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Research Article

Postural Control During Sit-to Stand and Gait in Stroke Patients

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ABSTRACT

Chou SW, Wong AMK, Leong CP, Hong WS, Tang FT, Lin TH: Postural control during sit-to-stand and gait in stroke patients. *Am J Phys Med Rehabil* 2003;82:42–47.

Objective: To investigate the relationship of sit-to-stand and gait performance in hemiplegic stroke patients.

Design: A total of 40 chronic stroke patients with hemiplegia and 22 age-matched healthy subjects were included in this study. Data of a motion analysis system and three force platforms were collected in a rehabilitation unit of a medical center.

Results: Laboratory sit-to-stand measurement and gait analysis were evaluated in both groups via three AMTI (Advanced Mechanical Technology Inc.) force platforms and a Vicon 370 system (six high-resolution cameras and one AMTI force plate), respectively. The sit-to-stand and gait parameters of hemiplegic patients were correlated significantly, especially in rising speed and the maximal vertical force of both legs during rising.

Conclusions: Hemiplegic stroke patients, who could stand up within 4.5 sec or who had a maximal vertical force difference of less than 30% of body weight between both legs, had better gait performance than the others did.

Key Words: Stroke, Hemiplegia, Sit-to-Stand, Gait Analysis

Sit-to-stand (STS) is performed many times daily and is an important prerequisite to the achievement of many functional goals. Transferring from a sitting to standing position requires large movements, particularly of the hip and the knee.[1–4] Changing the initial ankle position also affects muscle onsets, duration of movement phases, and joint excursion.[5]

Symmetry, steadiness, and dynamic stability are three elements of postural control.[6] Asymmetric dynamic posture and movement is the most prevalent locomotor deficit of stroke-related hemiparesis.[7–9] Winstein et al.[8] reported that a standing balance asymmetry reduction does not reduce the asymmetric limb movement patterns associated with hemiparetic locomotion, concomitantly, despite the obvious correlation between standing balance and locomotor control mechanism.[10] However, our previous studies proved that a significantly lower rate of force rise and greater postural sway, while rising or sitting, is useful in identifying patients who are at risk of falling.[11] That report also contains supportive laboratory evidence of a stroke patient who lost functional mobility and locomotion capability, based on dynamic balance responses (center of force sway patterns) and motor control activities (electromyography patterns), during STS.[12] Restoration of a secure STS and ambulation are emphasized in stroke rehabilitation; however, correlation between the two has not been studied. In measuring the outcome rehabilitation, ambulatory function is emphasized because it significantly influences a patient's chance of returning to his or her premorbid environment.[13]

Moreover, the stroke rehabilitation programs always discharge patients as soon as possible because of cost constraints. A home-based training model, which improves gait training, is extremely important for ambulatory rehabilitation. However, the main primary objective of this project was to investigate the correlation of kinematic data from STS and gait parameters between healthy subjects and hemiplegic stroke patients. Our hypothesis is that the ability of STS and ambulatory performance is closely related in stroke patients. Those patients who have better STS motor control also have better gait performance. STS functional training might be an appropriate task for a stroke patient to improve muscle strength and motor control of the affected leg to achieve better gait performance.

METHODS

A total of 40 hemiplegic stroke patients, 30 men and 10 women, and 22 age-matched healthy subjects, 14 men and 8 women, participated in this study (Table 1). The mean age was 60.0 ± 10.4 yr for the stroke patients and 60.8 ± 7.4 yr for the healthy subjects. The patients were medically stable and their illnesses, such as hypertension and diabetes mellitus, were under control. In contrast, the age-matched subjects were generally healthy, without any neurologic or musculoskeletal deficits. All subjects had no obvious deficits of cognition and were able to understand and follow the instructions to stand up independently. Based on clinical observation, they also had no active arthritis or peripheral neuropathy in the lower limbs, no cerebellar signs, no Ménière syndrome, and no Parkinsonism. In addition, each subject signed an informed consent statement before participating in this study.

All patients had a single stroke (proved by computed brain tomography) with hemiplegia. The mean duration since the time of stroke was 2.8 ± 2.0 yr (Table 1). Cortical lesions were noted in 25 patients, and subcortical lesions were noted in the other 15 patients. All patients underwent rehabilitation programs and

TABLE 1
Subject data

	CVA Patients (n = 40)	Normal Subjects (n = 22)	P Value
Age, yr	60.0 ± 10.4	60.8 ± 7.4	0.775
Sex, M/F	30/10	14/8	
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Brunnstrom stage, II–III/IV–V	18/22		
Spasticity (Ashworth scale grade 1–2/3–4)	24/16		
Duration of stroke, yr	2.8 ± 2.0		
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Body weight, kg	61.6 ± 6.4	59.9 ± 8.2	0.118
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Laboratory Measurement

STS Task. An AMTI force platform (Advanced Mechanical Technology Inc, Waterton, MA), which assessed anteroposterior and mediolateral sway and vertical forces in addition to the center of pressure (COP), was used to measure the ground reaction force under each foot. The subjects, barefoot and dressed in shorts, were seated on an armless, backless chair, which was adjusted to the height of the subject's knee, determined as the distance from the lateral knee joint. Their feet were parallel, one foot on each force plate, with the medial border of the feet 10–15 cm apart. Each subject's ankle was placed at about 10 degrees of dorsiflexion, and the knee angle was approximately 100 to 105 degrees of the flexion.

Subjects were then instructed to stand at their usual self-paced, comfortable speed. After the command "ready, set, start," the task began at "start," and when the vertical force equaled body weight, the rising phase ended. After about 30 sec of standing, subjects were instructed to sit normally. Notably, three trials were performed for each strategy and used for further analysis.

Gait Analysis. A Vicon 370 system with six high-resolution cameras (Oxford Metrics, Oxford, UK) and three AMTI force-plate systems were used to assess the three-dimensional kinematic data of all subjects. The six cameras had a frame rate of 60 frames/sec and used infrared light–emitting diode strobes. Lightweight retroreflective markers were attached to the skin over the following bony landmarks: sacrum (S2), anterior superior iliac spines, lateral thigh, knee-joint axes, lateral shank, lateral malleoli, and second foot ray. These points form the Vicon Clinical Manager marker set.[14] Then, to capture the trajectories of those markers, subjects walked at their typical speed along a 10-m walkway. Simultaneous information of the ground reaction force was collected via three force platforms. A component of the ground reaction force was perpendicular to the platform (i.e., the vertical force), and the other orthogonal components were horizontal (i.e., typically the anteroposterior and mediolateral forces). Three acceptable trials with a single step on a single-force platform were collected and averaged for further analysis. Comprehensive parameters were measured and determined from both affected and unaffected legs in kinetic data. The symmetric index of the step length was calculated by dividing its absolute difference of the unaffected and affected sides by their average.

Data Analysis

Data were coded and entered on an IBM-compatible computer and analyzed. Means were compared with a t test or a one-way analysis of variance, and proportions were compared with a χ^2 test. In addition, Pearson's correlation coefficients presented the correlation analysis. Statistical significance was set at $P < 0.05$.

RESULTS

Table 2 lists the comparison of STS and gait parameters between hemiplegic stroke patients and normal subjects. When subjects were instructed to stand with a self-paced speed, the required mean time was 4.5 sec in stroke patients and 1.9 sec in healthy controls ($P < 0.01$). The overshoot, caused by the acceleration of the body mass during rising, was the maximal vertical force represented as the percentage of the subject's body weight. Force of the

TABLE 2
Comparisons of STS and gait parameters between hemiplegic stroke patients and normal subjects

	CVA Patients (n = 40)	Normal Subjects (n = 22)
STS parameters		
Duration, sec	4.8 ± 1.6[a]	1.9 ± 0.5
MaxVF, %BW	66.6 ± 8.8	67.6 ± 11.0
MaxVFdiff, %BW	29.2 ± 12.0[a]	10.4 ± 3.1
COP X, cm	9.8 ± 4.1[a]	6.1 ± 2.5
COP Y, cm	9.9 ± 4.4	8.6 ± 2.1
Gait parameters		
Velocity, %BH/sec	16.7 ± 9.6[a]	52.9 ± 6.7
Cadence, steps/min	65.1 ± 19.9[a]	95.5 ± 8.9
Step length, %BH	16.1 ± 5.9[a]	33.2 ± 3.6
Stride time, sec	2.10 ± 0.91[a]	0.94 ± 0.05
Single support, %GC	20.5 ± 8.6[a]	36.8 ± 2.0
Double support, %GC	51.5 ± 13.0[a]	26.7 ± 3.0
Symmetry index	0.71 ± 0.18[a]	0.94 ± 0.05

BW, body weight; BH, body height; GC, gait cycle; STS, sit to stand; CVA, cerebrovascular accident; MaxVFdiff, maximal vertical force difference between two legs; BW, body weight; COP X, center of pressure in mediolateral displacement; COP Y, center of pressure in anteroposterior displacement; Symmetry index, step length ratio between two legs (≤1).
[a] $P < 0.01$.

TABLE 3

Correlation between gait and STS parameters of hemiplegic patients

Gait Parameters	Velocity	Cadence	Step Length	Stride Time	Single Support	Double Support	Symmetry Index
STS Parameters							
Duration	-0.733^a	-0.481^a	-0.729^a	0.344^b	-0.772^a	0.474^a	-0.518^a
MaxVF, %BW							
MaxVFdiff, %BW	-0.655^a	-0.542^a	-0.615^a	0.348^b	-0.721^a	0.408^a	-0.519^a
COP X	-0.353^b	-0.329^b			-0.316^b		
COP Y							

STS, sit to stand; MaxVFdiff, maximal vertical force difference between two legs; BW, body weight; COP X, center of pressure in mediolateral displacement; COP Y, center of pressure in anteroposterior displacement.

$^aP < 0.01$.

$^bP < 0.05$.

stroke patients was only slightly less than that of the healthy subjects. The COP sway (i.e., the mediolateral or anteroposterior excursion of the COP) for the whole body was also calculated during STS performance. Hemiplegic stroke patients had a significantly increased mediolateral COP sway, but they did not attain a significant difference in their anteroposterior COP sway. The anteroposterior COP sway of healthy subjects was more pronounced than the mediolateral one. Gait parameters analysis of hemiplegic stroke patients demonstrated a significant decrease in walking velocity, cadence, step length, and single support and increased stride time, double support, and asymmetry (Table 2).

Table 3 shows the correlations between gait and STS parameters of the hemiplegic patients. In addition, speed of rising and maximal vertical force difference of both legs during rising were the main major parameters that were related closely to gait.

A comparison between standing mean duration and gait parameters revealed that the hemiplegic patients who could stand up within 4.5 sec had significantly better velocity, cadence, stride time, and single and double support (Table 4). Also, a comparison of the maximal vertical force difference between two legs during rising and gait performance confirmed that the patients with a difference equal to or less than 30% of their body weight had an enhanced gait parameter performance (Table 5).

DISCUSSION

Duration of STS. Herein, as in some other studies, a significant difference exists in the time required in STS between hemiplegic stroke patients and healthy control subject.[15–21] Pai and Rogers studied STS transfer at both self-selected fast and natural speeds in healthy subjects (30–38 yr of age).[4] From STS, the maximum oscillation in the anteroposterior direction was significantly greater at fast speeds than natural speeds, suggesting that the faster movement had greater instability during the STS transfer. Yoshida et al.[15] proved that healthy elderly sub-

TABLE 4

Comparisons of gait parameters between different sit-to-stand (STS) durations in the hemiplegic patients

STS Parameter	Duration, ≤4.5 sec	Duration, >4.5 sec	*P* Value
Gait Parameters			
Cadence, steps/min	72.9 ± 12.4	58.0 ± 22.2	0.013^a
Velocity, %BH/sec	21.2 ± 10.9	12.3 ± 5.0	0.002^b
Stride time, sec	1.7 ± 0.3	2.5 ± 1.1	0.005^b
Step length, %BH	17.9 ± 6.9	14.2 ± 4.1	0.045^a
Single support, %GC	25.6 ± 7.9	15.5 ± 6.0	0.000^b
Double support, %GC	43.3 ± 12.0	59.7 ± 10.0	0.000^b
Symmetry index	0.76 ± 0.16	0.66 ± 0.19	0.076

BH, body height; GC, gait cycle.

$^aP < 0.05$.

$^bP < 0.01$.

TABLE 5

Comparisons of gait parameters between different maximal vertical force differences between two legs during sit to stand (STS) in hemiplegic patients

STS Parameter	Difference, ≤30.0%BW	Difference, >30.0%BW	*P* Value
Gait Parameters			
Cadence, steps/min	74.4 ± 14.7	58.2 ± 19.6	0.006[a]
Velocity, %BH/sec	20.5 ± 10.7	13.7 ± 7.6	0.024[b]
Stride time, sec	1.7 ± 0.4	2.4 ± 1.1	0.009[a]
Step length, %BH	17.0 ± 6.2	15.3 ± 5.7	0.374
Single support, %GC	25.7 ± 8.5	16.3 ± 6.1	0.000[a]
Double support, %GC	45.2 ± 12.5	56.7 ± 12.6	0.006[a]
Symmetry index	0.74 ± 0.19	0.68 ± 0.18	0.294

BW, body weight; BH, body height; GC, gait cycle.
[a] $P < 0.01$.
[b] $P < 0.05$.

jects required more time than younger individuals did to stabilize the anteroposterior sway during rising. Our stroke patients, who had just relearned how to rise from sitting, and thus fared poorly in automatic balance engram, were unable to perform this speedy adjustment. Those explain why our stroke patients with fast STS speed had improved motor control[12] and gait performance. Therefore, STS control may be related closely to ambulation ability.

Body Weight Distribution of STS. After a stroke, the automatic program for rising becomes asymmetric because of weakness of the affected side and loss of postural control. Kelso et al.[17] suggested that joint afferent information was not crucial for movement control. However, Engardt and Olsson[16] reported that the sensory function degree of stroke patients did not influence body weight distribution in either rising or sitting down. In stroke patients of that study, the paretic leg was 37.9% of body weight, whereas in the normal control group, it was 50.5% of body weight and 49.5% of body weight for each leg, respectively. In addition, hemiplegic patients with a vertical force difference equal to or less than 30% of body weight displayed superior gait parameters.

Clinical Application. Hill et al.[18] determined that only 7% of patients discharged from rehabilitation met four of the community ambulation criteria. The absence of ongoing exercise or activity programs is a major oversight in stroke management, which exacerbates disabilities and handicaps. Furthermore, several investigators reported that stroke patients did not maintain functional gains after the cessation of rehabilitation. Exercise classes are one way to provide ongoing maintenance or improvements after discharge. Dean et al.[22] reported on the efficacy of a task-related circuit class to improve the performance and endurance of locomotion functions (STS, walking, reaching in sitting and standing positions, and stair ascent and descent) in chronic stroke patients. Although such classes provide the opportunity for exercise and social interaction, they may not be convenient for every stroke patient to attend.

In this study, STS motor control is related closely to gait performance. Hemiplegic patients who could perform STS within 4.5 sec, or with a vertical force difference equal to or less than 30% of body weight, might walk better, as demonstrated in most gait parameters (Tables 4 and 5). Further improvements to this study include a task-specific, home STS training program, with equal weight distribution on both legs and a faster rising speed. In turn, this will result in improved motor performance of trunk control and walking ability.

CONCLUSION

Hemiplegic stroke patients who could stand up within 4.5 sec or who had a maximal vertical force difference of less than 30% of their body weight between both legs had better gait performance than other stroke patients.

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Table 2 lists the comparison of STS and gait parameters between hemiplegic stroke patients and normal subjects. When subjects were instructed to stand with a self-paced speed, the required mean time was 4.5 sec in stroke patients and 1.9 sec in healthy controls ($P < 0.01$). The overshoot, caused by the acceleration of the body mass during rising, was the maximal vertical force represented as the percentage of the subject's body weight. Force of the

TABLE 2
Comparisons of STS and gait parameters between hemiplegic stroke patients and normal subjects

	CVA Patients (n = 40)	Normal Subjects (n = 22)
STS parameters		
Duration, sec	4.8 ± 1.6[a]	1.9 ± 0.5
MaxVF, %BW	66.6 ± 8.8	67.6 ± 11.0
MaxVFdiff, %BW	29.2 ± 12.0[a]	10.4 ± 3.1
COP X, cm	9.8 ± 4.1[a]	6.1 ± 2.5
COP Y, cm	9.9 ± 4.4	8.6 ± 2.1
Gait parameters		
Velocity, %BH/sec	16.7 ± 9.6[a]	52.9 ± 6.7
Cadence, steps/min	65.1 ± 19.9[a]	95.5 ± 8.9
Step length, %BH	16.1 ± 5.9[a]	33.2 ± 3.6
Stride time, sec	2.10 ± 0.91[a]	0.94 ± 0.05
Single support, %GC	20.5 ± 8.6[a]	36.8 ± 2.0
Double support, %GC	51.5 ± 13.0[a]	26.7 ± 3.0
Symmetry index	0.71 ± 0.18[a]	0.94 ± 0.05

BW, body weight; BH, body height; GC, gait cycle; STS, sit to stand; CVA, cerebrovascular accident; MaxVFdiff, maximal vertical force difference between two legs; BW, body weight; COP X, center of pressure in mediolateral displacement; COP Y, center of pressure in anteroposterior displacement; Symmetry index, step length ratio between two legs (≤1).

[a] $P < 0.01$.

TABLE 3
Correlation between gait and STS parameters of hemiplegic patients

Gait Parameters	Velocity	Cadence	Step Length	Stride Time	Single Support	Double Support	Symmetry Index
STS Parameters							
Duration	−0.733[a]	−0.481[a]	−0.729[a]	0.344[b]	−0.772[a]	0.474[a]	−0.518[a]
MaxVF, %BW							
MaxVFdiff, %BW	−0.655[a]	−0.542[a]	−0.615[a]	0.348[b]	−0.721[a]	0.408[a]	−0.519[a]
COP X	−0.353[b]	−0.329[b]			−0.316[b]		
COP Y							

STS, sit to stand; MaxVFdiff, maximal vertical force difference between two legs; BW, body weight; COP X, center of pressure in mediolateral displacement; COP Y, center of pressure in anteroposterior displacement.
[a]$P < 0.01$.
[b]$P < 0.05$.

stroke patients was only slightly less than that of the healthy subjects. The COP sway (i.e., the mediolateral or anteroposterior excursion of the COP) for the whole body was also calculated during STS performance. Hemiplegic stroke patients had a significantly increased mediolateral COP sway, but they did not attain a significant difference in their anteroposterior COP sway. The anteroposterior COP sway of healthy subjects was more pronounced than the mediolateral one. Gait parameters analysis of hemiplegic stroke patients demonstrated a significant decrease in walking velocity, cadence, step length, and single support and increased stride time, double support, and asymmetry (Table 2).

Table 3 shows the correlations between gait and STS parameters of the hemiplegic patients. In addition, speed of rising and maximal vertical force difference of both legs during rising were the main major parameters that were related closely to gait.

A comparison between standing mean duration and gait parameters revealed that the hemiplegic patients who could stand up within 4.5 sec had significantly better velocity, cadence, stride time, and single and double support (Table 4). Also, a comparison of the maximal vertical force difference between two legs during rising and gait performance confirmed that the patients with a difference equal to or less than 30% of their body weight had an enhanced gait parameter performance (Table 5).

DISCUSSION

Duration of STS. Herein, as in some other studies, a significant difference exists in the time required in STS between hemiplegic stroke patients and healthy control subject.[15–21] Pai and Rogers studied STS transfer at both self-selected fast and natural speeds in healthy subjects (30–38 yr of age).[4] From STS, the maximum oscillation in the anteroposterior direction was significantly greater at fast speeds than natural speeds, suggesting that the faster movement had greater instability during the STS transfer. Yoshida et al.[15] proved that healthy elderly sub-

TABLE 4
Comparisons of gait parameters between different sit-to-stand (STS) durations in the hemiplegic patients

STS Parameter	Duration, ≤4.5 sec	Duration, >4.5 sec	*P* Value
Gait Parameters			
Cadence, steps/min	72.9 ± 12.4	58.0 ± 22.2	0.013[a]
Velocity, %BH/sec	21.2 ± 10.9	12.3 ± 5.0	0.002[b]
Stride time, sec	1.7 ± 0.3	2.5 ± 1.1	0.005[b]
Step length, %BH	17.9 ± 6.9	14.2 ± 4.1	0.045[a]
Single support, %GC	25.6 ± 7.9	15.5 ± 6.0	0.000[b]
Double support, %GC	43.3 ± 12.0	59.7 ± 10.0	0.000[b]
Symmetry index	0.76 ± 0.16	0.66 ± 0.19	0.076

BH, body height; GC, gait cycle.
[a]$P < 0.05$.
[b]$P < 0.01$.

TABLE 5

Comparisons of gait parameters between different maximal vertical force differences between two legs during sit to stand (STS) in hemiplegic patients

STS Parameter	Difference, ≤30.0%BW	Difference, >30.0%BW	*P* Value
Gait Parameters			
Cadence, steps/min	74.4 ± 14.7	58.2 ± 19.6	0.006[a]
Velocity, %BH/sec	20.5 ± 10.7	13.7 ± 7.6	0.024[b]
Stride time, sec	1.7 ± 0.4	2.4 ± 1.1	0.009[a]
Step length, %BH	17.0 ± 6.2	15.3 ± 5.7	0.374
Single support, %GC	25.7 ± 8.5	16.3 ± 6.1	0.000[a]
Double support, %GC	45.2 ± 12.5	56.7 ± 12.6	0.006[a]
Symmetry index	0.74 ± 0.19	0.68 ± 0.18	0.294

BW, body weight; BH, body height; GC, gait cycle.
[a] $P < 0.01$.
[b] $P < 0.05$.

jects required more time than younger individuals did to stabilize the anteroposterior sway during rising. Our stroke patients, who had just relearned how to rise from sitting, and thus fared poorly in automatic balance engram, were unable to perform this speedy adjustment. Those explain why our stroke patients with fast STS speed had improved motor control[12] and gait performance. Therefore, STS control may be related closely to ambulation ability.

Body Weight Distribution of STS. After a stroke, the automatic program for rising becomes asymmetric because of weakness of the affected side and loss of postural control. Kelso et al.[17] suggested that joint afferent information was not crucial for movement control. However, Engardt and Olsson[16] reported that the sensory function degree of stroke patients did not influence body weight distribution in either rising or sitting down. In stroke patients of that study, the paretic leg was 37.9% of body weight, whereas in the normal control group, it was 50.5% of body weight and 49.5% of body weight for each leg, respectively. In addition, hemiplegic patients with a vertical force difference equal to or less than 30% of body weight displayed superior gait parameters.

