DUAL-TASK WALKING PERFORMANCE: RELATIONSHIP TO STROKE CHARACTERISTICS

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ABSTRACT

Background: Previous work suggested that outdoor walking is one of the top concerns among community-dwelling stroke individuals. And most outdoor mobility activities involve dual-tasking. When a cognitive task was imposed during walking, there may be degradation of performance of the walking or/and the cognitive task, in a phenomenon called dual-task interference. How the extent and pattern of dual-task interference is influenced by component task complexity and stroke characteristics remain understudied.

Objective: To examine (1) how complexity of the component tasks influence dual-task cognitive and mobility performance in individuals with chronic stroke; (2) the association between dual-task performance and stroke characteristics (location of lesion, severity); and (3) the association between dual-task performance and satisfaction with community reintegration.

Study design: This was a cross-sectional study. Individuals with chronic stroke were tested on various combinations of dual-task conditions during walking.

Main outcome measure: Participants were classified to two groups: cortical involved stroke and subcortical stroke based on their CT or MRI reports. The severity of cognitive deficit was measured by Montreal Cognitive Assessment (MoCA) and Wisconsin Card Sorting Test (WCST). Mini-Balance Evaluation System Test (Mini-BESTest) and Fugl-Meyer Assessment (FMA) were used to test the balance and motor control deficits. The Reintegration to Normal Living Index (RNLI) was used to quantify the degree of satisfaction with community reintegration after stroke. The dual task protocol used in this study involved a combination of the mobility task and cognitive task. The former had two different complexity levels [low: walking on level ground (LGW) for 1 minute vs. high: obstacle crossing walking (OBW) for 1 minute]. Four aspects of gait performance were measured: velocity (distance, stride length, stride time),

variability (stride length and stride time variability), asymmetry (stride velocity asymmetry) and postural stability (peak frontal trunk velocity).The cognitive component task used in the testing protocol was a serial subtraction task which also had 2 levels of complexity [low: serial subtraction by three (SS3) vs. high: serial subtraction by seven (SS7)].

Results: Eighty participants [44 men; mean (SD) age: 62.2 (6.5)] were included in the final analysis, with 27 cortical involved stroke and 53 pure subcortical stroke individuals. The cognitive performance, and velocity related gait parameters (walking distance, stride time, stride length) under DT conditions deteriorated significantly when comparing with the respective values in the single-task condition ($p<0.01$). On the other hand, compared with single-task walking, better postural stability (i.e., smaller peak frontal trunk velocity) was observed under DT conditions ($p<0.01$). Also, the increased difficulty level of the mobility task (level ground walking vs obstacle crossing) among DT conditions did not change the cognitive performance significantly. Likewise, the increased complexity level of the cognitive task (SS3 vs. SS7) also did not impact the gait performance significantly. Overall, there was no significant difference in DT gait and cognitive performance between cortical involved stroke and subcortical stroke group ($p>0.05$). Negative associations were found between stride length during DT walking and perseverative errors (%) on the WCST ($p<0.05$). Lower MoCA scores were significantly associated with poorer DT cognitive performance as measured by the correct response rate (NCR). Lower Mini-BESTest and FMA scores were associated with poorer DT gait performance. Finally, poorer DT performance was associated with lower RLNI scores.

Conclusion: Significant dual-task interference occurred in individuals with chronic stroke, when a serial subtraction task was imposed during walking, regardless of the difficulty level of the component tasks used. Those who have more severe motor and cognitive deficits tended to have poorer DT performance, which in turn was related to lower level of satisfaction with community reintegration.

PUBLICATIONS

A. Peer-reviewed journal articles

1. Chan, A. C., Pang, M. Y., Ouyang, H. and Jehu, D. A. (2019), Minimal clinically important difference of four commonly used balance assessment tools in individuals after total knee arthroplasty: A prospective cohort study. *Journal of Injury, Function and Rehabilitation.* Accepted Author Manuscript. doi:10.1002/pmrj.12226

2. Pang, M. Y. C., Yang, L., Ouyang, H., Lam, F. M. H., Huang, M., & Jehu, D. A. (2018). Dual-Task Exercise Reduces Cognitive-Motor Interference in Walking and Falls After Stroke: A Randomized Controlled Study. *Stroke*, 49(12), 2990-2998.

3. Chan, A. C., Ouyang, X. H., Jehu, D. A., Chung, R. C., & Pang, M. Y. (2018). Recovery of balance function among individuals with total knee arthroplasty: Comparison of responsiveness among four balance tests. *Gait & posture*, 59, 267-271.

B. Conference Abstract

1. Ouyang HX., Pang MYC. The relationship between stroke location, executive function, motor task complexity and dynamic stability under dual task walking. *Hong Kong Physiotherapy Association Conference*, 25 May 2019, Hong Kong

2. Ouyang HX., Pang MYC. The relationship between stroke characteristics, task complexity and dual task walking performance. *Asian Confederation for Physical Therapy Congress*, 25 November 2018, Philippines.

3. Tsang C., Ouyang H X., Jehu DAM., Pang YCM. Dual task walking speed is predictive to falls in individuals post-stroke. *Hong Kong Physiotherapy Association Conference*, 8 October 2018, Hong Kong.

4. Chan CMA, Jehu AMD, Ouyang HX, Pang YCM. Minimal clinically important difference of four commonly used balance assessment tools in individuals after total knee arthroplasty. *Hong Kong Physiotherapy Association Conference*, 28 October 2017, Hong Kong.

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10. LIST OF ABBREVIATIONS

ADL	activities of daily living
ANOVA	analysis of variate
BG	basal ganglia
COM	center of mass
COP	center of pressure
CMI	cognitive-motor interference
DT	dual task
FMA	Fugl-Meyer Assessment
GRF	ground reaction force
HRQOL	health-related quality of life
LGW	level ground walking
LR	loading response phase
Mini-BESTest	Mini-Balance Evaluation System Test
MoCA	Montreal Cognitive Assessment

NCR	number of correct response
OBW	obstacle crossing walking
Q1/ Q3	25% quantile/ 75% quantile
RNLI	Reintegration to Normal Living Index
ST	single task
SS	serial subtraction task
SS3	serial subtraction by three
SS7	serial subtraction by seven
VF	Verbal Fluency Tasks
WCST	Wisconsin Card Sorting Test

11. Supplementary information (Outliers detection and conversion)

1. Chapter 1 introduction

1.1 Epidemiology of aging population

Unprecedented socioeconomic development, great improvements in survival rates at young ages in developing countries [1], and a reduced mortality rate among the elderly in developed countries [2] have allowed the life expectancy of most people to reach the 60s or above [3]. A recent report from the World Health Organization [4] noted that Japan's proportion of elderly people (≥60 years) exceeded 30% in 2015, and this proportion will approach 25% in most countries by 2050. Meanwhile, populations are aging much more quickly than ever before. The proportion of elderly people in China increased from 10% to 20% within only 20 years, whereas this increase took 150 years in France. The greater pace of this trend requires more efficient and effective measures to deal with its consequent challenges.

Increasing age is often accompanied by subtle impairment of bodily functions at various levels (e.g., molecular or cellular) [5, 6]. As time progresses, these subtle impairments may accumulate to result in more obvious adverse symptoms, an increasing vulnerability to environmental challenges, and an increased risk of various diseases. A recent study showed that each day, 10,000 people in the United States turn 65 years old, and 80% of them have at least one chronic disease [7]. Although developing countries have seen a reduction in disability related to infectious disease, they have seen an increasing trend of physical and mental limitations [4]. There has also been a marked increase in disability related to cerebrovascular disease in China [8].

1.2 Stroke — a high risk disease in aging populations

Stroke, also known as brain attack, occurs in two situations: 1) when a brain blood vessel bursts or 2) when a clot blocks the brain's blood supply. Because the population is aging, stroke will continue to be an important public health concern [9]. From 1990 to 2013, the incidence of stroke and the number of survivors increased significantly in both men and women [10-12].

1.2.1 Epidemiology of stroke

Many studies have shown that although the mortality rate for age-specific stroke has decreased globally over the past 20 years, the number of people who had a stroke still rose dramatically from 1990 to 2013 [9, 12-14]. In 2013, nearly 25.7 million people were living post stroke (71% ischemic), of whom 10.3 million were new cases (one third ischemic), and 6.5

million stroke victims did not survive (half ischemic) [15]. It is predicted that 23 million new stroke incidents will occur by 2030 [16]. Furthermore, the increased number of strokes in younger people (<65 years) has caused additional concern [9, 12-14].

In the United States, 795,000 strokes occur each year, including 610,000 new strokes and 185,000 recurrent strokes [17]. More specifically, each year from 1997 to 2016, about 8% of people at 65 years and older experienced a stroke [11]. Stroke is also a major cause of death in the United States (about 140,000 per year) [18]. Stroke is also a serious public health issue in Hong Kong, with more than 24,000 strokes reported yearly, and 90% of stroke patients surviving [19]. Not only is stroke a major global cause of premature death (i.e., <60 years), it is also a major cause of disability in this group [4].

1.2.2 Functional factors related to individuals after stroke

The increasing survival rate after stroke has translated into an increased number of stroke survivors living in the community. Stroke has thus become a major cause of disease burden. It often leads to a wide range of long-term disabilities, including physical limitations, psychosocial disorders, and cognitive deficits [20]. It is reported that about 2.5% of people have stroke-related disabilities and that more than 50% of elderly people (>65 years) with stroke have a mobility deficit [17].

1.2.2.1 **Physiology of typical gait**

1.2.2.1.1 Neural control of normal gait

Locomotion in humans is based on vertical body support, lateral and forward stability, and forward propulsion [21-23]. While walking, each individual joint movement interacts dynamically with other parts of the kinematic chain [23], and the whole body movement during walking results from the interplay between the neural and musculoskeletal systems [24].

Walking requires muscle synergy [25, 26]. There is co-activation and coordination across multiple muscles as a fixed pattern in each module. Multiple modules are involved in balance control [27] and walking [28-30]. Notably, gait and reactive balance control share a set of muscle modules [31].

Adequate prior postural stability is a prerequisite for locomotion [32, 33]. The trunk and lower extremity extensors mainly support the vertical antigravity posture. Under the regulation

of the cerebellum, support and balance control are mainly controlled by the pontomedullary reticular formation and the vestibular nuclei in the brainstem [22, 34-39]. The pontomedullary reticular formation also activates the spinal rhythmic network [22, 35, 39, 40]. In mammals, locomotor rhythm and pattern generation are controlled by spinal central pattern generators [41]. However, in humans evidence shows that rhythmic patterns, such as the activation coordination between antagonist muscles, are produced by modularly organized motor neuron pools, which are driven by spinal locomotor pattern generators [42]. During volitional locomotion, cortical modulation [43, 44] of the brainstem and the spinal network [43, 45-47] largely control the relevant motor modules. The initiation of locomotion requires activation of various cortical areas that project to the brainstem and spinal cord [40, 48], after which locomotion is usually achieved without conscious awareness. In contrast, the premotor cortices will be involved in intentional gait modification under obstacle-crossing conditions [40]. The cerebellum connects the cerebral cortex and the brainstem to regulate volitional and automatic processes, likely by receiving and integrating the signals from both [22, 38, 40]. Furthermore, locomotor adaptation and learning processes are highly associated with the cerebellum [22, 38]. The basal ganglia (BG) is also responsible for the volitional and automatic walking processes by receiving inputs from the cerebral cortex and projecting to both the cortex and the lower motor pathway [40, 49]. In summary, simple walking should be a result of automatic processes, which has advantages over cognitive processes that require attention [50, 51].

1.2.2.1.2 Biomechanical description of gait

The biomechanical characteristics of gait in healthy people are usually repeatable and generally include two stages: the stance stage and the swing stage [52]. Taking the leading leg as an example, the stance stage has five subphases: 1) initial contact (heel strike), 2) loading response (foot flat), 3) mid-stance (single leg supporting), 4) terminal stance (heel off), and 5) pre-swing (between heel off and toe off). The swing phase has three subphases: 1) initial swing (toe off), 2) mid-swing (contralateral single leg supporting), and 3) terminal swing (heel strike). Various muscles are activated in these subphases. During the loading response phase (LR), the lower limb extensors (i.e., the hip and knee joints) help with shock absorption and inhibit the trunk's forward momentum with sagittal deceleration. In the late LR phase after the foot becomes flat, the plantar flexors further account for restraining the trunk's forward momentum [53]. During the transition to single-leg support, the ground reaction force (GRF) from the

anterior direction and calf stabilization of the tibia provide the knee extension stability. During the mid-stance phase, the plantar flexors contribute to support the body weight and forward progression. During the pre-swing phase, the further contractions of the plantar flexors generate the momentum to push off. Next, the low activation of hip flexion muscles advances the limb to swing. The ankle dorsiflexors help foot clearance in the preparation and initiation of swing phases, and they decelerate foot drop during the terminal swing and LR phases.

At optimal speed, energy is saved by transferring vertical momentum from gravity to forward kinetic momentum during the late stage of stance [54] and with a special swing trajectory [55]. The metabolic cost occurs mainly in the redirection of the center of mass (COM) during the transitions between consecutive steps [56] and leg oscillation during the swing phase [57]. Mechanical asymmetry between the two legs during step-to-step transitions can impair metabolic optimization [58, 59].

1.2.2.1.3 Gait adaptability

In daily life, the ability to adjust gait and adapt to various external walking environments and internal functional states is essential. For example, to guarantee safety on a slippery floor, our body reduces the shear stress and increases friction with the ground by adjusting our muscle stiffness, step length, LR phase duration, and toe grip [24, 60, 61].

1.2.2.2 Mobility deficits after stroke

Gait deficits are common in stroke survivors who have a peripheral motor control deficit and impairment of central regulation.

1.2.2.2.1 Neural control of post-stroke gait

Muscle weakness and voluntary motor control deficit are two pronounced symptoms post stroke [62, 63].

1.2.2.2.1.1 Stroke location and neural adaptation

Generally, there are two levels of stroke based on location: cortical and subcortical. Of ischemic strokes, 4-16% are in brainstem, of which 54% are in the pons, 28% in the medulla, and 14% in the midbrain [64]. The dorsal pons and medulla, which contain the pontomedullary reticular formation and the vestibular nuclei, are rarely impaired (10%) [65-69]. About 2-6% of ischemic strokes occur in the cerebellum [70, 71], where medullary infarction is common [65,

67]. To note, about 90% of strokes do not involve the brainstem or cerebellum, which modulate the automaticity of gait [72]. Another phenomenon is that various stroke locations (motor cortex, basal ganglia, frontal and parietal cortex, descending motor pathways) can lead to similar patterns of motor deficit [73], which suggests that multiple levels of the motor system control a small portion of the related motor components [74, 75].

Among the important mechanisms of gait alteration are neural adaptive processes, such as compensation [76]. As mentioned in previous work, the cerebellum, which is involved in the adaptive process, is not usually affected by stroke. After a stroke, the brain activation pattern also experiences gradual change. During the acute stage, walking-induced activation is in the contralesional cortex, and then it gradually transfers to normal ipsilesional activation [77]. The unaffected hemisphere was found to have an increased fiber volume in the corticoreticular pathway [78].

1.2.2.2.1.2 Muscle weakness and spasticity

Disruption of the corticospinal tract, without direct injury to the peripheral neuromuscular system or spinal cord, contributes to post-stroke muscle weakness [73], and this common symptom primarily contributes to post-stroke motor deficit.

During a long recovery, voluntary motor control improvement is often accompanied by spasticity and stereotyped movements. Specifically, within the first month post stroke, about 4-27% individuals have spasticity, whereas the prevalence of spasticity increases to 17-43% after 3 months post stroke [79]. However, debate persists regarding the influence of spasticity on gait patterns after stroke [80-82]. Altered mechanical muscle fiber properties such as increased resistance to joint movement contribute more to walking disorders than abnormal reflexes [81]. The unilateral nature of vestibule-spinal pathways may be highly associated with the distinct lateralization of abnormal muscle tone (i.e., hypertonia and spasticity) after a stroke, especially the antigravity muscle groups [83].

Both voluntary and automatic processes can activate paretic muscles. Whereas spastic dystonia is triggered by tonic muscle stretch, spastic co-activation is triggered by volitional command [84]. In stroke individuals, muscle co-activation is especially frequent in both legs while walking [85], perhaps as a compensatory strategy to adapt to impairment in balance during

step-to-step transition [85-87]. Muscle co-activation does not hinder the maximum walking speed increase [88], whereas it is related to a higher energy cost [87].

1.2.2.2.1.3 Muscle coordination in modular organization

Walking is generated by muscle coordination with modular organization. In normal walking, four modules of the leg are activated during walking [75]. Post-stroke walking causes a reduction in modules activated during walking; only 58% of unaffected legs activated all four modules, and 45% and 36% of affected legs activated two to three modules, resulting in slower walking speed, greater step length asymmetry, and reduced propulsion [75]. The prevalence of existing modules merging may improve the automaticity of body support, especially on the hemiplegic side [31]. However, the interference between subtasks (i.e., weight acceptance and propulsion impulse) caused by abnormal extensive modules leads to poor walking performance (i.e., poor acceleration generation) [75, 89].

Specifically, to improve body support, frequent muscle synergy from the gluteus medius, quadriceps, and plantar flexors during the stance stage also likely results in greater stiffness of the proximal joints [90, 91]. In contrast, reductions in activation of the tibialis anterior during the stance phase and the plantar flexors during the swing phase [75] lead to an abnormal foot contact pattern [75, 92-94]. Further, the activation timing also changes after a stroke. During the LR phase, early activation of the plantar flexors results in increased ground friction [60], greater deceleration of ankle dorsiflexion [95], and early trunk forward deceleration [53].

1.2.2.2.2 Spatiotemporal characteristics of gait post stroke

Walking function is adversely influenced in about 80% of chronic stroke survivors [96]. The circumduction gait first is attributed to a lack of toe clearance during the swing phase and accompanying compensation adjustment by the hip abductors [97], tilting of the pelvis on the affected side [98, 99], and lateral flexion of the trunk toward the nonparetic side [100]. A typical stroke gait usually includes prolonged knee hyperextension during the loading phase, an insufficient peak knee flexion angle during the swing phase, decreased momentum at push-off, and decreased stability during the stance stage, resulting in poorer automaticity of walking [94, 97, 101, 102]. The gait mode commonly used for stability on a slippery floor has some similarities with the gait pattern seen after a stroke: gentle contact with the ground with a flat

foot, toe grip, one-peak of GRF during the single-leg standing phase, and greater limb stiffness from muscle co-activation [60, 61]. As for trunk kinematics during walking, thoracic rotation exceeded pelvic rotation by 15% in stroke survivors when compared with healthy controls [103]. Coordination between the thorax and pelvis plays some role in gait velocity [103-106]. Furthermore, during level walking, increased trunk frontal excursions are found in individuals post stroke[100].

1.2.2.2.2.1 *Walking speed*

The first aspect of gait deficit after stroke is decreased gait velocity. Post-stroke walking speed ranges from 0.23 m/s to 0.95 m/s [63, 103, 107]. Other studies have shown that although the mean (± SD) walking speed in stroke survivors ranged from 0.39±0.26 m/s to 0.78±0.38 m/s, that in healthy older adults ranged from 1.15±0.21 to 1.40±0.23 m/s [108-112]. The minimum gait speed for smooth community ambulation is 0.8 m/s [113]. Furthermore, both stride length and cadence are reduced after stroke. A significant linear relationship exists between cadence and velocity, with an average speed of 0.33 m/s and a cadence of 90 steps/min, and any further increase results mainly from a stride increase [114]. When compared with healthy elderly, if the speed is above 0.33 m/s, a trade-off is made between cadence and stride length in stroke survivors, with equal or higher cadence and equal or shorter stride length, if the speed is the same for the two groups [115]. When improvement on the Fugl-Meyer scale and the Barthel functional independence index approach a plateau 3 months after a stroke, the gait speed can continue to increase until 18 months [116]. Another study of the kinematic and kinetic variables of gait showed that gait velocity accounts for 41% of the variance, followed by asymmetry between legs (13%) [102].

