these parameters represent traditional balance measures, which are widely employed in clinical practice to assess individuals' postural control capacities during unperturbed stance [21]. Three trials were performed and their mean was used for further analysis. For all the assessed CoP variables, intraclass correlation coefficients (ICC) were  $\geq 0.75$ , indicating an excellent intersession reliability [21].

#### *Pressure-Sensitive Walkway*

The walking pattern was determined during steady-state walking on an instrumented 10-metre walkway using the GAIT-Rite® System (Havertown, Pa., USA). Participants walked with their own footwear at their own speeds, initiating and terminating each walk a minimum of 2 m before and after the 10-metre walkway to allow sufficient distance to accelerate to and decelerate from a steady state of ambulation across the walkway. Distribution of pressure during walking was monitored at 80 Hz, enabling spatiotemporal gait data to be collected. Because data from the left and right strides were not statistically different, only data from the left side were analysed. Besser et al. [4] reported that 5–8 strides are necessary for 90% of individuals tested with GAITRite instrumentation to have reliable mean estimates of spatiotemporal gait parameters. Temporal and spatial parameters of gait seem to be important in the assessment of mobility in community-dwelling elderly adults [22]. Thus, in a first step, means and standard deviations (SD) of stride time, stride length, and stride velocity were computed. Stride time was defined as the time (s) between the first contacts of two consecutive footfalls of the same foot. Stride length was defined as the linear distance (cm) between successive heel contacts of the same foot. Additionally, stride velocity (cm/s) was calculated as stride length divided by stride time. To determine gait variability, coefficients of variation (CV) were calculated for the above-mentioned parameters according to the

following formula  $[(SD/mean) \times 100]$  and used as outcome measures [23]. The smaller the CV value, the safer the walking pattern. Intraclass correlation coefficients for the calculated gait parameters ranged from ICC 0.79 to 0.98 [1].

#### Force Platform

Participants performed maximal vertical countermovement jumps (CMJs) while standing on a one-dimensional force platform (KistlerP type 9290AD, Winterthur, Switzerland). The vertical ground reaction force was sampled at 500 Hz. During the CMJs, subjects stood in an upright position on the force platform and were instructed to begin the jump with a downward movement, which was immediately followed by a concentric upward movement, resulting in a maximal vertical jump. Participants performed 3 CMJs with a resting period of 1 min between jumps. For each of these trials, subjects were asked to jump as high as possible. The mean of 3 trials in terms of maximal jumping power (W/kg) was taken for further data analysis. The intraclass correlation coefficient was calculated for CMJ power and amounted to ICC = 0.81.

#### Questionnaire

The 'Freiburg questionnaire for everyday and sports activities' [16] assesses basic physical activity level (e.g. gardening, climbing stairs), leisure time physical activity level (e.g. dancing, bowling) and sports activity level (e.g. jogging, swimming) of people between the ages of 18 and 78. Significant test-retest reliability was reported for the summed physical activity level ( $r = 0.56$ ). Cross-correlation with maximum oxygen uptake revealed a significant correlation coefficient of  $r = 0.42$  [16].

The MMSE is a valid test of cognitive function. It separates patients with cognitive disturbance from those without such disturbance. Test-retest reliability of the MMSE is high with  $r = 0.89$ . Cross-correlation with the Wechsler Adult Intelligence Score revealed a correlation coefficient of  $r = 0.78$  [17]. According to Folstein et al. [17], a MMSE total score of less than 20 separates patients with dementia or functional psychosis from cognitively independently functioning participants and those with anxiety neurosis or personality disorder.

The CDT is a sensitive screening test for the evaluation of executive function [18]. The elderly participants were instructed to draw numbers in a given circle to make the circle look like a clock. Thereafter, subjects were asked to draw the hands of the clock to a point in time of their choice which, at the end of the test, they had to write down in digital form. Depending on the study consulted, inter-rater reliability for the CDT ranges between 75.4 and 99.6% [18]. Test-retest reliability can be classified as high with an  $r$  value of 0.90 [24]. Cross-correlation with the MMSE revealed a correlation coefficient of  $r > 0.50$  [25]. As a result, the test distinguishes between pathological and normal test performance.

#### Statistical Analyses

Data are presented as group mean values  $\pm$  SD, unless otherwise stated. A multivariate ANOVA was used to detect differences between the study groups in all baseline variables. Balance and strength parameters were analysed in separate  $2 \times 2$  [groups (INT, CON)  $\times$  tests (before, after)] ANOVA with repeated measures on test. Post-hoc tests with the Bonferroni-adjusted  $\alpha$  were conducted to identify the comparisons that were statistically significant. The classification of effect sizes ( $f$ ) was determined by

calculating partial  $\eta^2_p$ . The effect size is a measure of the effectiveness of a treatment and it helps to determine whether a statistically significant difference is a difference of practical concern.  $f$  values of 0.10 indicate small, of 0.25 medium and of 0.40 large effects [26]. An a priori power analysis [27] with an assumed type I error rate of 0.05 and a type II error rate of 0.20 (80% statistical power) was conducted for measures of balance function [12] and revealed that 13 persons per group would be sufficient for finding statistically significant interaction effects. All analyses were performed using the Statistical Package for Social Sciences (SPSS) version 19.0. The significance level was set at  $p < 0.05$ .

## Results

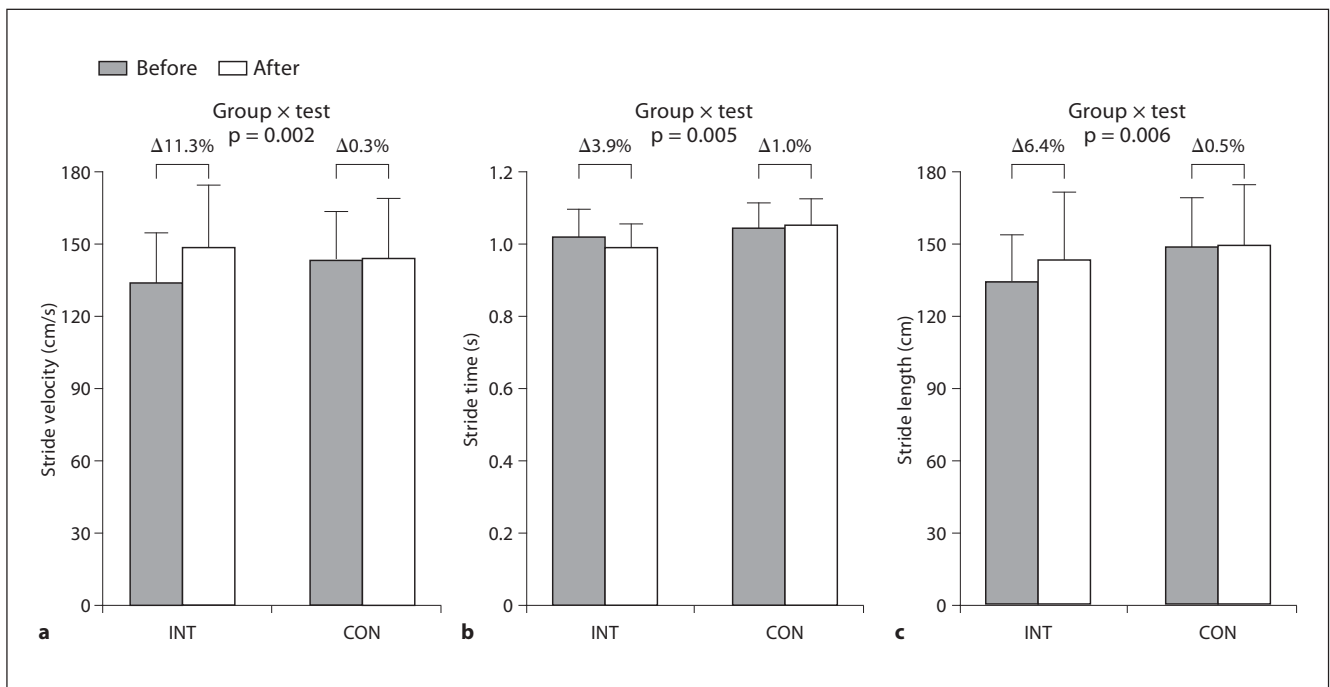
At baseline, all subjects met the inclusion criteria (i.e. MMSE; CDT) for participating in this study. The investigated results in the MMSE and the CDT indicate that the older adults of this study were cognitively healthy (table 1). Findings regarding the 'Freiburg questionnaire for everyday and sports activities' revealed that our participants could be classified as physically active (table 1). All subjects received treatment or control conditions as allocated. Fourteen participants completed the salsa dance programme and none reported any adverse events. Programme compliance was excellent with participants of the INT group completing 92.5% of the scheduled dancing sessions. Overall, there were no statistically significant differences in baseline values between the two experimental groups.

#### Standing Performance

The analysis based on performance during standing detected a main effect of time for the parameter CoPml [ $F(1, 54) = 4.39, p = 0.05, \eta^2_p = 0.15, f = 0.42$ ], and a tendency towards a significant group  $\times$  test interaction [ $F(1, 54) = 3.20, p = 0.09, \eta^2_p = 0.11, f = 0.35$ ] for the variable CoPap. The inclusion of additional CoP parameters (e.g. CoPtot, CoParea, CoPspeed) did not reveal further significant findings (table 2).

#### Walking Performance

*Stride Velocity.* The analysis indicated a significant main effect of test [ $F(1, 54) = 13.00, p < 0.001, \eta^2_p = 0.33, f = 0.70$ ] as well as a significant group  $\times$  test interaction [ $F(1, 54) = 11.73, p < 0.01, \eta^2_p = 0.31, f = 0.67$ ]. Post hoc analysis found that participants in the INT group significantly increased their stride velocity over the training period ( $p = 0.001, \Delta 11.3\%$ ) while the participants in the CON group showed no significant changes (fig. 1a). The main effect of group [ $F(1, 26) = 0.01, p > 0.05$ ] was not significant.



**Fig. 1.** Performance changes during the dancing period in stride velocity (a), stride time (b) and stride length (c) while walking on a pressure-sensitive walkway for the INT group compared to the CON group (mean ± SD).

**Table 2.** Outcome measures (ANOVA with repeated measures on test)

Measure	INT (n = 14)		CON (n = 14)		p value	
	before	after	before	after	time	time × group
<b>Standing</b>						
CoPtot, mm	1,984.4 ± 584.8	1,744.6 ± 670.7	2,192.3 ± 437.1	2,140.9 ± 457.7	0.076	0.243
CoPml, mm	1,210.5 ± 342.7	1,078.5 ± 441.0	1,448.8 ± 358.9	1,310.4 ± 297.4	0.046	0.960
CoPap, mm	1,315.0 ± 437.5	1,145.5 ± 459.9	1,335.1 ± 332.8	1,401.3 ± 403.4	0.440	0.085
CoPspeed, mm/s	67.1 ± 19.5	59.3 ± 23.0	74.3 ± 14.7	72.9 ± 15.6	0.093	0.241
CoParea, mm <sup>2</sup>	15.6 ± 9.2	13.8 ± 7.4	16.4 ± 8.4	14.7 ± 9.6	0.461	0.994
<b>Walking</b>						
Stride velocity, cm/s	133.8 ± 20.2	148.9 ± 25.8	141.8 ± 14.4	142.2 ± 14.2	0.001	0.002
Stride time, s	1.02 ± 0.07	0.98 ± 0.07	1.04 ± 0.06	1.05 ± 0.07	0.018	0.005
Stride length, cm	136.8 ± 22.0	145.5 ± 26.8	147.6 ± 15.0	148.4 ± 13.3	0.001	0.006
Stride velocity CV, %	2.7 ± 1.5	2.4 ± 1.1	2.3 ± 1.0	2.4 ± 0.7	0.637	0.542
Stride time CV, %	1.7 ± 1.0	1.9 ± 0.6	1.4 ± 0.7	1.6 ± 0.4	0.332	0.916
Stride length CV, %	1.9 ± 0.8	1.9 ± 1.1	1.9 ± 0.8	1.7 ± 0.6	0.612	0.609
<b>Power</b>						
CMJ power, W/kg	14.0 ± 2.8	15.7 ± 3.5	16.2 ± 2.2	19.2 ± 2.9	0.000	0.098

Values are means and SDs.

*Stride Time.* The analysis revealed a significant main effect of test [ $F(1, 54) = 6.35, p < 0.05, \eta^2_p = 0.20, f = 0.50$ ] as well as a significant group  $\times$  test interaction [ $F(1, 54) = 9.28, p < 0.01, \eta^2_p = 0.26, f = 0.59$ ]. Post hoc analysis found that participants in the INT group significantly decreased their stride time over the training period ( $p = 0.001, \Delta 3.9\%$ ) while the participants in the CON group showed no significant changes (fig. 1b). The main effect of group [ $F(1, 26) = 3.62, p > 0.05$ ] was not significant.

*Stride Length.* The analysis detected a significant main effect of test [ $F(1, 54) = 13.47, p < 0.001, \eta^2_p = 0.34, f = 0.72$ ] as well as a significant group  $\times$  test interaction [ $F(1, 54) = 9.15, p < 0.01, \eta^2_p = 0.26, f = 0.59$ ]. Post-hoc analysis found that participants in the INT group significantly increased their stride length over the training period ( $p = 0.001, \Delta 6.4\%$ ) while the participants in the CON group showed no significant changes (fig. 1c). The main effect of group [ $F(1, 26) = 0.86, p > 0.05$ ] was not significant.

*Stride-to-Stride Variability.* In terms of gait variability, the analysis failed to detect significant main effects of time, group and group  $\times$  test interactions for the CV of the stride velocity, time, and length parameters (table 2).

#### *Power Performance*

With regard to CMJ power, the analysis detected a significant main effect of time [ $F(1, 54) = 41.75, p < 0.001, \eta^2_p = 0.74, f = 1.69$ ]. The main effect of group [ $F(1, 26) = 4.32, p > 0.05$ ] and the interaction effect of group  $\times$  test [ $F(1, 54) = 3.11, p > 0.05$ ] were not significant (table 2).

## **Discussion**

To the authors' knowledge, this is the first study that has investigated the impact of salsa dancing on intrinsic fall-risk factors (i.e. deficits in postural control and muscle power of the leg extensors) in older adults. Eight weeks of progressive salsa dancing resulted in: (a) a tendency towards significant improvements in selected measures of static postural control; (b) a significantly enhanced gait pattern in terms of increases in stride velocity and length, and concomitant decreases in stride time, and (c) no significant changes in gait variability and muscle power of the leg extensors.

The present findings are in accordance with the literature regarding the effects of dancing on measures of balance function in older adults. Federici et al. [11] assessed the impact of Latin dance in a randomized controlled clinical trial on measures of balance in community-based inactive seniors. Study participants (age range 56–68

years) were randomized to either a dance or a control group for 3 months. While the dance group participated in 60-min Latin dance (e.g. Merengue, Bachata) classes twice a week, the control group did not engage in any physical activity. Before and after the intervention period, balance was assessed using 4 different clinical tests (the Tinetti, Romberg, improved Romberg and Sit-Up and Go tests). The findings indicated significant improvements in balance capability in the dance group. Conversely, the control group showed a slight but not statistically significant deterioration in balance function. Outcomes from a short 4-item psychosocial survey (smoking, alcohol consumption, sexual habits, sleep quality) developed by the study investigators also demonstrated improved subjective assessments of sleep quality and sexual activity among subjects in the dance group. Furthermore, 17 of the 20 dance group subjects reported moderate to great satisfaction with the dance activity. Based on their results, the authors concluded that Latin dance may improve balance and hence be a useful tool in reducing the risk of falling in older adults.

In another study, Shigematsu et al. [13] determined the effects of dance-based aerobic exercise on indices of falling in healthy community-dwelling women aged 72–87 years. The intervention group performed an aerobic dance exercise (side stepping, fast walking, forward/backward stepping, leg lifts, etc.) for 60 min, 3 days per week for a total of 12 weeks. Most of the activities were accompanied by music with changing tempo. The main outcome measures included balance tests (i.e. single leg balance with eyes opened/closed, functional reach), strength tests (i.e. hand grip strength, keeping a half squat position), locomotion/agility tests (i.e. walking time around 2 cones, 3-min walking distance), and motor processing tests (i.e. hand-reaction time, foot tapping). After the dance programme, the intervention group showed significantly greater single-leg balance with eyes closed, improved functional reach and decreased walking time. However, measures of strength were not significantly influenced by dancing. The lack of finding regarding the impact of dancing on leg extensor power in our study can most likely be explained by the high fitness/mobility level of our participants with average sports-related physical activities of 11.5 h/week and an average spontaneous stride velocity of 133.8 cm/s. In fact, Frey et al. [16] reported a mean physical activity level of 9.9 h/week including basic, leisure time and sports-related activities for seniors aged 70 years and older. In addition, Oberg et al. [28] examined habitual gait speed in subjects aged 10–79 years and found that women and men between the ages of 70 and 79 years

walked with an average speed of 115 cm/s. Thus, our participants' physical activity and fitness/mobility levels appear to be above the average values of older age-matched adults. Moreover, the training stimulus during salsa dancing might not have been specific enough to induce improvements in muscle power. It has frequently been reported that power training or high-velocity strength training have the potential to produce gains in muscle power in older adults [for a review see 29]. Thus, the principle of training specificity explains why we did not find improvements in leg extensor power in our study.

The present study revealed significant increases in stride velocity in the salsa dance group as compared to the control group. Given that the magnitude of age-related reduction in gait speed varies between 0.1 and 0.7% per year [28] and that decreases in gait speed are associated with an increased risk of falling [30] and functional decline [31], it is of great relevance that salsa dancing had the potential to increase gait speed in older adults. In fact, Hoxie and Rubenstein [31] reported that a walking speed of 122 cm/s is necessary to cross intersections safely, and observed that 96% of individuals aged 65 and over walk at a slower gait speed than this when crossing an intersection. Thus, the regular performance of salsa dancing may delay the onset of functional and mobility limitations and could help preserve the quality of life and independence of older adults.

This study did not detect significant effects of salsa dancing on spatiotemporal measures of gait variability in older adults. In contrast to our findings, Trombetti et al. [32] were able to examine significant decreases in stride length variability after 6 months of varied multi-task exercises, mostly performed to the rhythm of improvised piano music (i.e. Jaques-Dalcroze eurhythmics) in community-dwelling adults aged older than 65. In addition, the music-based exercise programme resulted in a reduced rate of falls and a lower risk of falling. Three methodological reasons can most likely explain the discrepancy in findings between our study and theirs. First, the duration of our salsa dance programme might not have been long enough to induce changes in measures of spatiotemporal gait variability. Thus, future studies should extend the intervention period beyond 8 weeks to find out whether additional adaptive processes in the gait pattern can be observed following salsa dancing. Second, in our subjects, spatiotemporal gait variability scores were already low at baseline (e.g. 1.7% stride time CV) indicating that the gait pattern was rather stable. In contrast, Trombetti et al. [32] reported a baseline stride time CV of 5.3%. Kressig et al. [33] were able to identify a critical threshold for stride time CV (>4%) that was strongly associated

with fall events in older inpatients. Based on these findings, it can be concluded that the gait pattern of our subjects was stable and risk of fall was low, whereas the gait pattern of the participants in the study by Trombetti et al. [32] was unstable and risk of fall was high. Third, with reference to the principle of training specificity, Jaques-Dalcroze eurhythmics may have the potential to improve gait variability due to the high demands of attention while moving to the melody and rhythm of improvised and quickly changing piano music. Salsa dance on the other hand lacks this improvised and unexpected music-imposed movement and pattern change, which might explain the missing effect on gait variability.

## Conclusions

This study proved that salsa dancing is a safe, feasible and highly enjoyable exercise programme for older adults. Salsa dancing seems to specifically be well suited for the promotion of static and particularly dynamic postural control, which makes it a useful intervention in reducing the risk of falling in older adults. However, if the goal is to induce improvements in spatiotemporal gait variability and muscle power, more specific training stimuli appear to be necessary. Recently, it has been reported that Jaques-Dalcroze eurhythmics has the potential to improve measures of gait variability and to reduce fall rate in older adults [32]. Furthermore, a recent systematic review on the effects of power training indicates that this training regimen enhances both muscle power and functional performance in older adults [29]. Taken together, these findings suggest that dance programmes should include improvising movement elements to the rhythm of music and power-specific exercise elements in order to effectively promote various components of postural control and force production. However, this hypothesis needs to be verified in future studies.

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**Publication (e)**

**Association between Serum Vitamin D Status and Functional Mobility in  
Memory Clinic Patients Age 65 and Older**

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## TITLE PAGE

### FULL TITLE

Association between Serum Vitamin D Status and Functional Mobility in Memory Clinic Patients Age 65 and Older

### ABBREVIATED TITLE

Vitamin D and functional mobility

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## ABSTRACT

### OBJECTIVES

To test whether serum 25-hydroxyvitamin D [25(OH)D] status is associated with functional mobility in seniors assessed in a memory clinic.

### DESIGN

Cross-sectional.

### SETTING

Outpatient memory clinic at a Geriatric University Hospital.

### PARTICIPANTS

Four hundred four memory clinic patients ( $\geq 65$  years) assessed in an ambulatory setting.

### MEASUREMENTS

Functional mobility was assessed with three endpoints: normal and fast walking speed and the Timed Up and Go (TUG) test by quartile of serum 25(OH)D concentrations. Multivariate analyses were performed adjusting for gender, age, and body mass index, history of falls, cognitive function (Mini-Mental State Examination, MMSE), and prescription drugs. Pre-planned subgroup analysis in less frail seniors (no previous fall and MMSE  $< 26$ ).