Clinical Application. Hill et al.[18] determined that only 7% of patients discharged from rehabilitation met four of the community ambulation criteria. The absence of ongoing exercise or activity programs is a major oversight in stroke management, which exacerbates disabilities and handicaps. Furthermore, several investigators reported that stroke patients did not maintain functional gains after the cessation of rehabilitation. Exercise classes are one way to provide ongoing maintenance or improvements after discharge. Dean et al.[22] reported on the efficacy of a task-related circuit class to improve the performance and endurance of locomotion functions (STS, walking, reaching in sitting and standing positions, and stair ascent and descent) in chronic stroke patients. Although such classes provide the opportunity for exercise and social interaction, they may not be convenient for every stroke patient to attend.

In this study, STS motor control is related closely to gait performance. Hemiplegic patients who could perform STS within 4.5 sec, or with a vertical force difference equal to or less than 30% of body weight, might walk better, as demonstrated in most gait parameters (Tables 4 and 5). Further improvements to this study include a task-specific, home STS training program, with equal weight distribution on both legs and a faster rising speed. In turn, this will result in improved motor performance of trunk control and walking ability.

CONCLUSION

Hemiplegic stroke patients who could stand up within 4.5 sec or who had a maximal vertical force difference of less than 30% of their body weight between both legs had better gait performance than other stroke patients.

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TUESDAY

The spasticity paradox: movement disorder or disorder of resting limbs?

J A Burne, V L Carleton and N J O'Dwyer

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PAPER

The spasticity paradox: movement disorder or disorder of resting limbs?

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Background: Spasticity is defined/assessed in resting limbs, where increased stretch reflex activity and mechanical joint resistance are evident. Treatment with antispastic agents assumes that these features contribute to the movement disorder, although it is unclear whether they persist during voluntary contraction.

Objectives: To compare reflex amplitude and joint resistance in spastic and normal limbs over an equivalent range of background contraction.

Methods: Thirteen normal and eight hemiparetic subjects with mild/moderate spasticity and without significant contracture were studied. Reflex and passive joint resistance were compared at rest and during six small increments of biceps voluntary contraction, up to 15% of normal maximum. A novel approach was used to match contraction levels between groups.

Results: Reflex amplitude and joint mechanical resistance were linearly related to contraction in both groups. The slopes of these relations were not above normal in the spastic subjects on linear regression. Thus, reflex amplitude and joint resistance were not different between groups over a comparable range of contraction levels. Spastic subjects exhibited a smaller range of reflex modulation than normals because of decreased maximal contraction levels (weakness) and significant increases of resting contraction levels.

Conclusions: Spasticity was most evident at rest because subjects could not reduce background contraction to normal. When background contractions were matched to normal levels, no evidence of exaggerated reflex activity or mechanical resistance was found. Instead, reduced capacity to modulate reflex activity dynamically over the normal range may contribute to the movement disorder. This finding does not support the routine use of antispastic agents to treat the movement disorder.

The paradox in relation to spasticity is that it has been clinically defined[1] and primarily studied in resting limbs, yet its clinical management is directed mainly at the associated movement disorder. Current directions in the treatment of spasticity include the use of antispastic agents such as botulinum toxin and baclofen to reduce overactive muscle activity. The rationale for this approach is that sustained overactivity in some way limits limb performance. This view is supported by the clinical definition of spasticity and numerous studies that report increased mechanical resistance and augmented tonic stretch reflexes (TSR) during passive joint rotation, particularly after stroke[2–7] and cerebral palsy.[8 9] On this basis, spastic limbs can be clearly distinguished from normal limbs at rest, in which slow stretches generally fail to elicit signs of increased tone or significant levels of TSR activity.[4 10–14]

Although it is more relevant to treatment, relatively little is known of spasticity in contracting muscle. Even a small voluntary background contraction leads to prominent TSR activity and increased passive resistance in normal limbs,[7 8 15 16] and there is then no clear demonstration that reflex magnitude[2 4 17–19] and joint resistance[20] are significantly higher in spastic limbs. Hence, it is unclear how, or if, spasticity contributes to the movement disorder in the affected limbs. It is possible, without clear evidence to the contrary, that the defining features of spasticity are a phenomenon confined to resting limbs. A more detailed knowledge of the properties of spastic muscle during active contraction is needed to guide future directions in treatment.

This paper reports a systematic study of the effect of muscle contraction on spasticity and outlines the implications for treatment. More specifically, we tested the possibility that a small rise in resting contraction levels could contribute to the observed increase in TSR activity and passive resistance in spastic muscles. In normal subjects, reflex amplitude and joint stiffness are linearly related to contraction level, at least for contractions below 50% of maximum.[16 21–29] Therefore, it was important to assess the effect of background contraction on reflex amplitude and joint resistance in normal and spastic limbs over a comparable range of contraction levels.

In practice, several problems complicate attempts to match contraction levels in normal and spastic limbs. Spastic limbs typically exhibit a much reduced range of contraction and subjects find it difficult to hold a target level of voluntary contraction or torque. In addition, traditional methods of electromyogram (EMG) normalisation are invalidated in weak spastic subjects, who will use a larger proportion of their maximum voluntary contraction (MVC) to achieve a given torque output. The problems associated with matching contraction levels in normal and spastic limbs have received little attention in past studies of reflexes and joint stiffness, and the effect of very small background contractions on reflex amplitude and joint resistance in spastic or normal subjects is not known.

Our study used a novel approach to the problem of controlling for differences in contraction level between subjects. We also used analysis techniques that permitted simultaneous estimation of reflex amplitude and resistive torque, so that these two variables could be directly correlated in each subject. TSR amplitude and mechanical resistance at the elbow were estimated in spastic and normal limbs at rest and at six small incremental levels of background isometric

Abbreviations: EMG, electromyogram; TSR, tonic stretch reflex; MVC, maximum voluntary contraction biceps muscle contraction to a maximum of 15% of MVC. These data permitted regression analysis of the relation between reflex amplitude and contraction level, and also between mechanical joint resistance and contraction level over this range in individual subjects. The derived slopes of these relations provide the first comparison of reflex amplitude and resistive torque in spastic and normal limbs over a similar range of contraction levels. Extrapolation of the regression lines back to zero contraction level gave estimates of reflex amplitude and mechanical joint resistance at a theoretical zero contraction level. Changes in passive tissue properties secondary to muscle shortening were excluded from consideration because the study was based on limbs that were free of significant contracture.

Previous studies have used a wide range of perturbations in terms of amplitude and frequency content, and this must have contributed to the conflicting results obtained. Reflex amplitude and joint stiffness show non-linear power relations with both stretch amplitude and frequency.[20 21 23 30 31] Recent studies have used peak to peak stretch amplitudes below 5° and frequencies above 30 Hz. Such stretches therefore reflect the highly non-linear properties of the stretch reflex, leading to reflex amplitude and joint stiffness estimates that are larger by an order of magnitude than those encountered in the clinical testing of joint resistance. In our current study, the stretch parameters were selected to reflect as much as possible the range used in clinical testing, so that the results would have relevance to spasticity as clinically defined.

MATERIALS AND METHODS

Subjects

Thirteen normal subjects (mean age, 45.8; SD, 9.3 years) and eight spastic hemiparetic subjects (mean age, 57.6; SD, 7.9 years) participated in our study. Table 1 summarises their demographic information. The inclusion criteria for normal subjects were that they fell within the approved age range (20–70 years) and were free of neurological and musculoskeletal abnormalities. Inclusion criteria for spastic hemiparetic subjects were that they were greater than one month post-stroke, possessed clinical signs of spasticity, accompanied by a minimum Ashworth score of 1, had sufficient strength and range of motion at the elbow joint to perform the experimental task, and could follow the test instructions. Subjects with major sensory impairment, antispastic or botulinum toxin medications, or an inability to attain the correct testing position as a result of soft tissue contracture and/or discomfort were excluded.

Anthropometric data, including segmental arm lengths and upper, mid, and lower forearm circumferences were collected for each subject so that calculations of elbow joint resistance could be normalised for the effects of limb volume. Our study was approved by the human ethics committee of the University of Sydney and informed consent was obtained according to the Declaration of Helsinki.

Stretch perturbation

Subjects were seated in a semi-reclining chair, with their right arm (normal subjects) or affected arm (stroke subjects) in 90° of shoulder abduction and 90° of elbow flexion. The height of the chair was adjusted so that the correct arm position could be attained. The semi-pronated forearm and hand were supported in a horizontally orientated adjustable cast, which was connected to a computer controlled DC torque-servo motor (Baldor Instruments, Sydney, Australia) via a vertically aligned motor shaft. The axis of rotation of the elbow joint was aligned with the axis of rotation of the motor shaft. Rotation about the elbow joint was constrained to the horizontal plane to eliminate gravitational effects.

Because spasticity can be detected by manual clinical testing and is clinically defined by this method,[1] we used a range of stretch amplitudes and frequencies comparable to those used clinically, achieving a maximum velocity of 90°/s. Otherwise, because reflex amplitude and resistive torque vary in a non-linear manner with stretch frequency and amplitude, estimates may be obtained that are larger by an order of magnitude than the values expected from clinical testing or reported here.

A broadband signal with an irregular profile and a frequency content of 0.1–3.0 Hz drove the perturbation. The signal was digitally generated from a random number sequence, which was subsequently low pass filtered by a fourth order Butterworth filter with a 3.0 Hz cutoff frequency. The resulting perturbation of the elbow was centred on 90° of elbow flexion and had a maximal amplitude ±15°. Preliminary studies showed that normal subjects could not voluntarily track the irregular perturbation profile on request. In addition, the results to be reported here showed the reflex EMG response to be consistently phase advanced with respect to the perturbation, confirming that voluntary muscle activity did not contribute significantly to the measures of reflex amplitude derived from the correlation analysis.

Recordings

Joint position was measured by a precision potentiometer (AXEM MC19S) attached to the lower end of the motor shaft. Resistive torque was measured by monitoring the amount of current supplied to the motor, because torque output is directly proportional to the current supplied. Before the experiment, the torque motor signal was calibrated by suspending a range of known weights from the manipulandum,

Table 1 Demographic information

Subjects	Age (years)	Sex	Location of CVA	Length of treatment* (months)	Time after stroke (months)	Handedness (L/R)	Arm tested (L/R)	Ashworth scale (0–4)	Contracture	MAS advanced hand activities	Antispastic medication
Stroke											
14	46	F	(L) MCA	5	22	L	R	1.5	Absent	1	Nil
15	48	F	(R) MCA	4.5	60	R	L	2	Absent	0	Nil
16	57	M	(L) MCA	4	86	R	R	3	Present	3	Nil
17	58	M	(L) MCA	1.5	26	R	R	1	Absent	5	Nil
18	58	M	(L) MCA	12	60	R	R	2	Absent	3	Nil
19	59	F	(L) MCA	3.5	60	R	R	1	Absent	0	Nil
20	70	M	(R) MCA	2	7	R	L	1.5	Absent	4	Nil
21	65	M	(L) MCA	2.5	16	R	R	1.5	Absent	6	Nil
Normal											
1–13	21–58	6F, 7M	–	–	–	12R, 1L	R	0	–	–	–

*Physiotherapy or occupational therapy.
CVA, cerebrovascular accident; L, left; MAS, Motor Assessment Scale; MCA, middle cerebral artery; R, right.

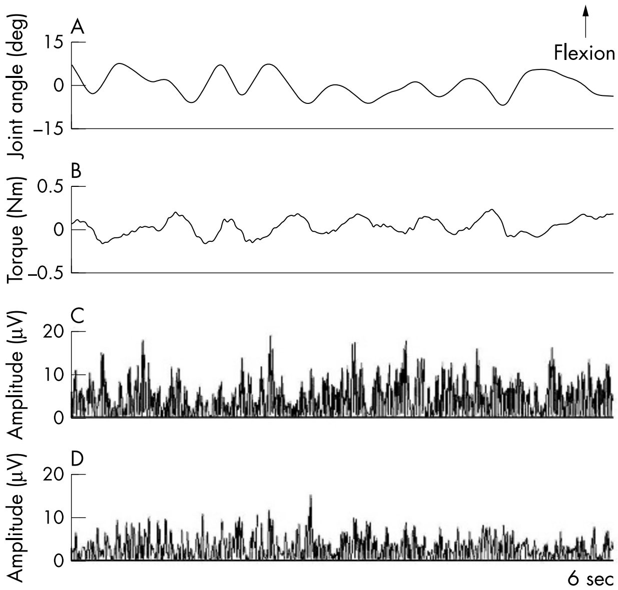

Figure 1 Samples of (A) joint angle, (B) resistive torque, (C) high pass filtered and rectified biceps electromyogram (EMG), and (D) rectified and filtered triceps EMG recorded during perturbation of the elbow by a broadband stimulus (0–3 Hz) in a normal subject during a 2.5% maximum voluntary contraction of biceps. Flexion is represented by an upward deflection of the position trace.

and was found to have a linear relation to torque over the testing range. Surface EMG was measured by bipolar silver–silver chloride electrodes, placed 2 cm apart over the central belly of the biceps brachii and the lateral head of the triceps muscles. Elbow joint angle, resistive torque (analogue filtered, 0.1–400 Hz band pass) and flexor and extensor surface EMG (analogue filtered, 5–400 Hz band pass) were recorded and digitised at 1000 Hz (Amlab2, Sydney, Australia).

EMG calibration

A series of MVCs of elbow flexor and extensor muscles was recorded before testing and mean MVCs were calculated digitally by software. Because MVC levels were not comparable in normal and stroke subjects, as a result of weakness in the stroke group, a second calibration method was preferred. Subjects were required to oppose several cycles of a 2 Nm peak to peak sinusoidal variation in torque at 0.3 Hz, applied about the elbow joint by the torque-servo motor. Concurrent measures of rectified flexor and extensor EMG activity were correlated against the torque signal. The gain of the EMG/torque relation was thus determined and used subsequently to convert the EMG signals from each subject into equivalent torque units. This was later used to normalise the flexor and extensor EMG data between subjects. The low torque level ensured that levels of co-contraction were also low relative to a normal MVC and in the same order of magnitude as those used during subsequent experimental trials.

Procedure

Subjects were positioned in the manipulandum, as described above, and instructed to relax their limb and not to assist or retard the limb perturbations. Two minutes of resting EMG was recorded before the perturbations. (A resting muscle was defined here by the absence of a voluntary contraction. No attempt was made to eliminate EMG using visual feedback.) Two consecutive 60 second perturbations of the limb were then recorded while the muscles were again at rest. In subsequent trials, subjects were instructed to maintain a constant target level of background contraction of the elbow flexor muscles against the resistance of the manipulandum throughout each perturbation of 60 seconds. A digital display of the root mean square and integrated biceps brachii muscle activity was provided to the subjects, and they were required to match this display to the target contraction level. Target contractions were set at approximately 2.5%, 5%, 7.5%, 10%, 12.5%, and 15% of MVC in normal subjects. Because of weakness in the stroke subjects, this meant that the target contraction levels frequently exceeded 15% of their MVC. In addition, because of persisting background EMG activity while attempting to rest, spastic subjects were frequently unable to achieve the lowest of these targets, resulting in fewer trials from these subjects. However, the accuracy of matching target contraction levels was not crucial to the results, and the true mean rectified EMG level for each perturbation was determined, in µV and equivalent torque units, by software during data analysis.

One minute of rest was allowed after four trials or as requested by the subject. On average, eight trials were performed.

Data analysis

The raw EMG signals were processed to produce a smoothed envelope of the raw signal, proportional to the level of muscle contraction (high pass filtered at 60 Hz, detrended, full wave rectified, and then low pass filtered at 3 Hz, using fourth order Butterworth filters). The torque and position data were passed through the same low pass filter before all signals were resampled at a 10th of the original sampling rate. Mean flexor and extensor EMG levels were digitally calculated at each contraction level.

Figure 1 shows samples of raw data. Cross correlation analysis[32] was performed to analyse the relations between the stretch stimulus and the flexor EMG, extensor EMG, and torque signals. The analysis provided measures of coherence square, gain, and phase between the signals. The output of the analysis for the stretch perturbation and torque signals is shown in fig 2A–C, with the power spectrum of the perturbation signal shown in fig 2D. The estimates are plotted as a function of stretch frequency. The coherence between the signals at each frequency was defined as the proportion of signal variance accounted for by the linear relation to the stretch stimulus (fig 2A). Gain was the ratio of the amplitude of the response to the amplitude of the stretch signal at each frequency (fig 2B). Phase estimated in degrees the advance or lag of the response with respect to the stretch for each frequency (fig 2C). Individual gain and phase estimates at any frequency with a coherence of less than 0.2 were eliminated from the analysis because of their low reliability as assessed from their 95% confidence intervals.

The viscoelastic resistance of the elbow joint was measured in two ways: first, via the torque angle gain (the ratio of the resistive torque and stretch signals) and, secondly, via the resonant frequency. The viscoelastic resistance estimates were also normalised for limb volume, estimated from volume measurements of each limb. All torque data presented in the results were normalised in this manner.

Joint resistance was also estimated by calculation of resonant frequency. At the resonant frequency, the resistive torque is a minimum because of the cancellation of elastic and inertial torques. Thus, the resonant frequency was determined as the frequency corresponding to a torque angle phase difference of 90°.[33] The resonant frequency increases with elastic tissue resistance and has thus been used as a measure of stiffness.[34] It has the advantage of being a simple method to isolate the elastic stiffness component from frictional and inertial components of limb and measuring equipment.

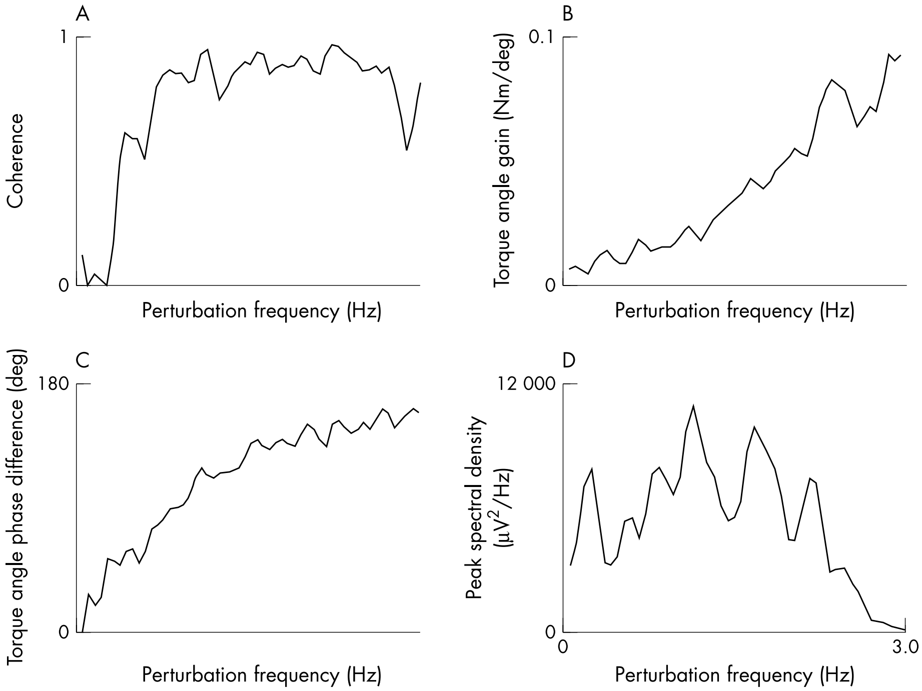

Figure 2 Estimates from correlation analysis of resistive torque and joint angle plotted against the frequency of the perturbation. (A) Coherence square, (B) torque angle gain, (C) phase difference, (D) spectral content of the position signal.

Statistical analysis

Descriptive and statistical analyses of the results were carried out using linear regression and ANOVA.

RESULTS

All EMG measurements were normalised using the torque based calibration procedure described in the methods. This showed that the normal and stroke groups generated similar levels of biceps and triceps muscle activity in µV/Nm of torque (table 2). Thus, there was no significant change in the EMG–torque relation in the stroke group. The MVCs of the biceps and triceps muscles were converted to torque units using the individual biceps and triceps EMG/torque gains. It was estimated using this method that the stroke group could produce approximately 20% of the normal maximal flexor and extensor torques. This was consistent with estimates of weakness derived from the MVCs for biceps and triceps measured in µV units. Stroke subjects produced on average only 25% of the normal MVC in biceps and triceps (table 2).

Because the EMG/torque conversion factor varied little between individuals, the statistical results were the same for both µV and torque units. Thus, the EMG data in the following sections are presented for simplicity in µV rather than torque units.

To determine the sensitivity of the experimental methods and analysis, the effect of the smallest voluntary contraction (2.5% MVC) on reflex gain and joint resistance was investigated in normal subjects. Normal group mean biceps gain increased from 0.05 µV/deg (SD, 0.04) at rest to 0.28 µV/deg (SD, 0.23) at 2.5% MVC ($p < 0.001$; one way ANOVA) and resistive torque increased from 0.06 Nm/deg (SD, 0.02) at rest to 0.09 Nm/deg (SD, 0.06) at 2.5% MVC ($p < 0.05$; one way ANOVA). Hence, both reflex gain and joint resistance were significantly increased above resting values by a contraction as small as 2.5% MVC. This shows that the 2.5% MVC increments between target contractions were sufficient to produce significant effects on both the stretch reflex and joint mechanics.

Table 2 Resting unperturbed data

	N	S	p Value
Biceps torque calibration (µV/Nm)	17	15	0.93
Triceps torque calibration (µV/Nm)	20	16	0.28
Biceps MVC (µV)	137	34	0.00001
Triceps MVC (µV)	112	28	0.00001
Mean resting biceps activity (µV)	0.6	1.9	0.01
Mean resting triceps activity (µV)	0.9	1.9	0.35

p Values were calculated using one way ANOVA.
MVC, maximum voluntary contraction; N, normal limbs; S, spastic limbs following stroke.

Reflex amplitude

Flexor and extensor TSR gain showed a non-linear increase with perturbation frequencies across the range 0–3 Hz. This gain–frequency relation (fig 3A) was fitted using least squares by a first order polynomial and the coefficients and intercepts then plotted against contraction level in each subject. The two coefficients and the intercept were linearly related to contraction level in normal and spastic muscles ($p < 0.0001$; linear regression). The slopes were not significantly different in normal and spastic muscles.

A simpler analysis of reflex amplitude was to average the TSR gain over all frequencies and to plot the mean gains against the mean biceps background activity. The analyses of these data produced the same conclusions as the method described above. Because the units (µV/deg) are more intuitive and easily related to past studies, they will be used below. Regression analysis confirmed the linearity of the relation between biceps TSR gain and contraction level in individual subjects. Individual r^2 values averaged 0.89 for the normal group and 0.81 for the stroke group. The slopes of individual regression lines were variable within normal and stroke groups. When compared by one way ANOVA, the normal and stroke groups were found to have similar slopes ($p = 0.86$) and similar Y intercepts ($p = 0.24$) (representing zero contraction level).