1.2.2.2.2.2 Asymmetry between legs

The temporal and spatial asymmetry between legs range from 44% to 82% in stroke survivors, with a shorter stance duration and longer swing duration in the affected leg and a shorter step length in both legs at different levels [117-120]. A shorter stance time of the paretic leg often results in a shorter step length with the nonparetic leg [121], and a greater self-selected gait velocity indicates a significantly lower asymmetry ratio (paretic/nonparetic) in stance duration, swing duration, and step length [117, 118, 122]. Even within one leg within the stance stage, the pre-swing phase is longer than the LR phase in the paretic leg [123]. It is surprising

that stride symmetry is not associated with age [124] but shows a positive relationship with stroke duration [125].

The imbalance in mechanical power between limbs can contribute to such asymmetry. Within a gait cycle, decreased push-off during the pre-swing stage and increased braking during the LR phase was generated to decelerate the COM for the paretic leg, whereas greater push-off is generated during the pre-swing stage to accelerate the COM for the nonparetic leg [126].

1.2.2.2.2.3 GRF

Postural stability can be also indicated by the GRF, which is assessed with a force platform. The GRF has three main directions during walking: upward, forward, and backward. The upward GRF for the paretic limb is significantly reduced, and the anterior-posterior component displays greater deceleration than acceleration propulsion [127-129]. The gait velocity is strongly associated with the propulsion of nonparetic deceleration and paretic acceleration [127] resulting from changes in the activity in three leg muscles (i.e., gastrocnemius, tibial anterior, rectus femoris) [130]. Furthermore, about 83% of stroke subjects use either a flat foot or a forefoot to touch the floor, with a reduction in vertical body movement [92-94, 131]. Some evidence has shown that the foot contact pattern (forefoot-, flatfoot-, and heel-initial contact) is highly related to the GRF pattern [94].

In addition, the relative positions of the foot and the COM can also influence acceleration and deceleration [132]. A reduced posterior position of the paretic leg during the pre-swing phase and a longer LR phase duration will reduce the propulsive impulse and increase the braking impulse, respectively [127, 132, 133]. Thus, the insufficient push-off power by lower activity in the plantar flexors decreases not only the gait velocity but also the flexion angle during the early swing phase after a stroke [109, 134, 135].

1.2.2.2.2.4 Balance control

Balance dysfunction, including quiet stance balance and balance control to self-initiated perturbations, is impaired in stroke survivors [136-139]. Reduced and asymmetrical lateral weight transfer speeds (stroke: 3.5-4.3 s; control: 2.6 s) and degrees (stroke, 65-85%; control, 95%) are seen [136, 138]. With respect to muscle activity, stroke survivors demonstrated more muscle onset latencies and disrupted anticipatory muscle activation sequences to both self-

induced perturbations [140] and external perturbations [141-146]. As for postural stability, the distance of the excursion of the center of pressure (COP) of stroke survivors is 1.5 to 5 times that seen in healthy elderly, especially in the frontal plane [147-153]. Another study that examined the kinetic modulation asymmetry index by using the ratio of the COP velocity between two legs revealed that the affected leg contributes about 30% to the total kinetic modulation activity [147]. Based on the ankle joint torques of both legs, Van Asseldonk revealed that the paretic leg helps 11-45% of balance maintenance [154].

Balance disorders after a stroke can be caused by motor disorders, sensory loss, perceptual deficits, and altered spatial cognition. The combination of impaired reactive postural adjustment and anticipated postural corrections with abnormal muscle co-activation contributed mainly to balance deficits. These dysfunctions often originate with cognitive impairments (sensory information integration, etc.) in which the right hemisphere is predominant [155].

The relationship between gait asymmetry and upright stability post stroke is significant [117, 156, 157], especially for weight-bearing on the paretic leg [117, 156]. Specifically, the Berg Balance Scale shows a negative association with step length and swing duration asymmetry [117] because the increased weight-bearing on the nonparetic side was related to an increase in the stance time on this leg, and decreased weight-bearing on the paretic side resulted in a decrease in the swing time on the nonparetic side, resulting in increased asymmetry of these two parameters [156]. These relationships were not attributed to the underlying leg impairment [72].

1.2.2.2.2.5 Gait adaptability

Safe walking in everyday life requires adjustment of one's walking pattern according to various environmental conditions. However, this ability can be severely impaired in stroke survivors. By using a presumed safety strategy to cross obstacles with greater toe clearance of the leading leg, shorter distances after an obstacle, and greater step times [158], stroke survivors still experience higher obstacle contact rates (14-28%) than healthy controls [159-161]. This phenomenon may be due to the increased anterior-posterior separation of the COP and the COM while crossing obstacles, resulting in damaged balance after stroke [162]. Another more specific reason is the delayed muscle initiation latencies (220 ms) in the knee flexors (the prime mover in this task) relative to age-matched control subjects (120 ms) [160, 161]. It is indicated that gait

adjustments while crossing obstacles must involve cognitive control instead of pure automation in stroke survivors [161].

1.2.2.3 *Cognitive deficits*

Cognitive impairment is another factor that causes disability and dependence in stroke survivors worldwide [163].

1.2.2.3.1 **Cognitive category and deficit after stroke**

The five commonly studied domains of cognition are 1) attention to a specific stimulus or task (i.e., focusing, shifting, dividing, or sustaining attention), 2) executive function (planning, organization of thoughts, inhibition, control), 3) visuospatial ability (visual search, drawing, construction), 4) memory (recall and recognition of visual and verbal information), and 5) language (expressive and receptive). However, these domains are not independent in daily life; telling the names of a category, for example, relies not only on verbal information storage and retrieval but also on sustained attention and expressive language skills.

In stroke survivors, several dimensions in various domains are incorporated for certain types of cognitive deficit: neglect (unconscious ignorance to specific direction of space), agnosia (unable to recognize object), apraxia (motor planning disorder), abstract thinking (advanced semantic understanding), and arithmetic. As modifiers, physiologic states and emotions (e.g., fatigue, apathy, and depression) also influence cognitive function.

1.2.2.3.2 Stroke location and volume

Stroke in cortical brain areas is more likely to demonstrate cognitive dysfunction. One study observed that about 80% of cortical stroke survivors had cognitive impairments, whereas subcortical or infratentorial stroke survivors experienced less than 50% of this deficit during the acute stage [164]. In addition to motor coordination, the cerebellum plays a role in cognition [165], as it not only has connections to the brain stem via neuronal circuits but also has many projections to other related brain areas [166]. Although a cerebellar stroke does not cause typical cortical symptoms such as aphasia or neglect [167], people with cerebellar damage (mostly because of stroke) demonstrate impairment in visuospatial ability [168], verbal working memory [169], and across multiple domains (e.g., executive function and abstract reasoning) [170]. The basal ganglia is also involved in cognitive control. Significant abnormalities in memory,

attention, visuospatial ability, and language were found in survivors of a pure basal ganglia stroke [171]. Furthermore, strokes in specific areas of the thalamus cause deficits in long-term memory, executive function, and attention [172]. Even slight but strategically located damage here can contribute to severe cognitive impairment [173].

In general, cognitive impairment tends to appear after strokes with a larger volume of lesions (27 vs. 9 cm^3) [164], but lesion size can only independently predict the recovery of visual memory [174]. Moreover, other studies showed that lesion size was related to the severity of aphasia during the initial stage but not to the degree of recovery in language [175, 176].

When classified by cerebral artery, early studies suggested that cognitive deficits appeared more frequently after infarcts of the anterior and posterior cerebral artery [177] or middle cerebral artery [178] than after those of the vertebrobasilar artery [177]. Other factors, including the stroke side (left) [179], type (hemorrhagic) [164], recurrence [180], and cause (cardioembolic) [181] were related to the subsequent cognitive decline [179].

1.2.2.3.3 Focal neuronal dysfunction

In the clinical setting, aphasia and spatial neglect are the two most common cognitive deficits from a focal brain lesion post stroke [182]. The neural substrate of various categories of aphasia or neglect has been well studied. Although Broca's aphasia is linked to impairment in the left posterior, inferior frontal gyrus, Wernicke's aphasia is associated with a lesion in the left posterior, superior temporal gyrus [183]. As for hemispatial neglect, the right inferior parietal lobule is responsible for the visuospatial component, the right dorsolateral prefrontal cortex is linked to the visuomotor component, and the deep temporal lobe regions are related to the object-centered component [184]. However, it has been argued that disruption in the cortical attentional networks contributes more to reginal neglect than to structural damage [185]. In contrast, it is indicated that executive function is not modulated only in the frontal cortex but is also controlled by a multilevel network that includes cortical, subcortical, and infratentorial areas according to neuropsychological [186] and functional imaging [187] evidence.

1.2.2.3.4 Diffuse neuronal dysfunction

Unlike focal lesions, which can contribute to specific cognitive deficits, diffuse brain damage leads to general slowing of mental processes, memory issues, and executive deficits

[188]. Diffuse dysfunction usually results from subtle pathologic changes, such as white matter abnormalities or small-vessel disease from accumulated subclinical infarcts, before it develops into cerebrovascular disease [189]. A previous study showed that a higher load of white matter hyperintensity had a significant relationship with a deterioration in cognitive function over a four year follow up post stroke [190]. White matter impairment and subclinical infarcts also suggest impaired cognitive performance after a stroke [191]. Specifically, cognitive impairment such as slowed mental processes and impaired attention and executive function shows a correlation with the degree of white matter hyperintensity in the basal ganglia of stroke survivors [192, 193]. Even in brain areas without detectable white matter abnormalities according to conventional magnetic resonance imaging (MRI), the greater sensitivity of diffusion tensor imaging allows it to recognize structural changes related to vascular cognitive impairment [194], specifically in the frontal and parietal regions [195]. In contrast, another study showed that although white matter hyperintensity was related to declines in mental speed, executive function, memory, and visuospatial ability, the regional correlation was relatively weak [196].

1.2.2.3.5 Hypoperfusion

Focal and diffuse deficits are both related to decreased blood flow in adjacent tissue, which combine with the infarction itself to contribute to focal cognitive deficits after ischemic stroke. Aphasia and neglect are linked more to the hypoperfusion around an infarction than to the infarction itself during the acute stage [197]. Cognitive impairment was found to be more severe in patients who have had a transient ischemic attack with single-hemisphere cerebral hypoperfusion than in those without; both are caused by carotid artery occlusion [198]. Even white matter hyperintensity is caused by compromised cerebral blood flow [199].

These cognitive impairments may be due to dilation of the cerebral artery and an increase in the oxygen extraction fraction after cerebral artery hypoperfusion. Reductions in cerebral gray matter attributed to hypoperfusion, specifically reduction in the thalamus [200], may contribute to cognitive impairment [201]. Additional evidence was found to support the relationship between global hemodynamic compromise and cognitive deficit in people with heart failure [202, 203]. It should be noted that gray matter abnormalities with no relevance to focal infarction may be associated with hypoperfusion. However, it has been suggested that alterations in cerebral

blood flow may influence the cognitive process, which involves wide brain regions on a whole-brain level [204].

1.2.2.4 Epidemiology and characteristics of falls

Falls are a multifactorial medical complication that occurs frequently post stroke [205-207]. The aging population [208] and increased post-stroke life expectancy [209] have also contributed to an increase in the prevalence of falls. The following sections briefly summarize the epidemiology of falls and related factors, mainly in the community-dwelling setting.

1.2.2.4.1 Fall rate

Each year, about 29% of adults above 65 years of age experience a fall [210]. This risk is even higher at all stages post stroke [211, 212]. In community-dwelling stroke survivors, the proportion of patients with falls ranged from 23-34% (3-4 months), 40-73% (half year), and 43-70% (one year) respectively [213-227].

Moreover, stroke survivors who have had a fall have a greater tendency to become recurrent fallers than age-controlled healthy subjects. The proportion of repeat fallers is about 15% among the healthy elderly [228-231] and 20-57% in community-dwelling people 6 to 12 months after a stroke [215, 222, 224, 232, 233]. Other studies found similar proportions of recurrent fallers (15%) among stroke survivors and healthy controls at 1 year [216, 220]. Studies have indicated that the wide range of fall rates found in long-term stroke survivors may be due to discrepancies in stroke characteristics and study methods, including duration, age [218, 219, 225], disability severity [216-219, 225], and data collection methods [234].

1.2.2.4.2 Fall circumstances

Most falls (39-90%) among community-dwelling stroke survivors occur while walking [214, 216, 220, 221, 224, 225, 235-237], followed by transfers [235]. Regarding the circumstances of the fall, similar results was found in stroke survivors and control subjects [229, 238], and falling in the direction of the more affected side [225, 235] or forward [225, 235] was the most common.

1.2.2.4.3 Fall time

An increasing trend has been seen in the incidence of falls post stroke: 25-37% (1-6 months) [236, 239], 40-50% (6-12 months) [221, 224], and 55-73% (one year after stroke) [233, 240]. Even nearly 10 years post stroke, when compared with age-controlled healthy, the fall risk in stroke survivors was more than twice as high as that in age-matched healthy controls [216].

The highest fall incidences are frequently reported during the setting transition stage right after their discharge from a medical institution [214, 215, 223]. This finding suggests that stroke patients with residual disabilities may not be sufficiently prepared for re-adaptation to the complex environment encounter during community-dwelling daily living.

1.2.2.4.4 Fall causes, risk factors, and associations

Fall related factors in stroke survivors are far from simple. “Losing balance” and “misjudgment” are two commonly reported reasons for falls in stroke survivors [214, 225]. Other studies have indicated that a balance deficit or misjudgment could be related to persistent stroke-related impairment, including sensorimotor function alteration, reduced attention, postural sway, weight distribution, abnormalities of vision and spatial awareness and of stance capabilities [241, 242].

Thus, the related risk factors are categorized in three areas: physical (e.g., gait and balance disorder) [214, 218, 220, 222, 224, 226, 243-249], mental (e.g., cognitive deficit, depression) [216, 225, 250], and participation (e.g., dependence level) [214, 218, 220, 222, 246, 250-252]. Specifically, delayed and insufficient or excessive muscle response to balance challenges [98, 109, 134, 135, 253, 254] and suboptimal automaticity in postural control [219, 226, 255] were more severe in fallers than non-fallers in people post stroke.

However, some studies about balance measurements were unable to discriminate fallers from non-fallers [221, 227, 255]. Conflicting results have also been reported regarding the fall prediction ability of quadriceps strength [222, 227], spasticity [220, 226], and increased body sway [216, 256, 257]. In contrast, falls in stroke survivors are neither correlated with age [217, 218, 220, 222, 232, 233, 258-261], gender [222, 232, 233, 237, 258, 259], nor with stroke location and type [217, 232, 233].

Moreover, two prediction models with sensitivity and specificity higher than 70% were built for fall prediction in community-living individuals post stroke. The first is based on a falls

baseline and a balance test [222], and the second includes memory, leg range of motion, stroke onset duration, and paretic side [235]. However, the predictive capability of these composite values seems comparable with that of a single functional test (Timed Up and Go, Stops Walking When Talking) [219, 226]. Above all, a more comprehensive model remains to be explored.

1.2.2.4.5 Fall consequences

The detrimental physical and psychosocial consequences from falls in stroke survivors are always a big concern. Soft tissue injury is the most prevalent adverse consequence of a fall [214, 223, 225]. Fractures comprise 1-15% of injuries in stroke survivors [205, 214, 223, 225, 236, 237, 262, 263], and this likelihood is higher than that in healthy control subjects [264, 265]. Further, wrist and hip fractures are the most common of all post-stroke facture types [264]; they are associated with osteoporosis, especially in the paretic limb [266], and susceptibility to fall on the paretic side [225, 235], limited affected arm stretching, and impaired frontal balance post stroke [147]. After a hip fracture, only 38% of stroke survivors regained independent mobility, whereas this rate was 69% in healthy control subjects [265]. Moreover, the mortality rate 3 months after fracture surgery was found to be twice that in healthy elderly subjects [267].

In addition to physical consequences, falls contribute to psychological threats, including fear of falling (32-88%) [268, 269] and anxiety and depression [214, 225, 270], which are also related to balance and gait deficit [271]. Together, they lead to activity restriction (44%) [272]. Further restriction in activity and dysfunction because of a fear of falling can easily result in less independence and a reduction in the performance of activities of daily living in individuals post stroke [273]. The further impairment of activities of daily living leads to social deprivation [214], and these adverse physical and mental consequences create a vicious circle. Last, the economic burden of post-stroke falls, especially those with fractures, cannot be ignored [207].

1.2.2.4.6 Dual task walking and fall risks

As mentioned above, it is well known that stroke survivors often fall while walking [211, 214, 220, 274, 275]. Loss of balance and distractions while walking are frequently reported reasons [225], and age [276-278], balance ability [279, 280], availability of sensory information [281], and stroke duration [245, 282] can affect the attentional demands of postural control. Previous studies have suggested that falls are more likely to occur in stroke survivors in

conditions in which substantial cognitive regulation is involved in walking activity (i.e., less walking automaticity) [219, 226, 255].

In healthy elderly, the following gait parameters during the dual-task (DT) walking test were found to be indicators of fall risk: gait velocity [283], step width, step time, step length [284], variability in stride time [285], and stride length [286]. Meanwhile, in stroke survivors, a significant reduction in stride length [255, 287] and increased medial-lateral direction sway [288] during DT gait was seen in fallers when compared with non-fallers. In addition, a previous study hypothesized that falls may be associated with the inability to prioritize dynamic postural stability in DT walking contexts [289]. In this respect, a risky "re-automation" of mobility control can be more susceptible to external disturbances [290]. Another study showed that the DT standing balance test cannot discriminate fallers from non-fallers, whereas a more complex DT walking test can [284]. This study supports the importance of the difficulty level of the DT (attention demanding level) [291], so it is crucial to identify how the task difficulty influences DT ability before establishing an effective DT measurement for fall prediction in stroke survivors.

1.2.2.4.7 **Summary**

In summary, the increased incidence of falls in stroke survivors poses a great challenge to rehabilitation because of its multifactorial adverse effect, and the occurrence of a fall may be attributed to a combination of many aspects. However, clinical tests (e.g., the Berge Balance Scale, the Tinetti test, and various functional walking tests) only aim at ability in limited aspects, but they cannot measure the subtle deficits that underlie non-optimal performance. Better knowledge of the influence of stroke on more challenging walking activity may improve the discrimination of people with a risk of falls from those without, and the prediction ability of DT assessment remains understudied.

1.2.2.5 **Limitations in community reintegration**

Community reintegration suggests re-adaptation to or development of new life roles and social relationships [292]. After hospital discharge and return to their family and the community, many people feel unsatisfied with their post-stroke community reintegration [293-298].

Studies have found an association between physical function [297, 299-302], balance self-efficacy [295], depression, poor quality of life, and limited participation in daily activities [294-296, 303-305] with community reintegration of stroke survivors. Furthermore, a factor analysis study found that motor control recovery, self-efficacy, executive function, and cognitive-motor interference (CMI) together accounted for 61.4% of community ambulation in older adults [306]. Stroke survivors with physical, psychosocial and cognitive functioning disability also experience impairment in community ambulation, which guarantees a basis for independence and offers a sense of inclusion in the community [307].

Indeed, a study of stroke survivors who returned to the community suggested that outdoor walking is among of the top preferences among the goals identified in clinical practice [308]. In real daily living, community ambulation is based on maintenance of postural stability while performing other tasks that demand attentional resources, such as walking while having a conversation or walking in a busy shopping mall. DT-related gait impairment was significantly associated with the subjects' functional independence (Barthel Index) level [309]. The field of "dual-tasking" has gained increasing attention in stroke rehabilitation [310].

To summarize, it has become increasingly necessary to facilitate the community reintegration and health-related quality of life (HRQOL) of stroke survivors [294, 311]. Relative stroke intervention strategies such as DT ability improvement still require further exploration.

1.3 CMI

DT scenarios are common in daily living, so a DT protocol is frequently applied to explore the effect on cognitive control in motor performance. CMI represents the deterioration in performance under DT conditions (a motor task with a cognitive task) compared with the performance operated separately [310]. This phenomenon was first investigated in the elderly population [312-315]. Specifically, Lundin-Olsson et al. observed that one fifth of elderly participants could not avoid a cessation of walking once a talking task was added [314]. Many other studies have also shown that the addition of a secondary cognitive task to walking contributed to a significant decline in gait velocity [315]. A similar behavioral change was also found in a DT test that involved standing balance. When older adults were asked to maintain equilibrium while standing on a stable force plate, the amount of postural excursion increased significantly after the serial-3-substraction task was added [313]. The CMI phenomenon was also

revealed to be more pronounced when the balance task was made more challenging (i.e., standing on a side-to-side tilting platform) [313].