### RESULTS

Among 404 seniors, mean 25(OH)D serum levels were 63.2 nmol/L (SD 33.9), and 41.3% were vitamin D deficient ( $< 50$  nmol/L). Seniors in the lowest 25(OH)D quartile ( $< 39$  nmol/L) had significantly worse functional mobility compared with seniors in the highest 25(OH)D quartile ( $> 81$  nmol/L): adjusted for all covariates, seniors in the highest quartile performed 9.4% better in normal ( $P = .02$ ) and 9.2% better in fast ( $P = .004$ ) walking speed, and 4.4% better in the TUG test ( $P = .24$ ). The association between 25(OH)D status and functional mobility was most pronounced in less frail seniors ( $P$  for trend

significant for all three mobility tests). Overall seniors with higher 25(OH)D status also had better cognitive function (MMSE score;  $P=.006$ ).

#### CONCLUSION

Among seniors assessed in a memory clinic, higher serum 25(OH)D status correlated positively with better functional mobility and better cognitive function. Given, the large number of seniors with vitamin D deficiency, 25(OH)D assessment may be warranted in this population at risk for both functional and cognitive decline.

#### KEY WORDS

Vitamin D, physical function, gait velocity, fall prevention, older adults

**MANUSCRIPT**

## INTRODUCTION

Traditionally, vitamin D has been linked to bone health and vitamin D supplementation is supported as an evidence-based strategy in fracture risk reduction among adults age 65 and older. In a most recent pooled analysis of source data of 11 double blind RCTs including 31,022 seniors, vitamin D supplementation at an actual median intake of 800 IU per day (range: 792 to 2,000 IU per day) reduced hip fracture risk by 30%.<sup>1</sup> Mechanistically, this benefit may be explained by the well-established positive effect of vitamin D on calcium absorption. Alternatively, several lines of evidence support a direct effect of vitamin D on muscle,<sup>2,3</sup> and several meta-analyses on trials of vitamin D supplementation support vitamin D as an effective strategy in fall prevention, as reflected in the American and British Geriatric Society Guidelines.<sup>4-6</sup>

At the same time the prevalence of vitamin D deficiency is reported to be 50% or more among large parts of the senior population worldwide.<sup>7</sup> Serum 25-hydroxyvitamin D [25(OH)D] represents the best clinical measure of systemic vitamin D status.<sup>8</sup> Seniors are at increased risk of vitamin D deficiency due to less time spent outside, use of sun protection, and institutionalization.<sup>7</sup> Further, with age the skin capacity to produce vitamin D from UVB-exposure is reduced by a factor of 4.<sup>9</sup>

In this large survey of seniors admitted to a memory clinic, we examined the association between vitamin D status and functional mobility. Further, we explored if this association differs between less frail and pre-frail seniors. Seniors who present at a memory clinic may be a target group for 25(OH)D assessment as they are at risk of further cognitive and functional decline. In the general senior population vitamin D deficiency has been associated with risk of nursing home admission,<sup>10</sup> reduced muscle strength and functional mobility,<sup>11</sup> increased risk of falls and fractures,<sup>12</sup> and higher risk of cognitive decline.<sup>13</sup>

## METHODS

### *Study Population*

In this survey, we include 404 consecutive memory clinic patients assessed in an ambulatory setting, age 65 and older from September 2008 to April 2011. This study was approved by the local ethics committee (Canton Basel).

The examination battery applied at the Memory Clinic of the Geriatric University Hospital Basel includes the Mini-Mental State Examination (MMSE, maximum score is 30 points, diagnostic range 0-10 = severe cognitive impairment, 11-20 = moderate cognitive impairment, 21-26 = mild cognitive impairment, 27-30 = normal cognitive function) as a measure of global cognitive function,<sup>16</sup> and a functional mobility assessment (measurements of Timed Up and Go (TUG) and gait analysis) at the Basel Mobility Center. Further, physical exam is performed by a physician including the record of height and weight, the medical history and the number of prescription drugs taken (self-report, report from care-givers and/or documented medical history). We used the latter as a surrogate for comorbidity. In addition, the physician explores the history of falls in the previous 12 months, including observations by accompanying caregivers. A fall is defined according to the Prevention of Falls Network Europe (ProFaNE) as 'an unexpected event in which the participant comes to a rest on the ground, floor, or lower level'.<sup>17</sup> Further, blood is drawn by nurses at the Memory Clinic for the assessment of 25(OH)D status and other relevant biomarkers.

We defined less frail and pre-frail individuals based on their cognitive performance in the MMSE and previous fall history (in the last 12 months). Less frail seniors had no previous fall and an MMSE score of  $\geq 26$ . Pre-frail seniors either had previous fall and MMSE  $\geq 26$  or had no previous fall and an MMSE  $< 26$ .

### *Functional Mobility Assessment*

For functional mobility 3 tests are evaluated: normal and fast walking speed, and the TUG test. Patients wore their normal clothes, their own shoes, and a safety belt. The test administrator walked beside and slightly behind the patient to provide assistance and grab the safety belt if balance loss occurred while walking.

### *Normal and Fast Walking Speed*

Patients were verbally instructed regarding the gait analysis testing procedure: first to walk at their usual speed (self-selected pace) and then as fast as possible (fast walking, but not running). No practice walks were performed before testing. Each walk was performed once.

### *Timed Up and Go Test*

The TUG assesses basic mobility in seniors and was conducted at the Basel Mobility Center prior to the walking speed assessments.<sup>18</sup> When performing the TUG, the time in seconds that it takes an individual to rise from an armchair with armrests, walk 3 m at their regular walking speed, turn, walk back and sit down again is measured using a stopwatch. A score of 14 sec or higher is associated with an increased fall risk.<sup>19</sup>

### *Serum 25-Hydroxyvitamin D Assay*

Blood samples for the determination of 25(OH)D concentrations were obtained by a nurse from the Memory Clinic and analyzed at the Laboratory of Immunology at the University Hospital Basel. An automated enzyme immune assay analyzer named DSX (Dynerx Technologies, Chantilly, VA) was used for 25(OH)D quantification in human serum. Samples were diluted with biotin labeled 25(OH)D and incubated in microtiter wells. Enzyme labeled avidin was added and bound selectively to complexed biotin followed by developing color using a chromogenic substrate. The absorbance of the stopped reaction mixtures were read in a microtiter plate reader, color intensity developed being inversely proportional to the concentration of 25(OH)D. The intra assay and inter assay coefficients of variation for 25(OH)D were 5.3% and 4.6%, respectively.

### *Statistical Analyses*

The baseline characteristics of the 404 memory clinic patients were summarized using means and standard deviations or frequencies and percentages, as appropriate (in all, in less frail (no previous fall and MMSE  $\geq 26$ ) and pre-frail (previous fall and MMSE  $\geq 26$ /no previous fall and an MMSE  $< 26$ ) seniors and by quartile of 25(OH)D status). Serum 25(OH)D levels were assessed as quartiles ( $< 39$ , 39 to 54, 55 to 81,  $> 81$  nmol/L). General linear models (GLM) were performed to evaluate differences in walking speed (normal and fast) and TUG by 25(OH)D quartile for all, less frail and pre-frail seniors



adjusted for age, gender, body mass index (BMI), MMSE, number of prescription drugs, and previous falls (yes/no). Analyses were conducted with SAS version 9.2 (SAS Institute, Cary, N.C.) software. All P values are two-sided.

## RESULTS

A total of 404 memory clinic patients (mean age 77.6, standard deviation (SD) 5.8, 53.5% female) were included in this survey. **Table 1** describes the study population for important covariates by the less frail and pre-frail status, and by quartile of 25(OH)D status. The overall mean MMSE score was 24.5 (SD 4.1) points (range 5 to 30 points). 34.4% (n = 139) of seniors took more than 3 prescription drugs, 28.2% (n = 114) between 3 and 5, and 37.4% (n = 151) none.

### *25(OH)D Status*

Mean 25(OH)D status was 63.2 (SD 33.9); 4.7% (n = 19) had serum levels below 25 nmol/L (severe deficiency), 41.3% (n = 134) had levels below 50 nmol/L (deficiency), and 69.8 % (n = 282) had levels below 75 nmol/L (threshold for optimal fall and fracture reduction).<sup>20</sup> Seniors with higher 25(OH)D status had a significantly higher MMSE score (P = .006).

### *Association Between 25(OH)D Status and Functional Mobility in all Seniors*

At the univariate level, seniors in the lowest 25(OH)D quartile (<39 nmol/L) had significantly worse functional mobility performance for all 3 functional mobility measures (normal and fast walking speed, and TUG) if compared to the highest 25(OH)D quartile (>81 nmol/L). Notably, there was a pattern that suggested all seniors in 25(OH)D quartile levels greater than 39 nmol/L had an equally better function than those in the lowest quartile. This pattern was maintained for all functional mobility measures also in the multivariate analyses after adjustment for age, gender, BMI, MMSE, prescription drugs, and falls (**Figure 1A, 1B, 1C**).

### *Association Between 25(OH)D Status and Functional Mobility in Less Frail and Pre-frail Seniors*

Compared to pre-frail seniors less frail seniors (no previous fall and MMSE  $\geq$ 26) showed a more pronounced association between all 3 functional mobility measures and 25(OH)D quartile level. Notably, in the subgroup of less frail seniors the pattern of association changed from a threshold of 39 nmol/L as observed on the total study population to a trend between better performance with higher 25(OH)D status. In less frail seniors this trend was significant for normal and fast walking speed and TUG performance (**Figure 2A, 2B, 2C**).

## DISCUSSION

In this large survey of 404 consecutive ambulatory memory clinic patients age 65 and older low serum 25(OH)D status was not only associated with a lower MMSE score, but also with decreased functional mobility. Including both less frail and pre-frail seniors as defined by their cognitive status and prior fall status, a 25(OH)D threshold of 39 nmol/L (upper end of the lowest quartile) was suggested for better functional mobility. However, in the subgroup of less frail seniors (n = 124), there was a significant trend of better functional mobility (normal and fast walking speed, and TUG) with higher 25(OH)D quartile status, with a desirable threshold of >81 nmol/L for optimal functional mobility.

Vitamin D has been linked to cognitive performance in seniors.<sup>21</sup> In a retrospective study of older patients assessed in a memory clinic, 25(OH)D status was positively correlated with the MMSE.<sup>22</sup> Another recent study evaluated the effects of vitamin D supplementation on cognition in seniors referred to a memory clinic and reported an 25(OH)D-associated improvement in MMSE score.<sup>23</sup> Our study confirms these findings documenting a significant association between higher 25(OH)D level and better cognitive performance assessed with the MMSE in seniors examined at a memory clinic.

Several previous studies,<sup>24</sup> including EPIDOS (Epidémiologie de l'Ostéoporose),<sup>15</sup> the Cardiovascular Health All Stars study,<sup>11</sup> and the population-based NHANES III study<sup>2</sup> support an inverse association between higher 25(OH)D status and faster walking speed among community-dwelling seniors. The benefit of vitamin D supplementation (800 to 1,000 IU) on TUG performance was recently confirmed in a recent meta-analysis among seniors age 60 years and older.<sup>14</sup> Our study extends to seniors assessed in a memory clinic supporting at the cross-sectional level a positive association between higher 25(OH)D status and functional mobility, including TUG and gait performance.

In the present study, 41.3% of individuals were vitamin D deficient and 69.8% did not reach the desirable threshold of 75 nmol/L for fall and fracture prevention.<sup>20</sup> These data are consistent with international reports where about 50% of ambulatory seniors are expected to have vitamin D deficiency,<sup>7</sup> and about 70% fall below a threshold of 75 nmol/L.<sup>1,2</sup>

As a surprise to the authors, less frail seniors (no previous fall and MMSE  $\geq 26$ ) expressed a more linear association between 25(OH)D quartile status and gait and functional mobility with a desirable 25(OH)D threshold of  $>81$  nmol/L for optimal performance. Comparing extreme quartiles in less frail seniors, the threshold of  $>81$  nmol/L was associated with an about 11% better performance in gait (normal and fast) and TUG compared to the lowest 25(OH)D quartile ( $<39$  nmol/L). Our expectation was that pre-frail seniors may be more susceptible to 25(OH)D status. However, including these seniors, only the lowest quartile was associated with worse functional mobility compared to the other quartiles suggesting a lower threshold of 39 nmol/L. This may be explained by an added level of impairment by a previous fall or reduced cognitive function, which may camouflage a positive association between 25(OH)D status and functional mobility.

Our study has several strengths. We measured 25(OH)D status, gait, and the TUG in a standardized way in a large consecutive sample of memory clinic patients. The consistency across the 3 tests applied lends credibility to our findings as does the observed pattern of association in all participants and most pronounced in less frail participants. Notably, our findings adjust for key covariates, including age, gender, BMI, cognitive function, number of prescription drugs, and previous fall (yes/no). A further strength of our study is its population, which extends previous findings to individuals at risk of cognitive and functional decline assessed at a memory clinic setting. Our study also has several limitations. A key limitation is its cross-sectional design where interpretation is limited to associations rather than causality. Although we were able to adjust for important confounders, we may have missed others, such as physical activity. However, physical activity is likely to be on the causal pathway between 25(OH)D and gait performance, which would have disqualified its inclusion in our analyses. Notably, exposure to sunlight, seasonal variations, dietary and supplement intake of vitamin D are reflected in the 25(OH)D status.

In summary and according to our findings a higher 25(OH)D status may contribute to better normal and fast walking speed, as well as quicker TUG performance in seniors referred to a memory clinic. Notably, this positive association may be most pronounced in less frail seniors and a desirable threshold for optimal function in this subgroup may be greater than 81 nmol/L. For the whole population assessed, including also pre-frail seniors, it seemed important to avoid a 25(OH)D status

below 39 nmol/L for functional mobility. Our data support measurement of 25(OH)D status in memory clinic patients, also for the observed positive association between higher 25(OH)D status and better cognitive performance.

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**Conflict of Interest:** None of the authors have conflicts of interest to declare.

**Author Contributions:** YJG: Test administrator for some of the TUG tests and gait analyses, literature search, analysis and interpretation of the data, and writing the manuscript. HBF: Contribution to the study plan, design analysis plan, statistical analyses and interpretation of results and critical revision of all drafts and the final manuscript. SAB: Conceptualization of the manuscript idea, test administrator for some of the TUG tests and gait analyses, and critical revision of the manuscript. IH: Test administrator for some of the TUG tests and gait analyses, critical revision of the manuscript. RWK: Conceptualization of the manuscript idea, interpretation of the data, and critical revision of the manuscript.

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FIGURES

Figure 1A.

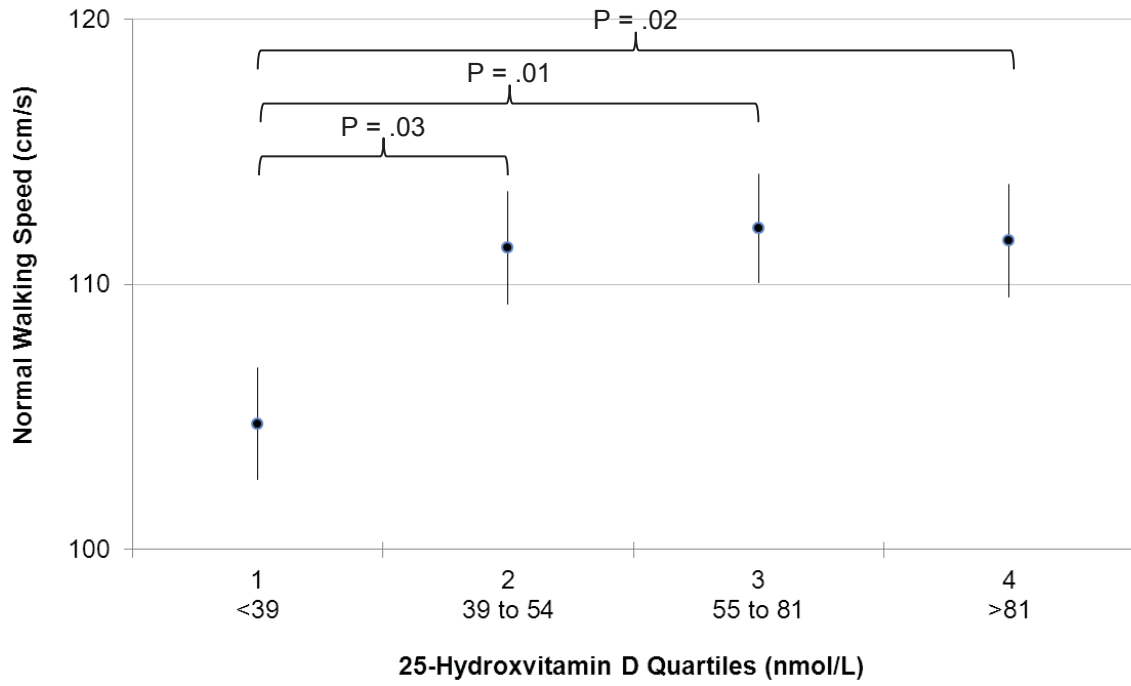


Figure 1B.

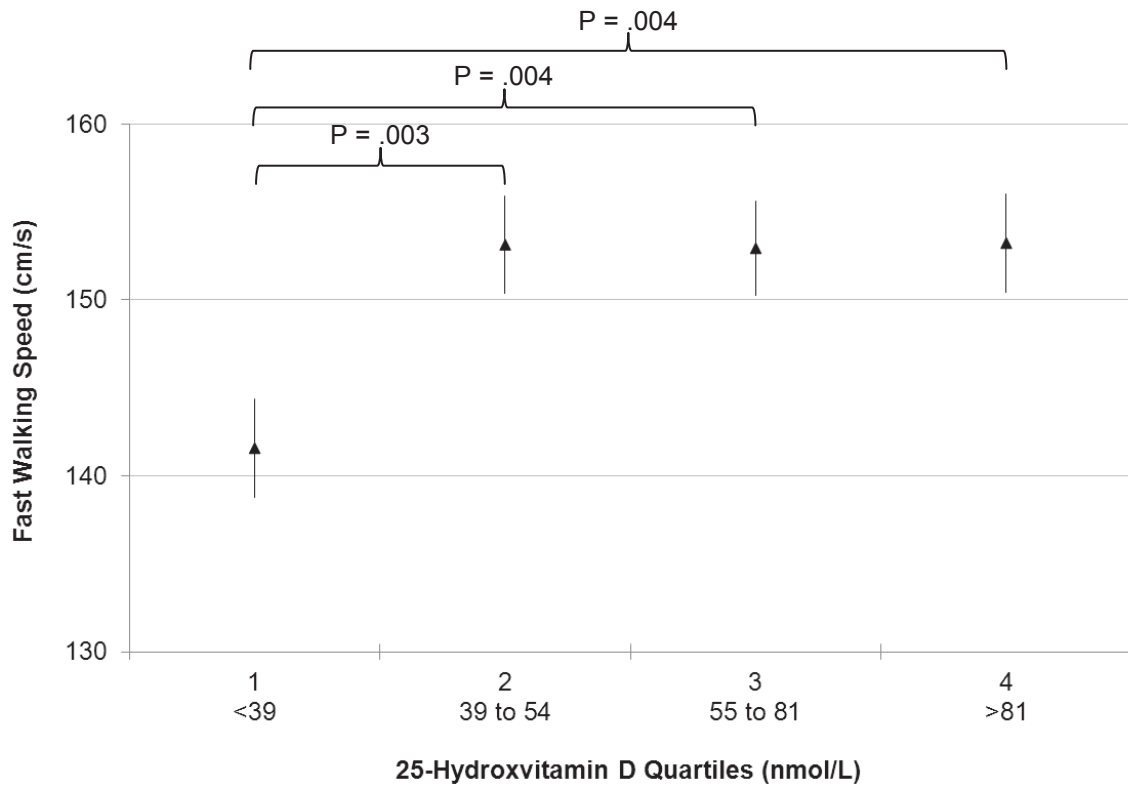
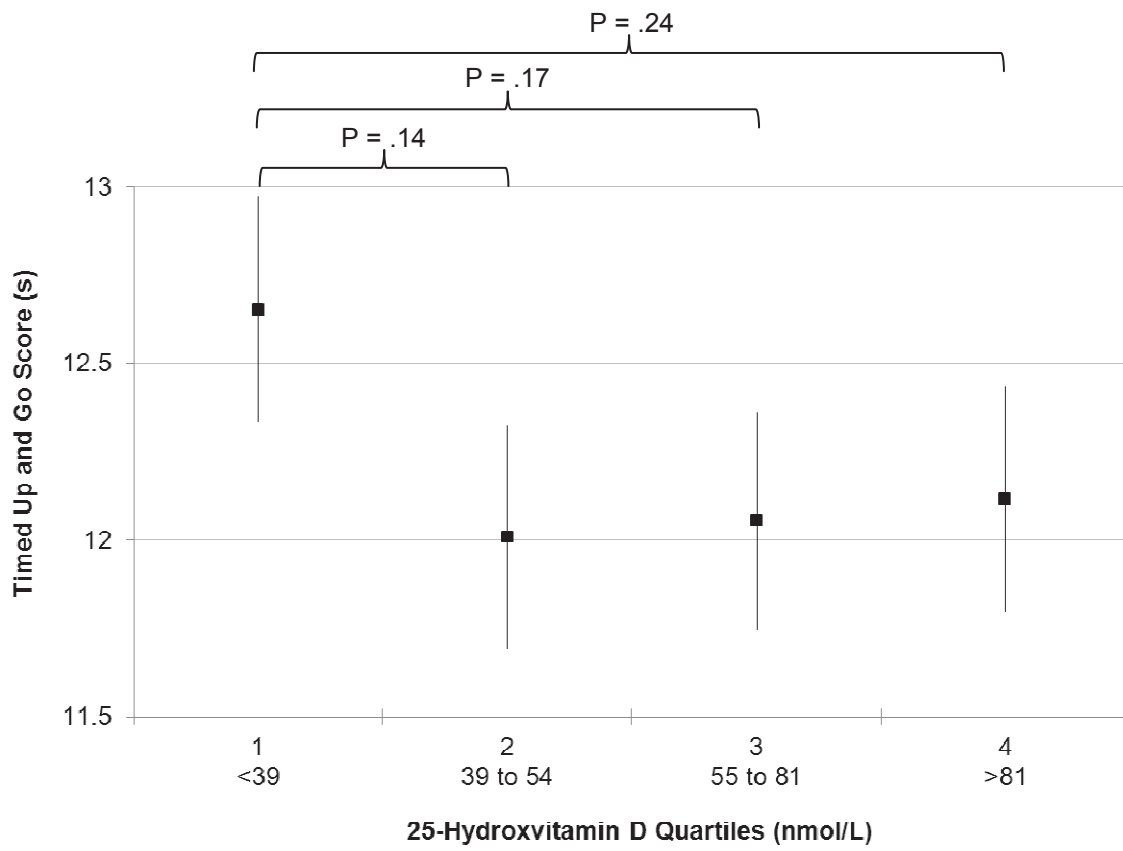


Figure 1C.