The group data relating biceps reflex gain and contraction level were obtained for the spastic and normal groups by pooling their individual regression statistics. Figure 4 illustrates the main findings. When plotted on the same axes

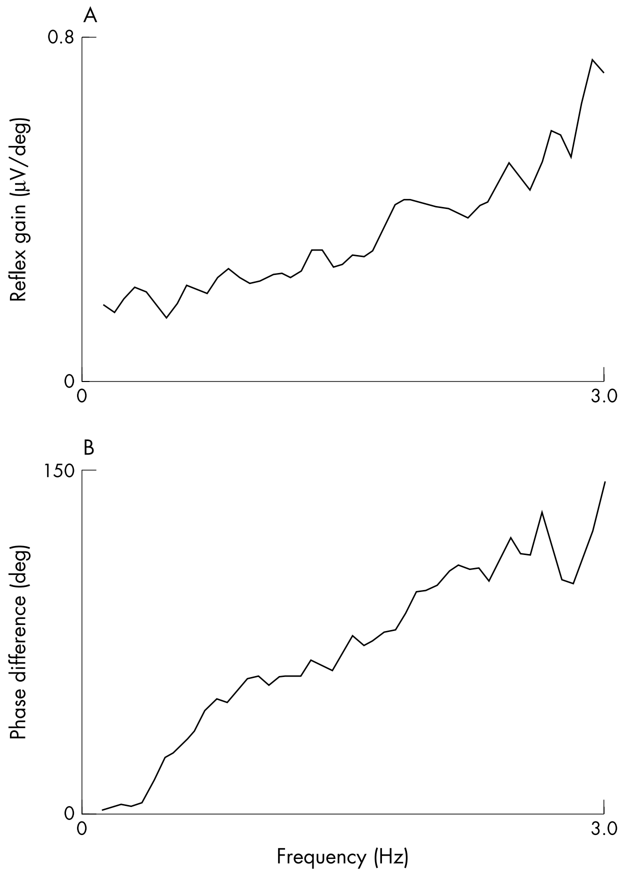

Figure 3 (A) Tonic stretch reflex (TSR) gain plotted against the frequency of the perturbation in a typical normal subject during a small 2.5% maximum voluntary contraction background contraction. (B) Phase difference of the TSR with respect to joint angle (stretch). A typical result is shown, increasing phase advance of the reflex with increase in frequency.

(fig 4A), their similar regression slopes showed that the gain was similar in both groups for any equivalent contraction level. However, it was clear that the lower limit was raised in the spastic group because of an increase of background contraction levels at rest, and the upper limit was decreased because of their lower MVC secondary to weakness. In the normals, the lower limit of gain modulation was not significantly different to zero and the upper limit was taken to be 50% of the group mean MVC. This estimate is consistent with a recent report on maximum reflex gain in a group of normal subjects.[21] The figure illustrates that the available range of biceps reflex gain modulation was reduced in the spastic group in proportion to their reduced range of contraction.

During the perturbation trials, the level of triceps muscle contraction was always less than 25% of the active biceps level, but still tended to increase with the biceps contraction level in the normal and stroke groups. As with biceps, regression analysis indicated a highly linear relation between TSR gain in triceps and the triceps contraction level. A one way ANOVA of individual subjects' slopes and intercepts again showed no significant difference in slope ($p = 0.85$) or Y intercept ($p = 0.22$) between the groups. That is, triceps reflex gain was similar in both groups over the range of contractions studied.

Reflex timing

During active contraction, the TSR phase was advanced with respect to muscle stretch. That is, the peak reflex EMG burst preceded the peak of muscle stretch (fig 3). When averaged over all frequencies, the mean phase advance was approximately 100° in both groups and did not change significantly with the level of biceps contraction.

The most impressive difference between the groups was in the resting data. In the resting normals, the reflex phase was retarded by approximately 100° relative to muscle stretch. However, in the resting stroke subjects, the reflex phase more closely resembled that seen in normals during contraction. They did not show the abrupt change from phase lag to phase lead seen in the normals with the onset of contraction ($p < 0.001$; one way ANOVA).

A similar pattern was seen in the phase of the triceps. Again, there was no significant difference between groups. Stroke subjects demonstrated a phase lead at rest, similar to the extensor phase in normal subjects during small voluntary contractions. This difference between groups in flexor and extensor EMG phase angle was significant ($p < 0.001$; one way ANOVA).

Mechanical resistance

The torque angle gain of the elbow joint depended on the frequency of the perturbation. At low frequencies, the torque angle gain was at a minimum and the torque was approximately in phase with position. Torque angle gain increased with frequency and the torque angle phase shifted toward 180° (fig 2B, C). These effects of frequency are predicted by the dominant contribution of tissue elasticity to resistive torque at low frequencies, and an increasing inertial contribution at higher frequencies according to the relation $I \propto f^2$ (where I is inertial resistance and f is the perturbation frequency).[33] An increase in tissue resistance would be reflected by an increased torque angle gain in the low frequency range and a shift in the inertial phase transition towards higher frequencies. Therefore, torque angle gain was averaged across the frequency range 0.1–0.3 Hz (where gain was relatively independent of frequency and the inertial contribution was approximately zero) to estimate elastic resistance.

The linearity of the relation between elastic resistance and biceps contraction level was also confirmed by regression analysis in individual subjects. The mean slope of the individual regression lines was lower in the stroke group than in normals (indicating reduced elastic resistance), but the difference was not significant ($p = 0.58$; one way ANOVA). Similar positive Y intercepts were obtained in both groups, indicating similar joint resistance at zero contraction level ($p = 0.94$; one way ANOVA).

This conclusion was further supported by the findings for resonant frequency, calculated under resting and contracting conditions. When plotted against contraction level for each subject, the resonant frequency also showed a linear increase with increasing contraction level, reflecting an increase in active tissue resistance. Individual regression analysis was used to compare the relation between resonant frequency and contraction level in the two groups. The slopes of the regression lines were not significantly different ($p = 0.69$; one way ANOVA). The positive Y intercepts were also very similar between groups ($p = 0.97$; one way ANOVA).

The mean data relating resonant frequency and biceps contraction level were obtained for the spastic and normal groups by pooling their individual data. When plotted on the same axes (fig 4B), their similar regression slopes showed that the resonant frequency was similar in both groups for any equivalent contraction level. However, it was clear that the available range of joint stiffness modulation was reduced in the spastic group. Hence, joint stiffness would be significantly different only below or above the reduced range

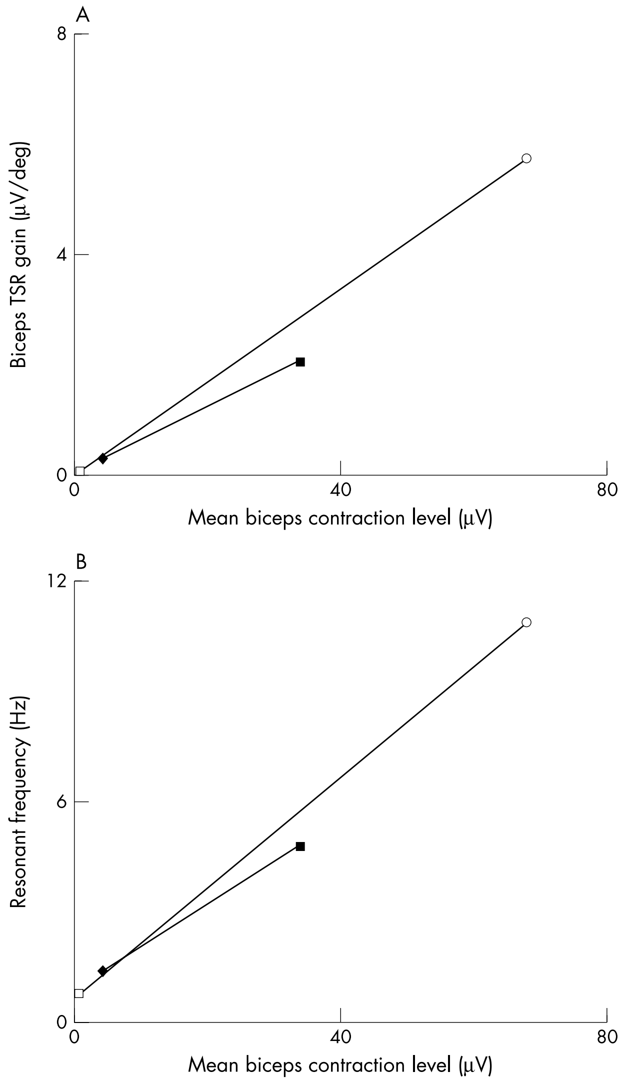

Figure 4 Linear regression lines from the pooled data relating (A) biceps tonic stretch reflex (TSR) gain and (B) joint stiffness (resonant frequency) to mean biceps contraction level in normal (open circle) and spastic (closed square) limbs. In both graphs, the slopes and zero intercepts are not significantly different, but the resting values are significantly different (see text). The figure illustrates that group differences in TSR gain or passive stiffness may be expected only above or below the reduced available range of background muscle contraction in stroke.

of contraction available to the spastic group. The first situation will be the case at "rest".

Resting perturbation data

To verify that the members of the experimental group were in fact spastic, as defined clinically, the data from the resting condition were compared in spastic and normal groups. This confirmed the findings of many past studies. The mean resting biceps TSR gain and background EMG levels were significantly increased, both approximately fivefold, in the stroke group during the perturbation ($p < 0.0001$; one way ANOVAs). The resting mechanical joint resistance (torque angle gain) was also significantly increased, approximately twofold ($p < 0.0001$; one way ANOVA). Furthermore, a significant positive relation was found between the resting torque angle gain and the resting biceps ($p < 0.0001$; linear regression) and triceps ($p < 0.001$; linear regression) EMG levels. Therefore, it can be concluded that the raised background contraction levels in the stroke group were related to both increased reflex gain and joint resistance.

Resting pre-perturbation data

Given the clear association between traditional measures of spasticity and raised background contraction levels during the perturbation, the mean resting levels of background contraction were analysed in the biceps and triceps muscles over the two minutes before the perturbation. In both muscles, the mean contraction level was higher in stroke subjects than in normal subjects, the difference being significant in biceps but not triceps (table 2).

Raised background contraction levels in resting stroke subjects during the perturbation were significantly related to the raised resting contraction levels in the same muscles before the perturbation and inversely related to the MVC in biceps ($p < 0.05$; linear regression). Hence, in stroke subjects, a small MVC and weakness were related to raised resting contraction levels and reflex gain in the same muscle.

DISCUSSION

The major difference found between the normal and spastic group, other than significant weakness in the last group, was a modest rise in the background levels of contraction when spastic limbs were at rest. As a consequence of this raised background contraction, when perturbations with amplitudes and frequencies comparable to those used clinically were imposed on the resting limb, the stretch reflex and the passive joint resistance were increased in the spastic subjects. However, the magnitudes of these increases were entirely in agreement with those predicted by regression analysis from the modest rise in background contraction. When the background contraction level was comparable, both reflex gain and joint mechanical resistance were also comparable between the two groups, so that there was no evidence of an increase in the intrinsic stretch reflex loop gain or passive joint resistance in the spastic group.

The results confirm earlier studies that found an approximately linear relation between reflex amplitude and low levels of voluntary contraction in normal subjects.[16 21 23–29] Furthermore, they show that this relation holds also in stroke. The finding that the slopes of the regression lines relating reflex gain and joint resistance to contraction level were not significantly different in the normal and stroke groups over the tested range means that both reflex amplitude and joint resistance fell within the normal range for any contraction level achieved by spastic subjects. This provides strong evidence that the intrinsic loop gain of the stretch reflex is not increased in spastic subjects.

The findings of our study underline the need to control for differences in contraction levels when comparing reflexes in different groups. There have been no attempts previously to quantify "resting" EMG levels or to assess the impact of incomplete relaxation on reflex gain or passive tissue resistance estimates in stroke subjects, although persisting activity in resting spastic muscles has been reported.[35] The group mean biceps background contraction during perturbations applied when spastic subjects attempted to relax was equivalent to 3.1% of the normal MVC (in the normal subjects it was 0.6%). Therefore, the spastic subjects exceeded the level required to increase reflex gain and joint resistance significantly in normals, where a voluntary background contraction of 2.5% of MVC produced significant increases in biceps reflex gain and joint resistance. The resting biceps reflex gain in spastic subjects was approximately five times higher than normal resting values. This increase was sufficient to influence joint mechanics, because resting reflex gain significantly correlated with resting joint resistance levels in the spastic limbs, but not the normal limbs. It can be concluded that the rise in resting background muscle activity is a primary factor in the greater prominence of spastic signs (viz, increased reflex gain and passive joint resistance) in resting rather than in contracting muscle, as seen here and in earlier studies.

Linear regression analysis showed that the maximal achievable reflex gain in spastic subjects was decreased proportionately to the degree of weakness. Their mean MVC was approximately 25% of the normal value in our study. Thus, if reflex gain is compared with normal muscles at high contraction levels that exceed the limited range of gain modulation in stroke, a relative decrease in gain may be observed.[2 4 17 18] Similarly, because joint resistance tended to increase in a linear manner with contraction level, there will be a reduction in the available range of joint stiffness modulation, with significant functional implications.

Also evident from our study, is the importance of the method used to calibrate the EMG when comparing normal and stroke subjects. Differences in calibration methods must have contributed to the conflicting findings on spasticity in previous studies. Calibration against MVC would have greatly altered the interpretation of the data reported in our present study. Such a method is of course invalidated by significant weakness in the stroke group. In view of the finding that the relation between torque production and EMG voltage was not significantly altered by weakness, EMG voltage was an appropriate unit for comparison.

Under the experimental conditions, there was no evidence that co-contraction of antagonist muscles or increased reflex activity in antagonist muscles contributed to spasticity. The ratio of mean flexor to extensor activity was similar in stroke and normal subjects at all levels of flexor contraction. Regression analysis in both flexor and extensor muscles of normal and stroke subjects showed that reflex gain was linearly related to contraction level, and that the slopes of these regressions were not significantly different in flexor and extensor muscles. The TSR phase analysis also gave no indication of an abnormal reciprocal relation between antagonist muscles. A shift in their relative phase would have provided evidence of abnormal reciprocal mechanisms, but both muscles maintained a normal phase advance of approximately 100° when contracted.[21] Therefore, our findings suggest that co-contraction does not occur as a result of changes in segmental reciprocal reflex mechanisms. This suggests that the abnormal patterns of co-contraction of muscle antagonists previously reported in spasticity[36–38] may be task specific, and thus of supraspinal origin, because they are not a feature of the simple isometric contractions studied here.

In our study, it was possible to estimate reflex gain, torque angle gain, and resonant frequency at a theoretical zero contraction level, by extrapolating their respective regression lines with respect to contraction level. No significant differences between groups were found. The intercept on the torque angle gain axis reflects the passive joint resistance component, and the findings indicate that it was small relative to active resistance in the resting stroke group. A small increase in passive resistance is unlikely to be detected by relatively insensitive clinical scales, and therefore is unlikely to contribute significantly to the clinical picture of hypertonia. Given *et al* estimated passive resistance at the elbow and also found no difference between normal and stroke subjects.[39] Although several studies have reported significant passive tissue contributions to spasticity,[39–45] the degree of relaxation in the subjects was not measured, except by visual inspection of raw EMG records. As the results of our present study show, without accurate matching of contraction levels, normal and spastic groups cannot be compared reliably.

However, an important measurement with regard to the question of passive resistance is the selection of subjects. Our current study is based on limbs that were free of significant contracture, as assessed clinically, and were able to be moved repeatedly through a range of 30° without significant discomfort. Therefore, the results do not bear on the potential contribution of passive tissue changes to spasticity in limbs with substantial contracture. The degree of contracture is probably an important variable in determining the relative magnitude of the passive component.

An increase in the velocity sensitivity of the stretch reflex has been reported in spasticity.[4] This has been attributed to an increase in the slope of the TSR–velocity relation with increasing severity of spasticity.[19 46] No evidence of a difference in the slope of the gain–frequency relation between normal and spastic muscle was found in our current study. TSR gain increased in a non-linear manner with perturbation frequency in normal (see also Neilson and Lance and Neilson and McCaughley[16 27]) and spastic muscles, but the slopes of the gain–frequency regression lines and their intercepts were not significantly different at equivalent contraction levels. Because the contraction levels in spastic muscle in the resting condition were not equivalent to normal, the effect was to displace the non-linear reflex gain–frequency relation upward on the Y axis and increase its slope. Thus, reported increases in velocity sensitivity and also of reduced velocity threshold[18 46–48] in spastic muscles may be explicable in terms of a normal velocity dependence of the TSR in the presence of a raised resting contraction level.

The rationale for the use of antispastic agents in treatment is that upper or lower limb performance is compromised by excessive spastic muscle activity of involuntary or reflex origin, and that performance may be improved by reducing this activity. Implicit in this approach is the view that the exaggerated reflex activity apparent at rest will translate into exaggerated reflex activity during voluntary movements. Some previous studies[2 4 17–19] have failed to demonstrate such increased activity under active conditions, and our present study supports and extends these findings. With accurate matching of background contraction between subjects, so as to assess the peripheral manifestations of spasticity independently of descending supraspinal influences, we found no evidence of increased muscle activity as reflected by increased mechanical resistance or increased stretch reflex loop gain. Therefore, the rationale for the routine use of antispastic agents was not supported.

It is clear that dynamic modulation of muscle reflexes occurs during movement tasks and that deficits in dynamic reflex modulation may accompany spasticity.[49] We have shown that the range of reflex gain modulation is reduced in spasticity as a result of raised resting contraction levels and weakness. Hence, task performance in the spastic movement disorder is more likely to be limited by disturbed central modulation of reflex activity than by a persisting increase in reflex activity (fig 4A, B).

An important qualification of the results is that the subjects selected for our study did not have significant degrees of contracture, so that the results do not exclude the possible contribution of muscle shortening and reduced range of movement to disability in some patients.

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LETTERS

Central pontine myelinolysis temporally related to hypophosphataemia

Central pontine myelinolysis (CPM) is known to be associated with the rapid correction of severe hyponatraemia. However, there have been case reports of CPM occurring in normonatraemic patients.[1] Here we describe two patients in whom chronic alcohol abuse led to profound hypophosphataemia that was closely temporally related to the development of CPM.

Case 1

A 29 year old woman was admitted for investigation of painless jaundice of 10 days' duration. She had consumed 100–140 units of alcohol a week for the preceding 18 months and had been noted to have mildly deranged serum transaminase levels one year previously.

On admission she was fully oriented with normal speech and gait. She had a mild postural tremor but no asterixis. A plasma biochemical profile showed her sodium to be 122 mmol/l, potassium 2.1 mmol/l, and urea 5.9 mmol/l. Serum creatinine was 182 µmol/l, phosphate 0.65 mmol/l, magnesium 0.59 mmol/l, and total corrected calcium 2.18 mmol/l. She was immediately given potassium and magnesium supplements, chlordiazepoxide, and intravenous vitamins including vitamin K and thiamine.

Three days after admission she developed a *Staph aureus* septicaemia secondary to a peripheral venous cannula infection. This required treatment with intravenous cefuroxime and flucloxacillin. She subsequently became drowsy and by day 10 had developed a severe spastic dysarthria and profound spastic tetraparesis. There was a bilateral lower motor neurone pattern of facial weakness and gaze evoked nystagmus. The clinical suspicion of CPM was supported by magnetic resonance imaging of the brain, which showed symmetrical signal hyperintensity in the pons on T2 weighted images, as well as generalised cerebral atrophy.

A review of the biochemistry results during her admission showed that the maximum increase in serum sodium concentration over a 24 hour period was only 7 mmol/l (from 123 to 130 mmol/l). Potassium and magnesium concentrations were corrected to the lower end of their normal ranges. However, she developed profound hypophosphataemia (0.16 mmol/l at nadir) which was rapidly corrected to 0.8 mmol/l within 72 hours. The rapid rise in plasma phosphate coincided with the onset of the patient's neurological deterioration. With supportive care she made a gradual recovery such that two months after admission she was safe to be discharged, with only a mild residual left hemiparesis and slight spastic dysarthria, which were improving.

Case 2

A 44 year old woman was admitted with a three day history of progressive dysarthria, seven days of difficulty in walking, and dysaesthesia affecting all four limbs and the perioral region. She had consumed at least 80 units of alcohol a week for several months before presentation.

Examination on admission revealed a mild tetraparesis, dysarthria, and subjective sensory loss in both legs and the left arm. Her admission blood profile revealed a plasma sodium concentration of 136 mmol/l and potassium of 3.4 mmol/l. The serum phosphate concentration was profoundly low at 0.13 mmol/l. T2 weighted and FLAIR sequence MRI done three days after admission showed abnormal signal within the central brain stem suggestive of CPM (fig 1).

She was treated with oral thiamine, multivitamins, and minerals including phosphate. She made a rapid improvement such that her dysarthria had resolved and gait improved sufficiently for her to be discharged 11 days after admission.

Comment

The pathophysiology of CPM is not well understood. Rapid correction of severe hyponatraemia is frequently implicated as a causative factor, but CPM has been reported in the presence of normonatraemia,[1] hypokalemia,[2] and hypophosphataemia.[3] In these cases a hypothesis based on osmotic trauma must be questioned.

Recently an apoptotic hypothesis has been proposed.[4] It is suggested that a depletion of the energy supply to glial cells might limit the function of their Na^+/K^+-ATPase pumps. This could reduce their ability to adapt to relatively minor osmotic stress caused by small changes in serum sodium concentration, and ultimately lead to apoptosis. A preliminary study of necropsy material from five cases of CPM compared with controls has provided some support for this theory. Using immunohistochemistry, an imbalance was shown between proapoptotic and antiapoptotic factors in glial cells with the appearance of oligodendrocytes.[5] Furthermore the serum sodium concentrations in two of the patients remained normal from the onset of symptoms to the time of death.

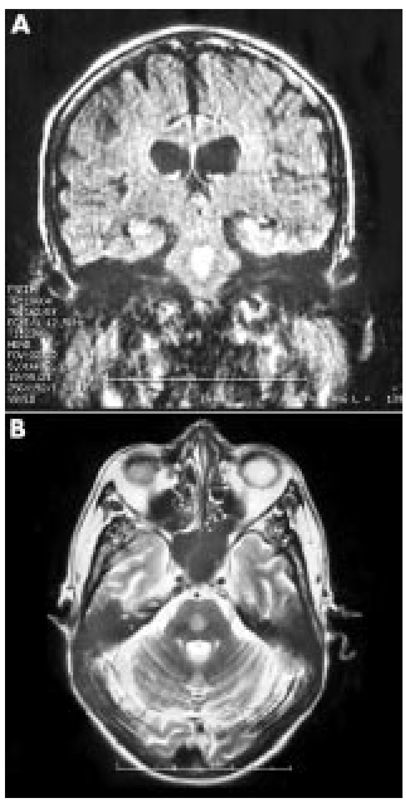

Figure 1 Coronal FLAIR magnetic resonance image (MRI) (A) and axial T2 weighted MRI (B) from case 2, showing high signal within the pons consistent with central pontine myelinosis.