As walking speed and automaticity are two distinct conceptions, a greater automaticity means a healthier locomotor control strategy with more independence and safety and a lower energy cost. It has thus been suggested that the degree of trade-off between gait automaticity and executive control under complex locomotion conditions can be evaluated by behavioral assessment of DT walking [50]. This approach gives a more comprehensive understanding to facilitate clinical rehabilitation.

1.3.1 CMI patterns

Plummer et al. [310] suggested nine potential cognitive-motor interaction outcomes: 1) no interference; 2) cognitive-related motor interference; 3) motor-related cognitive interference; 4) mutual interference; 5) motor facilitation; 6) cognitive facilitation; 7) motor-priority trade-off; 8) cognitive-priority trade-off; and 9) mutual facilitation. However, most previous studies showed a performance deterioration of either single-task (ST) component or both while dual-tasking, which is supported by the central capacity limitation theory [316].

Vuillerme et al. [317] proved that the addition of an easier cognitive task led to improved postural stability, and a U-shaped nonlinear relationship was shown between balance control and the difficulty level of the secondary cognitive task [318]. A motor-priority trade-off CMI pattern was observed in a recent study that added a finger-tapping task to a digit-memorization task in stroke survivors[319].

Three other studies showed that work involving a standing position (i.e., greater demand on postural control) may actually improve work productivity relative to a sitting position [320-322]. One possible explanation may be that standing suppresses the default-mode cognitive processing (i.e., mental wandering) that may occur in a relaxed sitting state. Suppression of the default mental wandering would in turn lead to better attentional focus, resulting in facilitation of the primary work performance.

In summary, CMI patterns are likely to be determined by gait automaticity, the difficulty of the cognitive or motor tasks performed, and the internal attention capacity level, which is linked to the severity of the motor or cognitive functional deficits. These factors determine the extent of the brain (especially cortical) regions activated and the amplitude of the activation during dual-tasking.

1.3.2 CMI performance

As the additional stroke-related impairment will further influence the cognitive motor interference performance, this section summarizes the findings regarding the CMI phenomenon in two separate populations: healthy individuals and stroke survivors.

1.3.2.1 **CMI in the healthy population**

When used in a healthy population, the DT assessment paradigm shows a higher function level but also great variation. In general, there are two types of DT category, cognitive-balance and cognitive-walking, but the cognitive and motor tasks have different complexities; the motor task varied from stance balance to dynamic balance [323-325], from level ground walking to obstacle walking, and from treadmill walking with various degrees of inclination [326], whereas the cognitive tasks involved working memory [323, 327], verbal fluency [324], serial subtraction (SS), and mobile phone use [328, 329]. The diversified DT test protocol generates no interference [330], motor interference [325, 326], or both [312, 324, 328, 329].

The CMI severity varies by age, with healthy older adults showing more severe CMI than the young [325, 331]. Moreover, the degree of CMI also depends on the type [327] and complexity of the single task applied; greater interference is observed when a more difficult task is used [312]. Al-Yahya et al. highlighted the impact of the cognitive state on DT capability in adults without disabilities [331]. Their review suggested a strong relationship between the cognitive state measured by the Mini-Mental State Exam and the CMI of walking velocity when the secondary task was a mental tracking task [331].

Another plausible explanation for the various CMI findings may be related to the automatic postural stability prioritization strategy. Subjects either worsened the performance of the motor task or both tasks [323] to guarantee the fundamental standing postural balance when competition of attention resources occurred between the two tasks. This hypothesis may be

supported by the finding that a cautious gait mode in the DT condition appeared to decrease fall risk [332]. The characteristics of a cautious gait mode include a decreased gait velocity, reduced step length, wider step width, and decreased heel contact speed. Moreover, another study revealed that healthy young subjects automatically prioritized the mobile phone task in the controlled environment with low-distraction, but allocated relatively equal attention to the mobile phone and walking tasks in the real-world environment [328]. This redistribution of attention may occur because subjects devoted greater effort into the cognitive task when basic postural stability was guaranteed. In contrast, if balance is challenged, they put more focus on the motor task (balance and walking).

However, the manner in which the difference in the secondary cognitive task type would influence the performance prioritization strategy remains unclear. One study compared the DT performance when the Stroop task was applied as the secondary cognitive task in the testing paradigm, compared to a visuo-motor reaction time task. It was observed that under DT conditions, the Stroop task resulted in less motor interference, whereas the visuo-motor reaction time task led to less cognitive performance interference [312].

Interestingly, the changes in gait parameters vary upon the addition of a cognitive task, which is also related to the complexity level of the mobility task involved [326]. The addition of an SS task to treadmill walking increased the step width and medial-lateral COM displacement. In contrast, when the inclination degree of the treadmill decreased from 0-10%, significant changes were found in walking speed, stride length, pelvis tilt and obliquity variability, pelvis rotation, and anteroposterior COM displacement [326]. During DT conditions, the gait variability was also increased [333].

1.3.2.2 **CMI in individuals post stroke**

In stroke survivors, the previously learned neuromuscular pathways to gait and postural control automaticity could be lost, contributing to a greater demand in attentional resources. Also, overall cognitive capacity may be reduced secondary to the higher-order lesion. Both factors may contribute to greater CMI in stroke survivors than in age-matched controls [255, 288, 334-340].

Post-stroke CMI is still a relatively understudied topic. Hyndman et al. [255] showed that in the DT condition (walking for 5 m while remembering a shopping list), the reductions in both

walking speed and cognitive recall were more severe in stroke survivors than in control subjects. In an obstacle-crossing task, Takatori et al. [338] observed that stroke survivors spent significantly more time crossing the obstacles, that the risk of heel-obstacle contact was higher than in the control group, and that this phenomenon was more pronounced in the DT condition when the obstacle-crossing task was combined with a verbal fluency task. More recently, Patel and Bhatt [307] studied a small sample of 10 stroke survivors and found that the CMI effect on gait speed was the most severe with the SS task, followed by the Stroop test and the visuomotor reaction time task. In contrast, the CMI effects on cognitive performance showed a different pattern, with the visuomotor reaction time task sustaining the most prominent degradation in DT condition, followed by the SS task, and Stroop test. The interference severity varied when the secondary task is working memory or word list generation [327]. Again, these results suggest that the degree of interference effects differed depending on the specific combination of walking and cognitive tasks [339, 341, 342] and that the same combination of cognitive and mobility tasks may induce a very different interference effect on mobility compared with that on cognition.

Some studies have examined the influence of dual-tasking on motor parameters other than speed. The sway of the COP decreased under DT conditions [255, 288, 343]. In contrast, one study [150] reported that stroke survivors demonstrated increased sway under DT conditions. DT walking included a decreased cadence, increased stride duration, and longer double-support duration [344, 345]. The temporal asymmetry of the gait was not significantly affected. The root mean square of the lateral trunk acceleration appeared to be increased in the frontal plane, but reduced along the sagittal and vertical planes during DT walking [346]. Manaf et al. suggested that temporal gait parameters (gait velocity and stride duration) were more likely to be influenced by dual-tasking than spatial gait parameters (stride length) [340]. This finding suggests that mobility impairment from stroke also include a reduction in the automaticity of gait in DT conditions [347].

A recent study examined the relationship between the complexity of the walking environment (a simple environment or an environment with static physical context or dynamic projector-augmented context) and the severity of cognitive-motor interference in people with stroke [348]. They found that a greater CMI was generated in the more challenging setting. The aforementioned automatic postural stability prioritization strategy was more obvious in stroke

individuals. Postural stability was prioritized over cognitive performance to ensure safe locomotion [343, 349].

The location and severity of the lesion should also be considered when examining the CMI phenomenon in stroke survivors. In a DT paradigm that involved hand movements, Dennis et al. found that the CMI score has a strong positive association with the contralesional dorsal premotor cortex (r =0.92). A similar but more fragile correlation was revealed in the ventral premotor and middle frontal gyrus. No independent association was found between hand motor dysfunction and CMI [350]. If CMI is explained by the theory that competition for the same attentional resources occurs in the brain cortex, the individuals with stroke in the brain cortex would demonstrate greater CMI than those with stroke in the subcortical brain area. Moreover, subjects whose lesion involves the neural substrate that controls the tested component tasks should show different performances than those whose lesion is located in other brain regions that do not play a major role in controlling the component tasks. The association between the severity of CMI and stroke lesion features remains understudied. Overall, the available evidence has highlighted the importance of the need to study how DT walking performance under different types and difficulties of cognitive and walking tasks would correlate with stroke severity and location. Unfortunately, no study has systematically examined this issue.

1.3.3 Potential mechanism of DT interference

What is the underlying CMI mechanism of during DT balance/mobility? The most popular theory is the “limited capacity model,” which states that (a) the operation of all cognitive tasks requires the involvement of attentional resources, (b) concurrent balance/mobility tasks also require related attentional resources, and (c) performance deterioration will occur if the overall requirement for such resources during dual-tasking exceeds the threshold of the individuals’ central capacity [310, 351].

However, hypotheses about how cognitive resources (brain’s information processing capacity) are applied under DT conditions are controversial: 1) modality-specific multiple resources: overlap hypothesis [352]; 2) modality-general single resource [353]: task-general whole-brain activation quota [354]. According to the overlap hypothesis, the degree of DT interference depends on the “functional cerebral distance” (i.e., functional similarity) between the brain areas involved in each component task alone. In contrast, the latter theory suggests that

an activation quota could exist at the whole-brain level. Some mutual inhibition mechanisms will regulate the discrete brain activity level of each single component task when the quota is used up under DT conditions [354]. To better understand the mechanism of DT, the role of executive function in DT regulation and the neural substrate of ST conditions should also be considered, especially for subjects with brain damage like a stroke.

1.3.4 Role of executive function in CMI

Executive function is like an umbrella that encompasses a variety of attention-demanding processes among multiple cortical systems [355] that monitor and coordinate goal-directed behaviors [356, 357] that involve planning, reasoning, or the selection and inhibition of appropriate responses [357-362]. Further, as a cornerstone of executive function [363], attention was originally defined as a cognitive process operating for the degree of significance allocated to certain stimuli [353] that have four functions, including focusing, selecting, and/or inhibiting a specific stimulus. Moreover, Norman and Shallice classified the executive control of applying attention under different conditions: 1) lower levels of attention for familiar and automatic conditions [364]; 2) higher levels of attention to solve challenging and novel situations [365].

Under DT circumstances, attention is shared between two component tasks. The degree of competition between the limited attentional resources largely determines the degree of DT interference, which considers both central capacity limitations and overlap hypothesis. Meanwhile, executive control was indicated to modulate task conflict, resource competition [366], and attention allocation [367-373] under DT conditions. It can also help organize lower, more automated cognitive processes to regulate behavioral performance when necessary [372].

1.3.5 Neural substrate of motor component task

Although simple rhythmic walking is relatively automatic and mainly involves the spinal cord, brainstem, and cerebellum [50, 374-380], walking activity in real-life often takes place in a complex environment (e.g., a busy crossroad or street with certain obstacles that cannot be avoided) that requires the ability to adapt the walking pattern, which requires a higher degree of visuo-motor coordination, resulting in regulation of this activity at a cortical level [381, 382]. Walking is regarded as a global brain activity because it requires cooperation among various cognitive processes, such as motivation, executive control, visuospatial ability, and sensorimotor coordination [383].

Indeed, Harada et al. [384] observed that when subjects walked at a higher gait velocity, more activation in the prefrontal cortex was found in the elderly, especially those with impaired gait performance. Specifically, a significant elevation was seen in prefrontal activity during the gait initiation stage, during adjustment in the gait velocity [385-387], and during challenging walking tasks [387-389], and during DT walking [387, 390]. Moreover, less variability in stride time during walking was significantly correlated with executive function as assessed by the Stroop test instead of memory [391]. Earlier studies found that obstacle cross walking performance is correlated with problem solving and executive function, but not with memory, in older adults [392, 393]. Increased prefrontal activity may also represent a compensation strategy for the insufficient walking automaticity by increasing executive control [394].

In addition to the frontal brain area, other cortices are also suggested to be involved in human walking, including the motor cortex [35, 379]; premotor cortices: [379, 380, 385, 395]; primary somatosensory cortices [377, 380, 396, 397]; and supplementary motor areas [377-380, 384, 396]. Other cortical areas include the cingulate cortex [380] and visual cortex [377-379]. To be noteworthy, the somatosensory cortex is activated less in subjects who walk more automatically [386, 398, 399]. Therefore, reduced automaticity during walking may be compensated by elevated cortical activation [384].

In addition, subcortical areas such as the basal ganglia [400] and limbic system hypothalamus thalamus [401] were also activated in walking. Specifically, it has been suggested that stride length may be controlled by cortical-basal ganglia circuits via the thalamus [35, 400], whereas cadence is regulated by the brainstem and spinal cord pathways [402, 403].

1.3.6 Neural substrate of cognitive tasks

Previous studies have revealed that the differences in the nature of secondary cognitive tasks also contribute to various CMI on both gait parameters and cognitive performance themselves [342, 404-406], and the neural substrate of various cognitive tasks remains poorly understood.

Cognitive tasks applied in the cognitive-motor DT testing paradigm can be categorized based on their attention demands and the cognitive processes involved in executing them. Each differs plausibly from the other domains at a behavioral and/or neuropsychological level [331].

The cognitive tasks used in the DT testing paradigm included mental tracking, verbal fluency, working memory (shopping list recall), reaction time (e.g., clock task), discrimination and decision-making (e.g., Stroop task), and sustained attention (e.g., a cup-holding task) [331]. Regardless, the operation of these cognitive tasks requires the involvement of attention. Although a wide range of brain areas are involved in various cognitive tasks, a shared activated brain structure is the prefrontal cortex[407-415], which is generally divided into two parts: a ventromedial and a dorsolateral division [416]. The former division was found to be linked to areas responsible for memory (hippocampus), emotional processing (amygdala), and high-order sensory processing (temporal and visual association areas), whereas the latter division was revealed to be correlated with motor control (supplementary motor area premotor cortex, basal ganglia), performance monitoring (cingulate cortex), and high-order sensory processing (association areas and parietal cortex) [416]. These neural networks integrate sensory and memory information to control actions and behaviors during cognitive tasks.

To avoid the inconclusive findings of previous studies due to an inconsistent DT paradigm and to help reveal the mechanism by which attentional resources are applied during dual tasking, this study included the most commonly used and well-studied cognitive task, the SS task. Ample previous studies have shed light on how this cognitive task with different major cognitive processes activates various brain areas.

1.3.6.1 **Neural substrate of SS task**

SS generally involves four sequentially cognitive processes: 1) covert production of numbers, 2) retrieval of arithmetic facts from memory, 3) execution of subtraction, and 4) storage of information in the working memory for the subsequent calculation [417].

Convincing evidence has been found regarding the neural substrates of this task, generally in the frontal and parietal areas [417, 418]. Different brain areas also control different cognitive process components of the SS task: the intraparietal sulcus for semantic memory of arithmetical facts, frontal areas (left inferior frontal gyrus, premotor and supplementary motor areas) for retrieval and execution of this memory, the right parietal area for proper alignment of digits, and the bilateral prefrontal cortices to maintain the digits needed for the subsequent mental SS [418].

Interestingly, one study found that a different calculation strategy affects the area of the brain activated. Intensive activation in the left dorsolateral frontal cortex with little activation in the inferior parietal cortex was demonstrated in the participants who used a verbal strategy, whereas in those who used a visual strategy, activation was shown in the bilateral prefrontal cortices and elevated activation in the left inferior parietal cortex [419].

1.3.6.2 **Neural substrate of other cognitive tasks in CMI testing paradigm**

Verbal fluency (VF) tasks require the individual to retrieve semantically or phonetically related words from the long-term storage in response to a specific cue [420]. The most common forms of VF are those that assess either category fluency or letter fluency. A semantically related verbal fluency test uses a categorical cue, whereas a phonetically related test uses a letter cue. In DT paradigms, a categorical fluency task such as the "word generation" task is often used, in which the patient is instructed to think of and verbalize as many items as possible within a fixed time.

Compared with the resting state, many brain imaging studies found distinct activation in the dorsolateral prefrontal cortex [411, 421, 422], left inferior frontal cortex (Broca's area) [411, 420-423], bilateral temporal [421], superior temporal regions [422], left medial temporal lobe [420], left superior parietal lobule [420, 421], and left thalamus [423]. These studies showed that these activation patterns can be a result of different brain areas regulating different process components of the semantic verbal fluency task. Temporal regions are the site of word storage [422] and retrieval [420], and the frontal cortex controls inhibitory modulation, which is the basis of intrinsic word generation [422]. The motor area in the parietal cortex may be related to speaking movements.

The third task is the auditory Stroop task. This task examines the ability for selective attention to relevant tasks and response inhibition to irrelevant tasks [424]. An auditory Stroop task requires the subjects to discriminate the pitch of four auditory files: the words "low" and "high" in low and high pitches. Previous studies showed that several brain regions may be associated with the neural substrate of the auditory Stroop task, including the dorsolateral prefrontal cortex [409, 425], right middle prefrontal cortex [426], precuneus [414, 415], anterior

cingulate cortex [425], right cerebellum, bilateral supplementary motor areas [415], middle occipital and inferior temporal cortices, and inferior parietal cortex [409, 425].

In the shopping list recall task, the subject is required to remember a list of shopping items and recall it after a certain period of time. It represents a process of short-term memory storage and manipulation of storage information. The neural substrate of this task may involve the prefrontal cortex [427], inferior parietal cortex [428], intraparietal sulcus, and frontal eye field [429].

The cognitive process in the cup-holding task is sustained attention, which involves maintaining attention on a set of stimuli for a prolonged period regardless of the sensory modality used (i.e., visual, somatosensory, auditory) [430]. The neural basis for this cognitive process was indicated in the right prefrontal and right superior parietal cortices [413, 431].

Last, as a combination of auditory-visuospatial integration and working memory, the clock task requires participants to locate the minute hand after hearing a time (e.g., up or down). Previous studies revealed that the posterior parietal cortex [432, 433] and the dorsal premotor area [432], contralateral parietal cortex [412, 434], and right middle prefrontal cortex [426] are involved in the clock test.

In summary, although some overlap of neural substrates exists, each task involves different mental processes. Among the various cognitive tasks used in previous CMI research studies, the neural bases of the SS task is the best established.

1.3.7 Neural substrates of DTs

The existence of neutral substrates that specifically regulate DT performance has long been debated. Both animal and human studies have provided insights, each with its own advantages and challenges.

1.3.7.1 **Neural substrates of DTs in animals**

Without the limitations in the temporal and spatial resolutions of human neuroimaging techniques, animal studies have used single-neuron-recording techniques to explore the CMI-specific neural basis. Evidence supports the notion that animals can learn dual tasking without a prohibitive training time [435]. Two areas in rats' brains were shown to be highly correlated with

DT processing: the agranular frontal cortex [436, 437] and the nucleus basalis magnocellularis [438, 439]. Moreover, the DT-specific type 1 neurons coexisted with other neuron types in the rat lateral agranular frontal cortex [436, 437]. In monkeys, hybrid neurons in the lateral prefrontal cortex may mediate the interference between two simultaneous tasks [440-442].

1.3.7.2 **Neural substrates of DTs in humans**

Previous neuroimaging studies generated divergent suggestions about the DT-specific location.

1.3.7.2.1 Neural substrate of CMI in healthy young adults

Findings are inconclusive in the healthy young population. Some studies suggested the existence of a specific brain area that regulates dual-tasking, and the areas proposed included the prefrontal cortex and parietal regions [443, 444], the premotor cortex and supplementary motor area [445], and left lobule V and the right vermis of the cerebellum [446]. In contrast, other studies have suggested that there may be no specific DT-related brain areas [447, 448].

1.3.7.2.2 Neural substrate of CMI in healthy elderly adults

The results collected from healthy elderly subjects were also inconsistent. Van Impe et al. examined the blood oxygen level dependent response of both elderly and young adults under both ST and DT conditions. Even though the older group showed increasing brain activation in the frontoparietal network during operation of the single visuomotor task, no structural interference (i.e., additional neural activation except for the neural basis of each component task) was found for either groups under the DT condition [449]. In contrast, Blumen et al. used an imagery walking and talking CMI paradigm, and fMRI images showed more activation during DT tasks than ST tasks in the cerebellar, precuneus, supplementary motor, and prefrontal regions [450]. Of note, Beurskens et al. also compared DT brain activation between the healthy young and old individuals. Their behavioral imaging study found little difference in prefrontal activation between ST and DT walking conditions in young adults, but in the elderly, the addition of a complex visual task to walking led to a substantial decrease in prefrontal activation [451].