**Figure 1 A, B, C show functional performance by quartile of 25-hydroxyvitamin D [25(OH)D] status in all 404 seniors.**

Figure 1 A shows normal walking speed (dot), Figure 1 B shows fast walking speed (triangle), and Figure 1 C shows Timed Up and Go performance (square) for all seniors by 25(OH)D quartile. We show least square means and the standard error around the least square means, adjusted for age, gender, body mass index, Mini-Mental State Examination score, number of prescription drugs, and fall history in the last 12 months (yes/no). For all 3 tests individuals in the lowest quartile of 25(OH)D status (<39 nmol/L) performed worse.

Figure 2A.

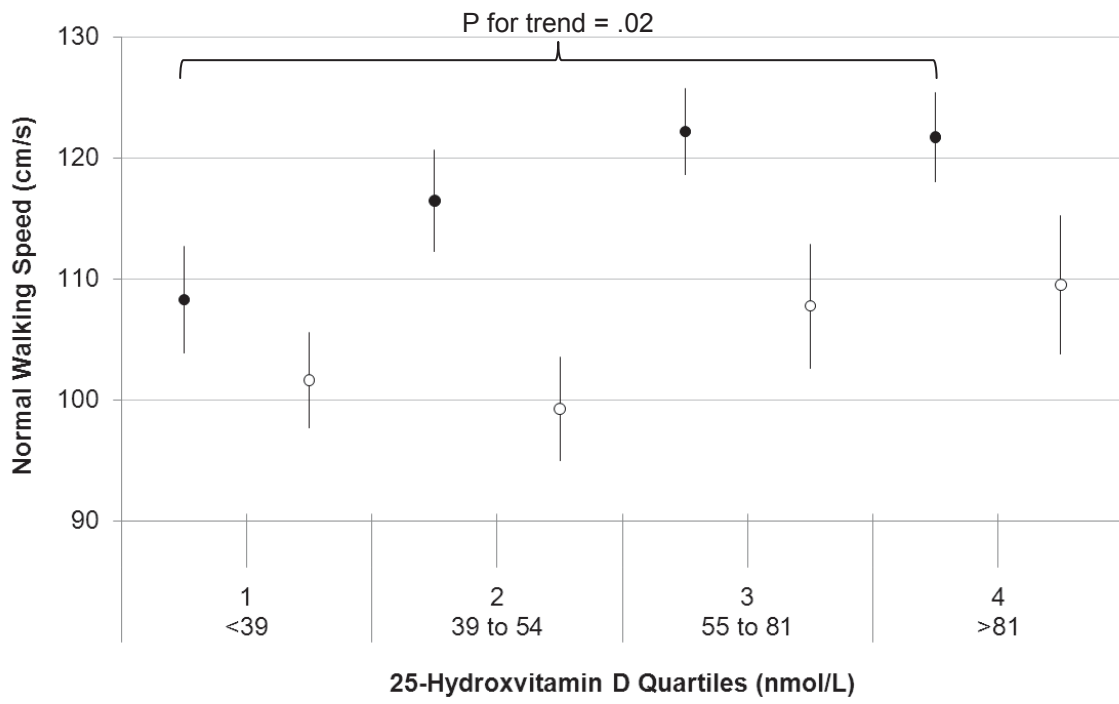


Figure 2B.

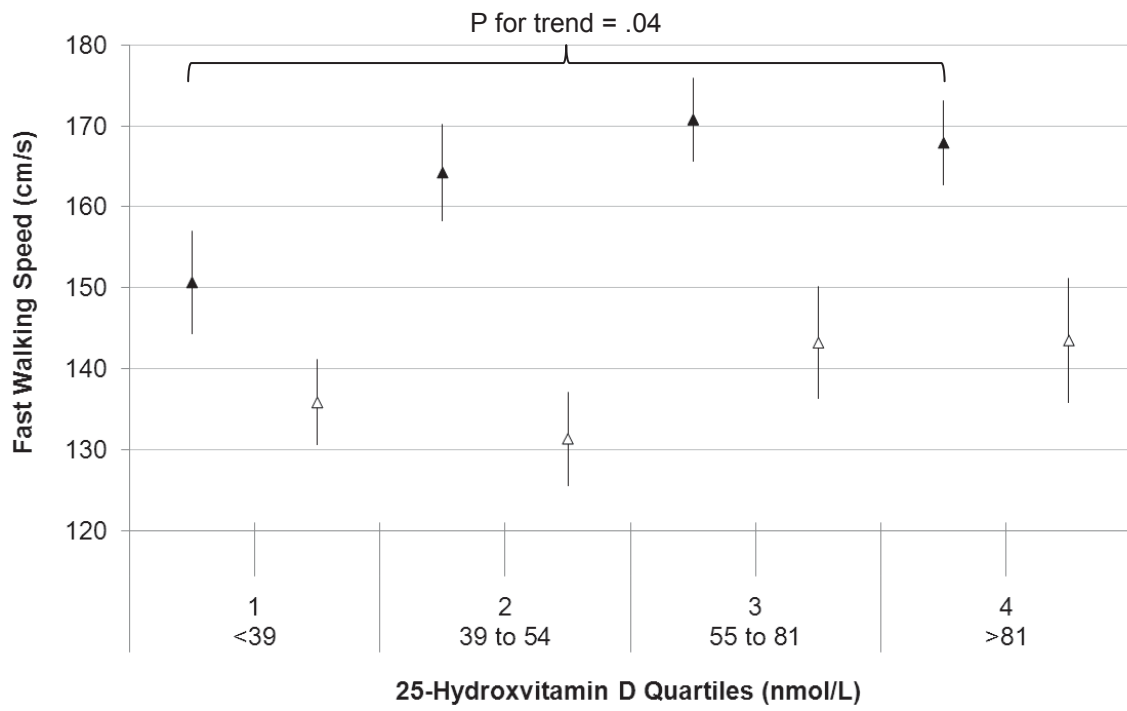
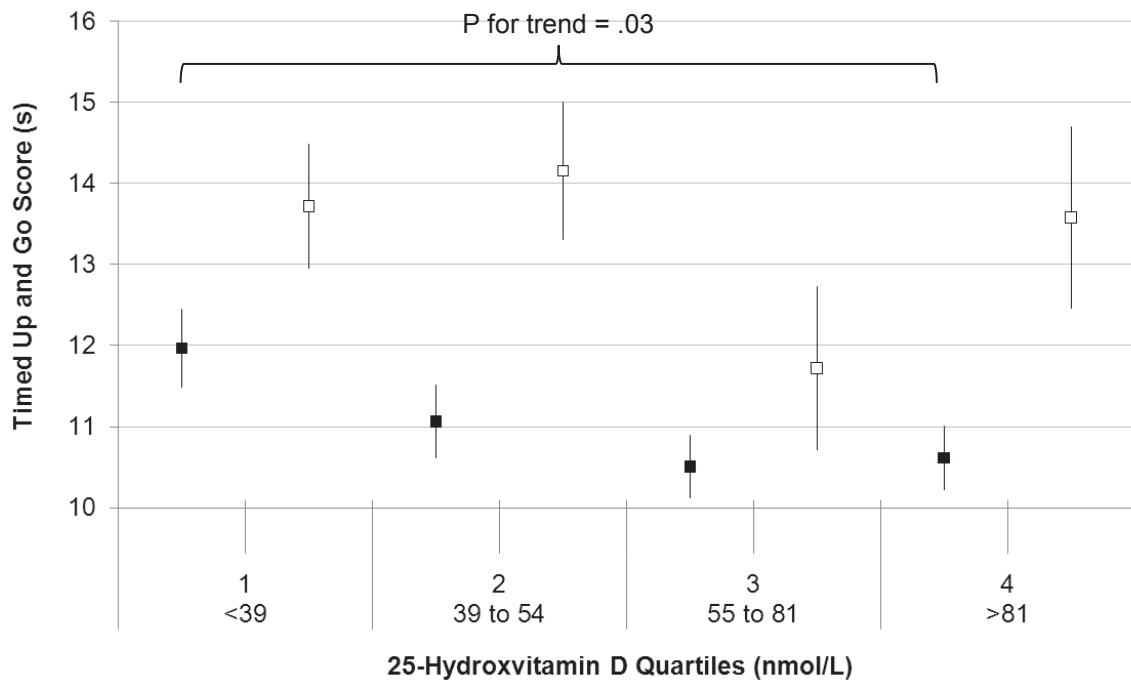


Figure 2C.





**Figure 2 A, B, C show functional performance by quartile of 25-hydroxyvitamin D [25(OH)D] status in less frail (n = 322) and pre-frail seniors (n = 82).**

Figure 2 A shows normal walking speed (dot), Figure 2 B shows fast walking speed (triangle), and Figure 2 C shows Timed Up and Go (TUG) performance (square) for less frail (filled marker) and pre-frail (open marker) by 25(OH)D quartile. We show least square means and the standard error around the least square means, adjusted for age, gender, body mass index, Mini-Mental State Examination score, number of prescription drugs, and fall history in the last 12 months (yes/no). Among less frail seniors, there was a significant trend between quartiles of 25(OH)D status and functional mobility for all 3 tests of functional performance among less frail seniors with a desirable threshold of >81 nmol/L for optimal gait and TUG performance. Such a trend could not be documented in pre-frail seniors. In pre-frail seniors, individuals in the lowest quartile had worse gait at a normal and fast pace compared to individuals in higher quartiles. For TUG performance, we could not document a significant association with 25(OH)D among pre-frail seniors.

TABLES

**Table 1.** Characteristics of Memory Clinic Patients Age 65 and Older by Less Frail and Pre-frail Status, and by Quartile of 25(OH)D Status

Characteristics	Serum 25(OH)D Level Quartile, nmol/L							P-Value <sup>†</sup>
	All n = 404	Less frail n = 322	Pre-frail n = 82	<39 n = 101	39 – 54 n = 97	55 – 81 n = 105	>81 n = 101	
mean ± SD								
Serum 25(OH)D, nmol/L	63.2 ± 33.9	65.3 ± 34.4	55.1 ± 30.8	29.8 ± 6.1	46.2 ± 4.9	66.2 ± 7.4	109.9 ± 30.1	<.001
Age	77.6 ± 5.8	77.1 ± 5.8	79.1 ± 5.4	78.9 ± 5.6	78.0 ± 5.8	76.2 ± 5.8	77.2 ± 5.5	.005
BMI, kg/m <sup>2</sup>	25.2 ± 4.9	25.4 ± 4.0	24.1 ± 3.3	25.7 ± 4.2	25.2 ± 4.0	25.7 ± 3.9	24.0 ± 3.3	.004
MMSE, score	24.5 ± 4.1	25.4 ± 3.6	20.8 ± 4.2	23.4 ± 4.4	24.4 ± 4.2	24.6 ± 4.0	25.4 ± 3.8	.006
TUG, time	12.1 ± 3.3	11.8 ± 3.0	13.3 ± 4.0	12.9 ± 3.2	12.0 ± 3.3	11.8 ± 3.2	11.8 ± 3.2	.06
Normal walking speed, cm/s	110.0 ± 22.7	117.7 ± 22.9	103.2 ± 20.8	102.3 ± 21.6	110.8 ± 23.4	113.5 ± 22.0	113.3 ± 22.2	<.001
Fast walking speed, cm/s	150.3 ± 31.6	153.9 ± 31.1	136.1 ± 30.0	137.3 ± 27.8	151.9 ± 32.9	155.3 ± 31.5	156.6 ± 30.6	<.001

\* Differences between groups were assessed using Student's t-test.

† Differences between 25(OH)D quartiles were assessed using analysis of variance.

BMI = Body Mass Index; MMSE = Mini-Mental State Examination; TUG = Timed Up and Go; 25(OH)D = 25-Hydroxyvitamin D.

**Publication (f)**

**The Effect of Three Different Types of Walking Aids on Spatio-Temporal Gait Parameters in Community-Dwelling Older Adults**

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Aging Clinical and Experimental Research, in review

## **Title**

The effect of three different types of walking aids on spatio-temporal gait parameters in community-dwelling older adults

## **Running head**

Effect of walking aids on gait in older adults

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## **Key words**

Mobility aids, gait, older adults, community-living

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## Abstract

**Background and aims:** Gait and balance impairments lead to falls and injuries in older people. Walking aids are meant to increase gait safety and prevent falls, yet little is known about how their use alters gait parameters. This study aimed to quantify gait in older adults during walking without and with different walking aids and to compare gait parameters to matched controls.

**Methods:** This retrospective study included 65 older ( $\geq 60$  years) community-dwellers who used a cane, crutch or walker and 195 independently mobile matched controls. Spatio-temporal gait parameters were measured with a GAITRite electronic walkway system during normal walking.

**Results:** When walking unaided, walking aid users had significantly worse gait than matched controls. Gait performances significantly improved when assessed with vs. without the walking aid for the cane (increased stride time and length, decreased cadence, stride length variability and double support), crutch (increased stride time and length, decreased cadence, stride time variability, stride length variability and double support) and walker (increased gait speed and stride length, decreased stride time, stride time variability, stride length variability, base of support and double support) users.

**Conclusion:** Gait in older adults who use a walking aid is more irregular and unstable than gait in independently ambulating older adults. Walking aid users have better gait when using their walking aid than when walking without it. The changes in gait were different for the different types of walking aids used. These study results may help better understand gait in older adults and differentiate between pathological gait changes and compensatory gait changes due to the use of a walking aid.

## Introduction

The ability to walk is one of the most relevant and important activities of daily living. It is central to the independence, health and well-being of older people. However, walking may be impaired by many factors such as acute or chronic diseases and physiological changes due to aging (1; 2). Impaired gait can negatively affect an individual's functionality, participation in social activities and quality of life (3). Gait disorders in older people are a risk factor for falling (4). Approximately one third of individuals over the age of 65 years sustain at least one fall over a one-year period (5; 6) and this increases to nearly half in adults over the age of 80 years (6). Falls represent an increasing public health problem with physical, psychological and social consequences.

Walking aids, such as a cane, crutch or walker, are frequently used by older people to cope with daily activities and to remain functionally independent and mobile (7; 8). These aids can maintain walking ability and improve balance by increasing the base of support, enhancing lateral stability and reducing lower-limb loading (7). In addition to benefits for ambulation, walking aids can have positive psychological effects, such as increased feelings of safety and confidence, resulting in improvements in physical activity levels and independence (9–11).

The association between walking aid use and risk of falls is less clear. The study by Rubenstein and Josephson (12) showed that the use of a walking aid was associated with a 2.6-fold (confidence interval: 1.2; 4.6) increased risk of falling. This may be due to improper use of the aid, tripping over the aid or the aid's impediment of compensatory stepping and grasping mechanisms during balance recovery to avoid a fall (13; 14). However, the increased fall risk associated with the use of a walking aid as reported by Rubenstein and Josephson (12) likely reflects the decreased functional status and mobility of the older people using the walking aids (those with gait disturbances, muscle weakness and increased fall risk are the ones most likely to use a walking aid) rather than due to the walking aid itself. When walking aids are appropriately chosen for clinical conditions (e.g., a standard walker instead of a front-wheeled walker for people with Parkinsonian gait disturbances), correctly sized (not too high or too low) and properly implemented, they can increase walking safety and thus may reduce the risk of falling.

Although walking aids are often used by those with gait impairments, little is known about the effects of different walking aids on gait parameters. Measurements of temporal and spatial gait parameters are used to identify gait deficits and to screen older people for their risk of falling (15). Impaired gait is characterized by reduced walking speed, shorter stride length and increased gait variability (16; 17).

Small changes in gait variability (stride length variability, stride time variability) have been identified as reliable fall predictors in older adults (17–20). Furthermore, increased base of support is also predictive of falls (19). Understanding how gait is influenced by different walking aids may help to distinguish between pathological gait alterations and healthy, compensatory reactions to the use of a walking aid. Although some normative gait data from a selected group of very healthy older adults has been previously described (21), data from population studies is needed to know what “normal” gait is in a representative population of older adults, including those who use walking aids.

The first objective of this study was to investigate whether people over the age of 60 who use a single-tip cane, a fore-arm crutch or a four-wheeled walker have differences in spatio-temporal gait parameters while walking normally (self-selected pace) with versus without their usual walking aid. The second objective was to compare these gait parameters to an independently mobile matched control group. We hypothesized that walking aid users would walk faster, would have a smaller base of support and a decreased stride time variability with their walking aid compared to walking without their walking aid. We also hypothesized that all gait parameters would be more variable in the group of walking aid users when compared to a matched control group.

## **Methods**

### **Study design and population**

In this retrospective, cross-sectional study, data was collected between January 2007 and October 2011 from patients at the Basel Mobility Center, University Hospital of Basel, Switzerland. The study was approved by the local ethics committee.

The data used for this study was extracted from an existing database. Inclusion criteria were as follows: (I) Age older than 60 years, (II) community-dwelling, (III) use of a walking aid during ambulation outdoors (those who used a walking aid only indoors were excluded, those who used a walking aid indoors and outdoors or only outdoors were included) for at least one month prior to their gait analysis, (IV) use of a single-tip cane, fore-arm crutch or four-wheeled walker, (V) available data for gait analysis with and without walking aid, and (VI) Mini Mental State Examination (MMSE) score available. Exclusion criteria were as follows: (I) Use of several different walking aids (e.g. cane for shorter distances and walker for longer distances), (II) use of a cane or crutch on both sides (because these subgroups of walking aid users were too small in this study to permit meaningful analysis), (III) improper use of the walking aid (moving cane/crutch with the ipsilateral rather than the contralateral

leg; holding the cane or crutch in air while taking multiple steps), (IV) severe neurological (normal pressure hydrocephalus, stroke with residual hemiplegia, Parkinson syndromes), orthopedic (severe osteoarthritis of the hips or knees, amputations with or without a prosthesis), or psychiatric illness (major depression, schizophrenia) causing inability to understand or follow task instructions or to walk 15 meters without assistance, (V) terminal illness with life expectancy less than 12 months.

Of the sample of 366 walking aid users, 65 fulfilled the eligibility criteria and were classified into one of three groups according to type of walking aid used: A single-tip cane (hereafter referred to only as cane), a forearm crutch (hereafter referred to only as crutch) or a four-wheeled walker (hereafter referred to only as walker). All walking aids were the personal property of the patients. No alternative walking aids were given and no setting adjustments of the aids were done at the Basel Mobility Center.

The patients with walking aids were matched to controls from the same database according to gender, age and MMSE.

### **Gait assessment**

The spatio-temporal parameters of gait were collected with the GAITRite<sup>®</sup> system (GAITRite<sup>®</sup> Platinum, CIR System, Sparta, NJ, USA), a 10-meter-long electronic walkway with integrated pressure sensors (22). The walking trials were performed according to the European guidelines for spatial-temporal gait analysis (23). The standard gait analysis at the Basel Mobility Center consists of five different walking tasks, whereas walking at self-selected normal walking speed (referred to as normal walking in this text) represents the first task. Normal walking with the aid (for those who had them) was performed as an additional sixth task. Details regarding the description of the gait analysis at the Basel Mobility Center have been reported elsewhere (15). Before testing, a trained evaluator gave standardized verbal instructions regarding the test procedure. In order to measure steady-state gait, the patients initiated and terminated each walk 1.25 m before and after the 10 m walkway allowing sufficient distance to accelerate and decelerate. Each subject performed one trial for each of the testing conditions. No practice trials were performed. To ensure safety, a belt was placed around each patient's waist for easy grasp by the trained evaluator who walked behind the patients during all trials. The patients performed all trials wearing their own footwear and used their own walking aid for the walking aid condition. A video camera was used during the gait analysis to allow detailed review.