The two patients presented here showed aclose temporal association between severe hypophosphataemia and the development of CPM. Both patients abused alcohol, and the first patient had moderate hyponatraemia with hypokalaemia. They may therefore have been particularly susceptible to CPM for a variety of reasons. It is possible, however, that severe hypophosphataemia adversely affected the Na^+/K^+-ATPase pump and finally triggered apoptosis and CPM. The temporal association of neurological deterioration with the rapid correction of profound hypophosphataemia in case 1 is unlikely to relate to osmotic stress in view of the small contribution of phosphate towards total osmolarity. The rapid change in plasma phosphate may, however, increase cellular stress, contributing to eventual apoptosis.

Both patients described here made good recoveries with phosphate replacement and supportive care. This suggests that widespread apoptosis had not occurred. In these patients the speed and degree of recovery might reflect the resolution of pontine oedema that could accompany less widespread or incomplete apoptosis.

There are useful practical conclusions to be drawn from the observed association of CPM with hypophosphataemia. First, one must suspect the diagnosis of CPM in susceptible patients even without "typical" electrolyte abnormalities. Second, as severe hypophosphataemia in itself has been correlated with increased mortality[6] it would seem prudent to check and treat low serum phosphate concentrations in susceptible patients. This particularly refers to alcohol abusers or malnourished patients treated with intravenous glucose, diuretics, and steroids which may lower serum phosphate concentrations.

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Spastic movement disorder: what is the impact of research on clinical practice?

One expects that convincing research results would have an impact on clinical practice. However, whether or not a new concept becomes transferred to an application in clinical practice is dependent on the medical field and on the therapeutic consequences. The issue discussed here concerns spasticity, a common motor disorder in, for example, patients who have had a stroke or a spinal cord injury.

The traditional concept

Over many years it was widely accepted that spasticity consists of muscle hypertonia (that is, "a velocity dependent resistance of a muscle to stretch"[1]) caused by exaggerated reflexes, leading to the spastic movement disorder.[2] This concept was based on animal experiments (for example, in the decerebrate cat[3]) and on the physical signs evident on clinical examination at the bedside. Consequently, the aim of any treatment was to reduce reflex activity by antispastic drugs. Possible differences in pathophysiology between the clinical signs of spasticity and the spastic movement disorder which hampers the patient were not considered.

The new concept

Early clinical observations[4] and studies in the 1980s on spastic movement disorders[5] clearly failed to support the traditional concept. In the subsequent 20 years an increasing number of studies using different technological approaches with electromyographic (EMG) and biomechanical recordings focused on the relation between muscle EMG and reflex activity and muscle tone during various functional[6–8] and clinical[9–12] conditions. All these studies fused into a new concept of spasticity (reviewed in several articles[13–15]). This concept has never been questioned in its basic aspects.

The new concept was based on the following observations. First, in the active muscle (that is, during movement) the presence of exaggerated tendon tap reflexes is associated with a loss of the functionally essential polysynaptic or longer latency reflexes, with the consequence that overall muscle activity is reduced during functional movements. Second, as a response to the primary lesion, changes in non-neuronal factors (muscle and connective tissue) compensate for the loss of supraspinal drive and essentially contribute to spastic hypertonia in both passive[9 12] and active[8] muscles.

The *scientific consequence* of this is that the physical signs obtained during the clinical bedside examination are an epiphenomenon rather than the cause of the functional condition (which impairs the patient). During movement, essential reflex mechanisms are involved which cannot usually be assessed by clinical testing. Consequently, the clinical examination required for diagnostic purposes has to be separated from functional testing, which should determine the therapeutic approach. For example, motor function can be assessed by a walking index, such as WISCI.[16]

The *therapeutic consequence* of these observations is that antispastic drugs should be used only with caution in the mobile spastic patient, as a decrease in muscle tone achieved by these drugs could be associated with an accentuation of paresis, impairing the performance of functional movements.[17 18] Consequently, spastic muscle tone is required so that a patient can walk again after a stroke.

Facts and consequences

Although this new concept has become well established scientifically in journals with a mainly scientific orientation during the past 20 years, there has been little transfer to clinical practice. This is reflected in recent review articles in journals with a practical orientation[19–21] read predominantly by clinical neurologists.

The following factors may contribute to the persistence of some old fashioned concepts in clinical neurology:

- The old concept was simple to understand and had a clear therapeutic consequence: the prescription of antispastic drugs. It is seemingly logical that exaggerated reflexes cause muscle hypertonia. The new concept is more complex and its implications—that antispastic drugs should *not* generally be used—make the doctor somewhat resourceless.
- It is not rewarding for a neurologist to take care of patients after a stroke and to have to explain that there are limited therapeutic options (that is, that it will be impossible to restore normal function, and that physical exercises will be more helpful than drug treatment).
- It is, of course of no interest for companies producing antispastic drugs to support graduate medical education in this new concept, with its limited opportunities for drug treatment.

The *consequences* of this experience should be as follows. First, scientific research results should be translated into an understandable and pragmatic format, to convince doctors and patients of the superiority of the new concept. Second, such a novel concept should initiate the development of new forms of treatment (for example, in the field of active physiotherapy); at very least it should be associated with a well structured physical treatment programme which allows the doctor to become involved. Third, the concept should emphasise that immobilised patients may benefit from the use of antispastic drugs (for example, in the management of spasms and for easier nursing); this would make the concept more acceptable to the drug companies. Finally, the concept should include perspectives and limitations of any possible achievements.

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Intracranial hypotension after chiropractic manipulation of the cervical spine

The aetiology of intracranial hypotension is not fully understood, but CSF leakage from spinal meningeal diverticula or dural tears may be involved. In the majority of patients without a history of mechanical opening of the dura the cause of intracranial hypotension is unknown and the syndrome is termed "spontaneous" intracranial hypotension. We report a case of intracranial hypotension ensuing after a spinal chiropractic manipulation leading to CSF isodense effusion in the upper cervical spine.

Case report

A 40 year old woman undertook a spinal chiropractic manipulation. The chiropractioner grasped the head of the supine patient and exerted axial tension while rotating the head. During this manoeuvre the patient complained of a sudden sharp pain in her upper neck, and the procedure had to be stopped immediately. Subsequently she complained of headaches and after 24 hours she developed nausea and vomiting. Her headaches worsened, and lying down gave the only measure of limited relief. On the sixth day she developed double vision and presented to the neurology department of a community hospital.

She had a right abducens palsy and pachymeningeal gadolinium enhancement on magnetic resonance imaging (MRI). The first

WEDNESDAY

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Research Articles

Does Balance or Motor Impairment of Limbs Discriminate the Ambulatory Status of Stroke Survivors?

ABSTRACT

Au-Yeung SSY, Ng JTW, Lo SK: Does balance or motor impairment of limbs discriminate the ambulatory status of stroke survivors? *Am J Phys Med Rehabil* 2003;82:279–283.

Objective: This study was performed to determine if ambulatory function is governed by motor impairment of limbs or balance ability in subjects with hemiplegia caused by stroke.

Design: Seven patients who walked with physical assistance (FIM™ 4) after stroke and 13 who walked independently with assistive devices (FIM 6) were compared with 13 healthy subjects. Motor impairment of limbs was evaluated with the Fugl-Meyer Assessment. The Berg Balance Scale and limit of stability test of the Smart Balance Master were used to evaluate balance ability.

Results: The FIM 6 group and the controls were best differentiated by motor impairment of the paretic limbs and limit of stability in the backward direction. Motor impairment of the upper limb and limit of stability in direction toward the paretic side separated the FIM 4 from the FIM 6 group. Upper limb motor impairment and the Berg Balance Scale consistently separated the three subject groups.

Conclusions: Motor impairment in the paretic upper limb and balance dysfunction should be addressed in treatments working toward independent ambulation.

Key Words: Motor, Balance, Ambulation, Hemiplegia

Recovery of independent walking is often set as a prime target in stroke rehabilitation. In a prospective study on the recovery of walking function after stroke,[1] nearly 30% of the subjects were still totally dependent or required assistance in walking even after rehabilitation. A survey including 58 subjects with stroke found that independent walking was rated as the most important factor when compared with distance, speed, and appearance of gait.[2] To tackle disability in walking, therapists have traditionally put special emphasis on strengthening the paretic lower limb, improving weight transfer to the limb, and walking with or without assistive devices. However, what should be the key target in developing ambulatory function toward independence? Restricted upper limb movements were found to affect the body kinematics for efficient locomotion.[3,4] Would motor impairment of the paretic upper limb caused by stroke also affect ambulatory function? The purpose of this study was to determine whether ambulation status of patients after stroke was governed more by balance ability or by limb motor impairment.

METHODS

Ethics approval was granted in March 1999 by the institution under which the study was conducted.

Subjects. A total of 20 patients with stroke who were attending a rehabilitation program in a day-hospital and 13 age-matched healthy individuals from a community center of the same district were recruited by convenient sampling. The patient subjects had first-ever stroke of ≤12 mo after onset, were aged >55 yr, had an Abbreviated Mental Test[5] score >7 to ensure ability to follow instructions, and were able to stand independently. Subjects were excluded if they had visual impairment, orthopedic or medical problems that would interfere with balance performance, premorbid or comorbid neurologic problems other than stroke, or were currently receiving medications known to affect balance. The subjects had an ambulatory function rating of 4 with the FIM™ instrument, which reflected their ability to walk only with assistive devices and physical assistance, or a rating 6 for their ability to walk independently with assistive devices.[6] Subjects of the two levels of ambulatory status were thus classified as the FIM 4 and FIM 6 group, respectively. The control group had no known history of diseases leading to physical impairment or other medical conditions requiring active treatment.

Procedures. All subjects were assessed by a single rater (J. T. W. Ng) for upper and lower limb motor function using the motor subsection of the Fugl-Meyer Assessment (FMA_{UL} and FMA_{LL}, respectively),[7] balance in performing activities with the Berg Balance Scale (BBS),[8] and the ability to shift the body's center of gravity (COG) in standing in the limit-of-stability (LOS) test with the Smart Balance Master (Neurocom International, Clackamas, OR). All assessments were completed in two sessions within 1 wk.

The FMA has been commonly used to evaluate one's physical progress after stroke. Its reliability and validity are well documented.[8,9] The motor subsection evaluates volitional movements within synergies, partially out of synergies and independent of synergies of shoulders to hands and hips to ankles. The movements performed are rated on a 3-point ordinal scale: 0 for complete failure and 2 for performance of full details. The full score of the FMA_{UL} is 66 and that of the FMA_{LL} is 34.

The BBS consists of a hierarchical series of 14 daily life activities that test one's ability to maintain balance in various positions, in transfers between positions, and during voluntary movements like turning around and stepping.[10] The rating of performance in each item is according to a 5-point ordinal scale, with the lowest score as 0. The BBS full score is 56. Reliability and validity of the scale as applied to older people or patients with stroke has been demonstrated in various studies.[11,12]

During the LOS test, the subjects wore a harness and stood on the force platform of the Smart Balance Master. They were required to lean their body about the ankle joint so as to move the COG position from the central starting position to targets shown on the screen at eye level. These peripheral targets were at a distance from the central starting position and were arranged in an elliptical manner at the boundary of the subject's theoretical LOS. Subjects were required to be tested at 60% LOS, which was confirmed from a pilot study as the maximal extent accomplished by five subjects with ambulatory status similar to the two FIM groups. From the LOS test, the results of endpoint excursion (EPE) and direction control (DC) of the COG positions during body shifting in forward, backward, and the two lateral directions were deduced by the system's built-in software. The paretic and contralateral side of the subjects with stroke corresponded to the nondominant and dominant side, respectively, of the controls.

EPE was the percentage of angular displacement of the COG on the primary attempt by the subjects to reach the target with reference to the theoretical maximum LOS angular displacement for normal adults. DC was the percentage that the COG excursion deviated from the shortest distance traveled by the COG from the center to the target.

TABLE 1
Demographic and clinical characteristics of the subjects

	FIM™ 4, Mean (SD)	FIM 6, Mean (SD)	Control, Mean (SD)	*P* Value
No. of subjects	7	13	13	—
Sex	4 M, 3 F	5 M, 8 F	3 M, 10 F	0.341
Age, yr	68.71 (9.01)	68.85 (6.64)	68.31 (3.95)	0.976
Height, m	1.55 (0.06)	1.54 (0.08)	1.53 (0.06)	0.748
Hemiplegic side	3 R, 4 L	4 R, 9 L	—	0.651
Type of stroke	4 I, 3 H	8 I, 1 H, 4 N	—	0.119
Months after stroke	4.14 (1.22)	3.94 (1.11)	—	0.714

M, male; F, female; R, right; L, left; I, infarct; H, hemorrhagic; N, no abnormality detected.

Statistical Analysis. Multivariate analysis of variance was used to test the differences in motor and balance performance between the FIM 4, FIM 6, and control groups. Linear contrast was then performed to test the differences between the FIM 4 and FIM 6 group and between the FIM 6 and control group. Although the overall level of significance was set at 0.05, the sharpened Bonferroni method[13] was used to adjust individual alpha level when multiple testing was performed. SPSS version 10.0 was used for all statistical analysis (SPSS, Chicago, IL).

RESULTS

As shown in Table 1, the three groups were similar in their demographic and clinical characteristics. Moreover, FIM 4 and FIM 6 were not significantly different in time after stroke onset when assessed.

Using multivariate analysis of variance, we found that the three groups were significantly different when all the dependent variables were examined simultaneously ($F = 20.2$; $df = 22, 38$; $P < 0.001$) (Table 2). Differences in the upper and lower limb FMA motor scores and BBS among the three groups were significant, with the FIM 4 group having the lowest scores. The three groups were also different in EPE and DC of all, except the contralateral, directions in the LOS test. Again, the FIM 4 group was the worst in performance.

Also shown in Table 2 are the results of linear contrast comparing between the FIM 4 and FIM 6 group and between the FIM 6 and control group, with alpha levels adjusted using the sharpened Bonferroni method because a series of contrasts had been carried out. Variables found

TABLE 2
Results of multivariate analysis of variance[a] for differences among the three groups

	Mean (SD)			*P* Value (Contrast)	
Variable	FIM™ 4	FIM 6	Control	FIM 4 *vs.* FIM 6	FIM 6 *vs.* Control
FMA_{UL}	16.1 (15.2)	32.6 (14.0)	66.0 (0.0)	<0.001[b]	<0.001[b]
FMA_{LL}	14.0 (3.4)	21.7 (5.8)	34.0 (0.0)	0.179	<0.001[b]
Berg Balance Score	29.3 (4.9)	46.0 (2.9)	55.6 (0.8)	0.005[b]	<0.001[b]
$EPE_{forward}$	34.5 (7.9)	47.5 (7.8)	50.3 (7.5)	0.006[b]	0.871
$EPE_{backward}$	31.0 (11.3)	36.2 (9.2)	46.2 (6.2)	0.282	0.007[b]
$EPE_{paretic}$	31.8 (8.8)	50.5 (10.0)	55.9 (7.7)	<0.001[b]	0.190
$EPE_{contralateral}$	45.9 (7.8)	54.4 (12.2)	56.1 (8.1)	0.269	0.879
$DC_{forward}$	52.5 (19.9)	70.0 (20.2)	89.4 (4.5)	0.055	0.012
$DC_{backward}$	−45.5 (62.5)	−6.2 (81.3)	66.2 (13.4)	0.245	0.004[b]
$DC_{paretic}$	52.8 (25.5)	79.3 (6.5)	85.8 (6.3)	<0.001[b]	0.165
$DC_{contralateral}$	79.2 (3.3)	76.6 (14.7)	86.6 (3.7)	0.955	0.048

FMA, Fugl-Meyer Assessment; UL, upper limb; LL, lower limb; EPE, endpoint excursion of the limit-of-stability test; DC, direction control of the limit-of-stability test. Subscripts are the directions of movement of the body's center of gravity. Paretic and contralateral for patient groups are, respectively, corresponding to nondominant and dominant for the controls.

[a] Multivariate analysis of variance. $F = 20.2$, $df = 22, 38$, $P < 0.001$.

[b] *P* value still significant after adjusting for the alpha value using the sharpened Bonferroni method.

to be useful in separating between the FIM 4 and FIM 6 group included, in order of statistical significance, FMA_{UL}, EPE and DC in direction of the paretic side, followed by BBS and EPE in the forward direction. On the other hand, in discriminating the FIM 6 from the control, FMA_{UL}, FMA_{LL}, and BBS were variables of a higher order of significance than DC and EPE in backward direction.

DISCUSSION

Subjects of the three levels of ambulatory status were different in all motor and balance parameters measured. Should all these aspects be targeted in stroke rehabilitation when training locomotion toward independence? There were reports on the positive relationship between lower limb impairment after stroke and independent ambulation.[14–17] Only one study on patients in the early stage of stroke confirmed that motor impairment of the upper limb was related to locomotion function.[18] We found that upper limb motor impairment was the top variable in the order of significance to discriminate patients of two different levels of ambulatory status (FIM 4 and FIM 6) after stroke and the healthy controls. With impaired upper limb movement, efficiency of locomotion could deteriorate because of altered body kinematics used as compensatory strategies.[4] In an observational study on people with stroke in the community, those who had a history of repeated falls were found to have upper limb motor function that was much more reduced.[19] In advancing ambulatory function from level 4 to 6 of FIM classification and from level 6 to complete independence, we could suggest that improving motor impairment of the paretic upper limb should be an important goal in stroke rehabilitation. On the other hand, lower limb motor impairment was in similar rank of significance as that of the upper limb in discriminating the FIM 6 group from the controls. Improving the motor function of the paretic lower limb should also be emphasized in the final stage of gait re-education.

The LOS test quantifies weight-shifting ability and stance postural control of an individual.[20,21] To what extent information from the LOS test reflects the ability of stroke subjects in ambulation is not clear. When compared with age- and sex-matched controls, subjects with stroke were found to have significant impairment in forward and backward weight shifting in standing from measurements obtained with force plates.[22] Another group of ambulatory subjects with stroke were tested on their ability to perform weight shifting to 50% limits of stability.[23] They had relatively less displacement of their body COG to both lateral directions than the healthy controls, although the difference was not significant. Dettmann et al.[24] found that impairment in shifting the body's COG in directions backward and to the side of paresis is related to gait speed. Our study supported impairment in COG displacement backwards discriminated the FIM 6 group from the control. On the other hand, the most distinguishable difference between the more dependent FIM 4 group and the FIM 6 was in weight-shifting performance to the paretic side. Our interpretation of this finding is that stance postural control problems are different at the two levels of ambulation status.

In the re-education of gait after stroke, weight-shifting exercise has been common. Different emphases of weight-shifting training should be introduced at different stages of gait re-education programs for stroke victims. Acquiring more efficient gait and independence would encourage survivors from stroke to be more active. Achieving better weight shifting to the weaker side should be an important goal for advancing ambulation status from FIM 4. To regain complete independence in ambulation, the problem in backward weight shifting should be addressed in the later stage of gait re-education.

Among all parameters evaluated, BBS consistently separated the three levels of walking status. In addition, BBS was relatively higher in order of significance in separating the FIM 6 group from the control than from the FIM 4 group. Improving balance should be an important goal in the advanced stage of rehabilitation aiming to achieve completely independent ambulation. Activities challenging balance as that in the BBS might be useful components in walking re-education programs. However, the possible benefits of such activities on ambulation have to be investigated with randomized, controlled trials before recommendations can be made.

Results of our study provided useful guidelines on emphasis in training ambulatory function after stroke. Motor impairment of the paretic upper limb and balance ability were consistently in high order of significance in discriminating among the three groups of subjects of different walking status. The two problems should therefore be addressed in stroke rehabilitation that aims to achieve independent ambulation.

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The acquisition of skilled motor performance: Fast and slow experience-driven changes in primary motor cortex

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ABSTRACT Behavioral and neurophysiological studies suggest that skill learning can be mediated by discrete, experience-driven changes within specific neural representations subserving the performance of the trained task. We have shown that a few minutes of daily practice on a sequential finger opposition task induced large, incremental performance gains over a few weeks of training. These gains did not generalize to the contralateral hand nor to a matched sequence of identical component movements, suggesting that a lateralized representation of the learned sequence of movements evolved through practice. This interpretation was supported by functional MRI data showing that a more extensive representation of the trained sequence emerged in primary motor cortex after 3 weeks of training. The imaging data, however, also indicated important changes occurring in primary motor cortex during the initial scanning sessions, which we proposed may reflect the setting up of a task-specific motor processing routine. Here we provide behavioral and functional MRI data on experience-dependent changes induced by a limited amount of repetitions within the first imaging session. We show that this limited training experience can be sufficient to trigger performance gains that require time to become evident. We propose that skilled motor performance is acquired in several stages: "fast" learning, an initial, within-session improvement phase, followed by a period of consolidation of several hours duration, and then "slow" learning, consisting of delayed, incremental gains in performance emerging after continued practice. This time course may reflect basic mechanisms of neuronal plasticity in the adult brain that subserve the acquisition and retention of many different skills.

The performance of many tasks improves, throughout life, with repetition and practice. Even in adulthood simple tasks such as reaching to a target or rapidly and accurately tapping a short sequence of finger movements, which appear, when mastered, to be effortlessly performed, often require extensive training before skilled performance develops. What changes occur in the adult brain when a new skill is acquired through practice? When, and after how much practice, do these changes occur? Functional reorganization of adult mammalian sensory and motor cortical representations has been found to occur in many different animal models of brain plasticity in the last two decades, advancing the idea that throughout life the functional properties of central nervous system neurons, as well as the neural circuitry within different brain areas, are malleable and retain a functionally significant degree of plasticity (e.g., refs. 1–4). These representational changes have been shown to be induced not only in response to lesions of peripheral or central sensory input or motor output pathways but also, in normal individuals, as a result of practice and experience. The advent of new brain imaging techniques, especially functional MRI (fMRI) (5), which allows repeated mapping of cortical representations as a consequence of long-term practice, provides a way to examine over an extended time frame the neurobiological correlates of skill learning in the adult human brain.

In this paper we briefly outline two characteristics of skill learning—the specificity and the time course of learning—which, we propose, can provide important constraints on the neural locus and substrates of adult skill learning. By using the learning of sequential finger movements as the main experimental paradigm, we review recent findings, mainly from our own work, suggesting that: (*i*) the acquisition and retention of motor skills may result in significant experience-related reorganization within specific motor cortical representations in the adult human brain; and (*ii*) these representational changes occur in several stages and are characterized by a distinct time course. We review our fMRI and behavioral data (6) and recent experimental data (7) from monkeys trained to perform complex motor tasks to demonstrate that long-term training results in highly specific skilled motor performance, paralleled by the emergence of a specific, more extensive representation of a trained sequence of movements in the contralateral primary motor cortex (M1). We then present fMRI as well as behavioral evidence for an important intermediate stage in the acquisition of the skill that is set in motion by a few minutes of practice and continues to evolve after practice has ended. This stage presumably is subserved by neuronal processes that require time to become effective. These processes may underlie the consolidation of motor experience and thus provide a basis for the long-term memory of the skill. Further, they may be related to similar processes that have been described in adult human perceptual skill learning (8, 9). The finding that a similar time course characterizes the learning both of different types of motor skills and of different perceptual skills lends support to the idea that the time course of skill learning

Abbreviations: fMRI, functional magnetic resonance imaging; M1, primary motor cortex.