1.3.7.2.3 Neural substrate of CMI in stroke survivors

Most DT studies in stroke survivors have been behavioral studies. Only one study conducted by Al-Yahya found that DT-originated elevation in fMRI activity in the bilateral inferior temporal gyrus, left cingulate gyrus, and left frontal pole was correlated with a DT-originated reduction in cadence of simulated walking among stroke survivors [452].

1.3.7.3 **Summary: neural substrates of DTs**

As summarized by Nijboer [453], four patterns describe the difference in neural activity while dual-tasking and for the sum of two single tasks: 1) over-additive, 2) additive, 3) under-additive, and 4) miscellaneous activations. Over-additive effects mean that the neural activation of the DT exceeds the sum of the corresponding STs. Additive activation is suggested when the degree of change in the activation signal during DT equals the sum of its STs. Under-additive activation represents brain activity during the DT that is less than the sum of the activity in during the STs. The last pattern is the mixed combination of the first three patterns [454].

The degree of brain activation is affected by the difficulty of the cognitive task and the motor task. Mirelman et al. [455] revealed intensified brain activity in the frontal cortex as the complexity of the calculation task increased (no counting, counting forward, and counting backward a series of “minus 7”) under DT walking conditions. In addition, the type of cognitive task may also affect the severity of CMI. Patel et al. [312] showed that the addition of the Stroop task led to the greatest deterioration in mobility performance, followed by the SS, verbal fluency, and visuomotor reaction time tasks. It was supposed that the Stroop test, which was a more novel task to the participants, may share more neural substrates (because a wider network is involved) with locomotion (e.g., the cerebellum and supplementary motor regions), resulting in more severe competition between them, whereas the neural substrates of working memory, verbal fluency, and reaction time tasks tend to centralize more within the prefrontal brain network, which suggests less overlapping with the correspondents in walking control [312, 382].

These results are inconclusive for three reasons: inconsistency with in the DT paradigm, difference in automatization of the component single tasks, and the lack of a comprehensive understanding of the limitations of neuroimaging resolution [354]. Behavioral lesion studies (e.g., stroke) in humans may be another appropriate approach to further explore the neural substrates of the DT mechanisms. Through comparing the results obtained from individuals with lesions in

different brain regions, the function and importance of certain brain areas in DT walking control may be identified.

1.4 Reliability and validity of CMI assessments

Our research team recently developed and validated a battery of DT balance/mobility assessments [456-458] and conducted studies to examine how CMI was affected by various combinations of cognitive and mobility tasks [341, 459]. The current study aimed to further build on this solid foundation and enhance our understanding of post-stroke CMI and the mechanism of dual-tasking.

1.5 Gaps in knowledge and study rationale

No investigations to date have assessed the association between CMI phenomenon post stroke and the stroke characteristics. Research is urgently needed to fill this knowledge gap in the field of stroke rehabilitation.

1.6 Objective and hypotheses

The objective of this study was to assess the association between DT performance and the location and severity of stroke with the manipulation of component task complexity. It was hypothesized that:

(1) increased complexity of a component task would lead to worsened DT performance;

(2) poorer DT performance would be observed after cortical strokes than after non-cortical strokes; and

(3) poorer DT performance would be associated with greater cognitive and motor deficits and worse community reintegration.

2 Chapter 2 Methods

2.1 Study design

In this repeated-measures cross-sectional study, individuals with stroke were assessed in various combinations of DT conditions while walking.

2.2 Subjects and sample size estimation

The subjects were recruited from the local community stroke self-help organization. The inclusion criteria were age of at least 50 years, community-dwelling status, diagnosis of a stroke confirmed by the individual's physician more than 3 months earlier, medically stable status, a score of at least 22 on the Montreal Cognitive Assessment (MoCA) [460], a Modified Rankin score of 2-3 [461], the ability to follow two-step commands, and the ability to ambulate without the physical assistance of another person for at least 1 minute. The exclusion criteria were expressive or receptive aphasia, other neurologic conditions (e.g., Parkinson's disease), other conditions that had a substantial influence on walking (e.g., rheumatoid arthritis), or other serious illnesses.

The power analysis for a three-way ANOVA (between-subjects factor: stroke location; within-subject factors: motor task complexity and cognitive task complexity) was conducted in G*Power 3.1.9.2 to determine a sufficient sample size. Using an alpha of 0.05, a power of 0.95, and a medium effect size of 0.06 (denoted by the partial eta squared ($\eta 2$); convention: small=0.01, medium=0.06, large=0.14) [462], including an attrition rate of 15%, a minimum sample size of 42 stroke survivors per cognitive test was required to detect a significant interactive effect between the complexity of the cognitive task and that of the mobility task (objective 1).

Because our study design includes two comparison groups, the desired sample size would be 84. (objective 2).

2.3 Experimental protocol and measurements

2.3.1 Demographic information

The relevant demographic information (e.g., age, medications) was collected in patient interviews. The discharge summary, CT report, or MRI report provided by the hospital where the

patient received inpatient rehabilitation contained the brain imaging findings and thus the location of the stroke. All the CT and MRI reports were written by the professional clinical examiners in hospital. And all the CT and MRI scans were done within the first two weeks post-stroke except the MRI scan of two subjects (one was done at the third month , the other was done at the sixth month post-stroke). Global stroke severity was measured by the Modified Rankin Scale [461] by one well-trained researcher. The following assessments were also administered to obtain a more comprehensive clinical profile of the study participants.

2.3.1.1 **Montreal Cognitive Assessment (MoCA)**

The MoCA was applied to measure general cognitive function. This test evaluates several aspects of cognitive function with a total score of 30. The feasibility of the MoCA to measure global cognitive function has been shown in a study with large sample size of stroke survivors [463]. The reliability and validity were found to be good to excellent for stroke survivors [460].

2.3.1.2 **Wisconsin Card Sorting Test (WCST)**

The WCST was created to measure abstract reasoning ability and cognitive flexibility in response to inconstant environmental contingencies (set-shifting) [464]. Mental flexibility is indicated by perseverative errors. A computerized version of the WCST was administered with the stimulus presentation software (Media Control Function; Digivox, Montreal, Canada). Throughout this test, four fixed reference cards—one red triangle, two green stars, three yellow crosses, and four blue circles—were placed in a row on top of the monitor. During each trial, a new test card was presented at the bottom of the screen. The participants were asked to match the testing card with one of the four reference cards based on one of three task principles: “sort by color,” “sort by shape,” or “sort by count” [465]. The participants were informed that once the matching was done, a mark would be given to indicate whether their choice was correct. If the matching was correct, the principle was kept for the following few matchings. However, the task rule changed at random, and the participants needed to shift the matching rule. The MoCA measures the general cognitive deficit level, and the WCST is a popular neuropsychological measurement applied to assess executive function [466], which is highly associated with the divided-attention process involved in dual-tasking. Perseverative errors represented the number of incorrect combinations made by combining with an incorrect combination standard. The greater the score of this item, the worse the mental flexibility.

2.3.1.3 **Reintegration to Normal Living Index**

The 11-item self-rated Reintegration to Normal Living Index was used to quantify the degree to which individuals achieved reintegration into normal social activities after a stroke. With a total score of 44, this scale contains two parts: 1) daily functioning (8 domains: indoor, community, and distance mobility; self-care; work and school activities; recreational and social activities; family role; personal relationships; presentation of self to others; and general coping skills) and 2) perception of self. The scoring is as follows: 1=Does not describe my situation, 2=describes a part of my situation, 3=describes most of my situation, 4=fully describes my situation. Moderate reliability of the items (k=0.41-0.66), except for item 7 and 11, which showed fair reliability (k=0.21-0.40), has been established [467].

2.3.2 Behavioral outcomes

Behavioral outcomes were measured by three tests: (1) the balance test, (2) the motor control test, and (3) the DT walking test.

2.3.2.1 **Mini-Balance Evaluation System Test (Mini-BESTest)**

The shortened version of the Balance Evaluation System Test was used to quantify the deficit of four different balance control systems: anticipatory, reactive postural control, sensory orientation, and dynamic gait. It is a 14-item test scored on a 3-level ordinal scale (0=severe, 1=moderate, 2=normal), for a total score of 28 [468]. The reliability and validity of the Mini-BESTest have been established in stroke survivors [469].

2.3.2.2 **Fugl-Meyer Assessment (FMA)**

The severity of stroke-related motor control deficits in the legs was measured using the 12-item leg subscale of the Fugl-Meyer Assessment (FMA) [470]. Items are scored on a 3-point ordinal scale (0=cannot perform, 1=performs partially, 2=performs fully), with a total of score of 24. Proximal hip/knee and distal ankle subscores were also calculated. The reliability, validity, responsiveness, and clinically important differences of the FMA have been well established in stroke survivors [471, 472].

2.3.2.3 **DT assessments**

The DT measurement protocol is illustrated in **Table** 1. In our DT protocol, each trial lasted 1 minute. The walking task had two difficulty levels (low: level ground walking vs. high: obstacle crossing walking). The cognitive tasks involved mental tracking. SS has been widely used as means of providing a distraction and a cognitive challenge, and the attention devoted to this task is not likely to change over time during a given test [363, 473, 474]. The cognitive task also has two levels of complexity (serial subtraction by three [SS3] and serial subtraction by seven [SS7]). The details are shown in Table 1. Overall, the protocol involved two ST conditions and four unique combinations of DT conditions. To prevent physical and mental fatigue, rest periods were given intermittently during the testing session.

First, the participants were instructed to perform the mobility task in the ST condition (i.e., no cognitive task imposed). The distance covered in 1 minute (in meters) and the incidence of obstacle-foot contact was recorded. The cognitive test was then performed in the ST condition (i.e., in a sitting position). The outcome variables for each category of cognitive task are displayed in Table 1. One minute was given for each cognitive test to match the amount of time designated for the walking test. The participants were then required to perform the mobility task in conjunction with the cognitive task (i.e., the DT condition). Again, 1 minute was given for each DT. A LabVIEW program was used to play the audio files and record the answers to the responses. The system was connected with a wireless loudspeaker and synchronized with an external wireless gait-tracking device (Mobility Lab, APDM, Inc., Portland) that allowed us to measure other gait parameters (stride length, cadence, and symmetry indices of step length, and stride time). A six-sensor configuration was used, including both ankles, both wrists, sternum, and waist. Each sensor included triaxial accelerometers, gyroscope, and magnetometer, and the signals were sampled at 1280 Hz with 14-bit resolution. The data were streamed wirelessly to a computer and automatically analyzed with the corresponding Mobility Lab™ software package. The IWalk plugin for Mobility Lab™ was chosen for its ability to measure the spatial-temporal gait parameters of interest. The start and stop were triggered simultaneously by the synchronization of the LabVIEW program. To minimize the sequence effect, the order of testing (choice of mobility and cognitive tasks) was randomized.

2.4 Statistical analysis

The literature strongly suggests that of the spatiotemporal gait parameters, the following are affected under the DT condition: stride time [475-477], stride length [476], stride time/length variability [391, 476, 478-482], and lateral gait instability [405]. Gait variability, which measures the shortest fluctuation in gait among strides [483], has been described as a marker of impaired control, arrhythmicity, and dynamic unsteadiness [484-490] because it can quantify gait automaticity [491]. It may be more sensitive than mean-based spatiotemporal gait measures to central impairment measured in DT walking [331, 492-497]. Gait variability of spatiotemporal parameters (e.g., stride time, stride length), expressed as the coefficient of variation, is calculated by means of a coefficient of variation according to the gait variable selected (SD/mean*100). Low variability values reflect the high automaticity of gait and are related to safety and stability in walking [480].

Moreover, two previous studies [498, 499] that applied factor analysis suggested that the human gait can be classified to four aspects: speed, variability, asymmetry, and postural stability. The ROM velocity of the mediolateral trunk movement was a direct marker for dynamic stability during walking [500-503]. Thus, the current study involved measurement of stride length, stride length variability, stride time, stride time variability, peak frontal trunk velocity, and swing time asymmetry [504] in the analysis. Swing time asymmetry: 2* │Left swing time asymmetry –right swing time asymmetry│/ (Left swing time asymmetry +right swing time asymmetry). As suggested by Plummer, analysis of only the DT's effect on gait would be inadequate, because different secondary cognitive tasks would impose different effects on walking. Analysis should include changes in both gait and cognitive task performance.

First, for comparison of demographic information between cortical and subcortical stroke survivors, an independent *t*-test was applied for normal distributed continuous variables, and a Mann-Whitney U test or chi-square test was chosen for nonparametric data.

To address hypothesis 1: 1) the motor parameters were analyzed with separate two-way repeated-measures ANOVA (two within-subject factors: cognitive task complexity [three levels: no cognitive task, easy cognitive task, difficult cognitive task] and motor task complexity [two levels: easy walking task, difficult walking task]) for conditions SS tasks, followed by post-hoc one-way ANOVA on cognitive complexity and subsequent paired-T test if necessary; and 2) the

cognitive parameters were analyzed with separate two-way repeated-measures ANOVA (two within-subject factors: cognitive task complexity [two levels: easy cognitive task, difficult cognitive task] and motor task complexity [three levels: sitting, easy walking task, difficult walking task]) for conditions with SS tasks, followed by post-hoc one-way ANOVA on motor complexity and subsequent paired *t*-test if necessary.

To address hypothesis 2, 1) the motor parameters were analyzed with three-way repeated-measures ANCOVA (one between-subjects factor: stroke location; two within-subject factors: cognitive task complexity [three levels: no cognitive task, SS3, SS7] and motor task complexity [two levels: level ground walking, obstacle crossing walking]; covariates: age, stroke duration), followed by post-hoc independent *t*-test if necessary; and 2) the cognitive performance was analyzed with three-way repeated measures ANCOVA (one between-subjects factor: stroke location; two within-subject factors: cognitive task complexity [two levels: SS3, SS7] and motor task complexity [three levels: sitting, level ground walking, obstacle crossing walking]), followed by post-hoc independent *t*-test if necessary. Other demographic variables that show a significant difference between the two stroke groups were also included as covariates if necessary. Age-related changes have been reported in executive function [505], gait disorders [506, 507], and postural stability in the elderly [508], and the progression of gait automaticity recovery, which is an important indicator of DT walking performance [509, 510], can be influenced by the time since the stroke.

To address hypothesis 3, the association between DT performance and Reintegration to Normal Living Index was analyzed with Spearman's ρ. The associations between DT performance and MoCA, WCST, Mini-BESTest score, and the Fugl-Meyer Assessment (indicators of stroke severity) were analyzed by Pearson's r test.

For all statistical analysis, the level of significance was set at 0.05, except for post-hoc analysis, for which a more stringent level of significance was used (p=0.01). Case-wise deletion was applied for subjects with major missing data points in the whole measurement set. For single missing data points, the regression method in Excel (formula: =forecast) was used. As suggested by Hoaglin (1987), the accepted range to find outliers was [511]:

Upper=Q3+ (2.2*(Q3-Q1)), Lower=Q1-(2.2*(Q3-Q1))

For extreme outliers, winsorization (i.e., transformation of statistics by limiting extreme values to lessen the effect of possibly spurious outliers) was applied to deal with outliers. To do

so, we converted the values of high outlying data points to the value of the highest data point that was not considered an outlier [512].

3 Chapter 3 Results

3.1 Participant characteristics

Ninety-three subjects were included in the measurements; five subjects did not have valid mobility data because of device measurement error, and eight subjects did not have stroke location information, one because the record was lost in the Hospital Authority and seven because of insufficient sensitivity of brain impairment on the early CT findings. Eighty subjects were thus included in the final analysis, 53 with pure subcortical stroke and 27 with cortical involvement (10 pure cortical stroke, 17 mixed stroke location). This sample size (56 subcortical stroke survivors and 28 cortical stroke survivors) would allow us to detect a difference in DT performance between the two different stroke types with a large effect size (Cohen's d=0.8) In general, the participants included in the final analysis had intact general cognitive function and mild to moderate impairment of motor control and balance function, as indicated by the total score of the MoCA (mean±SD, 27.13±2.07), FMA (mean±SD: 24.93±4.74), and Mini-BESTest (mean±SD: 19.54±4.32). Regarding the comparison between strokes with cortical involvement and those with subcortical involvement, only the FMA showed a slight but significantly higher score in the cortical group than in the subcortical group (p=0.02). More details are shown in Table 2.

3.2 Verification of the difficulty level of the mobility and cognitive task in testing protocol

First, in the ST condition, the number of correct responses (NCR) on the SS7 task was significantly lower than that on the SS3 task (mean difference: 8.30; 95% CI: 7.26-9.34; p<0.01), which confirms that the SS7 task was more difficult than the SS3 task. Also, in the ST condition, all measured mobility parameters changed significantly between level ground walking and obstacle crossing (p<0.01) with the exception of the peak frontal trunk velocity (mean difference: -1.39; 95% CI: -2.73, -0.05; p=0.04), which showed a marginally significant difference between

the level ground walking task and the obstacle crossing task. Therefore, the obstacle crossing task was shown to be more difficult than the level ground walking task. In summary, we were successful in designing a DT testing protocol that involved a mobility component task and a cognitive component task that each included two difficulty levels.

3.3 Influence of task difficulty on DT cognitive and mobility performance

The results revealed a significant main effect of the difficulty level of the mobility task ($F=50.30$, $p<0.01$, $\eta p\ 2=0.39$) and the cognitive task ($F=328.14$, $p<0.01$, $\eta p\ 2=0.81$) on cognitive performance (i.e., NCR), indicating that cognitive performance declined significantly when the difficulty level of either the mobility task or cognitive task was increased. The interactive effect between mobility task difficulty and cognitive task difficulty on cognitive performance ($F=11.76$, $p<0.01$, $\eta p\ 2=0.13$) was also significant. More information can be found in Table 3.

Regarding the mobility performance, a significant main effect was found for the difficulty level of the mobility task for all measured gait parameters ($p<0.01$). Also, a significant main effect was found for the difficulty level of the cognitive task on walking distance ($F=141.30$, $p<0.01$, $\eta p\ 2=0.64$), stride length ($F=80.34$, $p<0.01$, $\eta p\ 2=0.50$), stride time ($F=67.67$, $p<0.01$, $\eta p\ 2=0.46$), peak frontal trunk velocity ($F=63.20$, $p<0.01$, $\eta p\ 2=0.44$), swing time asymmetry ($F=16.59$, $p<0.01$, $\eta p\ 2=0.17$) and stride time variability ($F=8.71$, $p<0.01$, $\eta p\ 2=0.10$), but not on stride length variability ($p>0.05$), indicating that these variables changed significantly when the cognitive demand was increased. The interactive effect of motor task difficulty × cognitive task difficulty was only significant for walking distance ($F=6.45$, $p<0.01$, $\eta p\ 2=0.08$).

Post-hoc analysis was first performed to compare the ST and DT conditions. Cognitive performance differed significantly when comparing the ST condition with all corresponding DT conditions ($p<0.01$). The addition of a cognitive task also contributed to a significant decline in walking distance, stride time, and stride length ($p<0.01$), but not in swing time asymmetry or stride length variability. Interestingly, subjects demonstrated a lower peak frontal trunk velocity (i.e., better postural stability) under DT conditions than under ST conditions ($p<0.01$). A significant increase in the stride time variability between the ST and DT conditions was only

seen when the mobility task was level ground walking ($p<0.01$). Table 4-7 showed more details about these comparisons.

Post-hoc analysis was also performed to compare the DT conditions. As the mobility task became more difficult (i.e., obstacle crossing task), the NCR did change significantly for the SS3 task ($p<0.01$) but not for SS7 task when compared with the level ground walking task ($p>0.01$), but all mobility parameters deteriorated significantly ($p<0.01$) except for stride length ($p>0.01$). For the same mobility task, as the cognitive task became more difficult (i.e., changing from SS3 to SS7), none of the gait parameters showed a significant change ($p>0.01$). Figures 1 to 4 illustrate the changing trend in all measured parameters as the task difficulty increased.