Primary outcome measures were the following nine spatio-temporal gait measures: Gait speed (cm/s), cadence (number of steps per minute), stride time (s), stride time variability (%), stride length (cm), stride length variability (%), base of support (cm), base of support variability (%) and double support (percentage of gait cycle). Variability variables were quantified as the coefficients of variation ( $CV = (\text{standard deviation} / \text{mean}) \times 100$ ).

### **Clinical evaluation and assessments**

Clinical assessment including a physical examination was performed by a physician or a trained research assistant. The following data was used for the present study: age, sex, height, weight, falls (defined as unintentionally coming to rest on the ground or other surface (24)) in the preceding 12 months (single-item question), fear of falling (single-item question), and relevant medical problems. Cognitive status was evaluated by the score of the Mini Mental State Examination (25), whereby cognitive impairment was defined as a score less than 24 out of a maximum 30 points. Basic mobility was assessed with the Timed Up & Go Test (TUG) (26). The TUG measures the time in seconds that it takes an individual to rise from a chair with armrests, walk 3 m, turn, walk back and sit down again. Older adults who require 14 seconds or longer to complete the task have a high risk for falls (27).

### **Statistical analysis**

Characteristics of baseline assessment and gait parameters were summarized descriptively using either means and standard deviations or frequencies and percentages, as appropriate. Analyses were performed between the walking aid group and the matched control group and between the subgroups according to the type of walking aid (cane, crutch, walker). Test for normality (Shapiro-Wilk test) and homogeneity of variance (Levene's test) were performed for all outcomes. For continuous variables, comparisons between the walking aid group and the matched control group were performed using the t-test and between subgroups using the one way analysis of variance (ANOVA) when normally distributed, or the Mann-Whitney U test and the Kruskal-Wallis test when not. Post hoc tests were completed when a statistically significant value resulted to determine where the difference occurred. Gabriel's procedure was applied in normally distributed gait parameters; Mann-Whitney test was applied in not normally distributed gait parameters, in this case level of significance was set at  $p < 0.017$ . The chi-square test or Fisher's exact test was used for nominal variables. Evaluation of the difference between the normal condition and the walking aid condition within the three subgroups was

completed by the paired t-test or the Wilcoxon test. Probability values less than 0.05 were considered statistically significant. Analyses were conducted using the SPSS version 19.0 (SPSS, Inc., Chicago, IL) software program for Windows.

## Results

### Study population

Of the 65 walking aid users included in this study, 40 used a cane (average age  $82.4 \pm 5.7$ , 25 females), 13 used a crutch (average age  $79.4 \pm 6.3$ , 9 females) and 12 used a walker (average age  $84.3 \pm 3.9$ , 8 females). The patient's duration of walking aid use ranged from one month to 15 years, with an average of  $2.7 \pm 2.7$  years and a median of two years. Eleven patients were not able to recall how long they had been using their walking aid. Patient's characteristics did not differ between the three groups of walking aid users (data not shown). Scores on the MMSE demonstrated that 49 (75.4%) had an MMSE score  $\geq 24$  points and 16 (24.6%) had an MMSE score  $< 24$  points. Performance on the TUG differed between the walking aid users. Those with a cane had the fastest TUG time (average  $17.0 \pm 4.4$  s), followed by the crutch users (average  $18.9 \pm 6.1$  s) and then the walker users (average  $21.1 \pm 9.2$  s). However, the TUG times did not significantly differ between the three groups ( $p = 0.095$ ).

A summary of descriptive data of the entire group of walking aid users and matched controls is shown in Table 1. Compared to the control group, the walking aid group experienced more falls in the previous twelve months ( $p = 0.003$ ), more often had fear of falling ( $p < 0.001$ ), had a higher BMI ( $p = 0.024$ ), and needed more time to perform the TUG test ( $p < 0.001$ ). Because of missing information for the variables falls, fear of falling and living arrangement, the number of patients in the walking aid group was reduced to 60, 56, 58 respectively and in the matched control group to 189, 185, 192 respectively.

### Gait measurement

Gait measures from the walking aid group as a whole without the use of a walking aid and the matched control group are summarized in Table 2. Gait performance for all investigated parameters ( $p < 0.001$ ), except for base of support variability ( $p = 0.179$ ), was significantly worse in the walking aid group compared with matched controls.

Description and statistics of gait parameters between the different walking aid users are shown in Table 3. Overall for the walking aid group, gait performance without the use of a walking aid was best in cane users and worst in walker users. Significant group differences were found for stride time variability ( $p = 0.024$ ) and double support ( $p = 0.026$ ) between all three groups. Significant post hoc differences were found for double support between cane and walker users ( $p = 0.036$ ). No significant post hoc differences were found for stride time variability (cane vs. crutch,  $p = 0.045$ ; cane vs. walker,  $p = 0.023$ , crutch vs. walker,  $p = 0.789$ ). When assessed with the use of their walking aid, no significant results were found between the three groups of walking aid users.

Differences between gait measures with and without the use of the individual walking aid are summarized in Table 4. Comparison of gait speed, stride time variability and double support are presented in Fig. 1-3. Use of a cane led to significantly improved performance in cadence ( $p = 0.002$ ), stride time ( $p = 0.004$ ), stride length ( $p = 0.002$ ), stride time variability ( $p = 0.004$ ) and double support ( $p = 0.013$ ). Use of a crutch led to significantly improved performances in all assessed gait parameters ( $p < 0.005$ ), except for gait speed and base of support measures. Use of a walker led to significantly improved gait performance in gait speed ( $p = 0.001$ ), stride time variability ( $p = 0.045$ ), stride length ( $p = 0.002$ ), stride length variability ( $p = 0.019$ ), base of support ( $p = 0.006$ ) and double support ( $p = 0.001$ ).

## Discussion

The aim of the present study was to quantify the effect of walking aids on spatio-temporal gait parameters in community-dwelling older people and to compare these gait parameters to an independently mobile matched control group. To date, no quantitative data exist on the comparison of gait alterations in experienced walking aid users during unassisted walking and during walking with a cane, crutch or walker. Our findings showed that the gait pattern among experienced walking aid users when they did not use their walking aid was more vulnerable and unstable compared to an independently mobile control group matched by age, sex and cognition. We were able to demonstrate that differences in spatio-temporal gait parameters during unassisted walking were relatively discrete between the three groups of walking aid users and that no between-group differences existed when the walking aid was used. We also showed that the use of a walking aid significantly improved walking ability within each of the three walking aid groups. Finally, the present study provides descriptive data of gait performance in community-dwelling older people using three different types of walking aids.

Gait speed is a well-known indicator of overall functional performance. Those with slower gait are at higher risk for functional as well as cognitive decline, institutionalization, falls and mortality (28). Gait speed of less than 60 cm/s is used to define slow gait, between 60 cm/s and 100 cm/s defines intermediate gait and more than 100 cm/s normal gait (28). In the present study, patients using walking aids had a significantly slower gait during unassisted walking compared to a matched control group (74.4 vs. 110.3 cm/sec). This indicates that the use of a walking aid is likely a marker for impaired gait and not that the use of a walking aid causes slower gait. In addition to gait speed, all investigated gait parameters, except for base of support variability, were significantly better in the control group than the walking aid group. Particularly gait variability is known as a marker for irregular and unstable gait and is associated with frailty (29) and an increased fall risk (17–19). Studies comparing gait parameters between fallers and non-fallers among older people have revealed that fallers have slower gait speed, increased double support, stride length variability and stride time variability (17–19). These findings are in accordance with our present study suggesting that walking aid users might have a greater likelihood of falling than independently mobile older people. The demographic characteristics of the present study support this notion showing that walking aid users had more falls in the previous 12 months than the matched controls (50% vs. 29%). In addition, the walking aid users reported to have fear of falling more often which is known to negatively influence gait performance (19) and is associated with an increased fall risk (30).

This study demonstrated that there were only discrete differences in spatio-temporal gait parameters among the three groups of walking aid user (cane, crutch, walker). These findings are in contrast to our expectations. Since the selection of the walking aid depends on the individual's functional level and the support of the device increases from cane to crutch to walker, it was hypothesized that cane users would show a better gait pattern than crutch users and that they in turn would perform better than walker users. Although differences in spatio-temporal gait parameters while walking unassisted were relatively discrete, the gait pattern of the cane users tended to be better than the gait pattern of crutch users and walker users with a significant difference in stride time variability and double support. Interestingly, neither a significant difference in one of the investigated gait parameters nor a tendency between the three groups during assisted walking was detected. From a clinical point of view, it would be of great interest to investigate if an initial objective gait analysis would help in the selection of an appropriate walking aid.

Within each subgroup of walking aid users, gait performance was significantly better in several gait parameters when assessed during walking with the walking aid compared to walking unaided. Using a walker had the greatest effect on spatial (stride length and its variability) and temporal (gait speed, stride time variability, double support) gait parameters. Particularly, an increase in gait speed of 14.5 cm/s was observed in the walker group whereas using a cane or crutch did not influence gait speed. Verghese et al. (17) reported that each 10 cm/s decrease in gait speed was associated with a 7% increased risk for falls. Based on the results in gait speed, it could be concluded that only the use of a walker provides a benefit. However, one should be aware that walking speed may be affected by other gait parameters. The increase in gait speed among the walker group arising from increased stride length could not be observed in the cane and crutch group due to the simultaneous reduction in cadence. Another explanation for the increase in gait speed may be that the use of a cane or crutch requires the user to lift the device in time with their stepping whereas the walker allows the person to push the device without lifting it. However, other gait parameters in addition to gait speed are needed to fully understand gait stability in regard to falls prevention.

The use of a mobility aid enlarges a person's supporting area (not to be confused with the base of support gait parameter; see Fig. 2), thereby improving balance (7). In this context, Bateni and Maki (7) suggest that a walker enlarges the supporting area more than a cane and therefore the potential to increase stability is even greater. Considering the base of support measured by the GAITRite system, patients within the walker group had a 4 cm decrease in their base of support during assisted walking. Maki BE (19) reported that a 4 cm increase in the base of support of was associated with an increased risk for future falls. Hence, changes in gait parameters seen in our study, particularly decreased base of support and double support, as well as increased stride length indicate that patients adopted a more stable gait pattern when using their walking aid. These changes are more pronounced in the walker group compared to the crutch group, and this in turn more than the cane group.

Another marker of gait stability is the stride-to-stride variability, which can be viewed as a marker of gait regularity. High stride-to-stride variability reflects gait instability (19). Our findings show that walking with a crutch or walker produced a gait pattern with decreased stride time variability and decreased stride length variability. The use of a cane significantly decreased stride length variability. Taken together, these findings indicate that patients in each group adopted a safer and less variable (i.e. more regular and thus more stable) gait when utilizing their individual walking aid. Previous studies have been shown that higher variability in stride time and stride length is associated with

increased falls in older adults (17; 19; 20). Hence, utilizing a cane, crutch or walker would indicate a lower fall risk in these three groups of experienced walking aid users when walking with their device than without it.

Walking is generally seen as an automatic motor task in healthy adults. However, there is growing evidence that older adults require more attention for motor control while walking than younger adults (31). A common situation where attentional demands are challenged is, for example, when people walk while simultaneously performing one or more additional tasks. The ability to safely and effectively use a walking aid during ambulation characterizes such an additional attention-demanding task. Thus, it could be speculated that the attentional demands associated with the use of a walking aid could well lead to an altered gait performance. To date, only two studies used a dual task paradigm to examine the attentional demands of walking aid use. Wright and Kemp (32) showed that the performance on a voice reaction time task during ambulation in 10 healthy young adults required greater attention using a standard pickup walker in comparison to using a rolling walker or walking unaided. Wellmon et al. (33) extended the work of Wright and Kemp (32) by investigating the same dual task paradigm in older adults who ambulated with either a rolling walker, a straight cane or used no device. Their results demonstrated that walking with a rolling walker required greater attention compared to not using an assistive device (33). In both studies, the increased attentional requirements under the dual task condition could only be measured in the voice reaction time task and not in gait performance.

Another way to reveal the attentional demands of using a walking aid is the comparison of gait performance between experienced walking aid users and first-time users. Studies investigating the effect of walking aids on gait in first-time users showed that gait performance remained unchanged or even worsened (34–37). In contrast, studies with experienced walking aid users demonstrated an improvement in gait performance (38; 39), similar to the results in the present study. Due to the wide variety of methodological procedures and study populations a final conclusion to guide clinical practice needs more research in this area. However, it is of utmost importance to provide prior training before the use of walking aids and to reevaluate its need after a certain time span to guarantee the safe and effective use of the device.

When interpreting the results a few factors need to be taken into consideration. First, the number of patients in the crutch and walker group was small compared to the cane group, which might have influenced study results. However, the statistical procedures used considered the different sample sizes and the distribution of the gait variables. Also, patients with a range of mobility and health status

were included. Unfortunately, health status was not consistently measured and therefore could not be classified. Finally, the reason for use of the chosen walking aid was not part of the standard assessment which means little or nothing was known about the actual need for such devices. Future studies should also include standardized measures of health status and co-morbidities as well as the reason for use and compare the effect of walking aids among different patient groups according to health status, reason for using or cognitive status.

## **Conclusion**

This study is the first to report on the effect of different types of walking aids on quantitatively measured gait parameters in community-dwelling older people. The findings of the present study demonstrate that the use of a cane, crutch or walker increased gait speed (only in walker group) and stride length, and decreased cadence (in cane and crutch group), stride time variability (in crutch and walker group), stride length variability and double support (in all three walking aid groups). The results suggest that these changes are a compensatory reaction to the use of the walking aid rather than an indication of a pathological gait pattern in this group of experienced older walking aid users. However, the walking aid group had a higher stride time variability and stride length variability, than the matched control group. Therefore, using a walking aid improved gait performance but not to a degree that it can be called a healthy, stable gait pattern. Therefore, the selection of a walking aid should depend on objective gait assessments and periodical reevaluation to ensure that it suits a person's functional requirements and physical capabilities.

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### **Figure legends**

Fig. 1 - Gait speed (A) and stride time variability (B) for walking with vs. without walking aid by walking aid group. \*Denotes significant differences within a walking aid group.

Fig. 2 - Schematic illustration of the base of support as measured by GAITRite and of the supporting area of a walker. Figure modified from Bateni and Maki (7).

Figures

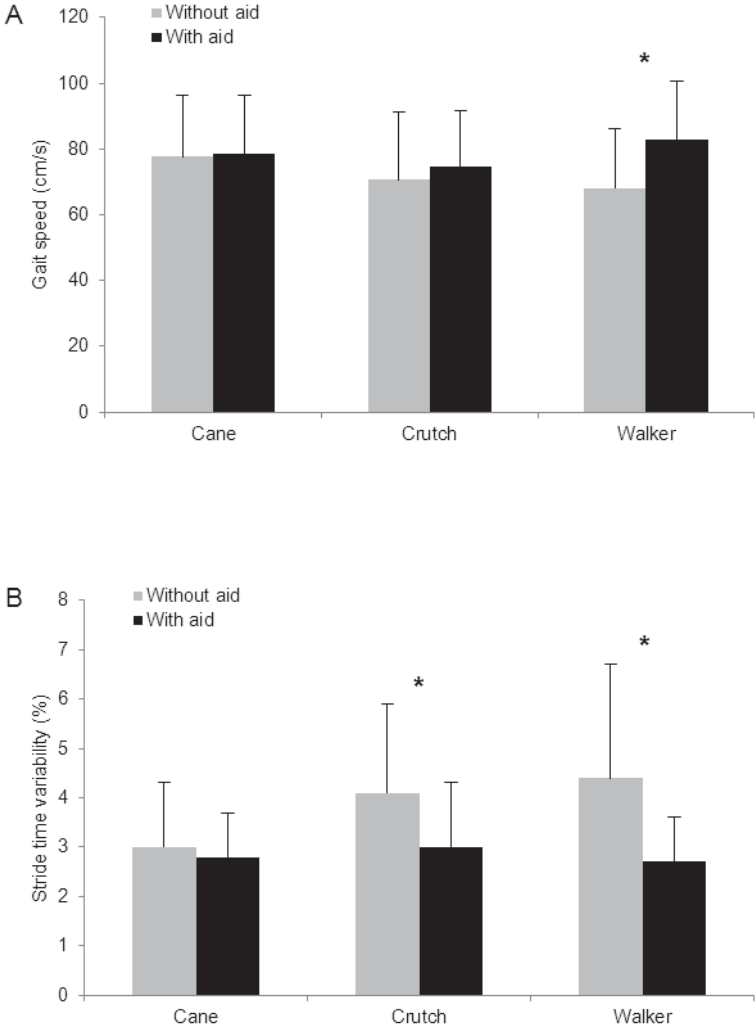


Fig. 1A to 1B

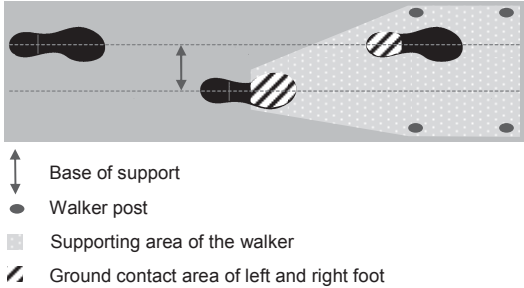


Fig. 2

## Tables

Table 1 - *Participants characteristics.*

Variable	Walking aid group (n=65)	Matched control group (n=195)	p-value
Age, years	82.1 ± 5.7	81.9 ± 5.4	0.732
Gender			1.000
Male, %	35.4	35.4	
Female, %	64.6	64.6	
MMSE score, points	25.4 ± 4.4	25.5 ± 4.2	0.906
Previous fall in the last 12 months <sup>a</sup>			0.003
none, %	50.0	70.9	
1 or more, %	50.0	29.1	
Fear of falling <sup>a</sup> , %	30.4	10.3	<0.001
Living arrangement <sup>a</sup> , %			0.663
Lives alone	43.1	46.4	
Cohabits	56.9	53.6	
Height, cm	164.7 ± 8.6	164.9 ± 8.8	0.877
Weight, kg	71.9 ± 13.6	68.5 ± 12.7	0.074
BMI, kg/m <sup>2</sup>	26.4 ± 4.1	25.1 ± 3.9	0.024
TUG, s	18.2 ± 6.0	11.6 ± 3.0	<0.001

<sup>a</sup>The number of patients in each group is less than the entire sample due to missing information. Values are means ± standard deviation or percentages. MMSE: Mini Mental State Examination. TUG: Timed Up & Go test.

Table 2 - Gait measures in normal walking without walking aid.

Gait parameter	Walking aid group (n = 65)	Matched control group (n = 195)	p-value <sup>a</sup>
Gait speed, cm/s	74.4 ± 19.0	110.3 ± 20.5	<0.001
Cadence, steps/min	100.3 ± 11.7	111.2 ± 10.7	<0.001
Stride time, s	1.1 ± 0.14	1.1 ± 0.11	<0.001
Stride time CV, %	3.5 ± 1.7	2.3 ± 1.0	<0.001
Stride length, cm	88.9 ± 18.7	118.9 ± 17.1	<0.001
Stride length CV, %	5.3 ± 3.0	3.0 ± 1.5	<0.001
Base of support, cm	11.9 ± 4.6	8.7 ± 3.3	<0.001
Base of support CV, %	24.6 ± 31.3	29.8 ± 25.3	0.179
Double support, % of gait cycle	36.4 ± 6.7	29.1 ± 2.7	<0.001

<sup>a</sup>Independent t-test. Values are means ± standard deviation. CV: coefficient of variation.



Table 3 - Gait measures with and without walking aid.

Gait parameter	Cane (n = 40)	Crutch (n = 13)	Walker (n = 12)	p-value
<b>Without walking aid</b>				
Gait speed, cm/s	77.6 ± 18.6	70.6 ± 20.5	68.2 ± 18.0	0.237 <sup>a</sup>
Cadence, steps/min	100.3 ± 11.5	98.7 ± 10.4	101.95 ± 14.4	0.789 <sup>a</sup>
Stride time, s	1.2 ± 0.15	1.2 ± 0.13	1.2 ± 0.15	0.939 <sup>b</sup>
Stride time CV, %	3.0 ± 1.3	4.1 ± 1.8	4.4 ± 2.3	0.024 <sup>b</sup>
Stride length, cm	92.6 ± 18.1	85.5 ± 19.4	80.4 ± 18.1	0.107 <sup>a</sup>
Stride length CV, %	4.7 ± 2.0	5.3 ± 2.9	7.2 ± 4.7	0.354 <sup>b</sup>
Base of support, cm	11.3 ± 3.9	12.2 ± 6.1	13.6 ± 4.9	0.297 <sup>a</sup>
Base of support CV, %	23.3 ± 25.2	26.0 ± 33.9	27.5 ± 46.6	0.587 <sup>b</sup>
Double support, % of gait cycle	34.7 ± 6.1	38.4 ± 6.9	39.9 ± 6.8	0.026 <sup>a</sup>
<b>With walking aid</b>				
Gait speed, cm/s	78.7 ± 17.8	74.7 ± 16.9	82.7 ± 18.0	0.355 <sup>b</sup>
Cadence, steps/min	95.5 ± 9.7	92.0 ± 9.5	98.5 ± 12.5	0.285 <sup>a</sup>
Stride time, s	1.3 ± 0.13	1.3 ± 0.14	1.2 ± 0.17	0.370 <sup>a</sup>
Stride time CV, %	2.8 ± 0.9	3.0 ± 1.3	2.7 ± 0.9	0.736 <sup>a</sup>
Stride length, cm	98.8 ± 18.9	96.7 ± 15.9	100.7 ± 17.6	0.699 <sup>b</sup>
Stride length CV, %	3.9 ± 1.5	3.8 ± 1.8	4.1 ± 2.0	0.915 <sup>a</sup>
Base of support, cm	10.7 ± 3.7	10.5 ± 5.2	9.6 ± 3.4	0.338 <sup>b</sup>
Base of support CV, %	21.2 ± 18.0	22.0 ± 21.5	12.1 ± 6.5	0.151 <sup>b</sup>
Double support, % of gait cycle	33.4 ± 4.9	35.7 ± 6.3	34.2 ± 4.7	0.373 <sup>a</sup>

<sup>a</sup>ANOVA. <sup>b</sup>Kruskal-Wallis test. Values are means ± standard deviation. CV: coefficient of variation.