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is determined by the time constants of a limited repertoire of basic neuronal mechanisms of plasticity subserving procedural memory throughout the adult cortex (10, 11).

Characteristics of Skill Learning

Skills constitute one of two distinct, broad categories of memory (12, 13). Although different taxonomies exist, the dichotomy accounts for deficits of fact and event memories ("what," declarative knowledge) on the one hand, and the preservation of skills and habits ("how to," procedural knowledge) on the other, in individuals and nonhuman primates with focal lesions to medial temporal lobe structures (12–15). Many instances of skill learning, both perceptual and motor, are specific for basic parameters of the training experience; that is, learning can be strongly dependent on simple physical attributes of the stimulus presented in training a perceptual task (e.g., refs. 16–18) or on factors such as the specific effector organs' positions, trajectories and sequence of trajectories experienced in motor training (e.g., refs. 6 and 19–21). For example, training to perform an arm movement aimed at a specific target location against a specific perturbation resulted in learning to compensate for the perturbation in the trained part of the workspace but showed little generalization to the rest of the workspace (19). Similarly, training to overcome a specific perturbation did not generalize to overcoming an identical perturbation in the orthogonal direction (20).

There is considerable anatomical and physiological evidence for a hierarchical organization of information processing in sensory and motor systems in the mammalian brain, such that many physical parameters of a sensory input, or a motor output, are selectively represented only in specific processing stages. The specificity of learning for a given parameter of the training experience implies, therefore, that only a discrete part (or subset of neurons) within a processing stream—that wherein the parameter is differentially represented—has undergone learning related changes. At a level of processing in which neurons respond invariantly, one would expect learning to generalize for that particular parameter. Thus, the finding of specificity in the learning of a given skill has been used to generate predictions on the possible neuronal loci and type of representations affected by the training experience (6, 16–19, 21–24). This is not to say that all skills are specific for low-level parameters of the training experience: indeed, one would predict otherwise whenever the relevant aspects of a task are represented at higher levels within the processing stream (25). Nevertheless, in many instances the degree of specificity has indicated discrete changes in low-level representations as an important locus of learning (25). This interpretation of the human behavioral data is supported by experimental animal studies that have revealed that the details of the representation of the sensory input in low-level processing areas engaged in the performance of a given sensory discrimination task change, so as to reflect, by evolving improved and enlarged representations, the specific behavioral experiences of the animals under study (26–29). Similarly, motor representations have been shown to undergo experience-specific reorganization after long-term training (7), whereas cortical representational maps, often on a much shorter time scale, have been found to be altered by manipulations of their sensory inputs (1, 2) or motor outputs (3, 30).

An important difference between declarative and procedural memory is the time course of learning. Declarative learning can be very fast and may take place even after a single event (13, 31). Procedural learning, in contrast, is slow and often requires many repetitions, usually over several training sessions, to evolve (12, 31). Thus, one may remember the contents of a book after a single reading but the skills of reading evolve over multiple practice sessions and require many repetitions to become established.

Several recent studies have examined the time course of experience-dependent perceptual learning (8, 9, 32–34). In these studies, adult individuals were found to gain an increase in perceptual sensitivity when given practice in basic sensory discrimination tasks. These studies indicate that improved perceptual performance often evolves in two distinct stages (8): first, a fast within-session improvement that can be induced by a limited number of trials on a time scale of minutes ("fast learning"), and second, slowly evolving, incremental performance gains, triggered by practice but taking hours to become effective ("slow learning"). In many instances, most gains in performance evolved in a latent manner not during, but rather a minimum of 6–8 hr after training, that is, between sessions (8, 33–35). Improvements in performance continued to develop over the course of 5–10 daily practice sessions, spaced 1 to 3 days apart, before nearing asymptotic performance. The skill then was retained for months and years (8). Because of the long-term retention and by analogy to the time course described in several paradigms of developmental plasticity (36, 37), the latent phase in human skill learning is thought to reflect a process of consolidation of experience-dependent changes in the adult cortex that is triggered by training but continues to evolve after the training session has ended (8). Furthermore, it was proposed that fast learning reflects the setting up of a task-specific processing routine for solving the perceptual problem whereby those representations that are relevant for task performance are selected. Slow learning, on the other hand, is thought to reflect ongoing, perhaps structural, modifications of basic perceptual modules within the selected representations (8, 25, 32, 38).

Recent studies suggest that a similar time course may characterize the acquisition of some motor skills by human adults (6, 20, 39). Studies conducted in the early decades of this century have described a latent consolidation phase in perceptuomotor tasks under the term reminiscence (see ref. 40). In the monkey, fast, within-session learning, as well as large incremental gains in performance over weeks of daily training sessions—"slow" learning—have been described in both perceptual and motor skill learning paradigms (7, 27, 29). The monkey data further suggest that the long-term changes that can be induced in different brain areas by the learning of motor (7, 41) and perceptual skills (29) may be subserved by similar mechanisms of plasticity. Although the data are limited by the small number of studies and the different time windows examined in each of these studies, the results lend support to the idea that although the nature of the practice-dependent cortical representational changes are determined by the specifics of the training experience, the time course of skill learning may be determined by the time constants of basic mechanisms of neuronal plasticity irrespective of the locus of plasticity.

"Slow" Learning and the Long-Term Reorganization of M1

The learning of many motor skills involves the formation of novel sequences of muscle activity and the reconstruction of existing muscle control architectures (3, 41, 42). A hallmark of such learning is improved speed of motor execution without reciprocal deterioration in accuracy (43), which indicates the acquisition of a new capability of the motor system rather than functional adaptation within the limits of a pre-existing motor gain control mechanism (44). In recent years, the learning of sequential finger movements—related to skills such as writing, typing, or playing musical instruments—has become an important paradigm for the study of the acquisition of motor skills by using imaging techniques (45–52). These studies however, have been confined to relatively short time intervals and were not designed to look at the effects of long-term training. Also, many of these studies were concerned not only with the issue of how the performance of a known sequence of movements becomes fast and accurate through practice (42–44), but also with the issue of how declarative knowledge of a given sequence, embedded in the task unknown to the subject, is acquired through motor performance (45, 46, 49).

To investigate the effects of long-term training on the performance of a given sequence of movements, we recently have used a simple sequential finger opposition task in which the effects of training in young, healthy adults could be tracked over several weeks by using both behavioral measurements and functional brain imaging (6). In this task, subjects were instructed to oppose the fingers of the nondominant hand to the thumb in one of two given sequences (Fig. 1*A*). The sequences were composed of five component movements and their mirror-reversed (tapped back to front) counterparts. Subjects were required to tap each sequence, with no visual feedback, as accurately and rapidly as possible. Speed and accuracy were independently scored. The results for speed are reproduced in Fig. 1 *B–D*. Although initial performance of the two sequences, in terms of speed and accuracy, did not differ (Fig. 1 *B* and *C*), 10–20 min of daily practice during which subjects were instructed to repeatedly tap a given sequence (the other sequence served as the unpracticed control) in a rapid self-paced and accurate manner induced large gains in performance. The speed at which the trained sequence could be performed increased across consecutive sessions, nearing asymptote after about 3 weeks of training, with more than doubling of the initial rate (Fig. 1*B*) and a concurrent gain in accuracy (6). This improvement was specific to the trained hand, with no significant transfer to the untrained hand (Fig. 1*D*). Moreover, the effects of training did not generalize to the performance of the control sequence (Fig. 1*C*). These behavioral results suggested that a specific, highly effective representation of the trained sequence of movements (rather than a representation of the individual component opposition movements) had developed as a function of training.

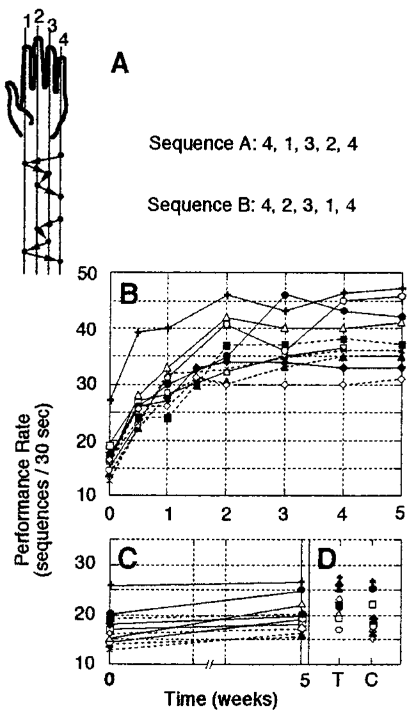

FIG. 1. The effects of long-term practice on sequence performance. (*A*) The two sequences of finger-to-thumb opposition movements used in our study (6). In sequence A the order of finger movements was 4,1,3,2,4 (numbering the fingers from index to little), and in sequence B the order was 4,2,3,1,4 as indicated by the arrows (matched, mirror-reversed sequences). Practice consisted of tapping the designated training sequence as fast and accurately as possible for 10–20 min a day, a few minutes at a time separated by half-minute rests. (*B*) Learning curves, trained sequence. Each curve (symbol) depicts the performance of a single subject as a function of time. Pre-training (time point 0), day 3 and 10 of training, and performance on the day of the subsequent weekly imaging sessions is shown for 10 subjects. The number of complete sequences performed in a 30-sec test interval (rate) increased from 17.4 ± 3.9 to 38.4 ± 5.8 (mean, SD; week 0 and 5 weeks of training, respectively; paired *t* test, $P < 0.001$). Accuracy improved, too, with the number of sequences that contained errors decreasing from a mean of 2.4 ± 0.9 to 0.5 ± 0.5 (paired *t* test, $P < 0.001$). (*C*) No significant improvement for the control sequence (performance rate 18.1 ± 3.7 to 19.4 ± 4.2; 0 and 5 weeks of training, respectively; paired *t* test, not significant). (*D*) There was little or no transfer of the learning effect to the contralateral (dominant) hand. Trained (T) vs. control (C) sequence performance rates, at week 5, were 22.3 ± 2.9 and 19.8 ± 4.0, respectively (paired *t* test, $P = 0.097$).

We conjectured that a strongly lateralized representation of finger movements—one in which a discrete population of neurons would encode the movements of one hand exclusively—would be a likely locus for this learning-related plasticity. To test this possibility, a long-term functional brain imaging study of M1 was undertaken (6). We focused on M1 because it contains a well-lateralized representation of finger movements; the cerebellum, which also contains lateralized representations of the hand, has been found to be less active with practice on a given sequence, even within the time frame of a single session (47, 48, 50, 52). Moreover, M1 has been indicated by studies in adult monkeys as a locus of manual skill learning (7, 53), and it is thought to be important in the initiation of voluntary motor actions, especially those associated with fine manipulative abilities (54). Finally, we considered a possible analogy to the results of several basic perceptual tasks in which primary cortical representations were shown to reorganize as a function of training and learning (2).

In the imaging study, six young adults were scanned once a week for 4–6 consecutive weeks—before, and then in parallel to training with one of the above finger opposition sequences, the other serving as the untrained control (6). The motor activity-evoked signal changes were measured by using a 4-T MRI system with a gradient echo, echo planar imaging sequence sensitive to local blood-oxygenation-level-dependent contrast. Each session consisted of 6–10 experimental sets with each set made of two performance intervals of 20-sec duration each (X1 and X2, respectively) separated by 40 sec of rest. In a set, either one sequence of movements was repeated in both performance intervals (X1 and X2) or a different sequence was performed in each activation interval assigned in a random but balanced manner. During all scanning sessions, both the trained and the control sequence were performed at a fixed, comfortable rate of 2 Hz, paced by the magnetic field gradient switch noise. Thus both rate and component movements were matched, and the only difference between sequences during scanning was the difference in practice histories. Data analysis consisted of determining those pixels in which signal intensity changed during each performance interval of a set, relative to the level at rest, and then comparing the two statistical maps generated from each set.

In the first scanning session, performed before any training was given, a comparable extent of the contralateral M1 was activated by the execution of both sequences. However, by session 4, which corresponded to 3 weeks of daily practice on the designated training sequence, and in all subsequent sessions, the extent of activation evoked by the trained sequence in M1 was significantly larger compared with the extent of activation evoked by the performance of the control, untrained sequence (Fig. 2 *a* and *b*). The area of evoked response in M1 for the trained sequence was larger in extent irrespective of the order in which the sequences were performed in the set. As in the initial, naive state, the activation in M1 appeared somewhat patchy (but to a lesser degree) and it did not extend beyond the hand representation itself, as indicated by control experiments,

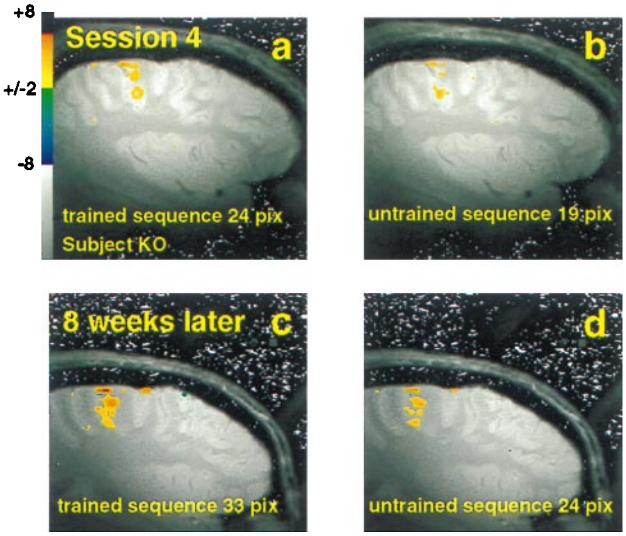

FIG. 2. Differential evoked responses in M1 to the trained vs. the untrained (control) sequence. Training and performance during scanning done with the left (nondominant) hand. (*a* and *b*) Emergence of differential activation after 3 weeks of daily practice on the designated training sequence. (*c* and *d*) Maintained differential activation 8 weeks later with no additional training in the interval. Sagital sections through the right hemisphere centered ≈35 mm from midline are shown: right, anterior; top, dorsal aspect of the brain. The activity-dependent blood-oxygenation-level-dependent signals evoked by the trained sequence are shown in *a* and *c*. Those evoked by the untrained sequence are shown in *b* and *d*. Z-score values are indicated by the pseudo-color scale. A surface coil was used, which had the advantage of providing enhanced signal-to-noise ratios, but at the cost of limiting the data to M1 and surrounding areas contralateral to the performing hand. Imaging parameters are given in ref. 6. The comparison is always to the control sequence, performed within the same set. No direct comparison is possible because of different shims and a somewhat different placing of the subject in the magnet and of the surface coil on the subject's head. The area of evoked signal in M1 was consistently larger in extent for the trained as compared with the untrained sequence by 3 weeks of training and remained so 8 weeks later.

in which single-digit and wrist extension-flexion movements, as well as eye (orbicularis oculi) closure were mapped. These results suggest that as the skill was acquired no significant expansion of the total hand representation area occurred. Indeed, the differential activation was accounted for by a subpopulation of pixels, in the hand area, that showed a significant response to the trained sequence, but little or no response to the performance of the untrained sequence (6). The more extensive blood-oxygenation-level-dependent signal evoked in M1 by the trained compared with the untrained sequence, persisted weeks after training was discontinued (Fig. 2 *c* and *d*). There was also no significant decrease in performance and, in fact, 1 year after training was stopped there was still significant retention of the skill.

These imaging data suggest that long-term practice results in a gradually evolving, specific, and more extensive representation of the trained sequence of movements in M1. The results are compatible with the idea that motor practice induces the recruitment of additional M1 units into a local network specifically representing the trained motor sequence (6). This interpretation is in agreement with the recent finding, in monkeys, of practice-dependent changes in the functional topography of M1 (7). Nudo *et al.* (7) found that after a few weeks of training on a task, which developed skilled manipulation, the evoked-movement digit representation, as well as the representation of task-related movement combinations in M1 gradually were expanded. A second important insight gained from our human imaging data is the indication that M1 may code not just single movements, but rather complex movement sequences, including those acquired in adulthood. This indication, too, is supported by the finding in monkeys that following long-term practice, co-contracting muscles used in the task come to be represented together in motor cortex, with those movement combinations that were used more frequently in training, more extensively corepresented (7).

An almost universal finding in animal studies of training-dependent cortical changes is the expansion, through recruitment of additional units, of the specific representation of the input or output that the monkey experiences (3, 30, 53) and, to a much larger degree, of the representation of inputs that are crucial to the performance of a behaviorally meaningful trained task (2, 7, 27–29). The finding of an enlargement of a sensory-motor representation of a body part in the setting of skill acquisition poses the question of how extensive such an enlargement can be. It suggests that the learning of a sequence of movements can in some instances interfere with or limit the learning of other sequences, or even result in an expansion of the representation of a body part, even at the cost of the representation of other, less used parts. Interference with a newly acquired skill may be possible, but only within a very limited time window (20, 39). The specificity of skill learning implies that different subpopulations of neurons within a representational domain participate in the representation of different task conditions, which in turn suggests a potential for many parallel skills within a given representation (38). Nevertheless, Pascual-Leone *et al.* (55) have found that in Braille readers, the sensory-motor cortical representation of the index finger used in reading was significantly larger, compared both to that of the nondominant index finger in those subjects and to that of the dominant index finger of non-Braille reading control subjects. Similarly, a recent study using magnetic source imaging revealed that the cortical representation of the left hand digits of string players, in primary somatosensory cortex was larger than that in nonmusician controls (56). Our results, on the other hand, as well as Nudo *et al.*'s monkey data (7) suggest that, rather than an enlargement of a specific effector organ's representation, training can result in a more extensive representation of a trained sequence of movements, i.e., a specific representation of skilled function rather than body parts. This finding is of importance because the human imaging data support the notion of M1 as a locus of the long-term acquired representation of specific motor skills.

A variety of motor tasks can be conceptualized as consisting of a serial sequence of simple movement components; the skilled generation of a sequence of movements then would be reduced to the problem of choosing the correct components in the proper order, determining the time at which each component movement is initiated and ensuring smooth continuity from one component to the next. Such a scheme, however, may not hold true in all cases of sequence performance (4, 41, 42). For example, in piano playing, a particular key press is subject to modification by succeeding elements of the given, well-rehearsed musical phrase (coarticulation) (57). Such anticipatory kinematic changes may explain why identical component movements are differentially represented in M1 when arranged in a trained sequence vs. an untrained sequence. Furthermore, there is evidence from monkeys showing that fingers do not move independently of each other and that each instructed movement is generated by combined activation of several muscles, many acting on more than one digit (54). Additionally, there is a large body of evidence demonstrating the complex overlapping representations of movements in maps of M1 (54). This evidence, together with the data of Nudo *et al.* (7) suggesting the training-dependent evolution of corepresentations of temporally correlated joint movements by single M1 units, provides a possible neural basis by which different sequences of individual digit movements can be represented by different patterns of activity in M1. Thus, the implementation of a sequence in M1 may be related to the representation of transitional movements (switching from one digit to the other) and temporally correlated movements (7), which would be dependent on the particular temporal ordering of the component movements in the sequence (41, 58). This order-specific aspect of the representation may be enhanced, extended, and consolidated by practice.

Fast Learning

Although the evolution of a sequence-specific, differential pattern of activation in M1 required extended practice over several weeks to be completed, some important changes occurred in the activity of M1 as early as the first imaging session (6). These changes related to the effects of the interval (first, X1, or second, X2) in which a given sequence was performed within a 2-min set, rather than to the sequence itself. We termed these interval-dependent signal modulations the "ordering effects." The difference in the extent of cortex activated in the two performance intervals of different sets is depicted in Fig. 3*A*. In the early sets of session 1, before any training was given, a consistent ordering effect was found: the performance of either sequence, irrespective of the sequence type, resulted in a larger area of evoked response when executed first (during interval X1) rather than second (during interval X2) in the set. We interpreted this finding as a habituation-like response across the 40-sec rest interval interposed between X1 and X2 (6). By the latter part of the first session, however, by which time each subject had typically performed six 2-min experimental sets over the course of approximately 30 min, this ordering effect was reversed. A larger extent of M1 was activated by a given sequence when executed second rather than first in the set. The interaction between activation period (X1 vs. X2) and sets (early vs. late), was significant [blocked two-factorial ANOVA, $F(1,27) = 4.946$, $P = 0.035$)] (Fig. 3*A*).

Is the switch in ordering effects a specific effect? That is, is it specific to the sequences that were repeatedly performed during the imaging session? To test this possibility, three subjects were given a new, third sequence, again composed of the same component movements (sequence C: 4, 3, 1, 2, 4; digit numbers as in Fig. 1*A*). This new sequence was introduced after the switch in ordering effects had occurred, that is when an enhanced response to the second sequence of the set was established for both sequences A and B. In all three subjects, the initial habituation-like pattern of the evoked fMRI responses to repetition returned on performing the new sequence, with a larger extent of activation during the first interval compared with the second interval of the set (Fig. 3*A*). Thus, the switch in ordering effect reflected the accumulating motor experience gained when subjects repeatedly performed the two sequences during the acquisition of the imaging data, indicating that the switch may represent a learning effect triggered by repetition of a motor sequence at a paced fixed rate.

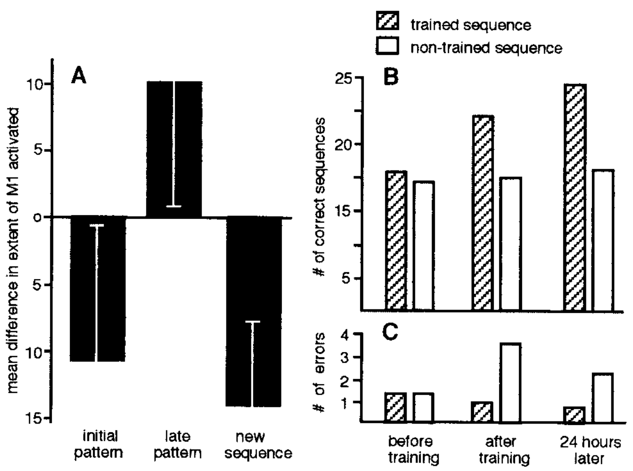

FIG. 3. Cortical and behavioral effects of short-term practice. (*A*) Cortical effects. The ordering effects during the initial imaging session: The mean difference in the extent of the evoked signal calculated as the difference in the number of pixels in M1 in which the signal changed above a threshold of $Z = 2$ during the respective activation intervals relative to rest, for each set (X2-X1, see text) during the two activation intervals of the initial and late sets of the session as well as when a new sequence was introduced is shown. Initial pattern: Averaged data from five subjects from the first two sets of each subject showing the initial ordering effect irrespective of sequence type, lesser extent of M1 activated during the second compared with the first interval. Late pattern: Averaged data from the two late sets in the session (sets 6 and 7) of five subjects showing the reversed ordering effect, irrespective of sequence type, larger extent of M1 activated during the second compared with the first interval. New sequence: Averaged data from three subjects (one set each) performing a new sequence, ordering effect reverted to the naive, initial pattern with smaller extent of M1 activated during the second compared with the first interval. (Bars = SD.) (*B* and *C*) Behavioral effects. Speed (*B*) and accuracy (*C*) of performance recorded during a test interval of 30 sec for two sequences (one randomly assigned to be trained or other the untrained control) before training (before), after a few minutes of externally paced performance of the designated trained sequence (after), and 24 hr later, with no additional training in the interval. Data from 12 subjects. An ANOVA showed that the effects of training, time and the interaction time*training were significant [$F(2,55) = 33.06$ $P < 0.001$, $F(1,55) = 26.83$ $P < 0.001$, $F(2,55) = 3.57$ $P < 0.03$, respectively, for speed; $F(2,55) = 29.58$ $P < 0.001$, $F(1,55) = 47.73$ $P < 0.001$, $F(2,55) = 6.34$ $P = 0.003$, respectively, for errors].