3.4 Influence of stroke location

Table 8 provides descriptive data for ST and DT gait and cognitive performance in the cortical and subcortical stroke groups. A significant main effect of stroke location was only found for peak frontal trunk velocity ($F=4.22$, $p=0.043$, $\eta p\ 2=0.05$) (Table 9). No significant main effect of stroke location or interactive effect between the stroke location and component task difficulty was found for other gait parameters. Post hoc analysis (Table 10) found that the peak frontal trunk velocity was marginally lower in the group with cortical involvement than in that with subcortical involvement under DT conditions with obstacle crossing ($p<0.05$). However, this effect was diminished after more stringent correction for multiple comparisons. To note, when FMA was included as the additional covariate, the main effect of stroke location for peak frontal trunk velocity became insignificant ($F=1.92$, $p=0.170$, $\eta p\ 2=0.03$).

3.5 Correlation between stroke characteristics and DT performance

Regarding the relationship between cognitive deficit and DT performance illustrated in Table 11, consistent negative relationships were found between stride length and perseverative errors (%) on the WCST ($r=-0.22$ to -0.29, $p<0.05$). When a more stringent level of significance was set (<0.01), this relationship remained significant for the DT condition with the obstacle crossing walking task but not for the DT condition with the level ground walking task. This suggests that a greater level of mental inflexibility was associated with a shorter stride length, especially in more challenging conditions. In addition, the MoCA total score had a significant positive relationship with NCR under most DT conditions ($p<0.01$), which indicates that better

global cognitive function as measured by the MoCA was associated with better cognitive performance in DT conditions.

More severe motor deficit was associated with poorer mobility performance in DT conditions. Specifically, a higher Mini-BESTest score (i.e., better balance ability) was associated with a longer walking distance ($r=0.61$ to 0.64, $p<0.01$), longer stride length ($r=0.41$ to 0.48, $p<0.01$), shorter stride time ($r=-0.44$ to -0.39, $p<0.01$) and less variability in stride length ($r=-0.44$ to -0.27, $p<0.01$) in DT conditions. Similarly, these gait parameters also demonstrated significant associations with FMA ($p<0.01$). Moreover, a higher FMA score was accompanied by a lower swing time asymmetry ($r=-0.39$ to -0.29, $p<0.01$) lower peak frontal trunk velocity in most DT conditions ($r=-0.29$ to -0.30, $p<0.01$). More details are given in Table 12. In addition, the walking distance in DT conditions was significantly related to community reintegration ($r=0.31$ to 0.33, $p<0.01$), as indicated by the Reintegration to Normal Living Index. Whereas, this relationship between RNLI and walking distance under LGW ($r=0.29$, $p=0.01$) and OBW ($r=0.27$, $p=0.02$) were less significant.

4 Chapter 4 Discussion

The results generally support our hypothesis that increased difficulty of the component tasks contributes to more compromised cognitive and mobility performance. Poorer DT walking performance is related to more compromised global cognitive function and motor recovery and to lower satisfaction with community reintegration.

4.1 Influence of task difficulty

In line with our hypothesis, with the addition of a secondary component task (regardless of the difficulty level), most walking parameters and cognitive performance showed significant changes from the corresponding values in the ST conditions. Three types of changing patterns were observed: 1) a decline in performance (increased interference): number of correct response (NCR, measure of cognitive performance), stride time variability (coupled with level ground walking only), distance, stride length, and stride time; 2) an improvement in performance (facilitation): peak frontal trunk velocity; and 3) no significant change in performance: stride

time variability (coupled with obstacle crossing only), stride length variability, and stride velocity asymmetry.

Moreover, for the same cognitive task, a further increase in the difficulty level of the mobility component task (changing from level ground walking to obstacle crossing) led to greater deterioration in motor performance in the DT condition. Cognitive performance, on the other hand, remained relatively stable. Likewise, in the same walking conditions, a further increase in the difficulty level of the cognitive component task (SS3 vs. SS7) resulted in greater deterioration in cognitive performance, whereas the mobility performance did not change significantly in DT conditions.

4.1.1 Comparison between ST and DT conditions

4.1.1.1 **Decline in performance upon addition of a secondary component task**

It is not surprising that the increased task complexity from the addition of a secondary task caused deterioration in both cognitive performance and most mobility parameters (i.e., mutual interference pattern). Most previous studies that involved cognitive-motor DT paradigms have demonstrated this phenomenon [342, 347, 513-519] [337, 513]. Specifically, impaired gait speed [255, 342, 513, 520, 521], stride length [255, 342], cadence [255, 342, 522, 523], and stride time [255, 335, 336, 342, 479, 521] were commonly found when comparing ST and DT walking tests in healthy elderly and stroke survivors.

This mutual interference pattern observed in stroke survivors can be explained in several ways. First, cognitive resources are limited [334, 524, 525]. In DT conditions, the cognitive load is increased. When the available cognitive resources are insufficient to satisfy the operation of two tasks simultaneously, performance was compromised. Second, the automaticity of motor control and/or cognitive processes may be defective [525-528] after stroke. Therefore, more cognitive resources would be required to accomplish the same task than in able-bodied counterparts. Third, the subjects may have used a compensatory “balance-first” strategy to deal with challenging DT situations [475]. The changes in gait parameters observed (increase in stride time and decreases in stride length, cadence, and speed) can be considered as compensation to enable better postural stability to guarantee safety during walking when faced with challenging and potentially fall-inducing DT conditions.

In contrast to our findings that cognitive performance was degraded in DT conditions, some previous studies also found cognitive facilitation (e.g., improved cognitive performance) during walking in stroke survivors when compared with cognitive ST performance [255, 335, 336, 342]. It was suggested that the similarity to the default mode of daily living (e.g., emphasize talking while walking) [312, 494, 529-532] together with the increased exercise-induced arousal [353, 533-535] contributes to cognitive facilitation before the overall demand exceeds a certain threshold [536].

The discrepancy in findings may arise from differences in the cognitive task type and central capacity in different populations. First, the SS task applied in this study required the subjects to hold updated information while performing a calculation task (i.e., mental tracking). This may increase the overall internal mental load than other cognitive tasks (e.g., verbal fluency) [537, 538]. The higher cognitive load imposed by the cognitive task resulted in a reduction in attention resources available for other concurrent tasks. Second, the SS task and gait control involve many of the same executive processes [331, 405, 539-541] and neural substrates [542-545] (i.e., parietal cortex). The competition for neural resources for the two concurrent tasks may also explain why a mutual interference pattern was observed rather than a cognitive facilitation pattern. Furthermore, as suggested by Plummer et al., when a greater potential threat to stability was imposed by increased DT complexity, the subjects would shift their focus back to the walking performance for safety reasons, thereby resulting in greater interference in cognitive performance [516].

4.1.1.2 **Improved postural stability upon addition of a secondary component task**

Contrary to our hypothesis, the postural stability–related parameter improved (as indicated by the lower peak lateral trunk velocity) with the addition of a cognitive task while walking. In line with our results, some previous studies also showed that postural stability was improved when a cognitive task was imposed during walking, which was characterized by lower COM velocity [476] and by less COP variability [546, 547] and medial-lateral trunk acceleration variability [548]. This “stability facilitation” in the DT condition was commonly observed with the external attention-diverting cognitive task [549-557]. For example, a decrease in the COP velocity was found in the healthy elderly during performance of a digit memory task [558].

Moreover, previous studies also showed that people focus more on postural control than on the concurrent cognitive task by stiffening the body [553, 559-562] and by reducing the exploratory activity (i.e., less diverted attention). These strategies may help to reduce the risk of falls when faced with a challenging DT condition that poses a serious threat to postural stability [281, 561].

Generally, facilitation of postural stability can be explained by two mechanisms. First, the voluntary safety-first strategy may be involved. The degree of ecological relevance, which is defined as the importance and similarity of the task to daily living [563] of the postural control, may play a crucial role in the posture-first strategy [554-557]. The perceived challenge may determine to some extent whether prioritization is given to postural control or to the concurrent cognitive performance [318]. Second, there may be automatization recovery on posture. Posture is mediated by both higher "controlled" and lower "automatic" levels of processing [564-566]. Thus, prioritization of posture over cognitive performance may be controlled with consciously controlled attention combined with an unconscious balance reaction. Increased attention upon the highly automatic postural control may actually increase the likelihood of disrupting coordination and stability [549, 567, 568]. A DT can thus help divert attention from postural control and prevent overcorrection [531], so that postural control becomes more automatic and effective [317, 318, 553].

Contrary to our results, a previous study found that the extent of the cognitive demand imposed by the secondary task can limit the beneficial effect of dual-tasking on postural control [318]. As stated in a recent review, although 30% of the studies reported significant enhancements in posture by dual-tasking, 50% reported significant deterioration, and 20% reported no effects [569]. A inverted U-shaped relationship between cognitive demand and postural stability was found in DT conditions [318]. Two studies stated that despite the high degree of automaticity, postural control may still require motor preparatory attention to facilitate multisensory integration and generation of motor commands [570, 571]. Thus, as the cognitive demand of the secondary cognitive task increased, facilitation of postural stability was seen first. The interpretation was that some kind of cognitive activity (e.g., mind-wandering) representative of the activation of default mode network [572, 573] is always engaged in single walking conditions [536, 574]. The cognitive load of such mind-wandering in ST walking conditions may be lower than that with the easy cognitive task in DT walking conditions, which reached the

optimal arousal level for postural facilitation (as indicated by decreased gait variability). As the cognitive demand continued to increase, there would be deterioration of postural stability, rather than facilitation. The Yerkes–Dodson law helps interpret the postural stability interference in the later stage of the curve as the arousal exceeds the optimal level for postural maintenance triggered by increasing the cognitive task demand [318, 569, 575]. This was supported by findings that an easy cognitive task (N-back 1 and 2) tended to decrease children's gait variability (i.e., better stability), whereas a harder cognitive task (N-back 3 and 4) increased the variability (i.e., worse stability) [536]. Taken together, whether deterioration or facilitation of the postural stability is induced by dual-tasking depends on the individual's position on the U-shaped curve based on their ST postural stability and DT capacity [318, 576].

4.1.1.3 Stride asymmetry and variability remained unchanged after addition of a secondary component task

In this study, the addition of an extra cognitive task during walking led to no significant change to stride length variability. The stride time variability increased significantly only during DT level ground walking but not during DT obstacle crossing walking. Mixed results for gait variability were found in previous studies, with non-significant results reported in some [492, 577, 578] and significant increases [479] and decreases in others [521], as the condition changed from ST to DT.

From a bio-behavioral perspective, two factors may influence gait variability in DT conditions. The first is related to the compensatory strategy adopted by the subjects [579]. As the conditions changed from ST to DT, significant reductions in stride length and cadence were seen, leading to a reduction in gait speed. These changes in the gait parameters may reflect a compensatory strategy to maintain stability during dual-tasking when fewer attentional resources are available for the walking task. With the overall reduction in the gait speed and smaller steps, the subjects may be able to keep their gait variability relatively stable despite the increase in cognitive demand. The second factor involves the minimal level of attention required to maintain automatic stepping [580]. The cognitive tasks used in this study may not take away this critical level of cognitive resources required [581] for automaticity of gait, thereby resulting in a relatively stable stride variability value as the condition changes from ST to DT. In summary, these results can be interpreted within the theory of selection, optimization, and compensation [582-584] as a tendency to selectively prioritize the task that is critical to survival [555].

As for gait asymmetry, as in our study, Hobert et al. found a non-significant change in swing time asymmetry with the addition of the SS7 task to level ground walking in a healthy elderly population [504], and Plummer et al. observed no significant DT effect on asymmetry of the swing-stance ratio in stroke survivors [585]. These researchers suggested that the lack of change in gait asymmetry in DT conditions resulted from the greater relation between gait symmetry and motor impairment severity, which remains relatively stable within a single measurement session [585]. This point was supported by our finding of a significant association between stride velocity asymmetry and the FMA score (Table 12).

4.1.2 Influence of task difficulty between DT conditions

For a given cognitive task, when a more difficult walking task was imposed (obstacle crossing vs. level ground walking), the DT cognitive performance was further impaired for SS3 task while remained relatively stable for SS7 task, whereas most measured DT mobility parameters showed further deterioration (decreased cadence and increased peak trunk frontal velocity, gait variability, and asymmetry). While Kelly et al. found no effect of walking task difficulty on cognitive performance [586], some previous studies, in contrast, found further impairment of cognitive performance as the difficulty level of the walking task [587] or balance task [278, 281, 555] was increased under DT conditions. According to previous work, three aspects could help explain the mixed results. First, the conflicting findings between Kelly et al. (which applied an auditory Stroop test) [586] and Lin et al. (which applied an n-back letter recall task) [587] may be a result of the distinct characteristics of the cognitive tasks applied in the DT paradigms. The difference in the overall cognitive load imposed may account for the difference in results. Second, differences in the sample characteristics may partially explain the discordance in results. For example, Lin et al [587] studied a much younger population. With intact attentional flexibility, healthy young individuals may have intentionally sacrificed the cognitive task to better maintain walking stability when the walking task was changed to the obstacle crossing condition. Lastly, the complexity of the walking and postural stability task would also lead to differences in results across studies. Maintenance of postural stability is more critical to survival than cognitive performance under challenging DT conditions. As a result, the subjects

would sacrifice the performance of the cognitive task when the risk of losing balance reached a critical point.

In contrast, for a given mobility task, when a more difficult cognitive task was given (SS7 vs. SS3), the DT mobility parameters remained relatively stable whereas the NCR showed a further significant decline. Consistent with our results, previous studies showed no effect of the complexity of the cognitive task on postural sway [588]. In contrast, some previous studies also found further impairment in mobility performance as the cognitive difficulty increased [496, 587]. This discrepancy may be attributed to differences in the SS task difficulty and the population studied. While Lövdén et al. compared DT walking with SS1 and SS3 in young healthy people [496], we compared DT walking with SS3 and SS7 in stroke survivors. Lövdén et al. found that as the SS task became more difficult, further deterioration in DT gait was observed during obstacle crossing but not during level ground walking [496]. Lin et al. found the same phenomenon in healthy young adults but not in older adults [587]. In summary, differences in the DT protocol and study populations can partly account for the differences in findings, because the type of cognitive tasks used may affect the cognitive load imposed, whereas the age of the subjects or the presence of a central nervous system disorder may affect the overall central cognitive capacity.

When the difficulty of either component task increased between DT conditions, the stride length showed little change much in this study. This stable stride length was accompanied by a longer stride time, which suggested compromised cadence. Previous studies indicated that a reduced gait speed in DT conditions in healthy elderly resulted from two strategies: a reduced stride length with maintained cadence [589-591] or maintained stride length with a compromised cadence [521, 592]. The former was mainly used by older adults who already walked slowly under DT conditions to prevent potential falls [593, 594] by consciously narrowing the distance between the COM and the base of support [595]. It was suggested that adjustment of the stride length requires more attention than cadence [592]. The more limited attentional resources in stroke survivors may partially explain why our results in stroke survivors are more in line with the latter strategy.

4.2 Influence of stroke location

Contrary to our hypothesis, none of the measured cognitive and walking parameters in the DT condition demonstrated a significant difference between the cortical stroke group and the subcortical stroke group. A cortical lesion after a stroke was suggested to result in greater impairment of executive control of both balance control and DT coordination [596] and more compromised processing resource capacity [597] because the neural substrates for both component tasks sustain more damage [290, 397, 415]. Thus, it was originally hypothesized that the cortical stroke group would experience more DT interference while walking. However, the current findings did not support this hypothesis.

Few studies have included a direct comparison of gait or cognitive performance between individuals with cortical and subcortical stroke. It was observed that patients with frontal lesions do not always show executive deficits, possibly because executive processes involve links between various brain areas, not exclusively with the frontal cortex [598, 599]. Another important factor is brain plasticity [600]. The brain can adapt to pathological changes by using alternative connections to bypass the damaged location [601, 602]. Researchers have confirmed that multisensor information may still be processed to a certain extent even when the damage includes multimodal areas of the cortex and specific areas of the sensory cortex [603]. This finding suggests that even if the neural substrate for regulation of DTs is damaged, the DT function may still be maintained by compensatory mechanisms that involve undamaged neural networks. This alternative brain activation is influenced by stroke level [604], time since the stroke [605-610], functional connectivity [611], and corticospinal tract lesion volume [612-615]. Brain plasticity may be an important factor that may explain the lack of between-groups differences in the results because our subjects were all in the chronic stage of stroke recovery, so substantial plastic changes in the brain may have taken place.

In addition, the insignificant differences in cognitive performance and other gait parameters between these two stroke subgroups may be attributed to the great heterogeneity of our subjects. For example, some subjects in the cortical stroke group had the lesion in one brain cortex (e.g., frontal or parietal cortex), whereas others had lesions in multiple brain cortices. The stroke location in the subcortical group was even more diversified, with lesions in the basal ganglia, corona radiata, and/or brainstem. This greater heterogeneity of sample characteristics

requires a larger sample size to determine a significant between-group difference. However, only 27 individuals with cortical stroke could be recruited, compared with the larger subcortical stroke group.

4.3 Relationships between stroke characteristics and DT performance

Consistent with our hypothesis, more impaired motor or cognitive function after stroke was related to worse DT performance. In addition, poorer DT performance was significantly associated with less-satisfactory community reintegration.

4.3.1 Relationships between cognitive deficit and DT performance

Only the stride length in DT conditions showed a consistent negative relationship with mental inflexibility. This relationship was stronger in DT with obstacle crossing walking than with level ground walking conditions. This was to some degree consistent with the findings of a previous study that found that the ability to walk and perform a simple cognitive task concurrently was explained by participant characteristics and motor factors alone, whereas walking while performing a complex cognitive task was explained by executive function except for the two aspects mentioned in the last sentence [616].

In contrast to our study, a significant relationship was found between executive function and walking speed [616] and stride time variability [617] during DT walking with the SS task in other studies. Two main factors may explain the discordance in results: the aspects of executive function tested and the participants' characteristics. Hall et al. separately tested various types of attention with a battery of neuropsychological tests [616] in community-dwelling elderly subjects. Yogev et al. assessed only selective attention using the Stroop test in patients with Parkinson's disease [617]. We chose chronic stroke individuals and measured mental inflexibility with the WCST, which involved the interplay of multiple levels of cognitive processing that include various types of attention.

Global cognitive function (as indicated by the MoCA score) was found to have only a moderate relationship with DT cognitive performance (NCR in SS task) but not with DT gait performance. The construct measured by MoCA was similar to that indicated by the NCR generated in the SS task in the DT condition, compared with the DT gait parameters. The MoCA may also have limitations in evaluating the motor-specific cognitive control in DT conditions

[618]. The MoCA has compromised sensitivity and specificity in detecting subtle impairment in speed of information processing [619] and advanced executive function control in dual-tasking. In addition, our inclusion criterion stated that all participants required an MoCA score above 22. The relatively high homogeneity in MoCA score in our sample may also partly explain the low correlation between MoCA score and DT gait parameters [620].

4.3.2 Relationships between mobility deficits and DT performance

It is not surprising that DT walking parameters were associated with leg motor function (FMA) and balance function (Mini-BESTest). Those who had better motor recovery in the legs and better balance ability also tended to perform better in DT walking. In line with our results, previous studies also observed that motor factors (i.e., leg strength, static and dynamic balance) always demonstrated a moderate to strong relationship with walking performance in various DT walking combinations in older adults [616].

4.3.3 Relationship between community reintegration and DT performance

Our findings suggest that walking distance in DT conditions was a good correlate of community reintegration. Previous studies also found significant associations between DT walking performance and activity participation in patients with Parkinson's disease [621] or cognitive deficits [622] and in the elderly [623]. Community ambulation may be one of the important mediators of the relationship between community reintegration and DT performance [624, 625], because a limited ability to adapt to changes in the environmental context as measured by DT walking may restrict life role participation. [624]. Specifically, efficient allocation of attentional resources between concurrent tasks is indispensable for behavioral adaptability and independent daily living [626, 627]. Given these findings, it is important to address the deficits in DT walking to promote community reintegration. A recent randomized controlled trial examined the effectiveness of a DT exercise program in individuals with chronic stroke and found a significant effect of reducing cognitive-motor interference during walking and fall incidence and related injuries [628]. Whether such a program has any effect on community reintegration awaits further research.