Table 4 - Gait measures of differences between test results without and with walking aid.

Gait parameter	Cane (n = 40)	p-value	Crutch (n = 13)	p-value	Walker (n = 12)	p-value
Gait speed, cm/s	+1.1 ± 14.2	0.626	+4.0 ± 12.1	0.251	+14.5 ± 10.6	0.001
Cadence, steps/min	-4.8 ± 9.0	0.002 <sup>a</sup>	-6.7 ± 8.4	0.019 <sup>a</sup>	-3.4 ± 12.2	0.394 <sup>a</sup>
Stride time, s	+0.06 ± 0.12	0.004 <sup>a</sup>	+0.089 ± 0.11	0.019 <sup>a</sup>	+0.042 ± 0.12	0.410 <sup>a</sup>
Stride time CV, %	-0.16 ± 1.4	0.480	-1.1 ± 1.4	0.016	-1.7 ± 2.6	0.045
Stride length, cm	+6.2 ± 11.2	0.002 <sup>a</sup>	+11.2 ± 9.9	0.006 <sup>a</sup>	+20.3 ± 9.4	0.002 <sup>a</sup>
Stride length CV, %	-0.76 ± 1.6	0.004	-1.5 ± 2.3	0.034	-3.2 ± 4.0	0.019
Base of support, cm	-0.52 ± 1.8	0.104 <sup>a</sup>	-1.7 ± 2.7	0.221 <sup>a</sup>	-4.0 ± 3.1	0.006 <sup>a</sup>
Base of support CV, %	-2.1 ± 17.3	0.502 <sup>a</sup>	-4.0 ± 15.1	0.422 <sup>a</sup>	-15.3 ± 41.6	0.182 <sup>a</sup>
Double support, % of gait cycle	-1.36 ± 3.3	0.013	-2.7 ± 2.8	0.005	-5.7 ± 4.1	0.001

P-values for paired t-test or <sup>a</sup>Wilcoxon signed rank test. Values are means ± standard deviation. CV: coefficient of variation.

**Publication (g)** (study protocol)

**Effect of Ginkgo Biloba Special Extract LI 1370 on Dual-Tasking in Patients with MCI: a Randomized, Double-Blind, Placebo-Controlled Exploratory Study**

Yves J. Gschwind

Stephanie A. Bridenbaugh

Urs Granacher

Andreas U. Monsch

Reto W. Kressig

ClinicalTrials.gov identifier: NCT01046292, in preparation



## 1. PROTOCOL TITLE

Protocol Identifying Number: GBE LI 1370

# **Effect of Ginkgo biloba special extract LI 1370 on dual-tasking in patients with MCI: a randomized, double-blind, placebo-controlled exploratory study**

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## 2. LIST OF ABBREVIATIONS

<b>AD</b>	Alzheimer Disease
<b>ADL</b>	Activities of Daily Living
<b>AE</b>	Adverse Event
<b>BMI</b>	Body Mass Index
<b>CI</b>	Clinical Investigator
<b>CNS</b>	Central Nervous System
<b>CO</b>	Co-author
<b>CIOMS</b>	Council for International Organizations of Medical Sciences
<b>CP</b>	Contact Person
<b>CPMP</b>	Committee for Proprietary Medicinal Products
<b>CRF</b>	Case Report Form
<b>CTU</b>	Clinical Trial Unit
<b>CV</b>	Coefficient of Variation
<b>DSM-IV</b>	Diagnostic and Statistical Manual of Mental Disorders IV
<b>EKBB</b>	Local Ethics Committee (“Ethikkommission beider Basel”)
<b>GG</b>	Ginkgo Intervention Group
<b>GBE</b>	Ginkgo Biloba Extract
<b>GCP</b>	Good Clinical Practice
<b>GMP</b>	Good Manufacturing Practice
<b>ICD</b>	International Classifications of Diseases
<b>ICH</b>	International Conference on Harmonization
<b>IEC</b>	Independent Ethics Committee
<b>IMP</b>	Investigational Medical Product
<b>IQCODE</b>	Informant Questionnaire on Cognitive Decline in the Elderly
<b>IRB</b>	Institutional Review Board
<b>MCI</b>	Mild Cognitive Impairment
<b>MD</b>	Medical Doctor
<b>ME</b>	Medical Expert
<b>MMSE</b>	Mini Mental State Examination
<b>MS</b>	Master of Science
<b>NOSGER</b>	The Nurses’ Observation Scale for Geriatric patients
<b>NSAIDs</b>	Non-Steroidal Anti-Inflammatory Drugs
<b>PAF</b>	Platelet Activating Factor
<b>PG</b>	Placebo Control Group
<b>PHD</b>	Doctor of Philosophy
<b>PI</b>	Principle Investigator
<b>PP</b>	Per-Protocol Analysis
<b>SA</b>	“Société Anonyme”

<b>SAE</b>	Serious Adverse Event
<b>SD</b>	Standard Deviation
<b>SIC</b>	Subject Identification Code
<b>SP</b>	Study Physician
<b>SPSS</b>	Statistical Package for Social Sciences
<b>SUSAR</b>	Suspected Unexpected Serious Adverse Reaction
<b>TUG</b>	Timed Up & Go
<b>UPN</b>	Unique Patient Number
<b>VKlin</b>	Regulations for clinical trials with remedies

### 3. ACTIVITY PLAN

	Routine clinical assessment (Visit 0)			Baseline (Visit 1)		GA 1 (Visit 2)	GA 2 (Visit 3)	Follow-up (Visit 4)
	Neuropsych. Assessment	Diagnosis Conference	Diagnosis Talk	Recruitment (house visit)	Intervention Start			
<b>Months</b>		approx. - 3			0	3	6	12
Allowed time frame				(Day 0)	(Day 1)	+/- 7 days	+/- 7 days	+/- 7 days
Eligibility (Inclusion/Exclusion Criteria)		x						
Informed Consent				x				
Study Inclusion				x				
<b>Neuropsychological Assessment</b>	x							
Mini Mental State Examination	x							
Physical Examination	x							
Vital Signs (BP)	x							
Medical History	x							
Blood Profile (incl. creatinine clearance, liver enzymes)	x							
<b>Gait Analyses (1-4)</b>	x					x	x	x
Demographic and Anthropometric Data	x					x	x	x
Randomization				x				
(Concomitant) Medication	x			x		monthly (months 0-12)		
Concomitant Symptoms				x		monthly (months 0-12)		
Study Information (IC/Patient Info.)			x					
Nihil Obstat (from family doctor)			x					
<b>Study Medication Administration</b>					months 0-6: Verum or Placebo / months 6-12: all Verum			
Drug Account Patient						x	x	x
Recalls						monthly (months 0-12)		
Adverse Events						monthly (months 0-12)		

GA = Gait analysis.

## 4. BACKGROUND

### 4.1 INTRODUCTION

The responsible and principal investigator of this investigator-driven study and PhD project of Yves Gschwind is Prof. Reto W. Kressig. This randomized, placebo-controlled, double-blind exploratory study will evaluate the effect of Symfona<sup>®</sup> forte with its active agent Ginkgo Biloba special Extract LI 1370 (GBE) on dual-tasking in patients with Mild Cognitive Impairment (MCI). All investigations will be conducted at the Basel University Hospital, Switzerland. The research is supported by the Acute Geriatric Clinic's research fund and an unrestricted educational grant by Vifor Société Anonyme (SA).

### 4.2 MILD COGNITIVE IMPAIRMENT (MCI)

According to the report of an international working group (Winblad et al., 2004) the diagnosis of MCI is based on the following 3 criteria:

- (1) The person is neither cognitively normal nor demented.
- (2) There is evidence of cognitive deterioration shown by either objectively measured decline over time and/or subjective report of decline by the person and/or a proxy informant in conjunction with objective cognitive deficits.
- (3) Activities of daily living are preserved and complex instrumental functions are either intact or minimally impaired.

Patients with MCI are further distinguished according to the cognitive domains affected: amnesic vs. non-amnesic and single vs. multiple domain. Thus, 4 subgroups of MCI exist: amnesic single domain, amnesic multiple domain, non-amnesic single domain and non-amnesic multiple domains. Once the clinical subclassification has been made, the proposed etiology of the clinical syndrome should be determined, similar to the evaluation that most clinicians perform in order to determine subtypes of dementia. For patients with amnesic impairment (single or multiple domain(s)) who had been diagnosed according to the previous MCI criteria (Petersen et al., 2001), the progression rate to Alzheimer Disease (AD) within 3 years was reported to be more than 40% (Palmer et al., 2007). This rate did not change when the new criteria that are outlined above were used (Palmer K, personal communication with Monsch AU). At the Memory Clinic of the Basel University Hospital, 17% of patients diagnosed with MCI convert to AD within one year. However, to this date, the question of longitudinal outcomes (deterioration to dementia vs. stable vs. improvement back) remains unclear.

#### 4.2.1 Role of Gait in Relation to Cognition (Executive Function) for Gait Safety in Older adults

The examination of spatio-temporal gait parameters in older adults enhances our understanding of movement control and is useful in quantifying outcomes of therapeutic interventions (Kressig and Beauchet, 2004). In particular, a safe and efficient gait is important for mobility and independence of the elderly (Nelson et al., 1999). In addition, the ability to adapt gait patterns to different situations has a central role in the safety of gait. In the elderly, the combination of daily living activities and walking becomes more difficult and often turns into a complex multi-task situation (Beauchet et al., 2007). Further, in conjunction with Alzheimer's disease, patients often develop considerable difficulties with gait and postural stability (Sheridan et al., 2003).

Walking, as an automated motor behavior, is mostly controlled by subcortical locomotor brain regions but might require higher levels of attention with increasing age due to sensorial losses such as low vision or peripheral polyneuropathy (Kressig and Beauchet, 2004). Locomotor function depends on executive function that can be affected in cerebral diseases such as MCI or dementia (Sheridan et al., 2003). Deficits in language and visual spatial skills can be caused by loss of attention and are common in patients with mild dementia and mild cognitive impairment (MCI) (Hulette et al., 1998). These executive dysfunctions may be controlled by the same brain networks responsible for the timing



and sequencing of motor activity (Sheridan et al., 2003). In the Einstein cohort Aging Study by Verghese et al. (2006), typical gait changes (irregular gait) were identified that preceded dementia by five years as diagnosed by neuropsychological and cerebral imaging assessments. Further, it was shown by Nakamura et al. (1997) that in subjects with dementia, reduced regional cerebral blood flow was significantly correlated with worsened gait patterns (i.e. decreased walking speed and increased gait irregularity with increasing severity degree of dementia).

#### **4.2.2 Gait Parameters and Postural Stability**

Gait variability is a quantifiable feature of walking that is altered (in terms of both magnitude and dynamics) in clinically relevant syndromes such as falling, frailty and neuro-degenerative disease (Sheridan et al., 2003). In the past, Maki (1997) showed that increased gait variability represents impaired motor control as well as an increased fall risk.

Today's most important gait parameter for postural stability in older walking adults is stride-to-stride variability (= gait regularity). Hereby, high gait variability corresponds to irregular gait whereas low gait variability corresponds to regular gait. Stride-to-stride variability is measured by the coefficient of variation ( $CV = [SD / \text{mean}] \times 100$ ) which is used as a clinical index of gait steadiness and has been found to be a sensitive predictor of falls in the elderly (Maki, 1997; Hausdorff et al., 2001; Allali et al., 2007; Priest et al., 2008). In fact, an increase in stride length of 1.7cm from one stride to the next doubles the likelihood of falling in the next six months (Maki et al., 1997, Kressig et al., 2008).

Stride time variability reflects the regularity of the walking rhythm which is considered an indicator of gait control (Hausdorff et al., 2001). Under normal walking and specifically under dual-task conditions (walking with simultaneous performance of other tasks, either motor or cognitive), high stride-time variability, a measure of gait unsteadiness, is strongly associated with impaired executive function and a high risk of falling in older people (Hausdorff et al., 2001; Sheridan et al., 2003; Hausdorff, 2005; Kressig et al., 2008). Hence, gait variability might represent a sensitive and relevant surrogate marker to measure the effects of therapeutic interventions in fall prevention (Hausdorff, 2005).

#### **4.2.3 Walking-Associated Dual-Tasking**

A main goal of using a dual-task paradigm while walking is to determine to what extent walking requires attention in an older subject. Normally, walking is a mostly automated behavior needing no or minimal attention. Dual-task-related gait changes provide an indicator of change in gait control (Beauchet and Berrut, 2006). Gait interference caused by dual-tasking is important for the occurrence of falls, because safe locomotion depends on efficient and mostly automated gait control (Beauchet et al., 2005c). Dual-tasking-induced gait changes are also used to explore the cortical involvement in gait control (Allali et al., 2006). In addition, there is growing evidence that gait changes are associated with the incidence of dementia and cognitive decline (Beauchet and Berrut, 2006).

#### **4.2.4 Two Types of Walking Associated Cognitive Tasks: Semantic and Working Memory Tasks**

Semantic verbal fluency relies on semantic memory counting backwards relies on working memory. The latter is a system for temporary storage and processing of information and is therefore more directly related to executive function (Beauchet et al., 2005a). Cognitive activity while walking, such as mental calculation may reduce gait velocity (Beauchet et al., 2005a; Priest et al., 2008). In addition, the required attentional demands for walking while simultaneously counting backwards may overload available central resources and explain major dual-task-related gait changes (Dubost et al., 2006; Allali et al., 2006). Verbal fluency (i.e. naming animals) on the other hand, assesses fluency and speed of mental processing (Sheridan et al., 2003). Consequently, combining an arithmetic task with walking could be related to competitive interaction with executive function in the elderly (Beauchet et al., 2005c).

Recently, Beauchet et al. (2005b) reported decreased gait speed and increased coefficient of variation (CV) of stride time when older subjects with a broad range of cognitive function disabilities (i.e. mild dementia) performed the dual-task of walking while counting backwards. These findings suggest that difficulties in the ability to appropriately allocate attention between two simultaneously performed tasks (walking and counting backwards) result in major competitive interactions with executive function (Beauchet et al., 2003, see also Sheridan et al., 2003). In other words, dual-task interference on gait is based on the cerebral capacity to divide attentional resources between gait and an additional task (Beauchet et al., 2005c).

In a recent pilot trial (Assal et al., 2008) Alzheimer's patients with impaired dual-task-associated gait performance (significant decrease of gait speed under a dual-task condition) normalized their dual-task-related gait speed after 6 months of treatment with Galantamine, a cholinesterase inhibitor commonly used in the treatment of Alzheimer's disease.

#### **4.2.5 Summary**

Deficits in executive function and attention are associated with typical gait disorders (decreased walking speed, increased gait variability) under dual-task conditions (walking while simultaneously performing cognitive tasks necessitates "divided attention"). A substance or drug with proven positive effects on cerebral concentration and attention might increase the ability to divide attentional resources in executive dysfunctional MCI patients and therefore positively influence gait performance under dual-task situations. Furthermore, this may improve gait safety in these patients with increased fall risk.

### **4.3 GINKGO BILOBA EXTRACT**

#### **4.3.1 Introduction**

Over the last three decades, the use of Ginkgo biloba special extract (GBE, standardized at 25% flavone glycosides and 6% terpene lactones) for the treatment of cognitive disorders has increased drastically. This results from a large number of pharmacological and clinical studies demonstrating the positive effects of ginkgo in elderly patients with cerebro-vascular insufficiency, impaired cerebral performance, cognitive impairment or mild to moderate dementia.

#### **4.3.2 Pharmacological Aspects**

Although the mechanism of action of ginkgo is only partially understood, the effects of ginkgo can be summarized in two main groups of actions: effects on microcirculation as well as antioxidant and neuroprotective effects.

GBE might benefit CNS and vascular conditions by improving blood flow to capillaries throughout the body including the CNS, eyes, ears, extremities, and other tissues. GBE likely improves circulation by decreasing blood viscosity and affecting vascular smooth muscle. GBE restores the balance between prostacyclin and thromboxane A<sub>2</sub>, resulting in improved vasoregulation. Therefore, GBE relaxes spasmodic contracting vasculature and constricts abnormally dilated vessels. Overall, ginkgo seems to increase cerebral and peripheral blood flow microcirculation and reduces vascular permeability (Diamond et al., 2000). Moreover, ginkgolides (obtained from the ginkgo leaf) competitively inhibit platelet activating factor (PAF) by binding to membrane receptors of various cells (Kudolo et al., 2002). GBE has strong antioxidant and free radical scavenging properties (Logani et al., 2000; Ahlemeyer et al., 2003). The flavonoids seem to prevent or reduce cell membrane lipid peroxidation (Oken et al., 1998), decrease oxidative damage to erythrocytes, and also protect neuronal mitochondrial function from oxidative stress (Eckert et al., 2003) and injury following ischemic episodes (Logani et al., 2000). There is preliminary evidence that GBE can inhibit toxicity and cell death induced by beta-amyloid peptides (Bastianetto et al., 2000; Bate et al., 2008). However, this has not yet been demonstrated in vivo. Ginkgo might also influence certain neurotransmitter systems, such as the cholinergic system

and seems to produce EEG changes similar to those caused by the acetylcholinesterase inhibitor tacrine (Itil et al., 1998).

#### **4.3.3 Clinical Data**

Numerous studies on patients with a cognitively impaired functioning have shown positive effects of GBE on memory (e.g. short term, verbal memory) (Graessel, 1992; Hofferberth, 1994; Semlitsch et al., 1995; Mix and Crews, 2002), learning rate (Graessel, 1992), speed of information processing (Allain et al., 1993), speed of responses (Rai et al. 1991) and attention (Hofferberth, 1994) as compared to placebo. Furthermore, a meta-analysis of 11 controlled trials with the GBE LI 1370 confirmed the effectiveness of the extract, while in one study the findings were inconclusive (Hopfenmüller, 1994). Since the study by Le Bars et al. (1997) showed the efficacy of GBE in patients with dementia, clinical researcher focused more on the efficacy of GBE in dementia and several studies confirmed these positive results (Maurer et al., 1997; Oken et al., 1998; Kanowski and Hörr, 2003; Mazza et al., 2006; Napryeyenko et al., 2007; Scripnikov et al., 2007). However, two studies did not show positive effects of ginkgo in patients with dementia (Van Dongen et al., 2000; Schneider et al., 2005).

Most studies evaluated the efficacy of the GBE by measuring cognitive performance. Only a few trials investigated the impact of GBE on functioning in everyday living or on mood (Trick et al. 2004; Woelk et al. 2007), although a positive effect on Activities of Daily Living (ADL) might represent the patient's most relevant clinical impression of improvement.

#### **4.3.4 Safety Data**

In general, according to published studies and reports, the use of Ginkgo seems safe and well tolerated. Birks and Grimley (2009) found no serious adverse effects for GBE compared to placebo (Birks and Grimley, 2009). A recent study by Mahadevan and Park (2008) supports these findings and reports a relatively low toxicity risk in association with the consumption of Ginkgo leaf products. Although rare, reported side effects include gastrointestinal disturbances, headaches or allergic skin reactions (Sierpina et al., 2003). Although rare, there were reports about individual cases of hemorrhages, mainly in high-risk patients. To date, however, a direct causal relationship between GBE intake and hemorrhages could not be established.

In conclusion, the use of GBE may be promising for treatment of certain conditions, although its long-term use still needs to be evaluated (Mahadevan and Park, 2008). In the present study, safety of participants will be assessed by evaluation of patient history at baseline and monthly recalls. In case of adverse events or side effects patients have to report the incident immediately to the principal investigator and clinical physician. All corresponding data and Serious Adverse Events (SAE) will be listed on the Case Report Form (CRF) and conveyed to the local ethics committee (EKBB) and Swissmedic.