Consolidation of Motor Experience

If the switch in ordering effect reflects learning, then one would expect a concurrent improvement in performance. We previously have reported that performing the two sequences during the initial imaging session resulted in a significant improvement in both speed and accuracy (6). Moreover, the pattern of enhanced response to repetition (a larger extent of M1 activated in the second compared with the first performance interval) was maintained during the second and third imaging sessions even for the untrained sequence, which was performed only during the weekly scanning sessions. This finding suggests a rather long-lasting effect in M1: the change in processing mode effected during the first scanning session was retained for at least 1 week. Taken together, these findings indicate that the accumulating motor experience gained through the paced tapping of a given sequence during the imaging session was, in itself, sufficient to trigger long-term effects in M1's representation of the sequence. The purpose of the following experiments was to investigate whether a limited amount of paced motor experience was sufficient to trigger delayed gains in the speed and accuracy of performance of a given sequence of movements. We were specifically interested in exploring the possibility that some performance gains become effective after practice has ended similar to the delayed gains described for perceptual skill learning (6, 25, 32–34).

Twelve young adults (23–42 years old; seven females, five males; all but one right-hand dominant) took part in these experiments. Subjects were instructed to accurately tap, by using their nondominant hand and with no visual feedback, the two five-element sequences of finger-to-thumb opposition movements depicted in Fig. 1*A*, as in our original study (6). Motor performance was recorded, during both testing and training, with a video camera at a frame length of 40 ms. Performance was tested before, immediately after, and then 24 hr after a single training session. During testing, as in our earlier study (6), subjects were required to tap each sequence as accurately and rapidly as possible over a test interval of 30 sec. Both speed (the number of sequences performed within the test interval) and accuracy (the number of times an out-of-sequence finger opposition movement was executed within the test interval) were scored independently, from the video recordings. In the training session, one of the sequences, randomly chosen, was tapped at a rate of 2 Hz, paced by a metronome, in six short training intervals of 40 sec each, separated by 2–3 min of rest.

Motor performance for the two sequences, before, immediately after, and on the day after training is shown in Fig. 3 *B* and *C*. Initial performance of the two sequences, in terms of speed and accuracy, did not differ. Training, however, induced a significant gain in both speed and accuracy for the trained sequence. Moreover, on the next day, with no additional training, a significant gain in both speed and accuracy, compared with the immediate post-training performance level, was found for the trained sequence only (Fig. 3 *B* and *C*).

Our results show that not all learning in a sequential finger opposition task is concurrent with practice. A limited amount of paced opposition movements was sufficient practice not only to improve performance during the session but also to initiate significant additional gains that affect performance by the next day; apparently, some gains require time to become effective and continue to develop after motor practice has ended. The concurrent gain in speed and accuracy, is characteristic of the acquisition of a new skill (44).

Delayed neuronal plasticity, which evolves hours after the inducing experience, has been demonstrated in several studies of the developing visual cortex in kittens (36, 37). These studies showed that the changes in neuronal properties induced by brief visual experience became effective, that is, consolidated, only after time, several hours to several days, was allowed to elapse. The notion of consolidation in these studies is consistent with the distinction between the "induction" and the "expression" and maintenance of plasticity suggested by studies of synaptic plasticity at the cellular and biochemical level (10, 11). It is also consistent with the kinetics of memory consolidation, in terms of its resistance to disruption, in animal and cellular models of learning (39). Karni and Sagi (8) have described similar delayed gains in the performance of adults emerging a minimum of 6–8 hr after training in a simple visual detection task. The term consolidation was suggested for the process, presumably initiated during the practice session, which underlies the improvement of performance hours after the training experience was terminated, and results in an enduring memory of the skill. Recently, while training subjects on moving a manipulandum against a force-field, Brashers-Krug *et al.* (20, 39) found evidence for an ongoing process of consolidation after training for one task condition was terminated. The introduction of a second task condition within a time window of several hours after the initial training disrupted long-term (overnight) improvement on the first task. Moreover, their data show that training not only results in within session (fast) gains, but also, provided enough time was allowed for the consolidation phase, in additional gains that are only apparent by the next day. Similar delayed gains in performance after a latent consolidation phase also have been described for a rotor pursuit task (J. Travis quoted in ref. 40). Altogether, these results indicate that human motor memory continues to evolve after the training session, and with the passage of time is transformed into a long-term trace. Furthermore, the data establish an important parallel between the time course of motor skill learning and perceptual learning and suggest the idea that the time course of skill learning may reflect the time constants of basic neuronal mechanisms of memory storage that are shared by different cortical representations in the adult brain.

Functional Stages in Skill Learning

Although the fractionation of skill learning into only two discrete phases is most likely an oversimplification (11), it provides an important conceptual framework for describing and accounting for the human skill learning data (6, 8, 22, 39). Our imaging data suggest that the acquisition of skilled motor performance occurs in two distinct phases in M1. First, a within-first-session switch in the representation of the repeatedly performed sequences of movements from a habituation-like decrease to an increase in the extent of motor cortex activated by a given sequence of repeated movements; and second, after about 3 weeks of training, the emergence of an enlarged, differential representation of the trained as compared with the untrained sequence of movements. Both stages of sequence learning are experience specific. The switch in ordering effects, or fast learning, occurs only for those sequences that have been repeated a critical number of times in the session, and it is correlated with a specific, significant gain in performance occurring within the session. The emerging, more extensive representation of the trained sequence of movements in M1 was a correlate of highly specific gains in performance that were incrementally acquired over a few weeks of daily practice (slow learning).

The switch in M1 processing mode may constitute an important step in initiating subsequent experience-dependent changes in M1. The imaging data show that the switched ordering effect that occurred in M1 late in the first imaging session was maintained, for the designated control sequence, for at least 1 week during which the sequence was not performed. This is not to say that the switch in M1 processing mode, and much of the behavioral effects that constitute fast learning, are products of major changes principally occurring in M1 within the time frame of a single session. The switch in ordering effects may reflect neural changes occurring in other parts of the distributed motor system (45, 47–52, 59–60). Psychophysical data from perceptual (8) and motor (39) learning tasks suggest that fast learning is mediated, at least in part, by brain regions distinct from those that subserve slow learning. It has been argued, based on electrophysiological data from monkeys, that brain regions active during the acquisition of a motor skill do not necessarily correspond to the regions that eventually will store the memory (4, 61). In humans, there is evidence from functional brain imaging studies that distinct brain areas are differentially activated during initial, naive performance compared with subsequent performance as learning proceeds both within a session [see for example Buckner (66) and Petersen (67) in this issue of the *Proceedings*] and across consecutive sessions (60, 62).

One should note, that in our study (6), the extent of activation in M1 for either sequence did not increase significantly during the initial scanning session. The learning related changes in M1 that occurred during the first session were related to the ordering effects within a time window of 40 sec. A number of positron emission tomography (PET) studies have examined changes in brain activations occurring within a single session as a consequence of practice in motor and sensory-motor tasks (45, 47–52). Although some studies have suggested that, as learning proceeded within the session, blood flow in M1 increased (47, 49), no significant changes in blood flow have been found in M1 when the rate of movements in the trained and untrained conditions were kept the same (50, 52). A recent PET study in which movement rate was controlled (45), as well as a transcranial magnetic stimulation study (46), found increased activity in M1 as learning progressed but only when subjects had no previous implicit knowledge of the sequence of finger movements. When explicit knowledge of the sequence was allowed to develop no significant learning-related M1 changes were found. However, in contrast to the M1 findings, several PET studies have found a consistent decrease in the activation of the cerebellum and prefrontal cortex (with conflicting observations concerning premotor cortex) as a function of practice within a session (45, 47–52, 60).

As the decrease in activation in areas projecting to M1 occurred over a similar time window as the switch in ordering effects that we observed in M1 within the first session, we proposed that this switch reflects changes in modulatory inputs to M1. This initial phase in the acquisition of the skill may be conceptualized as the setting up of a sequence-specific routine (6). Our working hypothesis is that, initially, the evoked response in M1 relates to the component movements of the sequences, which being identical, exert a smaller, i.e., habituated, response on repetition across a time window of 40 sec. By the end of the session, however, after the two sequences each have been repeated a few tens of times, the switch in ordering effect reflects the fact that a given sequence of movements constitutes a special entity of behavioral significance: it is consistently performed as a sequence rather than as unordered component movements. An experience-dependent change from representation of component movements in an explicit sequence to a representation, rather "automatic" (45, 48, 60), in M1 of the sequence as a unitary motor plan can be related to the decrease of activation in the cerebellum and prefrontal cortex through a decreasing need for movement by movement internal monitoring.

Although important changes occur on a short time scale, our results clearly demonstrate that skilled performance of the trained sequence is not the product of a single training session. Both the imaging and the behavioral data show that the initial changes in ordering effects and the gains in performance acquired during the first session were retained after the session and then consolidated; however, it took about 3 weeks of practice on a daily basis for performance to approach asymptote. The correlate of this acquired proficiency was an enlarged representation of the trained, relative to the untrained, sequence in M1. The emergence of this differential in the evoked fMRI signal corresponded in time to the attainment of maximal near asymptotic performance on the trained sequence. This, however, may be a result of a limitation in the sensitivity of our measurement, and it remains to be seen whether a differential representation of the trained sequence begins to evolve even earlier than the attainment of asymptotic performance. Nevertheless, our results have provided what we believe is direct evidence that long-term motor training can result in significant experience-dependent reorganization in the adult human motor cortex. These data provide an important link with a growing body of data in the nonhuman mammalian brain of representational changes associated with the acquisition of skills.

Two main mechanisms have been proposed for the changes induced in motor and sensory representational maps as a function of experience: (*i*) the transcription dependent improvement and growth of new connections and synapses (e.g., 34, 63); and (*ii*) the unmasking, or disinhibition, of previously existing lateral connections between neurons within a representational domain through internal or external modulating inputs (3, 30, 64). The latter mechanism can induce changes on a short time scale and may subserve fast learning; the former has been invoked to explain the delayed, time-dependent nature of developmental cortical plasticity and cortical reorganization compensating for injury and subserving learning. These mechanisms are not mutually exclusive, however, and one may conjecture that the pre-existing lateral connections between local populations of neurons, whose outputs result in different sets of movements, provide a basic network that short-term experience may unmask and subsequent practice may selectively improve (63, 65). Thus, our results support the idea that adult skill motor learning is contingent on the functional architecture of the motor system but, at the same time, modifies it.

Conclusions

The human imaging data together with the behavioral measurements of the effects of training over time lead to three important insights into the neurobiological substrates of skill learning in the adult brain. First, practice can set in motion neural processes that continue to evolve many hours after practice has ended. Thus, even a limited training experience can induce behaviorally significant changes in brain activity, and initiate important long-term effects that may provide the basis for the consolidation of the experience. Second, although many brain areas may be important in the initial stages of acquiring a new skill, an important substrate of skill proficiency can be an enlarged, better representation within the earliest level of processing in which a differential representation of those experience parameters that are critical for the performance of the task is available. This may be a basis for the specificity of procedural knowledge for basic parameters of the training experience. It is very likely the case that different parts of the distributed motor system, including subcortical structures, take part and subsequently represent acquired skills. Nevertheless, the data are consistent with the proposal that local changes in discrete representations subserve the long-term memory of skills. Third, motor skill learning requires time and has two distinct phases, analogous to those subserving perceptual skill learning. An initial, fast improvement phase ("fast learning") is followed by a slowly evolving, post-training incremental performance gains ("slow learning"). The hypothesis is that fast learning involves processes that select and establish an optimal routine or plan for the performance of the given task. Slow learning, on the other hand, may reflect the ongoing long-term, perhaps structural, modifications of basic motor modules; it may be implemented through time-dependent strengthening of links between motor neurons as a function of correlated activity, and their recruitment into a specific representation of the trained sequence of movements.

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Time Course of Functional and Biomechanical Improvements During a Gait Training Intervention in Persons With Chronic Stroke

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Background and Purpose: In rehabilitation, examining how variables change over time can help define the minimal number of training sessions required to produce a desired change. The purpose of this study was to identify the time course of changes in gait biomechanics and walking function in persons with chronic stroke.

Methods: Thirteen persons who were more than 6 months post-stroke participated in 12 weeks of fast treadmill training combined with plantar- and dorsiflexor muscle functional electrical stimulation (FastFES). All participants completed testing before the start of intervention, after 4, 8, and 12 weeks of FastFES locomotor training.

Results: Peak limb paretic propulsion, paretic limb propulsive integral, peak paretic limb knee flexion ($P < 0.05$ for all), and peak paretic trailing limb angle ($P < 0.01$) improved from pretraining to 4 weeks but not between 4 and 12 weeks. Self-selected walking speed and 6-minute walk test distance improved from pretraining to 4 weeks and from 4 to 12 weeks ($P < 0.01$ and $P < 0.05$, respectively for both). Timed Up & Go test time did not improve between pretraining and 4 weeks, but improved by 12 weeks ($P = 0.24$ and $P < 0.01$, respectively).

Discussion and Conclusions: The results demonstrate that walking function improves with a different time course compared with gait biomechanics in response to a locomotor training intervention in persons with chronic stroke. Thirty-six training sessions were necessary to achieve an increase in walking speed that exceeded the minimally clinically important difference. These findings should be considered when designing locomotor training interventions after stroke.

Video Abstract available (see Video, Supplemental Digital Content 1, http://links.lww.com/JNPT/A63) for more insights from the authors.

Key words: *gait, locomotor training, stroke*

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INTRODUCTION

According to the World Health Organization, 15 million people worldwide experience a stroke each year. One of the primary concerns for persons who experience stroke is the ability to regain walking function.[1] Consequently, significant effort is focused on gait retraining during rehabilitation after a stroke, and efforts to develop and improve locomotor retraining programs are a major focus of rehabilitation research.[2-5] The primary focus of much of this research has been on the development of novel interventions, using treadmills, body-weight support and robotics.[4-6] However, less attention has been paid to the time course of changes in the variety of deficits that are targeted with these interventions.

On the basis of the specific needs of the individual, gait training interventions after stroke may target a variety of deficits including walking biomechanics and energetics, walking endurance and/or speed, walking activity, or some combination of these and others.[7] Several studies have examined the time course of improvements in walking speed with the intervention after stroke[5,8]; however, there are no studies that have simultaneously examined the time course of changes in walking speed, endurance, and gait biomechanics. Improvements in gait biomechanics after stroke are thought to be important because of their connection to walking function and safety.[9-14] Poststroke intervention studies have associated improvements in specific gait biomechanics with improvements in walking speed after stroke,[11,15] and thus, many poststroke gait interventions focus on improving biomechanics *and* walking function.[16-19] There are likely different mechanisms underlying the change in each of these deficits; therefore, it is anticipated that changes in various deficits will occur on different timescales. For example, changes in the neural activation of muscle can occur on a short timescale (eg, several sessions),[20] suggesting that changes in gait biomechanics might change with a more rapid time course than walking speed or endurance. To the extent that there is a relationship between improvements in gait biomechanics and improvements in walking function and that these may change on different timescales, it is relevant to examine the time course of changes in both biomechanics and walking function with poststroke intervention.

By examining how gait-related variables change over the course of training, we may be able to determine the minimal number of training sessions required to produce a given change. As an example, in a 6-month treadmill training study focused on improving cardiovascular fitness in persons with chronic stroke, improvements in peak and average VO_2 were observed after 3 months of training, but no further improvements were found between 3 and 6 months of training.[21] Without the 3-month measurement point, the authors may have erroneously concluded that 6 months of their training intervention was required to see the gains observed.

For these reasons, in the process of developing a novel locomotor training intervention for persons poststroke, we designed a study that allowed us to examine the time course of changes in a variety of walking parameters. The purpose of this study was to identify the time course of changes in gait biomechanics and walking function in persons with chronic stroke. As indicated previously, because changes in the neural activation of muscle and motor learning can occur on a relatively short timescale (eg, several sessions),[20,22] we hypothesized that gait kinematics and kinetics would change with a more rapid time course than measures of walking function with this intervention, but that all variables would show improvement after 12 weeks of training.

METHODS

Participants

Thirteen subjects (age, 61 ± 8.3 years; 7 males) with poststroke hemiparesis participated in this study (Table 1). Participants were recruited from local physical therapy clinics, stroke support groups, and newspaper advertisements. All participants were more than 6 months after a single stroke, able to walk continuously for 5 minutes at their self-selected speed without the assistance of another person, and had enough passive range of motion so that their paretic ankle joint could reach within 5 degrees of the neutral position with the knee flexed (ie, participants could have no more than a 5-degree plantarflexion contracture). Exclusion criteria included congestive heart failure, peripheral artery disease with claudication, diabetes not under control via medication or diet, shortness of breath without exertion, unstable angina, resting heart rate outside the range of 40 to 100 beats per minute, resting blood pressure outside the range of 90/60 to 170/90 mm Hg, inability to communicate with the investigators, pain in lower limbs or spine, total knee replacement, cerebellar involvement, and neglect (star cancellation test[23]). All participants provided written informed consent to participate in a study that had been approved by the Human Subjects Review Board of the University of Delaware.

Testing

All participants completed testing before the start of intervention, and after 4, 8, and 12 weeks of fast treadmill training combined with plantar- and dorsiflexor muscle functional electrical stimulation (FastFES) locomotor training. All assessors were blinded to previous assessment data at each testing session. The clinical evaluation and training was completed by the same tester (MR), whereas gait analysis testing was completed by another tester (TK).

Clinical Evaluations

Participants completed clinical tests to evaluate their walking. These included (1) the 10-m walk test to measure short-distance self-selected (comfortable) and fastest walking speeds[24]; (2) the 6-minute walk test as a measure of walking endurance[25]; and (3) the Timed Up & Go (TUG) test as a measure of functional mobility that requires participants to stand up from a chair with armrests, walk 3 m at their comfortable speed, turn around, return to the chair, and sit down.[26] The clinical evaluation and training were completed by the same tester (MR).

Gait Analysis

Participants walked at their self-selected overground speed on a split-belt treadmill to measure specific gait impairments. The treadmill was instrumented with 2 independent 6 degree of freedom force platforms (AMTI, Watertown, MA) from which ground reaction force (GRF) data were collected at 2000 Hz. Retroreflective markers (14-mm diameter) were placed bilaterally over the pelvis, thigh, shank, and foot segments and on the medial and lateral malleoli, at the medial and lateral knee joint lines, greater trochanters, and iliac crests. Kinematic data were collected using an 8-camera Vicon Motion Capture System (Vicon MX, Los Angeles, CA) at 100 Hz. Two 20-second trials were collected. For safety, participants held on to a handrail during walking and wore a harness that was attached to an overhead support. No body weight was supported by the harness.

Training

Subjects participated in FastFES training administered by a physical therapist 3 times a week for a total of 12 weeks. Training speed was initially determined as the fastest speed the subject could maintain for 4 minutes of continuous walking. This speed was re-evaluated every 4 weeks and increased as possible at each 4-week interval using the same criterion. Each training session consisted of both treadmill and overground walking. First, participants completed 4 treadmill walking bouts of 6 minutes each for a total of 24 minutes of treadmill walking. During each of the 4 bouts, FES to the paretic ankle dorsi- and plantarflexor muscles was delivered during the first, third, and fifth minutes. During the second, fourth, and sixth minutes, FES was turned off and participants were encouraged to walk with the same pattern as during FES. This alternating pattern of FES delivery was designed to maximize potential motor learning[27] and to minimize muscle fatigue. Seated rest breaks (~5 minutes) were provided between consecutive walking bouts. The 4 bouts were followed by a final bout comprising 3 minutes of walking with FES on the treadmill, followed

Table 1. Subject Characteristics at the Pretraining Evaluation

Subject	Sex	Age, yr	Side of Hemiparesis (Center or Right)	Time Since Stroke, mo	Assistive Device Used (Community)	Orthotic Used (Community)	Self- Selected Gait Speed, m/s	Fugl-Meyer (LE) Score
1	Male	67	Left	22		AFO	0.70	21
2	Male	51	Left	111			0.90	24
9	Male	58	Right	110			0.50	15
53	Male	71	Right	70	SC	AFO	0.50	14
98	Male	66	Right	19	SC		0.30	21
108	Male	70	Left	21	SC		0.50	13
110	Female	65	Right	15	NBQC		0.70	18
120	Female	52	Left	33			0.80	19
128	Female	65	Right	18			0.50	18
129	Female	54	Right	55			0.50	17
136	Female	58	Right	12	SC	AFO	0.30	13
137	Male	46	Right	8		AFO	0.40	15
142	Female	70	Left	9	SC		0.30	22

Abbreviations: AFO, ankle foot orthosis; LE, lower extremity; NBQC, narrow-based quad cane; SC, straight cane.

immediately by 3 minutes of overground walking in the hallway at their fastest possible speed without FES. During overground walking, participants were encouraged to reproduce the same walking pattern as practiced with the FES on the treadmill.

Electrical Stimulation

Self-adhesive surface electrical stimulation electrodes were attached over the ankle dorsiflexor (2”×2” [5.08 cm × 5.08 cm], TENS Products, Grand Lake, CO) and plantarflexor (2”×5” [5.08 cm × 12.7 cm], ConMed Corp, NY) muscles. For the dorsiflexor muscles, one electrode was placed over the motor point of the tibialis anterior and the other over the distal portion of the tibialis anterior muscle belly. For the plantarflexors, the electrodes were oriented horizontally and placed on the dorsal aspect of the leg over the proximal and distal portions of the gastrocnemius muscle.[28] A Grass S8800 stimulator in combination with a Grass Model SIU8TB stimulus isolation unit was used to deliver electrical stimulation (Grass Instrument Division, Quincy, MA).