4.4 Limitations and future research directions

This study has several limitations. First, the results can only be generalized to stroke survivors. Second, the sample size for the cortical stroke group was small. More subjects in this group could help to better assess the effects of stroke location in a future study. Third, no healthy control group was included for comparison. Fourth, only one cognitive task was applied in our study which could limit our understanding of patients' DT ability under various DT scenarios in daily life. Thus, future work is recommended to include more cognitive tasks with high ecological relevance and well-established neural basis in the DT protocol. Finally, real-time brain activity was not measured during dual-tasking. A future study should incorporate brain imaging techniques to examine the neural mechanisms associated with DT walking in stroke survivors.

5 Conclusions

In conclusion, the results of this study can help clinicians to identify the most appropriate domains of walking adaptability and provide suggestions on the selection of task complexity in DT assessment for chronic stroke individuals. DT measures of gait may represent a promising tool for detecting subtle disability or disease progression [629] because they are highly related to functional deficit and community reintegration post stroke.

6 References:

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7 APPENDICES

7.1 Ethical approval

To Pang Marco Yiu Chung (Department of Rehabilitation Sciences)

From TSANG Wing Hong Hector, Chair, Departmental Research committee

Email rshtsang@ Date 24-Mar-2017

Application for Ethical Review for Teaching/Research Involving Human subjects

I write to inform you that approval has been given to your application for human subjects ethics review of the following project for a period from 13-Mar-2017 to 12-Mar-2019:

Project Title:	Dual-task walking performance: relationship to stroke characteristics.
Department:	Department of Rehabilitation Sciences
Principal Investigator:	Pang Marco Yiu Chung
Project Start Date:	13-Mar-2017
Reference Number:	HSEARS20170227004

You will be held responsible for the ethical approval granted for the project and the ethical conduct of the personnel involved in the project. In the case of the Co-PI, if any, has also obtained ethical approval for the project, the Co-PI will also assume the responsibility in respect of the ethical approval (in relation to the areas of expertise of respective Co-PI in accordance with the stipulations given by the approving authority).

You are responsible for informing the Human Subjects Ethics Sub-committee in advance of any changes in the proposal or procedures which may affect the validity of this ethical approval.

TSANG Wing Hong

Hector Chair

Departmental Research Committee

7.2 Consent form

香港理工大學康復治療科學系科研同意書

科研題目：步行時雙重任務表現：與中風特性的相關性研究

科研人員： 彭耀宗教授 （香港理工大學康復治療科學系教授）

陳智軒教授 （香港理工大學康復治療科學系講座教授）

鍾志強博士 （香港理工大學康復治療科學系科學主任）

曾秀蘭小姐 （香港理工大學康復治療科學系博士研究生）

歐陽卉熙小姐（香港理工大學康復治療科學系碩士研究生）

科研內容：

日常生活中涉及多種認知和步行並存的雙重任務，能有效地及安全地進行這些事項對於活動自理尤為重要。就中風病人而言，當認知任務同時進行期間步行能力尤其受到影響。此次研究旨在探討中風病人在不同程度的雙重任務下之表現與中風特性之間的關係。

我們誠邀閣下蒞臨香港理工大學進行以下評估：

1. **認知能力**：請對給出的聲音作出快捷及正確的回應，倒數，記憶，及說出物件名；

2. **步行能力**：請分別在平坦的地面上及放有障礙物的地面上持續步行一分鐘；

3. **雙重任務活動**：請一邊步行，一邊進行如上的認知活動；

4. **問卷**：閣下需要完成一系列的量表以評估閣下日常生活及生活質素；

5.下肢機能及平衡：我們會要求閣下進行一系列下肢的動作及活動，以評估下肢受中風影響的嚴重程度及平衡能力。

上述測試將持續 1.5 小時到 2 小時。為了防止疲勞,測試之間允許休息。

對項目參的益處和潛在危險性：

參與此項研究能讓閣下對自己在步行時的認知表現及雙重任務能力有更深入的了解。研究的結果，將會提供重要的資料，有助於設計臨床上的運動處方。測試過程中，將會提供間歇的休息時間。閣下如果感到不舒服，測試將會終止。沒有任何其他已知的危險性存在於是項研究之中。參與是次研究乃自願性質。

保密性：

此項研究收集所得的個人資料及數據絕對保密；除相關研究人員之外，閣下的姓名或個人資料將不會被公開。

參加者同意書

本人_____已瞭解此次研究的具體情況。本人願意參加是項研究計劃，並有權在任何時候、不論任何原因放棄參與此項計劃，而此舉不會導致我受到任何懲罰或不公平對待。本人明白參與此項計劃的潛在危險性以及本人的資料將不會洩露給與此計劃無關的人員，我的名字不會出現在任何影帶或出版物上。本人亦明白製作人員可剪輯本人之訪問或錄音或錄影片段，而片段將製作成教學用具，作為教學用途或於學術會議中播放。

本人可以用電話 2766- 來聯絡此計劃負責人彭耀宗教授。若本人對此計劃之研究人員有任何投訴，可以聯絡部門科研委員會秘書鍾靜妍女士(電話：2766)。本人亦明白，參與此計劃需要本人簽署一份同意書。

簽名（參與者） ：_____ 日期 ：_____

簽名（證人） ：_____ 日期 ：_____

7.3 Sample of assessments

7.3.1 Demographic information

Name: _____ Gender: Male/ Female Age_____

Body weight :_____(kg) Body Height:_____(cm)

First Onset of stroke:_____ Duration of stroke_____

Type of stroke: Ischemic / Hemorrhagic / Others (Please specify: ___) Paretic leg: L/ R

Orthosis: No/Yes (indoor_____/outdoor_____ during test_____)

Waling aids: No/Yes (indoor_____/outdoor_____/ during test_____)

(0,None / 1,cane,stick / 2,quadripod / 3,walking frame / 4,wheelchair)

Lesion area from MRI/CT _____ Dominant side: _____ Living status_____

Occupation (Pre/post)： ____/___ Smoking (Pre/post): ____ Drinking (Pre/post): _____

Exercise habit: Pre (Frequency/intensity/type): _____

Post: _____

Past 1 year fall history (time/numbers/ direction/cause/injury/follow medical care):

_____

_____

Present Medical Condition:

_____

_____

Medicine:

_____

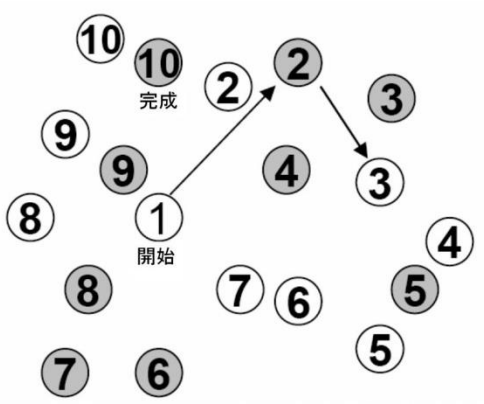
_____

Surgical history:

_____

7.3.2 Montreal Cognitive Assessment Hong Kong version (HK-MoCA)

視覺空間/執行性



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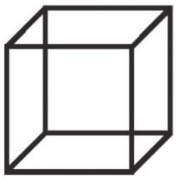
複製圖形



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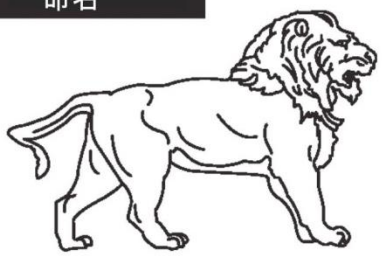
畫時鐘 (十一點十分)
(3 分)

[ ] 輪廓　[ ] 數字　[ ] 時分針

分數 ___/5

命名



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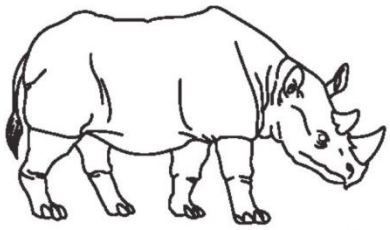

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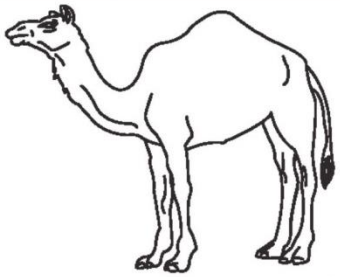

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___/3

記憶

讀出詞語再由病者重複
以上步驟做兩次
5分鐘後回憶

	面孔	絲絨	教堂	雛菊	紅色
第一次嘗試					
第二次嘗試					

不用計分

專注

讀出數字 (每秒一個)

病者須把數字向前重複[ ] 2 1 8 5 4

病者須把數字向後重複[ ] 7 4 2

___/2

讀出數字: 當數字 '1' 出現時病者必須用手敲打桌面
(如≥2錯誤便不給予分數)

[ ] 5 2 1 3 7 4 1 1 8 0 6 2 1 5 1 7 4 5 1 1 1 4 1 7 0 5 1 1 2

___/1

由100開始連續 7減算

[ ] 93　[ ] 86　[ ] 79　[ ] 72　[ ] 65

4 或 5 個正確減算得 **3 分**，2 或 3 個正確得 **2 分**，1個正確得 **1 分**，沒有正確得 **0 分**

___/3

語言

重複:

姨丈買魚腸[ ]

西施四十四歲[ ]

___/2

流暢: 一分鐘內能說出的動物名稱的數目 [ ] (N ≥ 11 個名稱)

___/1

抽象

相似點: 例如: 香蕉 – 橙 =生果　[ ] 火車 – 單車　[ ] 手錶 – 間尺

___/2

延遲記憶

須回憶詞語 不可給提示	面孔 [ ]	絲絨 [ ]	教堂 [ ]	雛菊 [ ]	紅色 [ ]	分數只給予沒有提示的正確回憶
類目提示 (見下表)						
多項選擇 (見下表)						

___/5

定向

[ ] 日　[ ] 月　[ ] 年　[ ] 星期　[ ] 地點　[ ] 地區

___/6

延遲記憶備註表

	類目提示	多項選擇
面孔	身體的一部分	鼻子、面孔、手
絲絨	紡織品的一種	牛仔布、棉花、絲絨
教堂	建築物的一種	教堂、學校、醫院
雛菊	花的一種	玫瑰、雛菊、鬱金香
紅色	一種顏色	紅色、藍色、綠色

總分 ___/30

如≤6年教育加1分
22分或以上為正常

7.3.3 Reintegration to Normal Living Index

1. 在家中，當我覺得有需要時，我能夠隨意走動（可能需要使用輪椅、其他器材或輔助）。

1	2	3	4
不能描述我的情況	描述我少部分的情況	描述我大部分的情況	完全描述我的情況

2. 在社區中， 當我覺得有需要時，我能夠隨意走動（可能需要使用輪椅、其他器材或輔助）。

1	2	3	4
不能描述我的情況	描述我少部分的情況	描述我大部分的情況	完全描述我的情況

3. 當我覺得有需要時，我能夠隨意出境外遊（可能需要使用輪椅、其他器材或輔助）。

1	2	3	4
不能描述我的情況	描述我少部分的情況	描述我大部分的情況	完全描述我的情況

4. 對於如何應付自我照顧的需要（穿衣、進食、如廁、洗澡），我感到自在（可能需要使用輪椅、其他器材或輔助）。

1	2	3	4
不能描述我的情況	描述我少部分的情況	描述我大部分的情況	完全描述我的情況

5. 我大部分的日子都用在我覺得有需要或重要的工作上（工作可以包括受薪工作、家務義工、上學...等等。可能需要使用輔助器材、監察、及/或協助）。

1	2	3	4
不能描述我的情況	描述我少部分的情況	描述我大部分的情況	完全描述我的情況

6. 當我想的時候，我能夠參與康樂活動（嗜好、手工藝、運動、閱讀、看電視、遊戲、電腦...等等）（可能需要使用輔助器材、監察、及/或協助）。

1	2	3	4
不能描述我的情況	描述我少部分的情況	描述我大部分的情況	完全描述我的情況

7. 當我覺得有需要或我希望時，我會和家人、朋友及/或工作上有往來的人一同參與社交活動（可能需要使用輔助器材、監察、及/或協助）。

1	2	3	4
不能描述我的情況	描述我少部分的情況	描述我大部分的情況	完全描述我的情況

8. 我認為我在這中所擔當的角色，可以切合自己及其他家庭成員的需要。（家庭的意思是與你一同居住的人，及/或並非與你同住但與你定期見面的親人。可能需要使用輔助器材、監察、及/或協助）。

1	2	3	4
不能描述我的情況	描述我少部分的情況	描述我大部分的情況	完全描述我的情況

9. 整體而言，我對我的個人關係（家人、親戚、朋友）感到自在。

1	2	3	4
不能描述我的情況	描述我少部分的情況	描述我大部分的情況	完全描述我的情況

10. 整體而言，當我與人共處時，我感到自在。

1	2	3	4
不能描述我的情況	描述我少部分的情況	描述我大部分的情況	完全描述我的情況

11. 我覺得我能夠應付得到人生中會發生的各項事件。

1	2	3	4
不能描述我的情況	描述我少部分的情況	描述我大部分的情況	完全描述我的情況

Total Score：_____

7.3.4 Fugl-Meyer Assessment (Lower Extremities)

E. LOWER EXTREMITY					
I. Reflex activity, supine position				**none**	**can be elicited**
Flexors: knee flexors				0	2
Extensors: patellar, achilles (at least one)				0	2
			Subtotal I (max 4)		
II. Volitional movement within synergies supine position				**none**	**partial**	**full**
Flexor synergy: Maximal hip flexion (abduction/external rotation), maximal flexion in knee and ankle joint (palpate distal tendons to ensure active knee flexion).	Hip	flexion		0	1	2
	Knee	flexion		0	1	2
	Ankle	dorsiflexion		0	1	2
Extensor synergy: From flexor synergy to the hip extension/adduction, knee extension and ankle plantar flexion. Resistance is applied to ensure active movement, evaluate both movement and strength (compare with the unaffected side)	Hip	extension		0	1	2
		adduction		0	1	2
	Knee	extension		0	1	2
	Ankle	plantar flexion		0	1	2
			Subtotal II (max 14)			
III. Volitional movement mixing synergies sitting position, knee 10cm from the edge of the chair/bed				**none**	**partial**	**full**
Knee flexion from actively or passively extended knee	no active motion less than 90° active flexion, palpate tendons of hamstrings more than 90° active flexion			0	1	2
Ankle dorsiflexion compare with unaffected side	no active motion limited dorsiflexion complete dorsiflexion			0	1	2
			Subtotal III (max 4)			
IV. Volitional movement with little or no synergy standing position, hip at 0°				**none**	**partial**	**full**
Knee flexion to 90° hip at 0°, balance support is allowed	no active motion or immediate, simultaneous hip flexion less than 90° knee flexion and/or hip flexion during movement at least 90° knee flexion without simultaneous hip flexion			0	1	2
Ankle dorsiflexion compare with unaffected side	no active motion limited dorsiflexion complete dorsiflexion			0	1	2
			Subtotal IV (max 4)			
V. Normal reflex activity supine position, assessed only if full score of 4 points is achieved in part IV, compare with the unaffected side				**0 (IV), hyper**	**lively**	**normal**
Reflex activity knee flexors, Patellar, Achilles,	0 points on part IV or 2 of 3 reflexes markedly hyperactive 1 reflex markedly hyperactive or at least 2 reflexes lively maximum of 1 reflex lively, none hyperactive			0	1	2
			Subtotal V (max 2)			
			Total E (max 28)			

F. COORDINATION/SPEED, supine, after one trial with both legs, eyes closed, heel to knee cap of the opposite leg, 5 times as fast as possible		**marked**	**slight**	**none**
Tremor	at least 1 completed movement	0	1	2
Dysmetria at least 1 completed movement	pronounced or unsystematic slight and systematic no dysmetria	0	1	2
		≥ 6s	**2 - 5s**	**< 2s**
Time start and end with the hand on the knee	at least 6 seconds slower than unaffected side 2-5 seconds slower than unaffected side less than 2 seconds difference	0	1	2
	Total F (max 6)			

7.3.5 Mini-BESTest: Balance Evaluation Systems Test

ANTICIPATORY ***SUB SCORE:*** **/6**

1. SIT TO STAND

Instruction: *"Cross your arms across your chest. Try not to use your hands unless you must. Do not let your legs lean against the back of the chair when you stand. Please stand up now."*

(2) Normal: Comes to stand without use of hands and stabilizes independently.
(1) Moderate: Comes to stand WITH use of hands on first attempt.
(0) Severe: Unable to stand up from chair without assistance, OR needs several attempts with use of hands.

2. RISE TO TOES

Instruction: *"Place your feet shoulder width apart. Place your hands on your hips. Try to rise as high as you can onto your toes. I will count out loud to 3 seconds. Try to hold this pose for at least 3 seconds. Look straight ahead. Rise now."*

(2) Normal: Stable for 3 s with maximum height.
(1) Moderate: Heels up, but not full range (smaller than when holding hands), OR noticeable instability for 3 s.
(0) Severe: ≤ 3 s.

3. STAND ON ONE LEG

Instruction: "Look straight ahead. Keep your hands on your hips. Lift your leg off of the ground behind you without touching or resting your raised leg upon your other standing leg. Stay standing on one leg as long as you can. Look straight ahead. Lift now."

Left: *Time in Seconds Trial 1:_____Trial 2:_____*
(2) Normal: 20 s.
(1) Moderate: < 20 s.
(0) Severe: Unable.

Right: *Time in Seconds Trial 1:_____Trial 2:_____*
(2) Normal: 20 s.
(1) Moderate: < 20 s.
(0) Severe: Unable

To score each side separately use the trial with the longest time.
To calculate the sub-score and total score use the side [left or right] with the lowest numerical score [i.e. the worse side].

REACTIVE POSTURAL CONTROL ***SUB SCORE:*** **/6**

4. COMPENSATORY STEPPING CORRECTION- FORWARD

Instruction: "Stand with your feet shoulder width apart, arms at your sides. Lean forward against my hands beyond your forward limits. When I let go, do whatever is necessary, including taking a step, to avoid a fall."

(2) Normal: Recovers independently with a single, large step (second realignment step is allowed).
(1) Moderate: More than one step used to recover equilibrium.
(0) Severe: No step, OR would fall if not caught, OR falls spontaneously.

5. COMPENSATORY STEPPING CORRECTION- BACKWARD

Instruction: "Stand with your feet shoulder width apart, arms at your sides. Lean backward against my hands beyond your backward limits. When I let go, do whatever is necessary, including taking a step, to avoid a fall."

(2) Normal: Recovers independently with a single, large step.
(1) Moderate: More than one step used to recover equilibrium.
(0) Severe: No step, OR would fall if not caught, OR falls spontaneously.

6. COMPENSATORY STEPPING CORRECTION- LATERAL

Instruction: "Stand with your feet together, arms down at your sides. Lean into my hand beyond your sideways limit. When I let go, do whatever is necessary, including taking a step, to avoid a fall."

Left
(2) Normal: Recovers independently with 1 step (crossover or lateral OK).
(1) Moderate: Several steps to recover equilibrium.
(0) Severe: Falls, or cannot step.

Right
(2) Normal: Recovers independently with 1 step (crossover or lateral OK).
(1) Moderate: Several steps to recover equilibrium.
(0) Severe: Falls, or cannot step.

Use the side with the lowest score to calculate sub-score and total score.

SENSORY ORIENTATION ***SUB SCORE:*** **/6**

7. STANCE (FEET TOGETHER); EYES OPEN, FIRM SURFACE

Instruction: "Place your hands on your hips. Place your feet together until almost touching. Look straight ahead. Be as stable and still as possible, until I say stop."

Time in seconds:_____
(2) Normal: 30 s.
(1) Moderate: < 30 s.
(0) Severe: Unable.

8. STANCE (FEET TOGETHER); EYES CLOSED, FOAM SURFACE

Instruction: "Step onto the foam. Place your hands on your hips. Place your feet together until almost touching. Be as stable and still as possible, until I say stop. I will start timing when you close your eyes."

Time in seconds:_____

(2) Normal: 30 s.
(1) Moderate: < 30 s.
(0) Severe: Unable.

9. INCLINE- EYES CLOSED

Instruction: "Step onto the incline ramp. Please stand on the incline ramp with your toes toward the top. Place your feet shoulder width apart and have your arms down at your sides. I will start timing when you close your eyes."