## **5. TRIAL OBJECTIVES AND HYPOTHESIS**

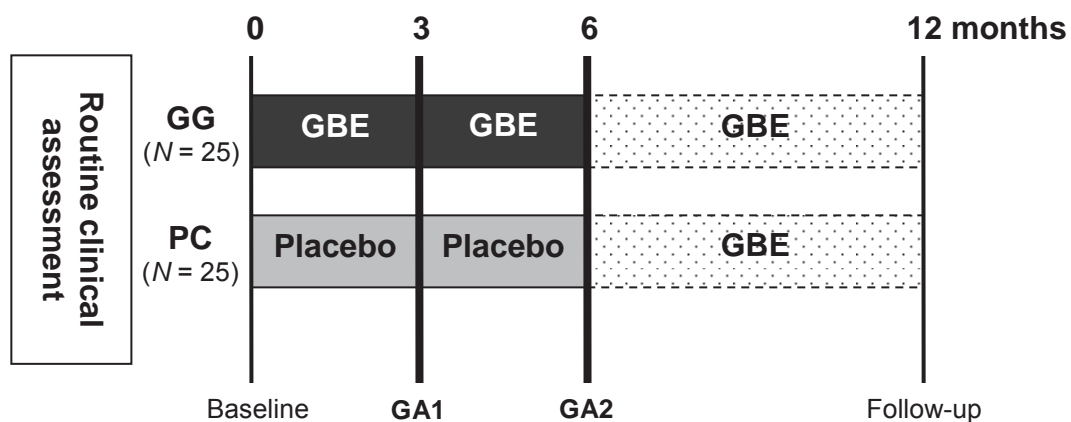
The aim of this study is to evaluate the effects of GBE in patients with MCI and impaired executive function as assessed by gait analysis while walking alone as well as under differing dual-task conditions. Therefore, we will evaluate the gait-related effects of GBE by measuring mean values and coefficients of variation of stride velocity, stride time and stride length for all walking conditions. In addition, we will determine if stride time variability ( $CV = [SD / \text{mean}] \times 100$ ), as the most sensitive parameter for gait safety while dual-tasking, can be positively affected by GBE. The primary endpoint in the evaluation of GBE efficacy is gait speed. The secondary endpoint is cycle time variability under dual-task

conditions. In addition, the study will enable further evaluation of safety and tolerability of the study medication in this study population.

We hypothesize that executive function-impaired MCI patients will exhibit a difference in gait variability under dual-task conditions after treatment with GBE compared to placebo controls.

## 6. STUDY DESIGN

### 6.1 INTERVENTION



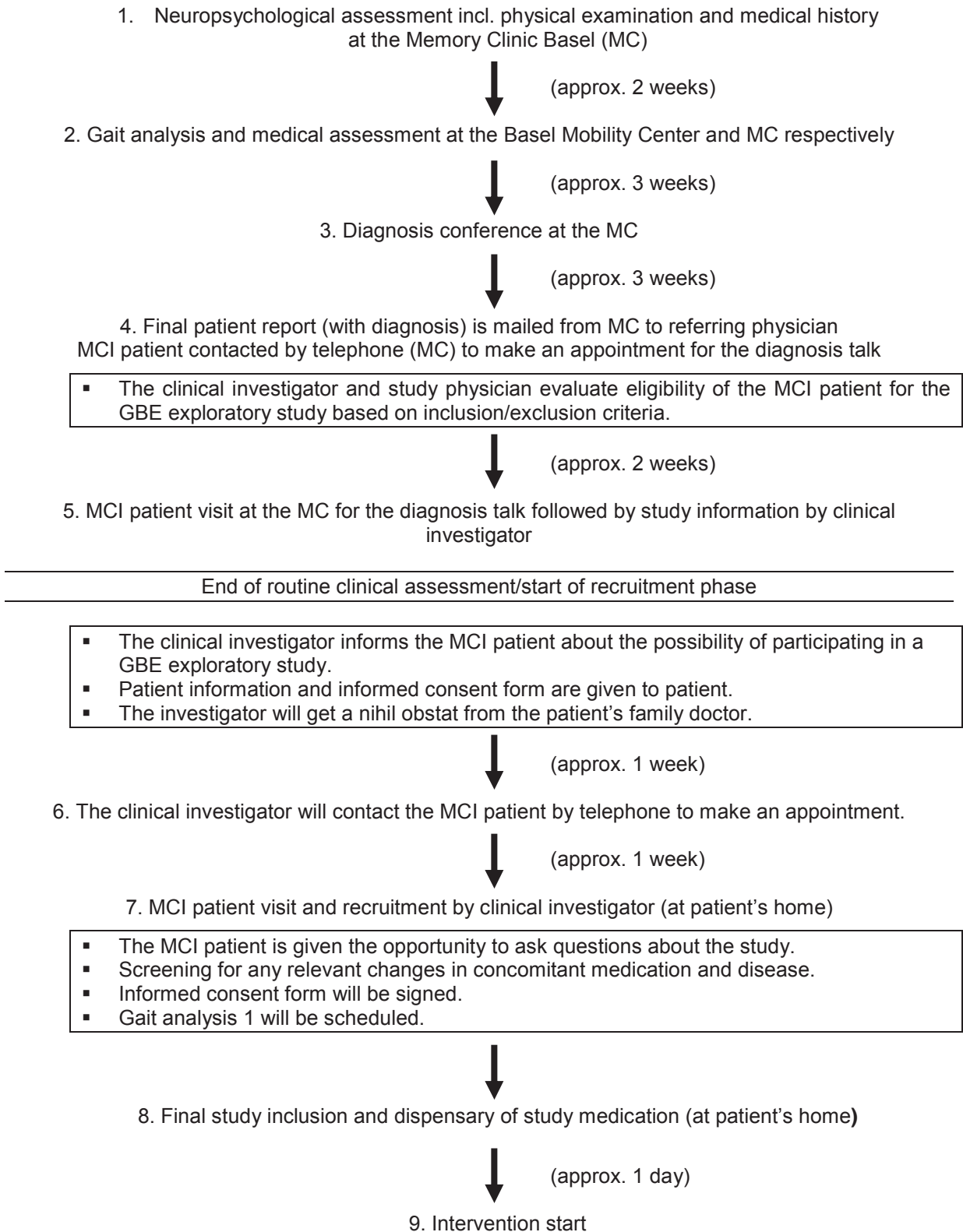
**Fig. 1.** Study design. GG = Ginkgo Group; PC = Placebo Group; GA1/GA2 = Gait analysis 1/2.

The participants will be randomly allocated to either the intervention group (GG) or the placebo control group (PC) at a ratio of 1:1. After six months, GBE will be administered to all participants for another 6 months (Fig. 1) free of charge. The daily administered dose (taken with meals in the morning and evening) will consist of twice-daily 1 capsule study medication containing 120mg Ginkgo biloba extract LI1370 (15mg = 25% flavone glycoside content and 3.6mg = 6% terpene lactone content) or an identically appearing placebo (same capsule in color (beige and brown) and size containing excipients and food coloring (E172)). In case patients omit the morning dose, they will be instructed to take the missing dose by noon. Should the omission of the morning dose be noticed during the afternoon, the missing dose must not be taken anymore and the administration of the evening dose should occur as usual. The same applies for omission of evening dose, which is allowed to be taken only until midnight.

At baseline and gait analysis 1 (Fig. 1) the subjects will receive the study medication for 3 months. At the time of gait analysis 2, the subjects will receive the study medication for the six month follow-up period. The supply of verum and placebo will be the responsibility of Vifor SA. The products will be packed and labeled according to the Good Manufacturing Praxis (GMP) annex 13. Both verum and placebo will be delivered to and stored at the Basel University Hospital Pharmacy in blisters of 10 capsules. The investigator will then get single doses of Symfona<sup>®</sup> forte or placebo according to demand. Hence, chain of custody and strict accounting, as well as secure storage conditions are provided throughout the distribution process.

## 6.2 VISIT AND ASSESSMENT SCHEDULES

### 6.2.1 Routine Clinical Assessment and Baseline (approx. – 3 to 0 months)



### 6.2.2 Gait Analysis 1 (after 3 months)

Physical examination	Demographic and anthropometric data
Gait analysis	Gait parameters
Clinical safety	Concomitant medication, AE/SAE review
Study medication	Compliance and dispensary of verum or placebo for further 3 months

### 6.2.3 Gait Analysis 2 (after 6 months)

Physical examination	Demographic and anthropometric data
Gait analysis	Gait parameters
Clinical safety	Concomitant medication, AE/SAE review
Study medication	Compliance and dispensary of verum for further 6 months

### 6.2.4 Follow-up (after 12 months)

Physical examination	Demographic and anthropometric data
Gait analysis	Gait parameters
Clinical safety	Concomitant medication, AE/SAE review
Study medication	Compliance

## 6.3 RANDOMIZATION

The randomization will be conducted independently by the study pharmacist from the Basel University Hospital Pharmacy to ensure that all investigators and participants are blinded. The randomization code will be broken by the study pharmacist after completion of the gait analysis at follow-up. Permuted block randomization (block sizes  $2n = 5$ ) is used to ensure treatment group numbers are evenly distributed.

## 6.4 ANONYMIZATION

Every study participant will receive a Subject Identification Code (SIC) called a Unique Patient Number (UPN). This number is consecutively assigned and does not allow recognition of subjects or personal data. For statistical analysis, follow-ups and public presentations, as well as for internal and external correspondence the UPN will be used exclusively. Hence, complete patient anonymization is always guaranteed. Consequently, personal data such as name or date of birth will remain anonymous.

# 7. SELECTION OF SUBJECTS

## 7.1 RECRUITMENT

Fifty individuals aged 50-85 years with Mild Cognitive Impairment (MCI) and dual-task dysfunction will be included in this study. Participants will be recruited from the Memory Clinic Basel, starting in autumn 2009. The diagnosis of MCI will be based on the comprehensive examination at the Memory Clinic Basel. This examination assesses the following cognitive domains: psychomotor speed, attention, memory, language, gnosis, praxis and executive function (see [www.memoryclinic.ch](http://www.memoryclinic.ch)). The

Nurses' Observation Scale for Geriatric patients (NOSGER, Spiegel et al., 1991) assesses the impact of cognitive dysfunction on every day life (Ehrensperger et al., submitted) and the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE; Jorm, 1994) assesses everyday cognitive functions compared to two years earlier. Irregular gait under dual-task conditions will be determined by gait analysis at the Mobility Center.

## 7.2 INCLUSION CRITERIA

- 50-85 years old (at recruitment).
- Swiss German or German speaker.
- Completed elementary school.
- Impaired executive function as measured by gait analysis and defined as a gait speed reduction  $\geq 10\%$  under dual-task as compared to normal walking (Springer et al., 2006).
- No dementia according to International Classifications of Diseases (ICD)-10 and Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV.
- MCI according to Winblad et al. (2004):
  - Cognitive decline (self/informant report or objective task).
  - Preserved basic activities of daily living and minimal impairment in complex instrumental functions.
- Written informed consent from each participant will be obtained before inclusion.
- Nihil obstat will be obtained from the participants' private physician.

## 7.3 EXCLUSION CRITERIA

- Current drug treatments with antipsychotics, Warfarin-like drugs (Coumarins or Clopidogrel), however, acetylsalicylic acid 100mg and 300mg is permitted).
- Current intake of Ginkgo biloba extract or Ginkgo intake during the last six months.
- Known hypersensitivity to Ginkgo biloba or its constituents.
- Diagnosed psychiatric disorders such as schizophrenia, bipolar disorders or severe clinical depression as determined by the study physician.
- Concomitant gait-relevant disorders such as severe cardio, pulmonary and cerebrovascular disorders, bleeding diathesis, polyneuropathy, severe orthopedic disorders, organic cerebral disease or epilepsy and low vision (if corrected vision in both eyes is below or equal to 0.2).
- Severe medical conditions e.g. chronic renal insufficiency (creatinine clearance (CL) calculated according to Cockcroft and Gault formula (Cockcroft and Gault, 1976), pathologic if  $CL < 30\text{ml/min}$ ), severe hepatic disorders (if liver enzymes are  $> 3\times$  normal values), cardio-vascular disease, uncontrolled hypertension (systolic blood pressure  $> 170\text{mm Hg}$  or diastolic blood pressure  $> 100\text{mm Hg}$ ) peptic ulcer, malignoma. For further explanation see also blood profile (appendix 14.1) where applicable.
- Participation in another clinical intervention study within the last 2 months.
- Use of a walking aid.
- Normal walking speed  $< 100\text{cm/s}$ .

During the study, the intake of substances listed in the exclusion criteria and the chronic intake of medications which may impair gait analysis is not allowed and leads to the exclusion of the patient from the study (see also Dropout Criteria). Co-medication with NSAIDs is permitted; however, caution is advised since interactions with drugs which impair blood coagulation cannot be excluded.

## 8. EFFICACY ASSESSMENT

### 8.1 STUDY PROCEDURES

#### 8.1.1 Analysis of Spatio-Temporal Gait Parameters

Gait analyses at baseline and after 3, 6 and 12 months will be conducted at the Mobility Center of the Basel University Hospital (Tab. 1). The GAITRite<sup>®</sup> system (GAITRite<sup>®</sup> Gold, CIR Systems, PA, USA) will be used to collect spatio-temporal gait data. All participants, after signing a separate informed consent form, will be photographed before testing and filmed (with audio) during gait analysis. The gait analysis will be performed according to the European guidelines for clinical applications of spatio-temporal gait analysis in older adults (Kressig and Beauchet, 2006). The GAITRite<sup>®</sup> system consists of an electronic walkway with integrated pressure-sensitive electronic surface of 7.32 x 0.61m that is connected to a computer. The pressure-sensors are placed every 1.27cm, giving a total of approximately 28'000 sensors. The data from the mechanically activated sensors are collected by onboard processors and transferred through a serial port. The data are sampled at a frequency of 60Hz. The following six gait variables will be selected based on their clinical relevance and their association with cognitive function in previous studies (Scherder et al., 2007): gait velocity (cm/s), cadence (steps/min), base of support (cm), base of support variability (%), cycle time variability (%) and swing time variability (%). In addition, data about age, height, weight, leg length, real and imagined Timed Up & Go (TUG) will be collected.

The participants will perform five walking tasks: walking alone at three different speeds and two walks at normal speed while simultaneously performing a cognitive task. Before testing, standardized verbal instructions regarding the test procedure will be given, as well as a visual demonstration if needed. No practice walks will be performed before testing. Subjects will be instructed to walk the entire walkway length of 14m. The electronically active walkway is 10m long and flanked at the beginning and end by 2m-long optically identical yet electronically inactive walkway sections. This is to ensure gait measurements under steady state conditions, with acceleration and deceleration phases of gait occurring on the electronically inactive 2m-long sections at the beginning and end of the active GAITRite<sup>®</sup> walkway, respectively. Subjects will be instructed to wear the same pair of shoes for all gait analyses. Every subject will wear a safety belt and be accompanied for each walk. No feedback of the walking performance will be provided to the subjects.



**Fig. 3.** Gait analysis at the Basel Mobility Center.



### 8.1.2 Walking Alone

Subjects will walk at their normal (self-selected and comfortable) pace, walk at a slow speed and walk at a fast speed. The testing will always begin with the normal speed trials. The order of the slow and fast conditions will be randomized. For slow speed trials, subjects will be instructed to walk slower than their normal pace. For fast speed trials, subjects will be instructed to walk as quickly as possible without running.

**Tab. 1.** Procedures of gait analysis.

<b>Gait analysis procedures</b>	<b>Unit of measurement</b>
Patient history	i.e. demographic data, footwear, etc.
Height	[cm]
Weight	[kg]
Body Mass Index (BMI)	[kg/m <sup>2</sup> ]
Leg length (left and right side)	[cm]
Timed Up & Go Test (TUG) real	[s]
Timed Up & Go Test (TUG) imagined	[s]
Uses armrest for TUG	[yes or no]
Stops walking when talking	[yes or no]
Normal walking	several gait parameters (e.g. velocity [cm/s])
Fast walking	several gait parameters (e.g. velocity [cm/s])
Slow walking	several gait parameters (e.g. velocity [cm/s])
Dual-task working memory (50 - 2s)	gait parameters including named numbers
Dual-task semantic memory (animals)	gait parameters including named animals

### 8.1.3 Walking while Dual-Tasking

After completing the above-mentioned walks, two walks under dual task conditions (presented in a randomized order for each gait analysis) will be performed. These will require the subjects to walk at their normal speed while simultaneously performing a cognitive dual task. For the verbal fluency task, subjects will be instructed to walk at their normal pace while simultaneously enumerating animals out loud. For the working memory task, subjects will be instructed to walk at their normal pace and simultaneously perform serial subtractions from 50 by 2s out loud. Subjects will be instructed to walk and simultaneously perform the cognitive task, yet no instructions regarding task prioritization will be given. During the dual tasks, subject's responses will be documented. If for safety reasons the security belt needs to be firmly held during an entire walk, participant responses to dual-task tests will be recorded by a hand-held recorder and transcribed to the test protocol immediately after the gait analysis.

## 9. SAFETY

### 9.1 DRUG ACCOUNTABILITY

The Basel University Hospital Pharmacy will document incoming study medication including badge number and expiry date. The investigator will document the dispensed and returned amount of study medication per patient. In addition, he will also record the amount of lost and destroyed study medication.

Participants are not allowed to dispense study medication to nonstudy subjects. They will be instructed to return the blisters on testing days (gait analysis 1, 2 and follow-up) to assess adherence to the verum and placebo intake regime. The investigator will count the remaining capsules and calculate approximate compliance ratios. In addition, compliance will be promoted by the same interviewer based on, at least, monthly contact with the participants (via email, text message or phone). Participants excluded from the study will be instructed to return remaining blisters and capsules to the Basel Mobility Center or to their local pharmacist. Study drop-outs will not undergo follow-up gait analysis.

### 9.2 STUDY MEDICATION LABELLING



Fig. 2. Study medication label.

## 10. STATISTICAL ANALYSIS

### 10.1 POPULATION FOR ANALYSIS

To our knowledge, no studies have yet examined the association between GBE and gait in MCI patients. Hence, this is the first study which addresses a possible effect of GBE on different gait parameters in this population, specifically under dual-task conditions. Due to a lack of existing estimates of standard deviation in the literature, no power analysis was conducted. However, the results of this exploratory study may provide valuable data for future research in this field.

### 10.2 STATISTICAL METHODS

Baseline characteristics and gait parameters will be descriptively summarized by using box-plots, means and standard deviations or frequencies and percentages, as appropriate. Then differences between the intervention and control group will be assessed using chi-square tests for categorical variables and Student's t-test or the Mann-Whitney U-test for continuous variables dependent on distribution of data. Comparisons between the before and after treatment conditions will be performed with a non-parametric Wilcoxon-test for paired samples. Statistical significance will be defined as  $P < 0.05$ . All statistical analyses will be conducted using the SPSS software program for Windows (SPSS, Inc., Chicago, IL).

### 10.3 INCOMPLETE DATA

To generate our results we will perform the per-protocol (PP) analysis. Consequently, all subjects who meet the dropout criteria will be excluded from PP analyses. Demographic data will be calculated for all participants. However, gait analysis data from drop-outs will not be included into PP analysis. By focusing only on the fully compliant subjects, we will be able to determine the maximal efficacy of the GBE (Symfona<sup>®</sup> forte) intervention. Adverse Events (AE) for all patients having taken the study medication at least once will be evaluated.

## 11. STUDY PRECAUTIONS

### 11.1 DROPOUT CRITERIA

A participant can withdraw and/or will be withdrawn from the study for following events:

- The patient wishes to stop participating in the study.
- Illness which impairs the performance of the study procedures or death.
- Significant deterioration of an initial medical condition.
- Side effects of GBE.
- Patients prescribed an anticoagulant medication after study onset.
- An illness or treatment listed as exclusion criteria which occur during the study.
- Necessity of antipsychotic, anxiolytic or sedative drugs and medication for acute severe depression after onset of the study.

Study drop-outs will not undergo follow-up gait analysis. The clinical investigator will inform the participant about their exclusion. If a dropout occurs due to medical reasons the study physician will report the incident to the subject's private physician. However, dropouts at any time will receive a report of their gait profile.

## 12. STUDY MANAGEMENT AND PRECAUTIONS

### 12.1 RESPONSIBILITIES AND COMMITMENTS

The right to stop participation in the study at anytime is reserved. This clinical trial will be conducted in accordance with the Declaration of Helsinki, ICH-Good Clinical Practice (GCP) standards, the approved protocol by the IEC, Swiss law and the applicable regulatory requirements. No deviation from the protocol will be implemented without prior review and approval of the IEC except where it may be necessary to eliminate an immediate hazard to a research subject. In such case, the deviation will be reported to the IEC as soon as possible.

### 12.2 SAFETY DEFINITIONS AND REPORTING PROCEDURES

#### 12.2.1 Definition and Obligation to Report (Serious) Adverse Events (SAE)

The investigator shall assume total responsibility for all reporting of adverse events to regulatory authorities and shall comply with all legal and regulatory requirements (ethics committee and Swissmedic) in respect of adverse event reporting in connection with the study.

#### 12.2.2 Adverse Event Documentation

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment (CPMP/ICH/377/95).

All adverse events occurring after the patient has signed the informed consent form must be fully recorded in the patient's CRF. Each event should be described in detail along with start and stop dates, severity, relationship to investigational product, action taken and outcome.

### 12.2.3 Reporting of Serious Adverse Events

All SAE must be reported to the sponsor within 24 hours of knowledge. SAE will have to be also reported to Swissmedic (vigilance@swissmedic.ch), the local ethics committee (EKBB) (ekbb@bs.ch) and Vifor SA (pharmacovigilance@viforpharma.com and confirmed by phone +41 58 851 67 27) within the notification period.

For documentation a trial specific SAE report form must be filled in. Collection of complete information concerning SAE is extremely important. If not available at time of the initial report, detailed information about SAE should be given in the follow-up report together with all relevant documentation. The investigator is responsible for submitting SAE to the responsible IEC.

A serious adverse event is defined as any untoward medical occurrence that at any dose (CPMP/ICH/377/95):

- Results in death or is life-threatening.
- Requires hospitalization or prolongation of existing hospitalization.
- Results in persistent or significant disability/incapacity.
- Is a congenital anomaly/birth defect.
- Requires a medical or surgical intervention in order to avoid any of the four above-mentioned medical occurrences.