For both the dorsi- and plantarflexor muscles, the stimulation amplitude was set using a stimulation train that was 300-ms long at a frequency of 30 Hz and with a pulse duration of 300 μs. For the ankle dorsiflexor muscles, stimulation amplitude was set with the subject seated and the foot hanging freely in a plantarflexed position. The stimulation train amplitude was gradually increased until the foot reached a neutral ankle joint position (0 degree) or the subject’s maximum dorsiflexion range of motion was achieved. The mediolateral placement of the electrodes was adjusted to minimize ankle eversion/inversion. For the ankle plantarflexor muscles, the stimulation amplitude was set while the subject stood so that the nonparetic foot was a step length ahead of the paretic foot with weight on both the paretic and nonparetic extremities. The amplitude was increased until either the stimulation train produced a plantarflexor force sufficient to lift the paretic heel off the ground or until the subject’s maximal tolerance was reached, whichever occurred first.

Two compression closing foot switches (25-mm diameter MA-153, Motion Lab Systems Inc., Baton Rouge, LA) were attached to the outside sole of the shoe of the paretic limb. One foot switch was placed under the fifth metatarsal head (forefoot switch) and the other under the lateral portion of the heel (hindfoot switch). The foot switches were used to control the timing of the FES during the gait cycle.

Timing of FES During Training

A customized FES system consisting of a real-time controller (cRIO-9004, National Instruments, TX), an analog input module (NI 9210), and a digital input/output module (NI 9401) were used to control the grass stimulator and deliver stimulation during the gait cycle.[28,29] The FES system delivered stimulation to the ankle dorsiflexor muscles from the time the paretic foot was off the ground (neither foot switch in contact with ground) to paretic initial contact (either foot switch in contact with ground). The ankle plantarflexor muscles of the paretic limb were stimulated from heel off of the paretic limb (hindfoot switch not in contact with ground), until the paretic foot was off the ground (neither foot switch in contact with ground). Recent publications from our laboratory have shown that this timing algorithm produced the desired effects of increased ankle dorsiflexion, increased anterior GRF, and increased knee flexion on the paretic limb during walking.[28,30]

The FES used novel, variable-frequency trains consisting of an initial high-frequency (200-Hz) 3-pulse burst followed by a lower frequency (30-Hz) constant frequency portion of the train.[28,29,31] That is, each time stimulation was delivered, the stimulation train began with 3 pulses that were each separated by 5 ms; all subsequent pulses within that same train were then separated by 33.3 ms. We used these variable-frequency trains because they are physiological-based patterns that take advantage of the catch-like property of muscle and have been shown to enhance gait performance after stroke compared with the more traditionally used constant-frequency train.[29]

Data Processing

Marker trajectories and GRF data were low-pass filtered (Butterworth fourth order, phase lag) at 6 and 30 Hz, respectively, using commercial software (Visual 3D; C-Motion, Rockville, MD). Lower limb kinematics were calculated using rigid body analysis and Euler angles using Visual 3D. Vertical and anteroposterior GRFs were normalized to body weight. Vertical GRFs were used to identify gait events (initial contact and toe-off). Strides were time-normalized to 100% of the gait cycle and averaged across trials for each participant.

We evaluated the following dependent variables before training and after 4, 8, and 12 weeks of training:

1. *Peak paretic propulsion*—peak value of the anterior GRF normalized to body weight
2. *Paretic propulsive integral*—integral of the anterior GRF from the onset of propulsion through the end of stance phase for the paretic leg

Variables 1 and 2 were chosen because the purpose of the plantarflexor FES was to increase plantar flexor force during push-off.

3. *Peak knee flexion during swing* phase was determined for the paretic leg.
4. *Peak trailing limb angle* was computed as the peak of the planar angle between the laboratory's vertical axis (along the sagittal plane) and a vector joining markers located on the lateral malleolus and the greater trochanter of the paretic lower extremity.

Variables 3 and 4 were chosen because the purpose of the plantarflexor FES was to increase plantarflexor force during push-off, with the paretic limb in greater extension during preswing. This increased plantarflexor force should result in greater knee flexion during swing.

5. Self-selected walking speed
6. Distance ambulated during the 6-minute walk test
7. Time on the TUG test

These measures of walking function (variables 5–7) were used to examine changes in the functional walking of the participants.

Statistical Analysis

The Kolmogorov–Smirnov test was used to test for normal distribution of data for each of the outcome variables. Because some variables were not normally distributed, nonparametric statistics were used. The Wilcoxon signed-rank test was used to compare data between the pretraining and 4-week testing sessions and between the 4- and 12-week testing sessions. We reasoned that if significant differences for a variable were not found between either of these 2 comparisons, then there was no effect of the intervention on that variable. If, however, there was a difference from pretraining to 4 weeks, but not from 4 to 12 weeks, we would conclude that maximum gains for that variable were achieved by 4 weeks. If there were differences between both time point comparisons, we would conclude that the variable continued to improve through the end of training (12 weeks). The alpha level was set at 0.05. All statistical analyses were performed using SPSS 19.0 (SPSS Inc, Chicago, IL).

RESULTS

The participants demonstrated a range of gait and functional impairments before training. Average pretraining self-selected walking speed was 0.5 ± 0.17 m/s, and the lower extremity Fugl-Meyer scores ranged from 13 to 24 (Table 1). Twelve of the 13 participants who were enrolled completed the 12 weeks of training and follow-up testing. The subject who did not complete training dropped out because of knee pain from an incident unrelated to the training.

Kinematics and Kinetics

Because of technical problems, GRF data from 3 participants were not available at all time points and therefore these participants' data were not included in the analysis of peak paretic propulsion and paretic propulsive integral. Both peak paretic propulsion and paretic propulsive integral improved from pretraining to 4 weeks (Figure 1A and B), but no differences were found between 4 and 12 weeks ($P > 0.05$ for both). Similarly, peak knee flexion and peak trailing limb angle improved from pretraining to 4 weeks ($P < 0.05$ and $P < 0.01$, respectively), but no differences were found between 4 and 12 weeks (Figure 1C and D).

Clinical Measures of Walking Function

Self-selected walking speed improved from pretraining (0.50 ± 0.17) to 4 weeks (0.61 ± 0.19) and again from 4 to 12 weeks (0.68 ± 0.22) ($P < 0.01$ and $P < 0.05$, respectively; Figure 2A). Similarly, distance covered during the 6-minute walk test improved from pretraining (214 ± 92) to 4 weeks (264 ± 107) and again from 4 to 12 weeks (304 ± 125; $P < 0.01$ and $P < 0.05$, respectively; Figure 2B). Time to complete the TUG test did not improve significantly between pretraining (21.5 ± 8.9) and 4 weeks (20.1 ± 9.3), but was improved by 12 weeks (17.6 ± 6.8; $P = 0.24$ and $P < 0.01$, respectively; Figure 2C).

DISCUSSION

The results of this study demonstrate that after 12 weeks of fast-speed locomotor training with functional electrical stimulation to the plantar- and dorsiflexor muscles, improvements were observed in kinematic and kinetic gait patterns and in functional walking. However, the time course of the improvements in the gait biomechanics was shorter than the time course of the improvements in functional measures. This information can assist clinicians in setting expectations for the time course of improvements with poststroke locomotor rehabilitation.

To our knowledge, this is the first study that has simultaneously examined the time course of changes in walking speed, endurance, and gait biomechanics following a locomotor training intervention in individuals after stroke. The data show that changes in the biomechanics of walking took place early in the training period and leveled off after subjects had trained for 4 weeks (12 sessions). However, the measures of function showed continued improvement, which has also been demonstrated by a number of studies that have examined the time course of improvements in walking function. Sullivan et al[5] studied the effect of body-weight-supported treadmill training in combination with upper extremity exercises that were administered 4 days per week for 24 sessions in persons after stroke. The results demonstrated a linear increase in walking speed between baseline and 12 sessions and between 12 and 24 sessions of training.[5] A 12-week intervention study that included body-weight-supported treadmill training, strength

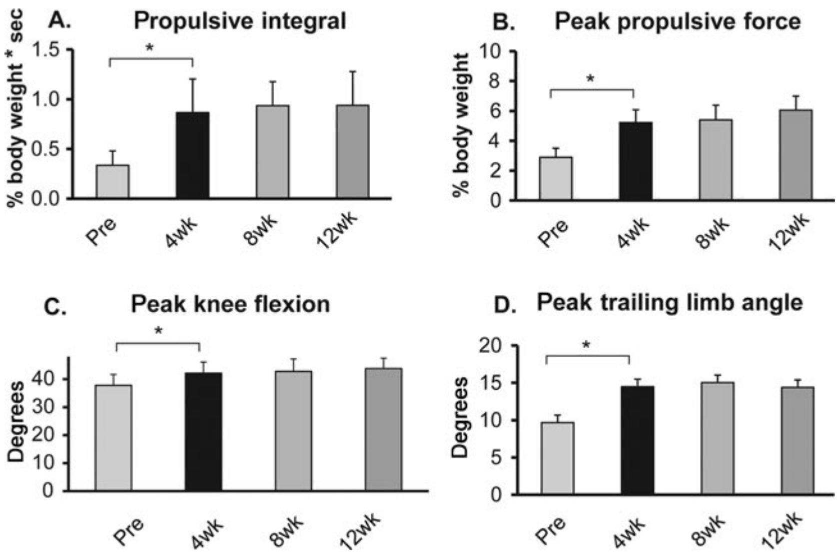

Figure 1. Results for the targeted kinematic and kinetic variables at a self-selected walking speed. From left to right, the bars in each figure represent the average results across participants before training (pre) and after 4, 8, and 12 weeks of training. Error bars are 1 SE. $*P < 0.05$ between time points.

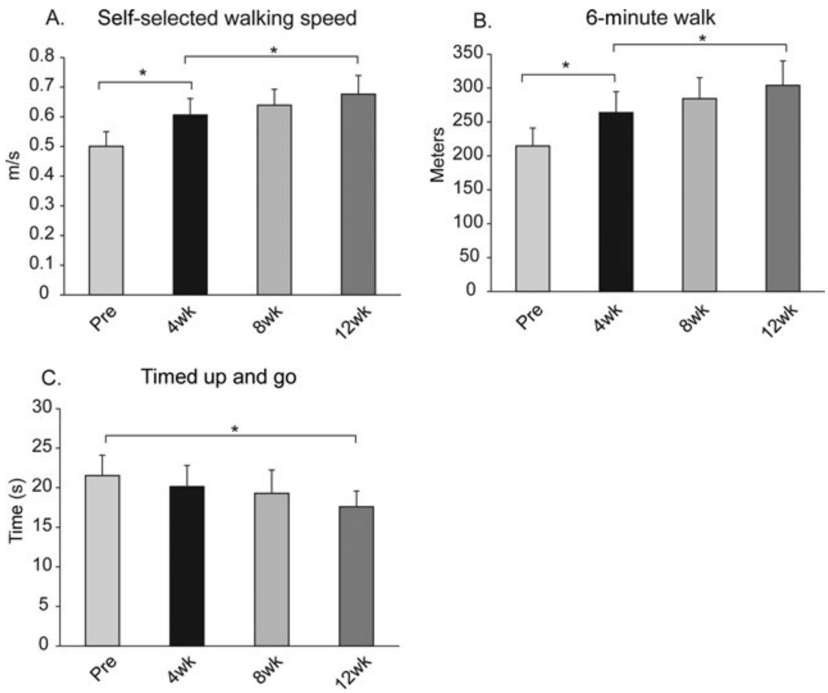

Figure 2. Results for the measures of walking function. From left to right, the bars in each figure represent the average results across participants before training (pre) and after 4, 8 and 12 weeks of training. Error bars are 1 SE. $*P < 0.05$ between time points.

training, and aerobic training 5 days per week in persons with stroke found that after 8 weeks of training (40 sessions), walking speed improvements during the 6-minute walk test appeared to plateau.[8] A 12-week intervention including body-weight-supported treadmill training and overground walking training 3 times a week in individuals with chronic stroke found that short-distance walking speed improved across all 12 weeks (36 sessions).[24] These findings are similar to those of the present study and support the assertion that walking speed and endurance continues to improve well after 12 sessions (4 weeks) of locomotor training in those with chronic stroke.

With respect to the functional measures, it is necessary to ask whether the improvements beyond 4 weeks (12 sessions) were not only statistically significant but also clinically meaningful. In the case of walking speed, the minimally clinically important difference (MCID) is 0.16 m/s in persons with stroke.[32] This value was not exceeded until the 12-week time point (after 36 sessions), indicating that to achieve a meaningful change in walking speed in these participants, 12 weeks of training was needed. MCID values do not exist for those with stroke for the 6-minute walk test or the TUG test. We do, however, know that the minimal detectable change (MDC) value for the TUG test is 3.7 seconds.[33] A reduction in the time taken to complete the test did not exceed this value until the 12-week time point (36 sessions). In the case of the 6-minute walk test, the change in distance exceeded the MDC value of 52 m[34] at the 8-week time point (24 sessions). Taken together these results suggest that to achieve meaningful and detectable changes in functional walking, 12 weeks (36 sessions) of intervention was required.

MCID values do not exist for those with stroke for the gait biomechanical variables presented. Evaluation of our results relative to MDC values for the gait biomechanics indicates that the changes observed exceed the MDC for trailing limb position and peak anterior GRF, but not for propulsive integral or peak knee flexion during swing.[35]

Walking function after stroke is thought to be influenced by a variety of factors including gait biomechanics, cardiovascular fitness, and biopsychosocial factors.[10,36-38] Improvements in gait biomechanics are thought to be important because of the connection between biomechanics and walking function and safety after stroke.[9-12,13,14] Many cross-sectional studies have demonstrated a relationship between specific deficits in gait biomechanics and walking speed after stroke.[9,12,39,40] Moreover, intervention studies have associated improvements in specific gait biomechanics with improvements in walking speed after stroke.[11,15] For example, cross-sectional studies have shown that increased plantarflexor power generation is associated with faster walking speed after stroke[9] and greater changes in this power generation are associated with greater improvements in walking speed.[15] Although this study was not designed to test a direct relationship between changes in gait biomechanics and walking function, our results do suggest that if biomechanical changes are important for improving walking speed or function, individuals after a stroke must devote additional time to learn to utilize the biomechanical changes to improve their walking speed and function. This is supported by the results of a recent study showing that improvements in a global measure of gait biomechanics (step length symmetry) at the end of a poststroke locomotor training intervention were associated with improved walking speed 6 months later.[18]

The results from this study provide clinicians with information about expected time frames for improvements in walking with rehabilitation after stroke that can be used in treatment planning and goal setting. Specifically, our results indicate that improvements in gait biomechanics will plateau before improvements in walking speed and endurance, and thus, expectations for each outcome should be set accordingly.

Limitations

The sample in this study is small. Future studies should examine the time course of changes in gait biomechanics and walking function during locomotor interventions in larger groups of persons with chronic stroke and should include follow-up testing.

It is possible that the specific time course of change for the various outcomes depends on factors such as type, intensity, and progression of training. Other studies have found a similar pattern of change in walking speed with differing locomotor training intensities and progressions,[8,24] suggesting that the results found here may be representative.

Biomechanical data were collected at the subject's self-selected speed at each time point. Although this congruence is important for relating the biomechanical data to the functional data, changes in speed could have played a role in the biomechanical changes.[41] However, the finding that improvements in biomechanics and function diverged after 4 weeks of training suggests that there may be a limit to the relationship between changes in walking speed and changes in biomechanics after stroke.

CONCLUSIONS

The results of this study demonstrate that after stroke, gait biomechanics and walking function both improved following a novel locomotor training intervention, but that each improved on a different timescale. Thirty-six training sessions were necessary to achieve an increase in walking speed that exceeded the MCID. This finding should be considered when designing locomotor training interventions after stroke.

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How do strength, sensation, spasticity and joint individuation relate to the reaching deficits of people with chronic hemiparesis?

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Summary

Hemiparetic subjects present with movement deficits including weakness, spasticity and an inability to isolate movement to one or a few joints. Voluntary attempts to move a single joint often result in excessive motion at adjacent joints. We investigated whether the inability to individuate joint movements is associated with deficits in functional reaching. Controls and hemiparetic subjects performed two different reaching movements and three individuated arm movements, all in the parasagittal plane. The reaching movements were a sagittal 'reach up' (shoulder flexion and elbow flexion) and 'reach out' (shoulder flexion and elbow extension). Joint individuation was assessed by getting each subject to perform an isolated flexion–extension movement at each of the shoulder, elbow and wrist joints. In addition, we measured strength, muscle tone and sensation using standard clinical instruments. Hemiparetic subjects showed varying degrees of impairment when performing reaching movements and individuated joint movements. Reaching impairments (hand path curvature, velocity) were worse in the reach out versus the reach up condition. Typical joint individuation abnormalities were excessive flexion of joints that should have been held fixed during movement of the instructed joint. Hemiparetic subjects tended to produce concurrent flexion motions of shoulder and elbow joints when attempting any movement, one explanation for why they were better at the 'reach up' than the 'reach out' task. Hierarchical regression analysis showed that impaired joint individuation explained most of the variance in the reach path curvature and end point error; strength explained most of the variance in reaching velocity. Sensation also contributed significantly, but spasticity and strength were not significant in the model. We conclude that the deficit in joint individuation reflects a fundamental motor control problem that largely explains some aspects of voluntary reaching deficits of hemiparetic subjects.

Keywords: movement; fractionation; hemiparesis; stroke; upper extremity

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Introduction

A leading cause of disability after stroke is hemiparesis, with poor control of arm, hand and finger movements. As a result, hemiparetic subjects commonly have abnormal reaching movements. In a horizontal plane, reaching deficits include decreased hand velocity (Wing *et al*., 1990; Roby-Brami *et al*., 1997), abnormalities in the initial direction of instructed movements (Beer *et al*., 2000), increases in the curvature or smoothness of the reach path (Levin, 1996; Rohrer *et al*., 2002) and co-contraction of elbow flexor and extensor muscles (Wing *et al*., 1990). Studies of reaching in the sagittal plane report similar deficits in velocity and path curvature (Trombly, 1993; Archambault *et al*., 1999).

Another impairment following stroke is the loss of independent movements of joints or body parts. These types of movements historically have been described as movement synergies (Twitchell, 1951). Attempts at isolated motions (individuation) of one body part are accompanied by excessive, unintended motion of linked segments (Schieber and Poliakov, 1998; Wittenberg *et al*., 1998; Beer *et al*., 2000; Lang and Schieber, 2003). Poor individuation has been quantified by measuring the finger movements of patients with hemiparesis. These studies have investigated specifically whether lesions of the motor cortex or corticospinal pathway affect individuation of finger movements (Schieber and Poliakov, 1998; Lang and Schieber, 2003). Lang and Schieber (2003) show that hemiparetic subjects' voluntary attempts to move the fingers often result in excessive motion at adjacent fingers and that certain digits were more impaired than others. Deficits in finger individuation presumably would affect many functional activities such as typing or playing a musical instrument.

It is not known whether impairments in functional arm movements (e.g. reaching) are related to individuation deficits. Poor reaching control could be due to a combination of many factors including poor individuation of upper extremity joints, weakness, spasticity and/or sensory loss. Deficits in the individuation of upper extremity joints have not been evaluated specifically, although some studies show that hemiparetic subjects are unable to isolate muscle activity when making many arm movements. In one study of isometric upper limb control, Dewald *et al*. (1995) report a reduction in the number of possible muscle combinations (i.e. movement patterns) in the paretic limb of hemiparetic subjects, compared with controls. Similarly, other studies report that abnormal coupling of isometric elbow and shoulder torques in the paretic limb of hemiparetic subjects is the predominant abnormality affecting upper limb motor control (Beer *et al*., 1999; Dewald and Beer, 2001). The patterns that they describe are very similar to the kinds of 'synergies' that are often observed clinically in hemiparetic subjects. These abnormal torque couplings suggest that hemiparetic subjects may have a fundamental problem generating, for example, an elbow extensor torque when they have to actively hold the shoulder against gravity. In another recent study, hemiparetic subjects were shown to be impaired in the overall distance that they could reach when moving in many different (mostly forward) directions (Kamper *et al*., 2002). This limitation in reaching space further supports the idea that activation of anti-gravity muscles at the shoulder can reduce the ability to generate elbow extension torques that are needed to make a 'reach out', similar to what was described in isometric reaching studies. Based on these data, one might expect that some reaching movements would be more impaired than others depending largely upon the pattern of motion and torques required at the shoulder and elbow.

One purpose of this study was to determine whether the ability to individuate joint movements predicts deficits when reaching in two specific directions: up, requiring shoulder flexion with elbow flexion, and out, requiring shoulder flexion with elbow extension. We chose these reaching directions to determine if coupling a shoulder flexion motion with elbow extension is more difficult for hemiparetic subjects than simply flexing at both joints. A second purpose was to determine the relative contribution of individuation, strength, spasticity and sensation to reaching abnormalities in hemiparetic subjects. Parts of this work have been reported previously in abstract form (Zackowski *et al*., 2001).

Methods

Subjects

Eighteen hemiparetic subjects and 18 age- and gender-matched control subjects participated in this study. Individual subject information is given in Table 1. The mean age of the hemiparetic subjects ($\pm$SE) was 55.0 $\pm$ 2.4 and that for the control subjects was 54.6 $\pm$ 2.4 years. For the hemiparetic group, a diagnosis of cerebrovascular accident was required for participation in the study. This was confirmed by a neurological examination and MRI. Hemiparetic subjects were tested between 1 and 269 months post-cerebrovascular accident (32 $\pm$ 62 months, mean $\pm$ SD) and on the side contralateral to their lesion. Control subjects were matched accordingly.

All hemiparetic subjects met the following inclusion criteria: (i) absence of ataxia and/or cerebellar damage, measured by clinical observation and MRI/CT images; (ii) absence of hemispatial neglect as noted by a score of 52–54 on the BIT star cancellation test; (iii) ability to follow directions as determined by a score of $\leqslant$1 on a subset of questions taken from the National Institutes of Health Stroke Scale (Brott *et al*., 1989); (iv) active range of motion on the affected side of at least 15° in the shoulder and elbow; and (v) passive range of motion on the affected side at least 75% of normal in the shoulder, elbow, wrist and fingers, with minimal to no pain. The Institutional Review Board at Washington University School of Medicine approved the protocol for this study. Informed consent was obtained from all subjects prior to testing.

Paradigm

Subjects were evaluated while making reaching movements and attempting to isolate joint movements. We also assessed all subjects for spasticity, strength and sensation deficits. Subjects performed two sets of fast reaching movements to a target, a 'reach out', and a 'reach up'. The target was a 40 mm Styrofoam ball suspended on a flexible wire in the sagittal plane (Fig. 1). Each subject was given an initial practice trial, and then 4–7 trials were recorded. For all trials, subjects were instructed to reach out and touch the target upon hearing a 'go' signal. The instruction was to reach as quickly as possible to touch anywhere on the target

For the 'reach out', subjects were seated with their back supported and with the hand to be tested resting on a pillow in their lap (an ~90° angle at the elbow joint). The target was placed in a position that required the subject to reach using ~40° of shoulder flexion and 40° of elbow extension to touch the target (position 1, Fig. 1A). For the 'reach up', subjects were seated identically to the reach out condition. However, the target was placed in a position that required the subject to reach using ~40° of shoulder flexion and 40° of elbow flexion to touch the target (position 2, Fig. 1A).