Time in seconds:_____

(2) Normal: Stands independently 30 s and aligns with gravity.
(1) Moderate: Stands independently <30 s OR aligns with surface.
(0) Severe: Unable.

DYNAMIC GAIT ***SUB SCORE:*** **/ 10**

10. CHANGE IN GAIT SPEED

Instruction: "Begin walking at your normal speed, when I tell you 'fast', walk as fast as you can. When I say 'slow', walk very slowly."

(2) Normal: Significantly changes walking speed without imbalance.
(1) Moderate: Unable to change walking speed or signs of imbalance.
(0) Severe: Unable to achieve significant change in walking speed AND signs of imbalance.

11. WALK WITH HEAD TURNS – HORIZONTAL

Instruction: "Begin walking at your normal speed, when I say "right", turn your head and look to the right. When I say "left" turn your head and look to the left. Try to keep yourself walking in a straight line."

(2) Normal: performs head turns with no change in gait speed and good balance.
(1) Moderate: performs head turns with reduction in gait speed.
(0) Severe: performs head turns with imbalance.

12. WALK WITH PIVOT TURNS

Instruction: "Begin walking at your normal speed. When I tell you to 'turn and stop', turn as quickly as you can, face the opposite direction, and stop. After the turn, your feet should be close together."

(2) Normal: Turns with feet close FAST (≤ 3 steps) with good balance.
(1) Moderate: Turns with feet close SLOW (≥4 steps) with good balance.
(0) Severe: Cannot turn with feet close at any speed without imbalance.

13. STEP OVER OBSTACLES

Instruction: "Begin walking at your normal speed. When you get to the box, step over it, not around it and keep walking."

(2) Normal: Able to step over box with minimal change of gait speed and with good balance.
(1) Moderate: Steps over box but touches box OR displays cautious behavior by slowing gait.
(0) Severe: Unable to step over box OR steps around box.

14. TIMED UP & GO WITH DUAL TASK *[3 METER WALK]*

Instruction TUG: "When I say 'Go', stand up from chair, walk at your normal speed across the tape on the floor, turn around, and come back to sit in the chair."

Instruction TUG with Dual Task: "Count backwards by threes starting at ___. When I say 'Go', stand up from chair, walk at your normal speed across the tape on the floor, turn around, and come back to sit in the chair. Continue counting backwards the entire time."

TUG: _____seconds; Dual Task TUG: _____seconds

(2) Normal: No noticeable change in sitting, standing or walking while backward counting when compared to TUG without Dual Task.
(1) Moderate: Dual Task affects either counting OR walking (>10%) when compared to the TUG without Dual Task.
(0) Severe: Stops counting while walking OR stops walking while counting.

When scoring item 14, if subject's gait speed slows more than 10% between the TUG without and with a Dual Task the score should be decreased by a point.

TOTAL SCORE: _____/28

8 LIST OF TABLES

8.1 Table 1 Experimental protocol.

Complexity	Description	Outcome variable
Mobility task: a 1-minute time period is given for all mobility tasks		
Low	Level ground walking: Walk along a rectangular-shaped walkway (6m×4m).	Distance (meters)
High	Obstacle crossing: Walk along a rectangular-shaped walkway (6m×4m) with obstacles (height: 9cm, length: 58cm) placed every 4 meters apart.	Distance (meters)
Cognitive task: a 1-minute time period is given for all cognitive tasks		
Domain: mental tracking		
Low	Serial 3 subtractions: Repeatedly subtract 3 from a random number between 500 and 600.	No. of correct digits (NCD)
high	Serial 7 subtractions: Repeatedly subtract 7 from a random number between 500 and 600.	No. of correct digits (NCD)

8.2 Table 2 Participant characteristics

Descriptive Statistics	Stroke(n=80)		Cortical (n=27)		Subcortical (n=53)		*p*
	Mean	SD	Mean	SD	Mean	SD	
Age	62.2	6.5	60.7	6.5	63.0	6.5	0.14
BMI	24.0	3.1	24.4	2.8	23.8	3.3	0.39
Number of comorbidities	2.3	1.4	2.3	1.5	2.3	1.4	0.97
Number of medications	3.9	2.3	3.7	2.2	4.0	2.4	0.51
Montreal Cognitive Assessment (Max:30)	27.1	2.1	27.4	1.7	27.0	2.2	0.54
Geriatric Depression Scale-short form (Max:15)	5.0	3.9	5.6	4.3	4.6	3.7	0.39
Mini-BESTest (Max:28)	19.5	4.3	20.4	3.9	19.1	4.5	0.12
Duration of stroke (month)	65.1	46.5	68.3	54.5	63.4	42.3	0.97
Fugl-Meyer assessment lower extremities (Max:34)	24.9	4.7	26.7	5.4	24.0	4.1	0.02*
WCST Perseverative Errors (%)	0.20	0.11	0.2	0.11	0.20	0.11	0.28
Reintegration to Normal Living Index (Max:44)	35.3	5.9	33.9	6.5	36.0	5.5	0.17
Stoke type (ischemic / hemorrhagic / others; n)	55/24/1		17/10		38/14/1		0.35
Involved stroke location (Frontal cortex/ parietal cortex/ temporal cortex/ basal ganglia/ internal capsule/ thalamus/brainstem; n)	17/12/12/49/16/7/20		17/12/12/11/2/1/3		0/0/0/38/14/6/17		NA
Paretic side(left/right; n)	48/32		18/9		30/23		0.39
Modified Rankin Scale (2/3; n)	68/12		21/6		47/6		0.20
Gender(female/male; n)	36/44		9/18		27/26		0.13
Walking aids indoor(none/stick/quadripod; n)	67/7/6		21/4/2		46/3/4		0.35
Walking aids outdoor(non/stick/quadripod/; n)	22/47/7		8/15/3		14/32/4		0.87
Walking aids during test (none/stick/quadripod; n)	64/11/5		21/3/3		43/8/2		0.63
Education level(Primary/Secondary/Tertiary; n)	21/43/16		6/14/7		15/29/9		0.61
Fall status past year (faller/non-faller; n)	20/60		8/19		12/41		0.50

Note： WCST: Wisconsin Card Sorting Task; *: $p<0.05$.

8.3 Table 3 Two-way ANOVA: Influence of task difficulty on cognitive (NCR) and gait parameters

		Two-way ANOVA		
		Main effect		Interaction effect
		MD	CD	MD×CD
Number of correct response (NCR)	F	50.30	328.14	11.76
	p	<0.001*	<0.001*	<0.001*
	ηp²	0.39	0.81	0.13
Distance	F	73.14	141.30	6.45
	p	<0.001*	<0.001*	0.002*
	ηp²	0.48	0.64	0.08
Stride Length	F	25.69	80.34	2.93
	p	<0.001*	<0.001*	0.062
	ηp²	0.25	0.50	0.04
Stride Time	F	73.24	67.67	1.86
	p	<0.001*	<0.001*	0.17
	ηp²	0.48	0.46	0.02
Peak frontal Trunk Velocity	F	20.35	63.20	1.80
	p	<0.001*	<0.001*	0.170
	ηp²	0.21	0.44	0.02
Swing time Asymmetry	F	7.74	16.59	4.40
	p	0.007*	<0.001*	0.02
	ηp²	0.09	0.17	0.05
Stride Length variability	F	179.06	2.59	1.50
	p	<0.001*	0.085	0.225
	ηp²	0.69	0.03	0.02
Stride Time variability	F	182.67	8.71	1.07
	p	<0.001*	<0.001*	0.347
	ηp²	0.70	0.10	0.01

Note： NCR: number of correct response; CD: cognitive difficulty comparison; MD: motor difficulty comparison.

*: $p<0.01$.

8.4 Table 4 Post-hoc paired-T test: Influence of task difficulty on cognitive performance (NCR).

	Number of correct responses			
①SS3 +LGW	14.61 ± 6.31			
②SS3 +OBW	13.36 ± 6.06			
③SS7 + LGW	8.26 ± 4.59			
④SS7 + OBW	7.71 ± 4.25			
⑤ SS3	17.68 ± 7.68			
⑥ SS7	9.38 ± 5.06			
	MD	95% CI		*p*
Motor task difficulty		Lower	Upper	
Comparison between DT conditions				
①②	1.25	0.32	2.18	0.009*
③④	0.55	-0.10	1.20	0.098
Comparison between ST and DT conditions				
⑤①	3.06	2.16	3.96	<0.001*
⑤②	4.31	3.22	5.41	<0.001*
⑥③	1.11	0.53	1.70	<0.001*
⑥④	1.66	0.97	2.36	<0.001*
Cognitive task difficulty				
Comparison between DT conditions				
①③	6.35	5.41	7.29	<0.001*
②④	5.65	4.66	6.64	<0.001*
Comparison between ST conditions				
⑤⑥	8.30	7.26	9.34	<0.001*

Note： NCR: number of correct response; SS3: serial subtraction three; SS7: serial subtraction seven; LGW: level ground walking; OBW: obstacle crossing walking; MD: mean difference.
*: $p<0.01$.

8.5 Table 5 Post-hoc paired-T tests: Influence of task difficulty on dual task walking distance, stride length and stride time.

	Distance	Stride Length	Stride Time
①SS3 +LGW	34.20±14.05	48.62 ±15.59	1.43 ±0.28
②SS3 +OBW	30.78±12.58	47.59 ±15.18	1.49 ±0.29
③SS7 + LGW	32.70±13.96	48.62 ±16.07	1.43 ±0.30
④SS7 + OBW	30.26±12.27	47.14 ±15.32	1.51 ±0.29
⑤ LGW	42.93±17.73	53.95 ±15.42	1.29 ±0.26
⑥ OBW	37.97±15.36	51.11 ±15.31	1.38 ±0.29

Motor task difficulty	MD	95% CI		*p*	MD	95% CI		*p*	MD	95% CI		*p*
		Lower	Upper			Lower	Upper			Lower	Upper	
Comparison between DT conditions												
①②	3.42	2.46	4.38	<0.001*	1.03	0.08	1.98	0.034	-0.06	-0.08	-0.04	<0.001*
③④	2.44	1.11	3.76	<0.001*	1.49	0.13	2.85	0.032	-0.09	-0.12	-0.05	<0.001*
Comparison between ST conditions												
⑤⑥	4.95	3.77	6.14	<0.001*	2.84	1.78	3.90	<0.001*	-0.09	-0.11	-0.07	<0.001*
Cognitive task difficulty												
Comparison between DT conditions												
①③	1.51	0.25	2.76	0.019	0.00	-1.35	1.35	0.995	0.00	-0.09	0.03	0.940
②④	0.52	-0.24	1.28	0.174	0.45	-0.28	1.18	0.222	-0.02	-0.05	0.00	0.055
Comparison between ST and DT conditions												
⑤①	8.72	7.25	10.20	<0.001*	5.33	4.23	6.43	<0.001*	-0.13	-0.16	-0.10	<0.001*
⑤③	10.23	8.37	12.09	<0.001*	5.32	3.73	6.92	<0.001*	-0.13	-0.16	-0.10	<0.001*
⑥②	7.19	5.90	8.48	<0.001*	3.52	2.63	4.41	<0.001*	-0.11	-0.14	-0.08	<0.001*
⑥④	7.71	6.44	8.98	<0.001*	3.97	3.10	4.85	<0.001*	-0.13	-0.16	-0.10	<0.001*

Note： SS3: serial subtraction three; SS7: serial subtraction seven; LGW: level ground walking; OBW: obstacle crossing walking; MD: mean difference.

*: $p<0.01$.

8.6 Table 6 Post-hoc paired-T tests: Influence of task difficulty on dual-task peak frontal trunk velocity and swing time asymmetry.

	Peak frontal Trunk Velocity				Swing time Asymmetry			
①SS3 +LGW	39.17±14.81				22.37±13.01			
②SS3 +OBW	41.87±15.12				25.81±12.12			
③SS7 + LGW	38.88±14.86				22.71±13.26			
④SS7 + OBW	41.04±15.31				25.93 ±12.23			
⑤ LGW	44.51±16.83				20.72±11.97			
⑥ OBW	45.90±17.25				24.08±11.91			
	MD	95% CI		*p*	MD	95% CI		*p*
Motor task difficulty		Lower	Upper			Lower	Upper	
Comparison between DT conditions								
①②	-2.70	-3.81	-1.58	<0.001*	-3.44	-5.26	-1.62	<0.001*
③④	-2.15	-3.33	-0.98	<0.001*	-3.22	-5.01	-1.43	0.001*
Comparison between ST conditions								
⑤⑥	-1.39	-2.73	-0.05	0.043	-3.36	-5.18	-1.53	<0.001*
Cognitive task difficulty								
Comparison between DT conditions								
①③	0.29	-0.54	1.12	0.490	-0.34	-2.01	1.33	0.683
②④	0.83	0.09	1.57	0.028	-0.12	-1.62	1.39	0.875
Comparison between ST and DT conditions								
⑤①	5.34	3.99	6.70	<0.001*	-1.65	-3.54	0.25	0.087
⑤③	5.63	4.23	7.03	<0.001*	-1.99	-3.55	-0.43	0.013
⑥②	4.03	2.60	5.47	<0.001*	-1.73	-3.34	-0.12	0.035
⑥④	4.86	3.44	6.29	<0.001*	-1.85	-3.47	-0.23	0.025

Note： SS3: serial subtraction three; SS7: serial subtraction seven; LGW: level ground walking; OBW: obstacle crossing walking; MD: mean difference

*: $p<0.01$.

8.7 Table 7 Post-hoc paired-T tests: Influence of task difficulty on dual task stride length variability and stride time variability.

	Stride Length variability				Stride Time variability			
①SS3 +LGW	0.10 ±0.04				0.07 ±0.03			
②SS3 +OBW	0.13 ±0.04				0.15 ±0.06			
③SS7 + LGW	0.10 ±0.04				0.07 ±0.04			
④SS7 + OBW	0.14 ±0.04				0.15 ±0.06			
⑤ LGW	0.09 ±0.03				0.05 ±0.02			
⑥ OBW	0.13 ±0.04				0.14 ±0.07			
	MD	95% CI		*p*	MD	95% CI		*p*
Motor task difficulty		Lower	Upper			Lower	Upper	
Comparison between DT conditions								
①②	-0.04	-0.04	-0.03	<0.001*	-0.08	-0.10	-0.07	<0.001*
③④	-0.03	-0.04	-0.02	<0.001*	-0.08	-0.10	-0.07	<0.001*
Comparison between ST conditions								
⑤⑥	-0.04	-0.05	-0.04	<0.001*	-0.09	-0.11	-0.08	<0.001*
Cognitive task difficulty								
Comparison between DT conditions								
①③					0.00	-0.01	0.00	0.376
②④					0.00	-0.01	0.01	0.764
Comparison between ST and DT conditions								
⑤①					-0.02	-0.02	-0.01	<0.001*
⑤③					-0.02	-0.03	-0.01	<0.001*
⑥②					-0.01	-0.02	0.01	0.219
⑥④					-0.01	-0.02	0.00	0.169

Note： SS3: serial subtraction three; SS7: serial subtraction seven; LGW: level ground walking; OBW: obstacle crossing walking; MD: mean difference.

*: $p<0.01$.

8.8 Table 8 Descriptive data of stroke location comparisons on motor performance.

	Number of correct response	Distance	Stride Length	Stride Time	Swing time Asymmetry	Stride Length variability	Stride time variability
Cortical involved							
①SS3 +LGW	14.93±5.96	35.30±13.68	48.23±17.11	1.40±0.30	22.32 ±14.66	0.09±0.04	0.06±0.03
②SS3 +OBW	13.56±6.23	31.84±12.54	47.55±16.10	1.48±0.32	24.93 ±11.53	0.13±0.03	0.16±0.07
③SS7 + LGW	7.37±3.71	33.33±13.59	47.85±16.72	1.42±0.31	22.04 ±13.39	0.09±0.03	0.07±0.04
④SS7 + OBW	7.30±3.52	31.58±12.77	47.47±16.01	1.49±0.32	24.97 ±11.34	0.13±0.04	0.16±0.06
⑤ LGW		45.43±16.80	54.75±16.36	1.25±0.27	21.54 ±12.01	0.09±0.03	0.05±0.02
⑥ OBW		40.24±15.32	51.45±16.64	1.36±0.32	23.39 ±12.98	0.13±0.04	0.15±0.10
⑦ SS3	18.30±7.20						
⑧ SS7	9.26±4.04						
Subcortical							
①SS3 +LGW	14.45±6.53	33.65±14.33	48.82±14.93	1.44±0.27	22.39 ±12.23	0.10±0.04	0.07±0.04
②SS3 +OBW	13.26±6.03	30.24±12.69	47.61±14.84	1.50±0.27	26.26 ±12.50	0.13±0.04	0.15±0.06
③SS7 + LGW	8.72±4.95	32.37±14.25	49.02±15.88	1.43±0.30	23.05 ±13.31	0.11±0.04	0.07±0.04
④SS7 + OBW	7.92±4. 95	29.59±12.07	46.97±15.12	1.52±0.28	26.41 ±12.73	0.14±0.04	0.15±0.06
⑤ LGW		41.65±18.20	53.54±15.06	1.32±0.26	20.30 ±12.05	0.09±0.04	0.05±0.02
⑥ OBW		36.82±15.40	50.94±14.76	1.39±0.27	24.42 ±11.44	0.14±0.04	0.14±0.06
⑦ SS3	17.36±7.97						
⑧ SS7	9.43±5.53						

Note：SS3: serial subtraction three; SS7: serial subtraction seven; LGW: level ground walking; OBW: obstacle crossing walking.

8.9 Table 9 Three-way ANCOVA: Influence of stroke location on DT performance.

		Main effect	Interaction effect		
		Stroke location	MD×Stroke location	CD×Stroke location	MD×CD ×Stroke location
Number of correct response	F	0.12	0.70	3.43	0.22
	p	0.726	0.498	0.068	0.804
	ηp²	<0.01	0.01	0.04	<0.01
Distance	F	0.30	0.017	1.922	0.52
	p	0.585	0.897	0.161	0.598
	ηp²	<0.01	<0.01	0.03	0.01
Stride Length	F	0.03	0.82	1.23	1.04
	p	0.865	0.369	0.291	0.350
	ηp²	<0.01	0.01	0.02	0.01
Stride Time	F	0.05	1.51	0.07	0.44
	p	0.828	0.223	0.937	0.633
	ηp²	<0.01	0.02	<0.01	0.01
Peak frontal Trunk Velocity	F	4.22	1.37	0.82	0.40
	p	**0.043***	0.246	0.440	0.669
	ηp²	0.05	0.02	0.01	0.01
Swing time asymmetry	F	0.01	1.78	0.78	0.32
	p	0.920	0.186	0.461	0.727
	ηp²	<0.01	0.02	0.01	<0.01
Stride Length variability	F	1.41	0.63	0.01	1.24
	p	0.239	0.429	0.991	0.292
	ηp²	0.02	0.01	<0.01	0.02
Stride time variability	F	0.05	1.51	0.10	<0.01
	p	0.828	0.223	0.748	0.985
	ηp²	<0.01	0.02	<0.01	<0.01

Note： CD: cognitive difficulty comparison; MD: motor difficulty comparison. *: $p<0.05$.

8.10 Table 10 Post-hoc independent T test: Influence of stroke location on dual task postural stability performance.

	Peak Frontal Trunk Velocity			
Cortical stroke				
①SS3 +LGW	35.11±12.75			
②SS3 +OBW	37.00±12.40			
③SS7 + LGW	34.65±12.55			
④SS7 + OBW	35.99±12.65			
⑤ LGW	40.85±15.51			
⑥ OBW	42.25±15.46			
Subcortical stroke				
①SS3 +LGW	41.24±15.46			
②SS3 +OBW	44.35±15.87			
③SS7 + LGW	41.04±15.58			
④SS7 + OBW	43.61±16.01			
⑤ LGW	46.38±17.31			
⑥ OBW	47.76±17.95			
		95% CI		
	MD	Lower	Upper	*p*
①	-6.14	-13.01	0.74	0.080
②	-7.35	-14.32	-0.38	0.039
③	-6.39	-13.28	0.50	0.069
④	-7.61	-14.66	-0.56	0.035
⑤	-5.53	-13.41	2.34	0.166
⑥	-5.51	-13.58	2.57	0.178

Note： SS3: serial subtraction three; SS7: serial subtraction seven; LGW: level ground walking; OBW: obstacle crossing walking; MD: mean difference.