Exceptions:

The hospitalization of a patient will not be considered as a serious adverse event, if:

- The hospitalization is required for routine analysis taking.
- The hospitalization is an elective treatment which was planned prior to the enrolment into the above-mentioned clinical study.

### 12.2.4 Suspected Unexpected Serious Adverse Reaction (SUSAR)

All SUSAR occurring in the framework of this clinic trial will be evaluated by the study physician. Required information will be processed by the study physician and then reported to Swissmedic. All three criteria (serious + related + unexpected) must be fulfilled and the identity of the blinded trial subject must be revealed. Council for International Organizations of Medical Sciences (CIOMS) form will be sent to vigilance@swissmedic.ch within seven days for lethal or life-threatening SUSAR (Art. 23, para, 1, VKlin) and within 15 days for other events requiring notification (Art. 23, para. 2, VKlin).

### 12.2.5 Safety Contact Information

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## 13. ETHICAL CONSIDERATIONS

### 13.1 BENEFIT AND RISK

All participants will profit from a complimentary treatment with Symfona<sup>®</sup> forte from Vifor SA for at least six months and its positive effects on cerebral microcirculation as well as its antioxidant and neuroprotective effects. In addition, all participants will receive a comprehensive report on their gait

performance. Further, the active agent Ginkgo biloba extract might be associated with improved gait parameters, leading to a safer gait among the elderly study participants.

In general, the participation in this study will help to increase the understanding of possible therapeutic interventions to improve mobility and daily functioning in the elderly. Results of our study may lead to better treatment strategies for older adults with MCI, thus not only improving cognition, but also improving gait performance under dual task and thus reducing fall risk.

Potential side effects of the Ginkgo product include gastrointestinal disorders, headaches or allergic skin reactions (erythema, skin swelling, pruritus). There have been a few reports of increased bleeding risk after surgery in patients with long-term treatment of Ginkgo biloba. To date, a causal relationship with Ginkgo biloba extract could not be established. However, it is recommended to advise the surgeon before surgery. Further, an enhancing interaction with warfarin-similar drugs for blood anticoagulation can not be excluded.

The study participation is voluntary and does not imply any remuneration. The expenses for public transport or taxi will be covered.

## 13.2 ETHICS AND PATIENT'S RIGHTS

Subjects will be included in the present study after reading the patient information and signing the informed consent forms. A score of at least 20/30 points on the MMSE (Folstein et al., 1975) will ensure that participants are mentally capable of providing consent.

The informed consent form and the informed consent form for video recording and photograph are approved by the legal department of the University Hospital Basel.

Participant's confidentiality will be maintained at all times. Personnel from the sponsor, from regulatory authorities and members of IEC are obliged to respect medical secrecy and to refrain from divulging the participant's identity or any other personal information they might fortuitously be aware of.

## 14. QUALITY CONTROL AND ASSURANCE

### 14.1 DIRECT ACCESS TO SOURCE DATA

The investigator will permit study related monitoring visits, audits, IEC reviews and regulatory inspections. Access to all source data (i.e. original records of clinical findings or information necessary for reconstruction and evaluation of the study) will be granted at all time.

Audits or inspections by regulatory authorities may include verification of documents, controlling of CRFs and electronic Case Report Forms (eCRFs) and site files. Hence, direct access to all documents and premises of the study site is mandatory.

### 14.2 MONITORING

The monitoring will evaluate the progress of the study, verify the accuracy and completeness of CRFs, ensure that all protocol requirements, applicable local authority regulations and investigator's obligations are being fulfilled, and resolve any inconsistencies in the study records. The extent of monitoring will be in the responsibility of the sponsor. The monitoring will be conducted by the Clinical Trial Unit (CTU) Basel.

An investigator site file (ISF) will be designed to gather all the information related to the study in the Mobility Center. Further, the ISF will permit evaluation of study conduct and compliance of the investigator with ICH-GCP. The ISF will be maintained and updated throughout the study and kept in a secure place.

### 14.3 FINANCES AND INSURANCE

The sponsor declares that he has taken out an insurance policy by the Zurich insurance company (Mythenquai 2, 8002 Zurich) for the total study length, covering the participants in respect of the risks involved in this study. In case of injury or disability deriving from participation in the study, the study participant is requested to inform without delay the physician responsible for the study.

### 14.4 DATA HANDLING AND CASE REPORT FORM

In this study personal data will be acquired. For this purpose, all relevant data of every patient will be documented in the eCRF. Entries in the eCRF must be consistent with the information recorded in the source documents and not contain any personal data of study participants. Data will be also generated by the GAITRite<sup>®</sup> system software. All data will be anonymized and only professional experts will have access (for trial-related monitoring, audits, Institutional Review Board (IRB)/Independent Ethics Commission (IEC) review, and regulatory inspections) to source data and documents. In addition, the local ethics committee (EKBB) will be able to access the original data. Data acquired in this study will be made available for follow-up studies. The confidentiality will be maintained throughout the entire study.

### 14.5 ARCHIVING OF STUDY MATERIAL

The investigator commits to archive study material in a safe place at the Basel University Hospital for at least 10 years. The investigator will maintain all study-related records, such as CRFs, medical records, laboratory reports, informed consent documents, Investigational Medical Product (IMP) disposition records, safety reports, information regarding participants who discontinued, and other pertinent data. Documents will be destroyed regarding Basel University Hospital policy.

### 14.6 PUBLICATION PLAN

The main publication will be created by Yves J. Gschwind as first author in mutual agreement with the sponsor. Subsequent publications of subgroups can follow thereafter and will have to be approved by the sponsor.

No unpublished data given to the investigator may be transmitted to a third party without prior written approval by the sponsor. No publication or communication involving the results of the study is authorized without prior written consent from the sponsor. In view of patent and confidentiality issues, however, the investigator must accept requirements on the timing of early publication. The investigator's name should not be used in any publication without the prior written permission of the investigator.

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## 16. APPENDIX

### 16.1 BLOOD PROFILE

Blood parameters	Unit	Blood parameters	Unit
<b>Chemogram</b>	mmol/l	<b>Hemogram</b>	
Sodium	mmol/l	Leukocytes	$\times 10^9/l$
Potassium	mmol/l	Erythrocytes	$\times 10^{12}/l$
Chloride	$\mu\text{mol}/l$	Hemoglobin	g/l
Creatinine	mmol/l	Hematocrit	l/l
Urea	$\mu\text{mol}/l$	- MCV	fl
Bilirubin	U/l	- MCH	pg
ASAT	U/l	- MCHC	g/l
ALAT	U/l	- EVB	%
GGT	U/l	- hypochrome Erythrocytes	%
Alcalic phosphatase	U/l	Thrombocytes	$\times 10^9/l$
Calcium	mmol/l	Neutrophils absolute (Seg+Stab)	$\times 10^9/l$
Albumin-corrected calcium	mmol/l	Lymphocytes absolute	$\times 10^9/l$
Phosphate	mmol/l	Monocytes absolute	$\times 10^9/l$
Uric acid	$\mu\text{mol}/l$	Eosinophile absolute	$\times 10^9/l$
Total protein	g/l	Basophile absolute	$\times 10^9/l$
Albumin	g/l	LUC absolute	$\times 10^9/l$
Globulin	g/l		
C-reactive protein	mg/l		
LDH	U/l	<b>Other</b>	
Creatine kinase	U/l	TSH	mIU/l
Pancreatic amylase	U/l	Serum folic acid	nmol/l
Fe (iron)	$\mu\text{mol}/l$	Vitamin B12	pmol/l
Transferrin	g/l	25-OH-Vitamin D	nmol/l
Transferrin saturation	%		
TEBK (calculated)	$\mu\text{mol}/l$		
Ferritin	ng/ml		
Soluble transferrin receptor	mg/l		
HbA1c	%		

## VII. Discussion

### 2.1 Main research findings

In this doctoral thesis research about the association between fall-related gait parameters, and several hypothesized fall prevention properties is presented. The main findings are as follows:

(a) Our first review article summarized important aspects of gait disorders, an increased risk of falling, and the association with attentional resources and dual-tasking. It was illustrated that exercise interventions, such as JDR and PRT are used as therapeutic interventions to improve gait, and decrease fall risk in older people.

(b) Our review about gait changes and fall risk highlighted the importance of gait analysis as part of fall risk assessment. Irregular gait is not an inevitability of older age, because targeted interventions based on a thorough fall risk assessment can influence gait in older people.

(c) Our third systematic literature review presented a summary of our work about fall prevention within the Best Practice Health Promotion (Via) project in collaboration with the Swiss Council for Accident Prevention (bfu) and Health Promotion Switzerland. The results consisted of a summary of current studies on fall prevention, with a particular focus on methodological quality and successful reduction of fall incidence in vulnerable older people. Characteristics of effective fall prevention programs in the fields of exercise, home modifications, appropriate footwear and walking aids were analyzed. The consolidated scientific findings intend to provide a basis for new national recommendations for the implementation of fall prevention interventions in vulnerable older people.

(d) Our salsa intervention trial showed the impact of salsa dancing on intrinsic fall-risk factors (i.e. deficits in postural control and muscle power of the leg extensors) in older people. We found a tendency towards an improvement of performance in postural control, gait (i.e. increases in stride velocity and stride length, and concomitant decreases in stride time), but no significant effect on gait variability and leg muscle power. In summary, it was shown that salsa dancing is an appropriate exercise for older people to improve dynamic postural control and reduce the risk of falling in older people.

(e) Our most recent cross-sectional study showed that older patients assessed at a memory clinic with 25(OH)D levels below 39 nmol/L had significantly worse functional mobility (normal and fast walking speed and TUG) compared to those with 25(OH)D levels above 81 nmol/L. This association was more pronounced in less frail seniors (no previous fall and MMSE  $\geq$ 26) compared to pre-frail (previous fall

and MMSE <26) older patients. In conclusion, 25(OH)D status measurement may be relevant for functional mobility in older people referred to a memory clinic.

(f) Another recent cross-sectional study improved the understanding of how spatio-temporal gait parameters are affected by walking aid use in community-dwelling older people. We were able to show that gait in older people who use a walking aid is more irregular and unstable than gait in independently ambulating older people. Walking aid users have better gait when using their walking aid than when walking without it. The changes in gait were different for the different types of walking aids used. These study results may help better understand gait in older people and differentiate between pathological gait changes and compensatory gait changes due to the use of a walking aid.

(g) Due to blinding of participants and investigators we were not able to show any preliminary findings about the influence of ginkgo biloba on spatio-temporal gait parameters in older people with MCI, but the intervention trial will soon be completed providing valuable information about ginkgo biloba as a possible treatment of gait stability for older people with MCI.

## **2.2 General discussion of research findings**

(a-b) Many studies have been using the dual task paradigm to assess the relationship between gait, cognition, and falls. Recent dual task research focused on older people suffering from cognitive decline who are more likely to experience gait disorders and falls compared to cognitively healthy older people.<sup>215</sup> In a most recent study, dual task spatio-temporal gait parameters predicted multiple falls in older people suffering from cognitive impairment.<sup>299</sup> This may be mainly explained by a negative effect on gait variability and gait velocity.<sup>300</sup> Improvement of gait performance (i.e. faster gait velocity and lower gait variability), in addition to cognitive performance, is therefore one of the major aims in older people with cognitive decline in order to improve dual-tasking and reduce fall risk.<sup>218</sup> Further, our review article illustrated that exercise such as JDR and PRT may improve gait performance and reduce fall risk. As discussed in chapter 1.13.2, a recent study showed the effectiveness of JDR on decreasing gait variability and fall rate.<sup>283</sup> In contrast, evidence about the effectiveness of PRT on spatio-temporal gait measures is low. A recent RCT reported that a 21-week muscle strength training may improve walking speed (while carrying 10.2 kg at both hands) in older men ( $56.3 \pm 9.9$  years).<sup>301</sup> In a small RCT with 27 older women ( $61.1 \pm 4.3$  years), lower limb strength exercises for 12 weeks improved walking speed, stride length, and cadence towards a gait pattern presented by young healthy individuals who are less prone to falls.<sup>302</sup> However, recent research confirmed the weak association between lower limb strength and mobility measures.<sup>303</sup> This may, at least in part, explain the lack of large RCTs in the literature reporting a positive effect of muscle strength and muscle power training on gait and related functional outcomes (e.g. fall risk reduction).

Future research needs to address the possible effect of muscle strength and muscle power on gait and fall-related outcomes in older people.<sup>304</sup>

(c) Current research on fall prevention emphasizes the implementation of research evidence into policy and practice.<sup>305</sup> As mentioned in our systematic review article,<sup>120</sup> key factors in fall prevention are the early detection of older people at risk for falls, adherence to exercise interventions, and development of evidence-based guidelines. The most recent Cochrane review about interventions for preventing falls in community-dwelling older people shows that group (rate ratio 0.71, 95%CI 0.63 to 0.82) and home-based (rate ratio 0.68, 95%CI 0.58 to 0.80) exercise programs, including balance and strength components, are effective in reducing rate of falls.<sup>146</sup> In support of our findings, there is further evidence that home safety assessment and modification interventions (risk ratio 0.81, 95%CI 0.68 to 0.97) are effective in reducing fall incidence.<sup>146</sup> However, multifactorial interventions are complex and their effective factors are not fully determined yet. Due to a lack of detailed information (e.g. type of exercise) in the literature, it still remains difficult to translate general guidelines on fall prevention into effective interventions.<sup>306</sup> The future development of new technologies may help personalize, monitor, and tailor fall prevention interventions (e.g. exercise).<sup>305,307</sup> Future research should also stress that exercise interventions have a range of health benefits (i.e. reduced depression and improved cognition) beyond affecting fall risk.<sup>306</sup>

(d) Previous research showed that deficits in gait, muscle power, and balance are important risk factors for falls in older people.<sup>36,303</sup> These factors may be improved by dancing exercises.<sup>295</sup> Our salsa trial was among the first studies investigating the effects of dancing on gait, postural stability, and muscle power in community-dwelling older people. We found that older people who participated in an 8-week progressive salsa dance program significantly increased stride velocity ( $133.8 \pm 20.2$  cm/s to  $148.9 \pm 25.8$  cm/s,  $P < .001$ ), increased stride length ( $136.8 \pm 22.0$  cm to  $145.5 \pm 26.8$  cm,  $P < .001$ ), and decreased stride time ( $1.02 \pm 0.07$  s to  $0.98 \pm 0.07$  s,  $P = .018$ ). Our results confirm findings from a previous study that reported stride velocity of  $135.0 \pm 16.0$  cm/s in 45 healthy older people.<sup>201</sup> The measured decrease in stride time and increase in stride length can be interpreted as an improvement in gait pattern<sup>33,91</sup> and postural stability.<sup>128</sup> However, we did not find any significant changes observed in gait variability measures (i.e. CV of stride time, CV of stride length) after the salsa training program. In contrast, a recent RCT showed that a 6-month JDR intervention significantly improved gait variability (CV of stride length, adjusted mean difference -1.4%, 95%CI -2.3 to -0.6,  $P < .002$ ) in older people.<sup>283</sup> These findings can be explained, at least partially, by the longer intervention duration when compared to our salsa trial. In addition, the higher gait variability measures at baseline (e.g. 2.3% vs. 1.7% CV of stride time) may have offered more range for improvement. Future RCTs need to confirm a possible effect of dancing interventions on spatio-temporal gait parameters and strength measures related to a reduction in fall risk and fall rate.

(e) To date, only a limited number of studies elucidated the association between 25(OH)D concentrations and gait in older people.<sup>144,308</sup> Our study was the first to examine the association

between functional mobility (normal and fast walking objectively measured with an electronic walkway system, and TUG) and serum 25(OH)D concentrations in older patients assessed at a memory clinic. Our findings regarding insufficient serum 25(OH)D concentrations (mean  $63.2 \pm 33.9$  nmol/L) are consistent with those of previous studies in older patients referred to a memory clinic,<sup>309</sup> but below the threshold of 75 nmol/L required for fall and fracture prevention.<sup>310</sup> We found a trend of better functional mobility with higher 25(OH)D quartile status, especially in less frail patients (no previous fall and MMSE  $\geq 26$ ) compared to pre-frail patients (previous fall and MMSE  $\geq 26$  or no previous fall and MMSE  $< 26$ ). These results extend previous findings of a cross-sectional study in older women which showed that only fast but not normal walking speed was significantly associated with higher serum 25(OH)D concentrations ( $< 25$  nmol/L vs.  $> 70$  nmol/L).<sup>144</sup> Our study showed that the entire sample of older patients walked with a mean walking speed greater than 100 cm/s under the normal walking condition which is considered an unimpaired normal walking speed (see chapter 1.6.3).<sup>28</sup> The unadjusted mean of older patients in the highest 25(OH)D quartile ( $> 81$  nmol/L) was 11.0 cm/s faster in normal walking speed, 19.3 cm/s faster in the fast walking speed, and 1.1 s faster in the TUG test compared to those in the lowest 25(OH)D quartile ( $< 39$  nmol/L). These differences in physical performance are clinically important,<sup>165</sup> because results of a prospective cohort study showed that any decrease in walking speed of 10 cm/s is associated with a 7% increased risk for falls.<sup>191</sup> A recent meta-analysis showed that the overall hazard ratio for survival for each 10 cm/s faster walking speed in community-dwelling older people was 0.88 (95%CI 0.87 to 0.90).<sup>28</sup> Further, a TUG score of 14 s or higher is associated with increased fall risk.<sup>234</sup> Older patients in the highest 25(OH)D quartile therefore tend to have a lower fall risk due to faster mean TUG scores compared to those in the lowest 25(OH)D quartile ( $11.8 \pm 3.2$  s vs.  $12.9 \pm 3.2$  s).<sup>234</sup> Future research is needed to establish a causal relationship between the underlying mechanisms of the effect of vitamin D on mobility and spatio-temporal gait parameters in older people.

(f) There is no data available in the literature on spatio-temporal gait data and the comparison of gait alterations in experienced walking aid users during unassisted walking and during walking with a cane, crutch or walker. Our results showed a significantly decreased gait performance in walking aid users when they did not use their walking aid compared to a matched control group (walking speed  $74.4 \pm 19.0$  vs.  $110.3 \pm 20.5$ , CV of stride time  $3.5 \pm 1.7$  vs.  $2.3 \pm 1.0$ , CV of stride length  $5.3 \pm 3.0$  vs.  $3.0 \pm 1.5$ , all  $P < .001$ ). When the walking aid was used, the walking ability within each of the three walking aid groups improved significantly. These findings are generally consistent with those of previous studies, demonstrating that experienced walking aid users can improve gait performance after they practiced walking with a walking aid.<sup>311</sup> In contrast, a small study with older people showed that novice use of walking aids may not affect walking performance compared to unaided walking.<sup>312</sup> Further, a recent observational study reported that older people prefer to choose the appropriate type of walking on their own.<sup>313</sup> Our results suggest that a cane is the most popular walking aid, probably due to its easy maneuverability and social acceptance.<sup>314</sup> However, a cane is rarely efficiently used<sup>314</sup> which is important for safety reasons, because using a walking aid incorrectly may increase the risk of falls.<sup>313</sup>



Future research is needed to determine which type of walking aid optimally affects gait in older people with mobility impairments.

g) Several studies examined the effect of ginkgo biloba on the conversion rate from MCI to dementia. In a large study with 3,069 older people (cognitive healthy and MCI), ginkgo biloba (240 mg/d) was not effective in reducing the incidence rate of dementia.<sup>269</sup> Recently, a large randomized placebo-controlled trial with ginkgo biloba (240 mg/d) also did not show any reduction in the risk of progression from MCI (memory) to AD in older people aged 70 years and older.<sup>315</sup> Although these findings suggest that ginkgo biloba may not benefit the treatment of dementia, there is evidence that long-term intake of ginkgo biloba can improve executive function and attention.<sup>316</sup> As discussed in chapter 1.8.6, executive function and attention properties are required for motor control and walking.<sup>30,195,203,229</sup> Previous research about ginkgo biloba and gait predominantly focused on patients with peripheral arterial disease<sup>317</sup> and intermittent claudication.<sup>318</sup> To the best of our knowledge, there is no data available in the literature about ginkgo biloba and its effect on gait performance (i.e. walking speed or gait variability) in older people suffering from cognitive decline. Similar to our current study, there is one other randomized controlled double-blind trial currently examining the effect of ginkgo biloba on mobility in older people with MCI.<sup>215</sup> However, results for both trials have not been published yet.

## **2.3 Important aspects regarding our research findings**

### **2.3.1 Characteristics of older people**

Older people are not a homogenous group, and individual diversity increases with age.<sup>10</sup> As a consequence, the ideals of active aging might not be achievable for all older persons, particularly if they have complex comorbidities or severe cognitive impairments.<sup>319</sup> However, older people should never be discriminated because of their health status,<sup>319</sup> and always receive the most appropriate therapeutic treatment.