8.11 Table 11 Correlations between cognitive deficit and DT performance.

	WCST Perseverative Errors (%)		MoCA	
	r	*p*	r	*p*
number of correct response (SS3+ LGW)	-0.19	0.086	0.33	0.003 **
number of correct response (SS3+ OBW)	-0.22	0.051	0.38	0.001 **
number of correct response (SS7+ LGW)	-0.17	0.131	0.38	0.000 **
number of correct response (SS7+OBW)	-0.18	0.105	0.29	0.010 **
distance (SS3+ LGW)	-0.14	0.230	-0.04	0.696
distance (SS3+OBW)	-0.17	0.139	-0.04	0.728
distance (SS7+ LGW)	-0.14	0.223	-0.07	0.564
distance (SS7+OBW)	-0.12	0.304	-0.08	0.466
stride length (SS3+ LGW)	-0.22	0.048 *	-0.01	0.905
stride length (SS3+OBW)	-0.29	0.010 **	-0.03	0.769
stride length (SS7+ LGW)	-0.25	0.023 *	0.00	0.992
stride length (SS7+OBW)	-0.28	0.011 *	-0.01	0.945
stride time (SS3+ LGW)	-0.06	0.608	-0.08	0.469
stride time (SS3+OBW)	-0.09	0.429	-0.03	0.817
stride time (SS7+ LGW)	-0.06	0.579	-0.01	0.942
stride time (SS7+OBW)	-0.04	0.754	-0.04	0.700
peak trunk frontal velocity (SS3+ LGW)	0.08	0.499	0.12	0.280
peak trunk frontal velocity (SS3+OBW)	-0.05	0.654	0.15	0.180
peak trunk frontal velocity (SS7+ LGW)	0.07	0.517	0.11	0.351
peak trunk frontal velocity (SS7+OBW)	0.02	0.832	0.15	0.181
swing time asymmetry (SS3+ LGW)	0.22	0.046	0.05	0.679
swing time asymmetry (SS3+OBW)	0.17	0.126	0.13	0.246
swing time asymmetry (SS7+ LGW)	0.20	0.074	0.02	0.839
swing time asymmetry (SS7+OBW)	0.15	0.177	0.19	0.095
stride length variability (SS3+ LGW)	-0.03	0.789	0.05	0.639
stride length variability (SS3+OBW)	0.13	0.251	0.06	0.598
stride length variability (SS7+ LGW)	0.16	0.163	-0.08	0.498
stride length variability (SS7+OBW)	0.08	0.495	0.08	0.490
stride time variability (SS3+ LGW)	-0.04	0.718	-0.10	0.360
stride time variability (SS3+OBW)	0.26	0.021	-0.15	0.199
stride time variability (SS7+ LGW)	-0.20	0.070	-0.07	0.568
stride time variability (SS7+OBW)	0.17	0.144	-0.07	0.536

Note： SS3: serial subtraction three; SS7: serial subtraction seven; LGW: level ground walking; OBW: obstacle crossing walking; WCST: Wisconsin Card Sorting Task; MoCA: Montreal Cognitive Assessment;

*: $p<0.05$, **: $p<0.01$.

8.12 Table 12 Correlations between Mini-BEST, FMA and DT performance.

	Mini-BEST		FMA	
	r	*p*	r	*p*
number of correct response (SS3+ LGW)	-0.07	0.569	-0.15	0.198
number of correct response (SS3+ OBW)	0.04	0.719	-0.18	0.109
number of correct response (SS7+ LGW)	-0.15	0.194	-0.21	0.064
number of correct response (SS7+OBW)	-0.13	0.258	-0.23	0.045 *
distance (SS3+ LGW)	0.62	<0.001**	0.55	<0.001**
distance (SS3+OBW)	0.64	<0.001**	0.57	<0.001**
distance (SS7+ LGW)	0.61	<0.001**	0.49	<0.001**
distance (SS7+OBW)	0.63	<0.001**	0.49	<0.001**
stride length (SS3+ LGW)	0.45	<0.001**	0.50	<0.001**
stride length (SS3+OBW)	0.48	<0.001**	0.53	<0.001**
stride length (SS7+ LGW)	0.41	<0.001**	0.44	<0.001**
stride length (SS7+OBW)	0.47	<0.001**	0.53	<0.001**
stride time (SS3+ LGW)	-0.44	<0.001**	-0.33	0.003**
stride time (SS3+OBW)	-0.40	<0.001**	-0.30	0.006**
stride time (SS7+ LGW)	-0.43	<0.001**	-0.35	0.001**
stride time (SS7+OBW)	-0.39	<0.001**	-0.35	0.001 **
peak trunk frontal velocity (SS3+ LGW)	0.14	0.216	-0.30	0.006**
peak trunk frontal velocity (SS3+OBW)	0.12	0.282	-0.30	0.007**
peak trunk frontal velocity (SS7+ LGW)	0.16	0.171	-0.24	0.032*
peak trunk frontal velocity (SS7+OBW)	0.10	0.377	-0.29	0.009**
swing time asymmetry (SS3+ LGW)	-0.15	0.192	-0.39	0.000**
swing time asymmetry (SS3+OBW)	-0.18	0.103	-0.34	0.002 **
swing time asymmetry (SS7+ LGW)	-0.11	0.356	-0.29	0.009 **
swing time asymmetry (SS7+OBW)	-0.21	0.060	-0.39	<0.001**
stride length variability (SS3+ LGW)	-0.44	<0.001**	-0.32	0.003 **
stride length variability (SS3+OBW)	-0.33	0.003 **	-0.34	0.002 **
stride length variability (SS7+ LGW)	-0.33	0.003 **	-0.29	0.010 **
stride length variability (SS7+OBW)	-0.27	0.016*	-0.31	0.005 **
stride time variability (SS3+ LGW)	-0.02	0.849	0.02	0.859
stride time variability (SS3+OBW)	-0.08	0.510	0.01	0.922
stride time variability (SS7+ LGW)	0.02	0.894	0.00	0.993
stride time variability (SS7+OBW)	-0.03	0.763	-0.07	0.560

Note： SS3: serial subtraction three; SS7: serial subtraction seven; LGW: level ground walking; OBW: obstacle crossing walking; Mini-BEST: Mini-Balance Evaluation System Test; FMA: Fugl-Meyer Assessment.

*: $p<0.05$, **: $p<0.01$.

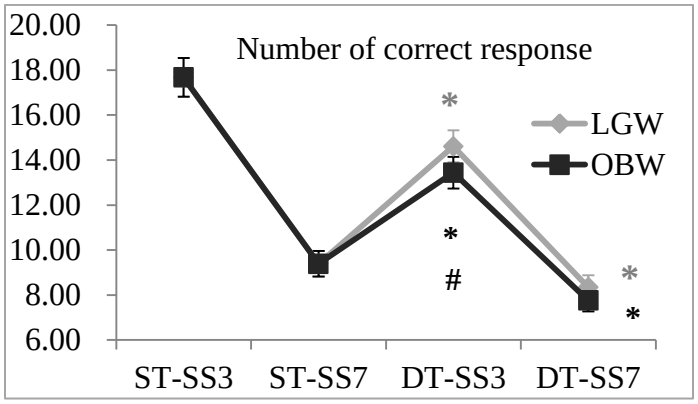
8.13 Table 13 Correlations between RNLI and DT performance.

	RNLI	
	r	*p*
number of correct response (SS3+ LGW)	0.09	0.431
number of correct response (SS3+ OBW)	0.23	0.038*
number of correct response (SS7+ LGW)	0.12	0.311
number of correct response (SS7+OBW)	0.17	0.143
distance (SS3+ LGW)	0.33	0.003**
distance (SS3+OBW)	0.31	0.006**
distance (SS7+ LGW)	0.33	0.003**
distance (SS7+OBW)	0.32	0.004**
stride length (SS3+ LGW)	0.14	0.211
stride length (SS3+OBW)	0.18	0.117
stride length (SS7+ LGW)	0.18	0.104
stride length (SS7+OBW)	0.13	0.240
stride time (SS3+ LGW)	-0.11	0.350
stride time (SS3+OBW)	-0.05	0.666
stride time (SS7+ LGW)	-0.06	0.582
stride time (SS7+OBW)	0.02	0.859
peak trunk frontal velocity (SS3+ LGW)	0.09	0.421
peak trunk frontal velocity (SS3+OBW)	0.16	0.148
peak trunk frontal velocity (SS7+ LGW)	0.11	0.342
peak trunk frontal velocity (SS7+OBW)	0.12	0.294
swing time asymmetry (SS3+ LGW)	0.15	0.196
swing time asymmetry (SS3+OBW)	0.04	0.719
swing time asymmetry (SS7+ LGW)	0.05	0.647
swing time asymmetry (SS7+OBW)	0.12	0.297
stride length variability (SS3+ LGW)	-0.12	0.304
stride length variability (SS3+OBW)	-0.06	0.613
stride length variability (SS7+ LGW)	0.01	0.938
stride length variability (SS7+OBW)	-0.07	0.523
stride time variability (SS3+ LGW)	0.08	0.508
stride time variability (SS3+OBW)	-0.11	0.330
stride time variability (SS7+ LGW)	0.06	0.574
stride time variability (SS7+OBW)	-0.08	0.465

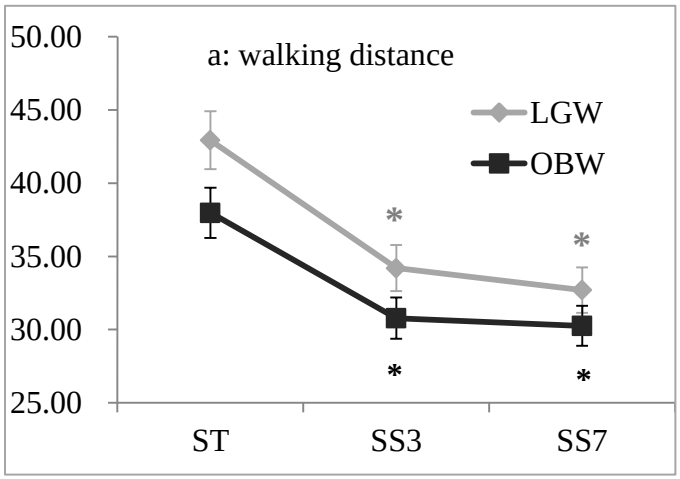
Note： SS3: serial subtraction three; SS7: serial subtraction seven; LGW: level ground walking; OBW: obstacle crossing walking; ABC: Activities-specific Balance Confidence Scale; RNLI: Reintegration to Normal Living Index.

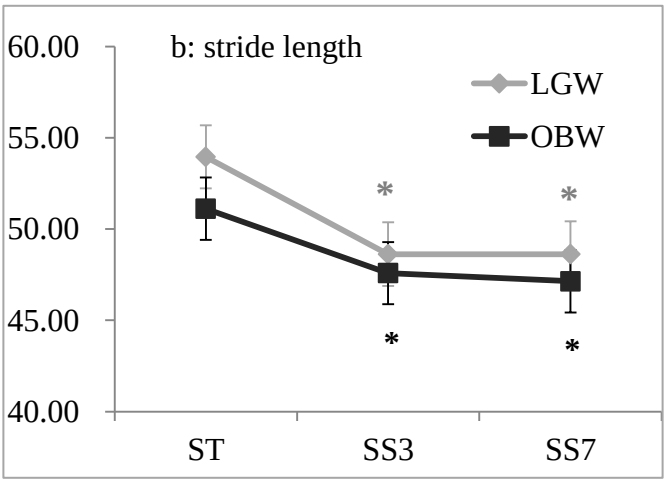
*: $p<0.05$, **: $p<0.01$.

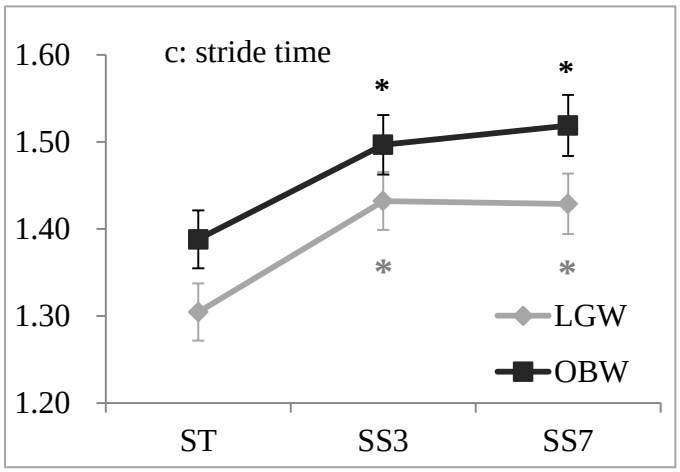
9 LIST OF FIGURES



Note: *: significant between ST and DT under level ground walking conditions; *****: significant between ST and DT under obstacle crossing walking conditions; #: significant between LGW and OBW under DT conditions. LGW: level ground walking; OBW: obstacle crossing walking.

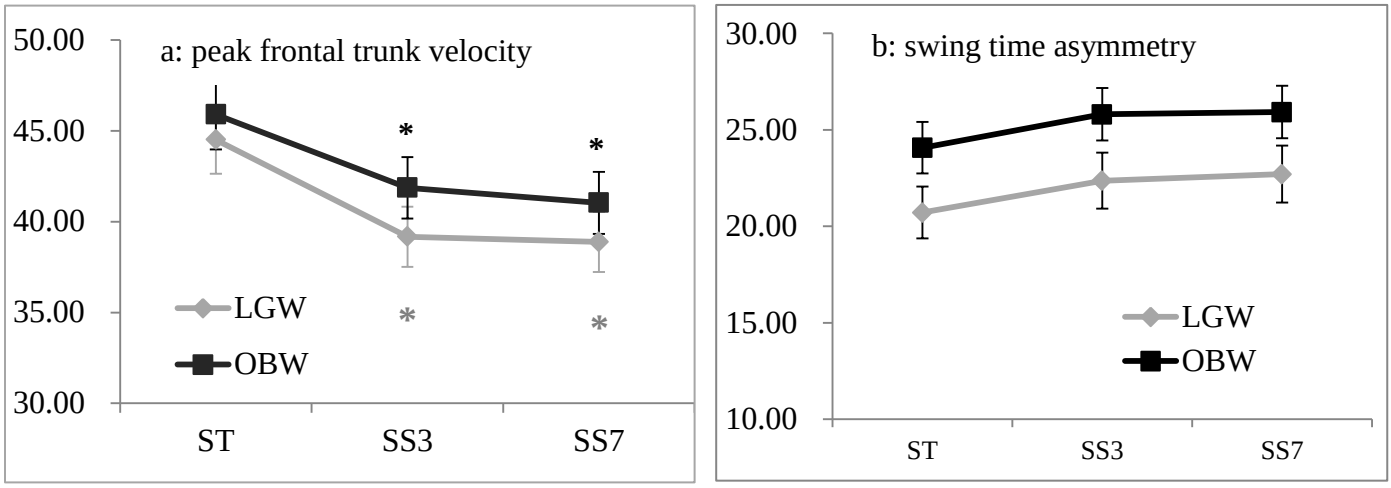






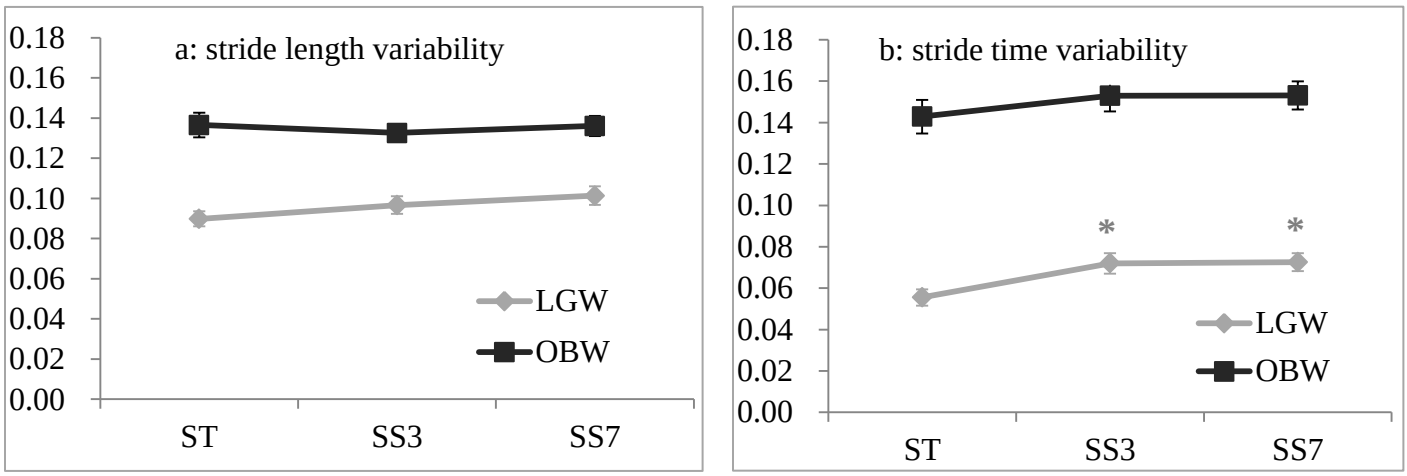
Note: *: significant difference between ST and DT under level ground walking conditions; *****: significant difference between ST and DT under obstacle crossing walking conditions; #: significant difference between SS3 and SS7 under DT conditions. LGW: level ground walking; OBW: obstacle crossing walking.

9.3 Figure 3 The changing trend of postural stability and gait asymmetry with increased task complexity**.**



Note: *: significant difference between ST and DT under level ground walking conditions; *: significant difference between ST and DT under obstacle crossing walking conditions; #: significant difference between SS3 and SS7 under DT conditions. LGW: level ground walking; OBW: obstacle crossing walking.

9.4 Figure 4 The changing trend of gait variability with increased task complexity**.**



Note: *: significant difference between ST and DT under level ground walking conditions; *: significant difference between ST and DT under obstacle crossing walking conditions; #: significant difference between SS3 and SS7 under DT conditions. LGW: level ground walking; OBW: obstacle crossing walking.

10 LIST OF ABBREVIATIONS

11 Supplementary information：Outliers detection and conversion

	Subject code	Outlier	Converted	Upper bound*	Lower bound #
number of correct response (SS7)	DT61	26	25	25.20	-7.20
number of correct response (SS3+ OBW)	DT61	33	27	32.40	-5.40
number of correct response (SS7+ LGW)	DT37	21	19	19.35	-3.60
number of correct response (SS7+OBW)	DT61	22	18	21.55	-6.80
stride time (LGW)	DT02	2.46	1.93	2.09	0.43
stride time (OBW)	DT02	2.44	2.12	2.28	0.41
stride time (SS3+ LGW)	DT02	2.62	2.17	2.35	0.43
stride time (SS3+OBW)	DT02	2.62	2.17	2.30	0.59
stride time (SS7+ LGW)	DT02	2.55	2.28	2.35	0.41
stride time (SS7+OBW)	DT02	2.62	2.31	2.41	0.56
stride length variability (OBW)	DT18	0.51	0.22	0.26	-0.01
stride length variability (SS3+OBW)	DT21	0.26	0.24	0.24	0.02
stride length variability (SS7+OBW)	DT28	0.30	0.25	0.27	<0.01
stride time variability (LGW)	DT03	0.28	0.10	0.10	<-0.01
	DT05	0.12	0.10		
	DT40	0.14	0.10		
	DT80	0.12	0.10		
	DT87	0.11	0.10		
stride time variability (OBW)	DT31	0.59	0.30	0.36	-0.08
stride time variability (SS3+ LGW)	DT03	0.26	0.15	0.15	-0.02
	DT60	0.17	0.15		
	DT78	0.17	0.15		
	DT93	0.24	0.15		
stride time variability (SS3+OBW)	DT90	0.43	0.31	0.37	-0.07
stride time variability (SS7+ LGW)	DT40	0.21	0.20	0.20	-0.07
swing time asymmetry (SS7+OBW)	DT21	92.21	56.4	71.84	-22.64

Note: *: Upper bound: Q3+ (2.2*(Q3-Q1)); #: Lower bound: Q1-(2.2*(Q3-Q1)).

Abbreviations: SS3: serial subtraction three; SS7: serial subtraction seven; LGW: level ground walking; OBW: obstacle crossing walking; MD: mean difference.