It is in the responsibility of the older people to try and maintain or increase physical activity and exercise<sup>218</sup> to keep functional abilities.<sup>289</sup> Engagement in regular exercise and physical activity, undertaking exercises as prescribed, and continuing to practice after completing a course or intervention are imperative for a positive effect on health outcomes.<sup>10,280</sup> However, a major limitation of such public health efforts are low rates of participation<sup>5</sup> and dropout rates around 27%.<sup>320</sup> To improve adherence to a therapeutic intervention, established principles of behavioral change should be integrated including social support of partners, regular performance feedback, and positive reinforcement.<sup>286,321,322</sup> Additionally, the type of exercise or physical activity is crucial, whereas interventions with music, rhythmic, and dance components seem especially suited for older people.<sup>171</sup> Furthermore, public policies and proven prevention strategies that are tailored to the old people are essential for the successful integration of fall-prevention evidence into practice.<sup>10</sup> Although fall

prevention interventions can be successfully translated from research into clinical practice,<sup>323</sup> the implementation of fall prevention programs depends highly on the request of older people. In older people fall prevention advice is regarded as useful, but often thought to be only relevant for more disabled older people.<sup>80</sup> If older people do not adhere closely to a fall prevention program, the most effective intervention remains useless.<sup>324</sup> Falls prevention should therefore include the consideration of older people's preferences to encourage intervention uptake, and identification of strategies to enhance intervention sustainability.<sup>77</sup>

### **2.3.2 Fall-related outcomes**

A major problem in fall research is the inconsistency in definition and reporting of falls.<sup>325</sup> Assessment of a fall is often subjective, self-reported, research-oriented, and requires extensive interviewing, therefore allowing differences for each study setting.<sup>36,82</sup> In addition, (non-injurious) falls in older people are commonly not reported due to fear of social consequences (e.g. referral to a nursing home),<sup>110,326</sup> and thus never attract the attention of a health care professional.<sup>40,82</sup> Older people also may forget a fall incidence and/or they tend to have different definitions of a fall than clinical researchers. As a consequence, a substantial number of falls is likely unreported, and the interpretation of fall-related outcomes remains difficult.<sup>82,325</sup> Despite differences in study populations, fall definitions, and fall recall, fall-related studies in older people provide useful insight in the etiology of falls.<sup>36</sup> The use of new technologies (e.g. body-worn sensors)<sup>307</sup> may be the next step solving several of these aforementioned problems in fall assessment.

Previous research showed that falls prevention interventions vary widely in terms of population setting, adherence, intervention, number of falls, cognitive status, and method of reporting falls,<sup>85,279</sup> because detailed measurements of outcomes are often expensive, invasive (i.e. blood profile), or require a high degree of expertise.<sup>45</sup> This frequently results in descriptions of interventions which do not provide sufficient details to permit evaluation of how an intervention may have affected fall risk or fall rate.<sup>279</sup> As a consequence, impact of therapeutic interventions (i.e. drug trials or exercise programs) cannot conclusively be evaluated and comparing results from different studies is complicated.<sup>81,86</sup> In this context a particular issue relates to the highly variable and difficult to interpret measures of therapeutic interventions.<sup>28</sup> Numerous methodological issues, including the use of different study populations, lack of clarity and consistency in definitions, variability in periods of follow-up, and the inevitable difficulties of retrospective recall of events<sup>106</sup> represent a challenge to effectively directing an intervention to improve mobility and functionality in older people.<sup>187</sup> In addition, the dose-response relationship needed to justify and refine exercise guidelines, particularly of exercise programs including cognitive health outcomes (e.g. in a multifactorial program), and the adoption of programs for specific populations (e.g. male gender, ethnic minorities, older people with low socioeconomic status), are substantially understudied.<sup>327</sup> Future research needs to address these problems to develop sustainable long-term interventions for older people.<sup>6,325</sup>

### **2.3.3 Potential for improvement in gait analysis**

Gait analysis becomes increasingly important for functional mobility assessment. However, a priority in gait analysis remains the understanding of normal gait due to a wide range of age groups, body geometry, and gender proportions.<sup>16</sup> In older people it is particularly difficult to distinguish normal from abnormal gait,<sup>16</sup> because even in healthy older people, some decline in gait performance is inevitable.<sup>188</sup> Although there is no consensual agreement on the definition of normal gait, normative and population-based data provide insight about the expected magnitude of certain gait parameters.<sup>188</sup> Another issue is the limited knowledge about meaningful change of spatio-temporal gait parameters (i.e. gait variability) in therapeutic interventions.<sup>196,328</sup> Future research will be required to determine normal gait and define criteria for effective gait change in different populations.<sup>165</sup> Addressing these issues will increase comparability between studies (i.e. normalization of gait and taking potential confounders into account),<sup>205</sup> and help to implement gait analysis into clinical practice.<sup>165</sup>

Despite some evidence in the literature the exact number of steps or strides required for a representative measurement of spatio-temporal gait parameters has not yet been determined.<sup>210,225</sup> Measuring a small number of steps or strides may not be accurate when measuring spatio-temporal gait parameters, and if the data is not measured reliably, the data may not be valid and meaningful.<sup>176</sup> Future research is needed to define standards and reference values in terms of how many strides have to be measured.<sup>24</sup> In terms of the applied walking tests, instructions given to the older people are often not specified in the literature.<sup>185</sup> Particularly, more information about the nature of dual tasks, in terms of instructions with specific task prioritization or emphasis to a single task would be needed.<sup>241</sup> Currently, there is no consensus on which additional attention-demanding task is most appropriate,<sup>116</sup> and optimally causes interference<sup>229</sup> in different older populations.<sup>84</sup> As a possible solution, a recent study suggested to improve validity by adjusting dual task performance relative to single task ability.<sup>229</sup> Nevertheless, more standardization regarding dual task gait analysis is required to improve comparability between gait laboratories and studies. Another important aspect in the field of gait and fall prevention research are gender differences.<sup>212</sup> Several factors that may differ between gait in men and women are still to be elucidated for optimization of gait analysis and effectiveness of therapeutic interventions.<sup>212</sup> Men appear to walk faster, with longer stride lengths, lower cadence, and greater stride times, swing times, stance times, and double support times compared to women.<sup>17,188</sup> However, gender differences in spatio-temporal gait parameters need further evaluation, particularly under dual task conditions,<sup>212</sup> in order to detect possible deficits and optimize gait and fall prevention interventions.

### **2.3.4 Difficulties in research with older people suffering from cognitive decline**

Identifying effective interventions that maintain or improve cognition, especially executive functions, are important to face the epidemic of dementia and related disorders such as fall risk.<sup>209,329</sup> However, a wide variety of outcome measures (whether they stem from physical or cognitive function tests), interventions, age groups, and cognitive impairments make it difficult to define general

recommendations.<sup>218</sup> In addition, a large proportion of older people with cognitive impairment vary largely in regard to their functionality and mobility.<sup>329</sup> At first, an improved operationalization of diagnostic criteria for cognitive decline, particularly in older people with MCI is needed,<sup>248</sup> which would then allow a better determination of dose and outcome in intervention trials of this population. In the search of the optimal interventions for older people suffering from cognitive decline there is increasing evidence for combining motor and cognitive interventions to improve dual-tasking and functional independence.<sup>8,218,330</sup> Performing neuropsychological tasks while walking may improve cognitive components of dual-tasking,<sup>331</sup> while exercise training may improve motor components of dual-tasking in older people.<sup>332</sup> Future research should therefore compare effects of sequentially and simultaneously combined motor and cognitive interventions in older people.<sup>8,330</sup> However, it has to be taken into consideration that older people with severe cognitive impairment may be unable to perform dual tasks properly, thereby increasing measurement error and make drawing conclusions impossible.<sup>174</sup>

### **2.3.5 Vitamin D supplementation for 25-hydroxyvitamin D deficient older people**

Despite a high prevalence of low 25(OH)D concentrations in the older population,<sup>131</sup> no generally accepted criteria for vitamin D deficiency have yet been established.<sup>132,140</sup> This hinders comparison among studies, because universally accepted criteria would be needed to overcome controversy regarding optimal 25(OH)D levels for achieving and maintaining health, gait stability, and fall prevention.<sup>133</sup> In addition, vitamin D supplementation may not uniformly exert a protective effect on muscle function, muscle strength, or physical function that normally occurs with aging,<sup>333</sup> particularly in older people with healthy vitamin D concentrations.<sup>333,334</sup> Muscle function may be improved in older people with deficient 25(OH)D levels, but no increase in fat-free mass, necessary for consistent improvement in strength, could be attributed to vitamin D supplementation.<sup>335</sup> To date, the only effective strategy to maintain or increase skeletal muscle mass and strength during healthy aging therefore remains exercise in form of PRT.<sup>333</sup> Vast literature is available on the relevance of PRT in older people, but uncertainty remains about the optimal type of PRT (e.g. principle of specificity),<sup>2,72</sup> especially in order to improve mobility and prevent falls.<sup>69</sup> In terms of the ideal PRT program, both muscle strength and muscle power should be generally emphasized so that those who are slow can get fast and those who are weak can get strong.<sup>63</sup> However, vitamin D remains a safe, inexpensive, and well-tolerated supplement with a high compliance in older people and positive health outcomes.<sup>131</sup>

### **2.3.6 Conclusion**

The findings presented in my doctoral thesis support the use of gait analysis in the routine clinical assessment of motor and cognitive function in older people.<sup>220,225</sup> Substantial evidence was provided for the probable positive effects of vitamin D, exercise, walking aids, and ginkgo biloba on spatio-temporal gait parameters. However, future research needs to announce which elements of these therapeutic interventions are most effective for improving gait stability in order to prevent falls,<sup>85</sup> and

how these elements are translated efficient, appropriate, and cost-effective into real-life of older people.<sup>7,13</sup> In conclusion, gait impairments and falls can be largely prevented, and older people who tend to walk with an unstable gait pattern or fall frequently may be enabled to walk safer and fall less often.<sup>151</sup>

## VIII. Abbreviations

AChEI	Acetylcholine esterase inhibitors
AD	Alzheimer's disease
ADL	Activities of daily living
bfu	Swiss Council for Accident Prevention
CHF	Swiss franc
CA	California
CI	Confidence interval
cm	Centimeter(s)
cm/s	Centimeter(s) per second
CNS	Central nervous system
Corp.	Corporation
CSF	Cerebrospinal fluid
CT	Computer tomography
CV	Coefficient of variation
d	Day
DE	Germany
DVD	Digital versatile disc
e.g.	exempli gratia (for example)
ff.	Following pages
Hz	Hertz
i.e.	id est (that is)
Inc.	Incorporated
IT	Italy
IU	International unit
JDR	Jaques-Dalcroze eurhythmics
LED	Light emitting diode
Ltd.	Limited
m	Meter(s)
MA	Massachusetts
MCI	Mild cognitive impairment
mg	Milligram(s)
min	Minute(s)
MRI	Magnetic resonance imaging
NL	The Netherlands
nmol/L	Nanomole(s) per liter
OR	Oregon

PA	Pennsylvania
PET	Positron emission tomography
PRT	Progressive resistance training
RCT	Randomized controlled trial
s	Second(s)
SD	Standard deviation
SE	Sweden
SPECT	Single-photon emission computer tomography
SUI	Switzerland
TV	Television
UK	United Kingdom
US	United States
USD	United States dollar
Via	Best Practice Health Promotion
vs.	Versus
25(OH)D	25-hydroxyvitamin D

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## X. Curriculum vitae

### Personal Details

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Last Name	Gschwind
First Name	Yves
Middle Name	Josef
Date of Birth	29/07/1982
Nationality	Swiss

### Academic Qualifications

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08/2009 – present	Doctor of Philosophy (PhD) in Sport Science PhD committee: Prof. Dr. Reto W. Kressig, Prof. Dr. Uwe Pühse, Prof. Dr. Heike A. Bischoff-Ferrari, Prof. Dr. Urs Granacher Faculty of Medicine University Hospital Basel and University of Basel, Switzerland
02/2008 – 01/2009	Master of Exercise and Sport Science Sports Performance Health Faculty Cumberland Campus, Lidcombe NSW The University of Sydney, Australia
10/2005 – 01/2008	Master of Science in Exercise and Health Sciences Prevention and Rehabilitation Faculty of Medicine Institute of Exercise and Health Sciences University of Basel, Switzerland  2008 Award for the Best Master's Thesis Graduate School of Sport Science Cleven Becker Foundation, Germany
10/2002 – 07/2005	Bachelor of Science in Exercise and Sports Sciences Major in Physical Education Major in Exercise and Health Sciences Faculty of Medicine Institute of Exercise and Health Sciences University of Basel, Switzerland
08/1998 – 06/2002	High School Humanistisches Gymnasium am Münsterplatz Major in Spanish Basel, Switzerland

## Professional Experience

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03/2009 – present	Research fellow (100%) Basel Mobility Center, Department of Acute Geriatrics University Hospital Basel, Switzerland
07/2008 – 12/2008	Research assistant (50%) Prince Of Wales Medical Research Institute Falls Balance and Research Group, Professor Stephen Lord, DSc Sydney, Australia
11/2007 – 12/2007	Internship at the Swiss Olympic Association (100%) Organization of the 2 <sup>nd</sup> Youth Sport Session Department of Education. House of Sport, Bern, Switzerland
10/2006 – 01/2008	Exercise instructor for older people (1 lesson per week) Retirement home 'Im Brühl'. Aesch, Switzerland
10/2005 – 01/2008	Health and fitness instructor (20-50%) Joggeli Fitness Club, Town Sports PLC. Basel, Switzerland
08/2004 – present	Exercise instructor for older adults (2 lessons per week) Sports Club of University Graduates est. 1931. Basel, Switzerland
08/2003 – 01/2008	Physical education teacher (approx. 100 hours in total) High school and secondary school level. Basel/Mumpf, Switzerland
04/2001 – 09/2005	Customer service (20-40%) Athleticum Sportmarkets. Basel, Switzerland

## Memberships

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09/2010 – present	Swiss Society of Sport Sciences (SGS)
05/2009 – present	Golden Key International Honours Society
08/2006 – present	International Olympic Academy Participants Association (IOAPA)
04/2005 – present	Swiss Snowsports Association (Instructor)

## Language Skills

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German	Native language
English	Proficient oral and written skills
French	Advanced skills
Spanish	Advanced skills
Italian	Basic skills

## PhD Lectures

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### Summer Semester 2012

2 ECTS Applied Statistics with “R”, Dr. Gilles Dutilh, Faculty of Psychology, University of Basel

### Winter Semester 2011/2012

4 ECTS PhD School in Rehabilitation Research 2011, Prof. Dr. Bength H. Sjölund,  
University of Southern Denmark

### Summer Semester 2011

4 ECTS Seminar: Statistics and SPSS, Dr. Erin Gerlach, Institute for Sport und Sport Sciences,  
University of Basel

1 ECTS Seminar: Biomechanics, Motion Analysis, Biocalorimetry and Clinical Research,  
Prof. Dr. Niklaus F. Friederich, Faculty of Medicine, University of Basel

### Winter Semester 2010/2011

2 ECTS Theory Seminar: Functional Neuroanatomy and Developmental Psychology,  
Prof. Dr. Pasquale Calabrese, Faculty of Psychology, University of Basel

1 ECTS Lecture: Main Features of Hospital Pharmacy and Clinical Pharmacy,  
Prof. Dr. Stefan Mühlebach, Department of Pharmaceutical Sciences,  
University of Basel

1 ECTS Seminar: Current Topics in Epidemiology and Public Health, Prof. Dr. Marcel Tanner,  
Swiss Tropical and Public Health Institute, University of Basel

### Summer Semester 2010

1 ECTS Colloquium: Scientific Paper Writing, Dr. Karen Thorpe,  
Department of Environmental Sciences, University of Basel

1 ECTS Mixed Methods Research and Evaluation, Prof. Dr. Manfred M. Bergman,  
Swiss School of Public Health, University of Basel

2 ECTS Seminar with Exercises: Applied Statistics I and II, Faculty of Psychology,  
Dr. Andrea H. Meyer, University of Basel

2 ECTS Lecture with Exercises: Statistics II – Inductive Statistics, Lic. rer. reg. Rainer Volman,  
Department of Human Geography, University of Basel

### Winter Semester 2009/2010

3 ECTS Seminar Statistics, Dr. Carmine Maiello, Research and Study Center for Pedagogies,  
University of Basel

## Publication List

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### Peer-reviewed Journal Articles

Gschwind YJ, Bischoff-Ferrari HA, Bridenbaugh SA, Haerdi I, Kressig RW. Association between serum vitamin D status and functional mobility in memory clinic patients Age 65 and older. *J Am Geriatr Soc*; submitted.

Haerdi I, Bridenbaugh SA, Gschwind YJ, Kressig RW. The effect of three different types of walking aids on spatio-temporal gait parameters in community-dwelling older adults. *Aging Clin Exp Res*; in review.

Granacher U, Muehlbauer T, Bridenbaugh SA, Wolf M, Roth R, Gschwind YJ, Wolf I, Mata R, Kressig RW. Effects of salsa dance training on balance and strength performance in older adults. *Gerontology* 2012;58:305-12

Wolf I, Bridenbaugh SA, Gschwind YJ, Kressig RW. Gait changes and fall risk. [Article in German]. *Praxis* 2012;101:1631-7.

Gschwind YJ, Wolf I, Bridenbaugh SA, Kressig RW. Basis for a Swiss perspective on fall prevention in vulnerable older people. *Swiss Med Wkly* 2011;141:w13305

Gschwind YJ, Bridenbaugh SA, Kressig RW. Gait disorders and falls. *GeroPsych* 2010;23:21-32.

### Non-peer-reviewed Journal Articles

Gschwind YJ, Bridenbaugh SA. Early detection of dementia and fall risk – the role of gait analysis. [Article in German]. *Der informierte Arzt*. 2011;6:39-41.

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### Research Reports

Gschwind YJ, Pfenninger B. Exercise for fall prevention. Manual for strength and balance exercises for fall prevention in older people. [Report in German]. Swiss Council for Accident Prevention (bfu). bfu-Fachdokumentation 2.104, Bern 2012, in print.

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## Publication List (continued)

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### Book Chapters

Gschwind YJ, Bridenbaugh SA, Kressig RW. Falls in older people. In: Likar R, Janig H, Schippinger W, Kada O, Cernic K, Pinter G (eds.). Strategies and concepts for the geriatric emergency care. [Book in German]. Vienna: Springer Verlag; submitted.

### Media Activities

Monsch AU, Langenegger S, Gschwind YJ. Alzheimer's disease. [Broadcast in German]. Gesundheit Sprechstunde, ed. Käch R, Swiss National Television (SF), broadcasted 31/03/2012.

Karpf C, Schlögl M, Bridenbaugh SA, Wolf I, Gschwind YJ. Eurhythmics helps older people to prevent falls. [Broadcast in German]. 7vor7 News, ed. Keller E, TeleBasel, broadcasted 19/09/2010.

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## Conferences and Courses

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### Presentations

Gschwind YJ. Fall prevention – what does really work? [Presentation in German]. Presentation at the 'Prevention and health promotion in older people: update 2012'. Nursing home Baar and Pro Senectute Canton Zug. Nursing home Baar. Baar, Switzerland, 14/11/2012.

Gschwind YJ. Best Practice – Fall prevention in older people. [Presentation in German]. Presentation at Old Age in the Course of Time Congress 2012. Swiss Society of Gerontology. University Miséricorde Fribourg. Fribourg, Switzerland, 02-03/02/2012.

Gschwind YJ, Wolf I, Bridenbaugh SA, Kressig RW. Mobility and functionality assessment in daily life. [Presentation in German]. Workshop at medArt Basel 2011. University Hospital Basel. Basel, Switzerland, 22/06/2011.

Gschwind YJ, Wolf I, Bridenbaugh SA, Kressig RW. Best Practice Health Promotion for older people. [Presentation in German]. Workshop at the 1<sup>st</sup> Network Congress Best Practice Health Promotion for Older People. Health Promotion Switzerland. Bern, Switzerland, 08/03/2011.

Gschwind YJ. Ginkgo trial. Movement Progress Report. Laboratory of Biomechanics and Biocalorimetry (LOB<sup>2</sup>) Basel. University of Basel. Basel, Switzerland, 14/04/2011.

Gschwind YJ, Kressig RW. Can Ginkgo improve MCI-related walking disorders? Study protocol presented at 3<sup>rd</sup> Young Researchers' Meeting. Alzheimer's Disease Forum Switzerland. Interlaken, Switzerland, November 19-21/11/2010.

Bridenbaugh SA, Gschwind YJ, Kressig RW. The fracture of a geriatric patient – more than broken bones! Presentation at the 5<sup>th</sup> General Meeting of AOTrauma's CPP Fracture Fixation in Osteoporotic Bone (Med Academy). University Hospital Basel. Basel, Switzerland, 25/03/2010.

### Poster Sessions

Gschwind YJ, Wolf I, Bridenbaugh SA, Kressig RW. Swiss perspective on fall prevention in pre-frail older people. Poster presentation at the PhD School in Rehabilitation Research 2011. University of Southern Denmark. Copenhagen, Denmark, 06-09/12/2012.

Gschwind YJ, Wolf I, Bridenbaugh SA, Kressig RW. Swiss perspective on fall prevention in pre-frail older people. Poster presentation at the Swiss Public Health Conference 2011. Public Health Switzerland. Basel, Switzerland, 25-26/08/2011.

### Selected Courses

Clinical Investigator Course. Good clinical practice, study implementation and study protocol (participant). Clinical Trial Unit (CTU), Study Coordination Centre, University Hospital Basel. Basel, Switzerland, 17-18 and 25/03/2010.

4<sup>th</sup> European GAITRite Meeting. Clinical applications of spatial and temporal gait analysis (organisation assistant and participant). Basel Mobility Center, University Hospital Basel. Basel, Switzerland, 24-26/09/2009.