All subjects also performed three upper extremity individuation movements; one initial practice trial was followed by 4–7 recorded trials for each type of movement. For 'shoulder individuation', subjects were seated with their back supported and their arm hanging down next to their body with the elbow extended (Fig. 1B). They were instructed to begin the movement upon hearing a 'go' signal and then carefully to raise their arm up to shoulder height, trying not to bend at their elbow or wrist. For 'elbow individuation', subjects

Table 1 *Hemiparetic subject information*

	Age	Sex	Diagnosis	Months post-stroke	Individuation index	Spasticity	Sensation	Strength
01	75	F	R. ischaemic frontal temporal parietal ischaemic infarcts	21	0.91	0.00	4.00	19.4
02	48	F	R. ischaemic frontal parietal infarcts	4	0.79	2.50	0.25	0.0
03	48	M	L. ischaemic basal ganglia and external capsule infarcts	12	0.91	1.17	0.50	25.5
04	52	F	L. haemorrhage in putamen	33	0.83	1.33	3.00	8.2
05	58	M	R ischaemic caudate body infarct	15	0.80	1.08	1.00	28.4
06	54	M	R. ischaemic pontine infarct	11	0.83	0.00	1.00	31.3
07	58	M	R. haemorrhage in putamen	50	0.59	2.17	4.00	31.8
08	59	M	L. ischaemic frontal temporal parietal watershed infarcts	1	0.32	2.00	4.00	2.7
09	57	M	R. ischaemic pons, midbrain infarct	10	–0.81	1.83	1.50	0.0
10	61	F	R. ischaemic frontal infarct	6	0.79	1.33	1.25	21.9
11	50	M	R. ischaemic subinsular infarcts	24	0.80	0.00	1.50	30.8
12	62	F	L. ischaemic frontal temporal parietal infarcts	66	0.75	0.83	2.50	17.2
13	39	M	R. ischaemic frontal temporal parietal infarcts	2	0.56	1.92	0.25	8.3
14	56	F	L. ischaemic basal ganglia, subcortical infarcts	19	0.85	0.75	0.50	22.1
15	75	M	L. haemorrhage in frontal parietal cortex	24	0.36	3.00	1.75	0.0
16	36	M	L. ischaemic basal ganglia, and frontal infarcts	11	0.83	0.00	0.50	45.2
17	56	M	L. haemorrhage in pons	1	0.91	0.33	4.00	19.7
18	51	F	R. ischaemic frontal temporal parietal infarcts	269	0.82	1.17	1.00	22.7

R = right side; L = left side. The individuation index is the averaged individuation index from shoulder, elbow and wrist individuation movements. Spasticity is the averaged modified Ashworth score (scale = 0–4) from the shoulder, elbow and wrist joints, normal tone = 0. Sensation is the average sensation assessed using Semmes Weinstein monofilaments from four sites on the arm. Normal = 0 (monofilament size 2.83); diminished light touch = 1 (monofilament, 3.61); diminished protective sensation = 2 (monofilament, 4.31); loss of protective sensation = 3 (monofilament 6.65); and unable to feel largest monofilament = 4. Strength is the average pounds of resistance measured from the shoulder flexors, elbow flexors and wrist extensor muscles.

were seated identically to the shoulder individuation movement and were instructed to bend their elbow carefully as far as possible, trying not to move at their shoulder or wrist. For 'wrist individuation', subjects were seated with their back supported, upper arm hanging down but with elbow flexed to 90° and their wrist flexed as far as they could comfortably hold it. Subjects were then instructed to extend their wrist carefully as far as possible, trying not to move at their shoulder or elbow.

Spasticity of the affected upper extremity was measured at the shoulder, elbow and wrist joints in the hemiparetic subjects using the MODIFIED Ashworth scale (see Table 1). For this measure, passive movements of flexion and extension of the shoulder, elbow and wrist are graded between 0 (no increase in muscle tone) to 4 (affected parts rigid in one position) (Bohannon and Smith, 1987). The modified Ashworth scale was designed to measure resistance to passive stretch, and is one of the most frequently used measures to grade spasticity (Bohannon and Smith, 1987; Gregson *et al*., 1999). It has been found to be a reliable and reproducible method of evaluating spasticity (Lee *et al*., 1989; Gregson *et al*., 1999). For this assessment, all subjects were positioned supine on a plinth.

The strength of the tested upper extremity was measured using a Microfet2 hand-held dynamometer. We measured strength of the shoulder, elbow and wrist flexor and extensor muscles (see Table 1). The strength testing protocol followed the protocol of Andrews *et al*. (1996), except that subjects were seated throughout the testing.

Fine touch sensation of the tested upper extremity was measured in the hemiparetic subjects using the Semmes Weinstein Aesthesiometer Monofilament test (Semmes, 1960) (see Table 1). This test demonstrates gradients of cutaneous sensibility. Four locations on the affected arm including the hand were tested.

Data collection

Kinematic signals were recorded from all subjects. Kinematic data for the reaching and individuation movements were collected in 3-D at 100 Hz, using an Optotrak motion measurement system (Northern Digital, Inc., Waterloo, Ontario, Canada). Infrared light-emitting diode markers were taped on the centre of the lateral surface of the index finger, head of the fifth metacarpal, wrist joint, elbow joint, shoulder joint and the target (Fig. 1).

Analysis

For reaching performance, we defined the start of movement as the time that the wrist velocity exceeded 5% of its peak. The end of the first reach was defined as the time and position at which the wrist velocity dropped to a minimum prior to subsequent corrective movements. Other measures of interest included: (i) peak wrist velocity; (ii) index end point error; and (iii) index finger path ratio. Peak wrist velocity was the maximum linear velocity reached by the wrist joint marker during this time. Index end point error was measured as the total distance between the tip of the index finger and the target at the end of the first reach movement. The index finger path ratio is a measure of the 'straightness' of the index finger path from the start of movement to touch of the target (Gilman *et al*., 1976). It is the ratio of the length of the path actually travelled to an ideal straight line between the start of movement and the position when the finger touches the target. A path ratio of 1 represents a straight path (normal), whereas a path ratio >1 represents an abnormally curved path. Hemiparetic subjects 08, 09 and 15 did not touch the target on every trial; in these cases, we chose the position of the index finger that was closest to the target as their end point.

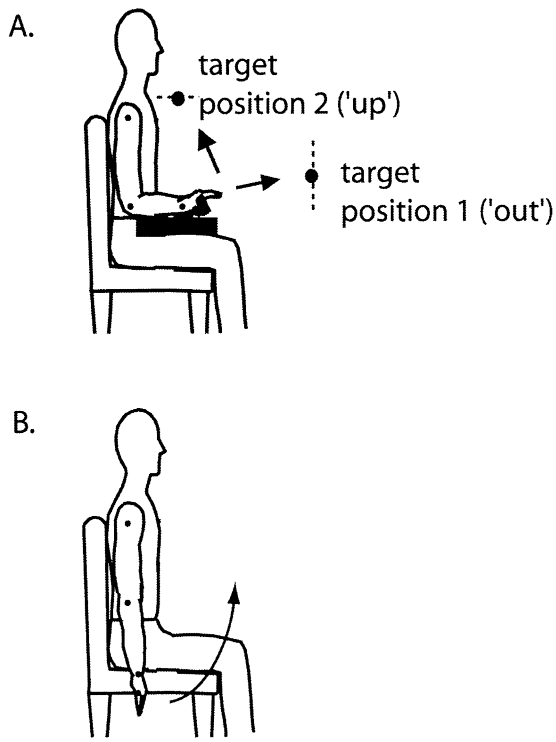

Fig. 1 Schematic of (**A**) reaching condition, target position 1 for reach 'out' and target position 2 for reach 'up'; and (**B**) shoulder individuation task. Dotted lines: delineation of under- versus overshooting. End point error was classified as an overshoot when the finger travelled above a horizontal line (reach up) and past a vertical line (reach out) through the target. Undershoot was when the finger fell below a horizontal line (reach up) and prior to a vertical line (reach out) through the target.

For individuation performance, the relative motion of instructed versus non-instructed joints using a measure of the normalized joint excursion was determined. We calculated flexion and extension joint angles for the shoulder, elbow and wrist from the 3-D position data; this was necessary since motions were not always perfectly constrained to the parasagittal plane. We did not consider other motions (e.g. shoulder abduction) in this analysis. Joint excursion is defined as the range of motion a joint went through during each isolated movement (regardless of whether the joint was 'instructed' or 'non-instructed'). The average joint excursion values were normalized by dividing the values by the excursion of that joint when it was the instructed joint. Thus, the normalized joint excursion is 1 when a joint is the instructed one and is usually <1 when it is a non-instructed joint. The normalized joint excursion was then used to derive the individuation index (Schieber, 1991). To quantify the degree to which non-instructed joints moved simultaneously with the instructed joints, methods initially developed by Schieber were modified (Schieber, 1991; Lang and Schieber, 2003).

The individuation index is a measure of how well a joint is able to move independently, i.e. without the other joints moving. The individuation index was calculated as 1 minus the average normalized joint excursion of the non-instructed joints, or:

$$\mathrm{II_j} = 1 - [(\sum_{i=1}^{n} | D_{ij} | - 1]/(n-1) \qquad (1)$$

where $\mathrm{II_j}$ is the individuation index of the *j*th joint, $\mathrm{D_{ij}}$ is the normalized joint excursion of the *i*th joint during the *j*th instructed movement, and *n* is the number of joints (*n* = 3). One is subtracted from the sum of the normalized path distances in the numerator and from *n* in the denominator to remove the normalized path distances of the instructed joint itself. The individuation index will be close to 1 for an ideally individuated movement in which the instructed joint moves with no movement of non-instructed joints and closer to 0 when more non-instructed joint movements occur simultaneously with the instructed joint movement. The individuation index can be negative if the normalized joint excursion for the non-instructed joints is >1. This would only occur if, for example, the elbow flexed more when it was the non-instructed joint versus when it was the instructed joint. A joint individuation index was calculated separately for each of the three individuation movements (shoulder, elbow and wrist) and also averaged to obtain an average individuation index for each subject.

Spasticity, strength and fine touch sensation measures were also evaluated. For spasticity, individual MODIFIED Ashworth scale scores from shoulder flexion, elbow flexion and extension, and wrist flexion and extension were measured; the average value from across the three joints was used for analysis. For strength, values from the shoulder flexors, elbow flexors and wrist extensor muscles were chosen because they were the anti-gravity (agonist) muscles in all movements. The three muscle groups were then averaged and used in all subsequent analyses. For sensation, in each subject, four sites were assessed on the affected arm and given a score based on the smallest monofilament that could be sensed at that location: normal = 0 (i.e. the subject can feel monofilament, 2.83); diminished light touch = 1 (monofilament, 3.61); diminished protective sensation = 2 (monofilament, 4.31); loss of protective sensation = 3 (monofilament, 6.65); and unable to feel the largest monofilament = 4. The four numbers were then averaged; this average value was the sensation score for that subject and was used in all subsequent analyses.

Statistica software (StatSoft, Tulsa, OK) was used for all analyses. Separate, repeated measures analyses of variance (ANOVAs) were used to test the reach movements, for differences due to group (control group versus hemiparetic group), condition (reach out vesus reach up) and group × condition interactions. Similarly, a repeated measure ANOVA was used to test the individuation movements for differences due to group (control versus hemiparetic), joint (shoulder, elbow and wrist) and group × joint interactions. In cases where ANOVA revealed significant differences, *post hoc* comparisons were made using Tukey's HSD test.

Pearson correlations were used to evaluate the relationships between individuation, spasticity, strength, sensation and months post-stroke in the hemiparetic subject group; a Bonferroni correction was also applied to adjust for multiple comparisons (Hayes, 1994). In addition, hierarchical regression analysis was used to test systematically whether strength, spasticity, sensation and/or individuation index best predicted the curvature of hand paths, end point error and peak velocity during reaching.

Results

Reach performance

All measures of reaching were abnormal in the hemiparetic group compared with controls. Hemiparetic subjects' performance was also different in the reach out versus reach up

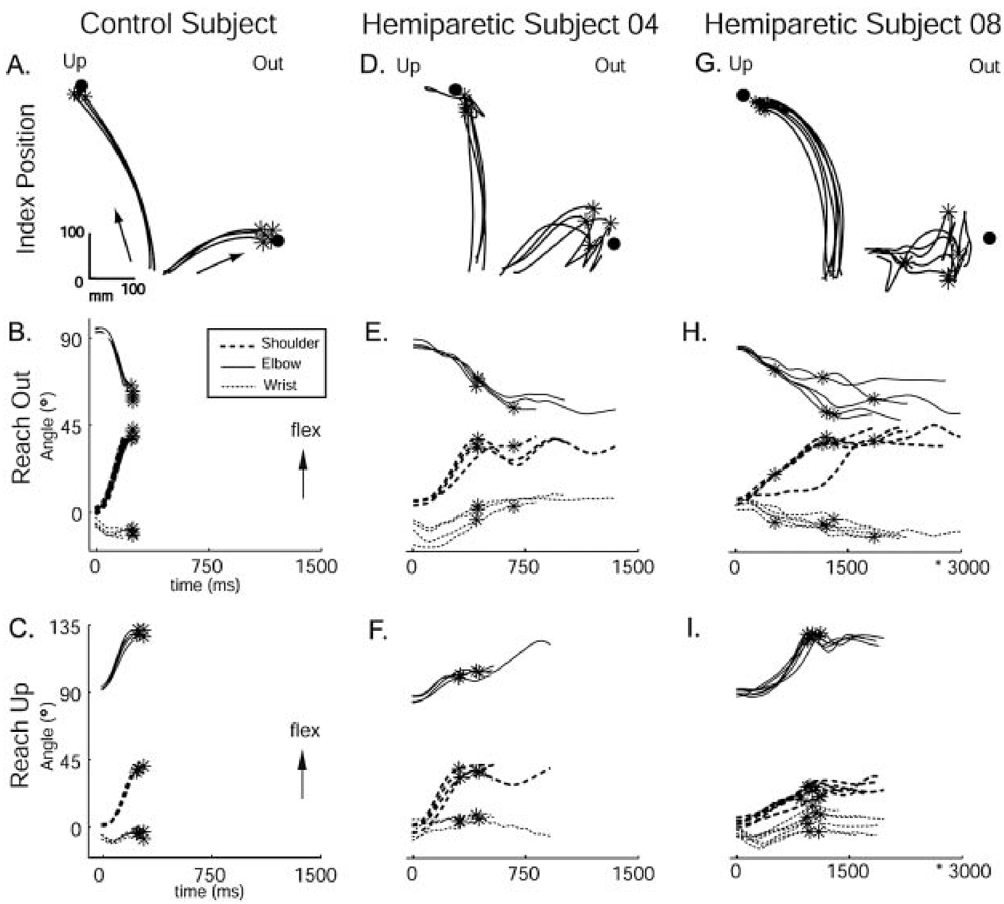

Fig. 2 Overlaid single trials for index finger paths, and associated excursions of the shoulder, elbow, and wrist joints from both reaching conditions ('up' and 'out'). (**A**) Control index finger paths for reaches 'out' and 'up'. (**B**) Control joint angle plots during the reach 'out'. (**C**) Control joint angle plots during the reach 'up'. (**D**) Hemiparetic subject 04 index finger paths. (**E**) Hemiparetic subject 04 joint angle plots during the reach 'out'. (**F**) Hemiparetic subject 04 joint angle plots during the reach 'up'. (**G**) Hemiparetic subject 08 index finger paths. (**H**) Hemiparetic subject 08 joint angle plots during the reach 'out'. (**I**) Hemiparetic subject 08 joint angle plots during the reach 'up'. Solid black circles: target. Asterisk: index end point position or time of index end point prior to corrective submovements. Angular excursions are graphed as follows: bold dashed traces, shoulder angular excursion; narrow solid traces, elbow angular excursion; narrow dashed traces, wrist angular excursion.

movements: when reaching up, reach paths were straighter and faster. Figure 2 shows plots of index finger paths and the corresponding joint angles during several trials of a reach up and a reach out movement. In each plot, the asterisk indicates the position/time of the end of the first phase of movement prior to corrective submovements. The asterisks therefore indicate end point error on the index path plots. In Fig. 2A, the index finger paths for a control subject are consistently directed straight toward the target and show little end point error (asterisk) for both types of reaches. Controls also produce smooth and consistent joint movements for both reach out (Fig. 2B) and up (Fig. 2C) movements. Two example subjects with hemiparesis are shown in Fig. 2D–I. Both subjects make straighter, less variable index paths when moving up versus out (Fig. 2D and G) and tended to undershoot the target more than controls in both conditions. Joint angles produced by the hemiparetic subjects were also more variable, with multiple reversals in direction, particularly for the reach out versus up condition (Fig. 2E and F, and H and I).

Figure 3 shows group mean bar graphs (±SE) for peak wrist velocity, index finger path ratios (curvature) and index end point errors for the reach out and up conditions. There was a significant effect of group on all measures, with hemiparetic subjects reaching more slowly, with greater path curvature and with larger end point errors compared with controls (Fig. 3A–C, all $P < 0.01$). There was also a significant effect of condition in that reaching up was faster ($P = 0.0001$) and straighter ($P = 0.008$), but with slightly larger end point errors ($P = 0.036$) compared with reaching out. In addition, there were significant interactions. Hemiparetic subjects improved the straightness of their reach when moving up versus out; this improvement was much greater than that of controls, who made straight

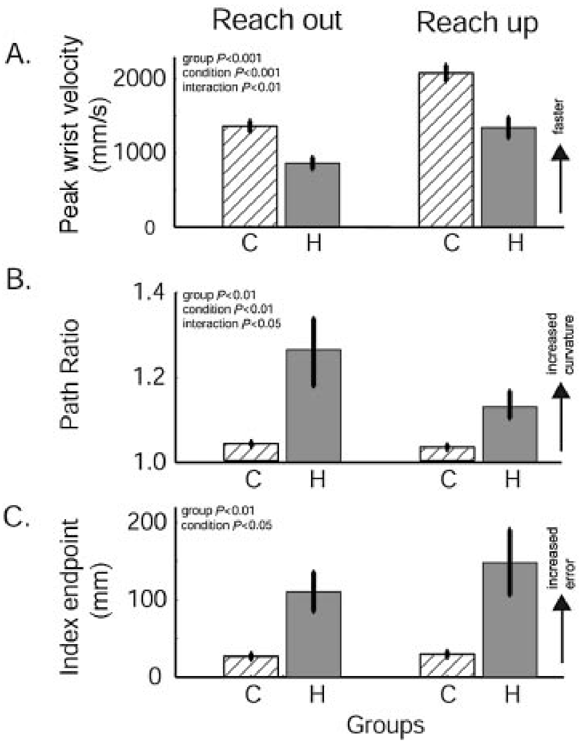

Fig. 3 Group averages for reach performance measures in reach out and reach up conditions. (**A**) Peak wrist velocity. (**B**) Index finger path ratio. (**C**) Index end point error (absolute distance from the target). Hatched bars, control group (C) mean ± SE; grey bars, hemiparetic group (H) mean ± SE.

movements in both conditions (group × condition, $P = 0.015$). Finally, hemiparetic subjects increased their speed when moving up versus out, but this improvement was not as great as that seen in the control group (group × condition, $P = 0.006$).

Upper extremity individuation

Subjects in the hemiparetic group had varying ability to individuate shoulder, elbow or wrist movements. Figure 4 shows plots of shoulder, elbow and wrist joint angles during several trials of shoulder, elbow and wrist individuation in a representative control and two hemiparetic subjects. During shoulder individuation trials, the control subject in Fig. 4A flexed his shoulder ~73° and consistently added <8° of combined movement at the elbow and wrist joints. This subject's individuation index was 0.97, indicating very good shoulder individuation. Similar patterns were observed for elbow and wrist individuation, resulting in individuation indices of 0.91 and 0.99, respectively.

Two example subjects with hemiparesis are shown in Fig. 4B and C; both had difficulty making individuated joint movements, although each shows a different pattern of joint movement. Subject 04 in Fig. 4B had a mild deficit in making individuated movements at the three joints tested and moved more slowly than controls. During attempted shoulder individuation (Fig. 4B, top), the shoulder was flexed 70°, in addition to 15° of elbow flexion and 20° of wrist extension; this resulted in an individuation index of 0.79. Similar patterns were observed for attempted individuation of elbow (Fig. 4B, middle) and wrist motions (Fig. 4B, bottom), resulting in individuation indices of 0.83 and 0.87, respectively. This subject always moved the most at the instructed joint, but typically had unwanted movement of the non-instructed joints.

Subject 08 had a severe inability to individuate movement of any joint and also moved slowly (Fig. 4C). This subject always moved most at the elbow, regardless of which of the three joints was the instructed one. When attempting to isolate shoulder movement (Fig. 4C, top), the shoulder was flexed 40° along with 65° of elbow motion and 20° of wrist motion, resulting in a very abnormal individuation index of –0.29. This index was negative because the wrist actually moved more in this condition than it did when it was the instructed joint, and the elbow moved to a similar extent during this condition and when it was the instructed joint (see Methods, Equation 1). This subject was best at isolating elbow movement (Fig. 4C, middle), with an individuation index of 0.71. Wrist individuation was poor (0.53) because the wrist moved only 10°, while the elbow moved nearly 60° (Fig. 4C, bottom).

Figure 5 shows the individuation indices for all joints tested from subjects in the control and hemiparetic groups. Controls typically showed very good individuation indices (close to 1), with the best indices occurring at the wrist and shoulder and slightly lower indices at the elbow. The hemiparetic subjects' indices were more variable, and often substantially lower than 1. This indicates that they were unable to move the instructed joint in isolation; instead, they had concomitant movements at the other joints of the arm. A few hemiparetic subjects had negative indices, most often during shoulder individuation. Negative indices were associated with the greatest abnormality; they indicate that one or more of the non-instructed joints (e.g. elbow or wrist) moved more during this condition (e.g. shoulder individuation) than when they were the instructed joints.

Group means for the individuation index are shown in Fig. 6. Note that controls perform best at the wrist and worst at the elbow. The hemiparetic group had significantly lower individuation indices for all three joints tested (all $P < 0.05$), but followed the same pattern as controls. Hemiparetic subjects also had deficits actively moving all joints. Table 2 shows the active range of motion for each joint when it was the instructed joint. The hemiparetic group showed significantly reduced range at all joints ($P < 0.01$), although the wrist was the most impaired in terms of active range of motion. Thus, in an absolute sense, the wrist was most impaired in its ability to actively move.

In addition to upper extremity individuation, hemiparetic subjects were each evaluated for spasticity, strength and sensation. Table 1 shows average individuation index, spasticity, strength and sensation measures, along with

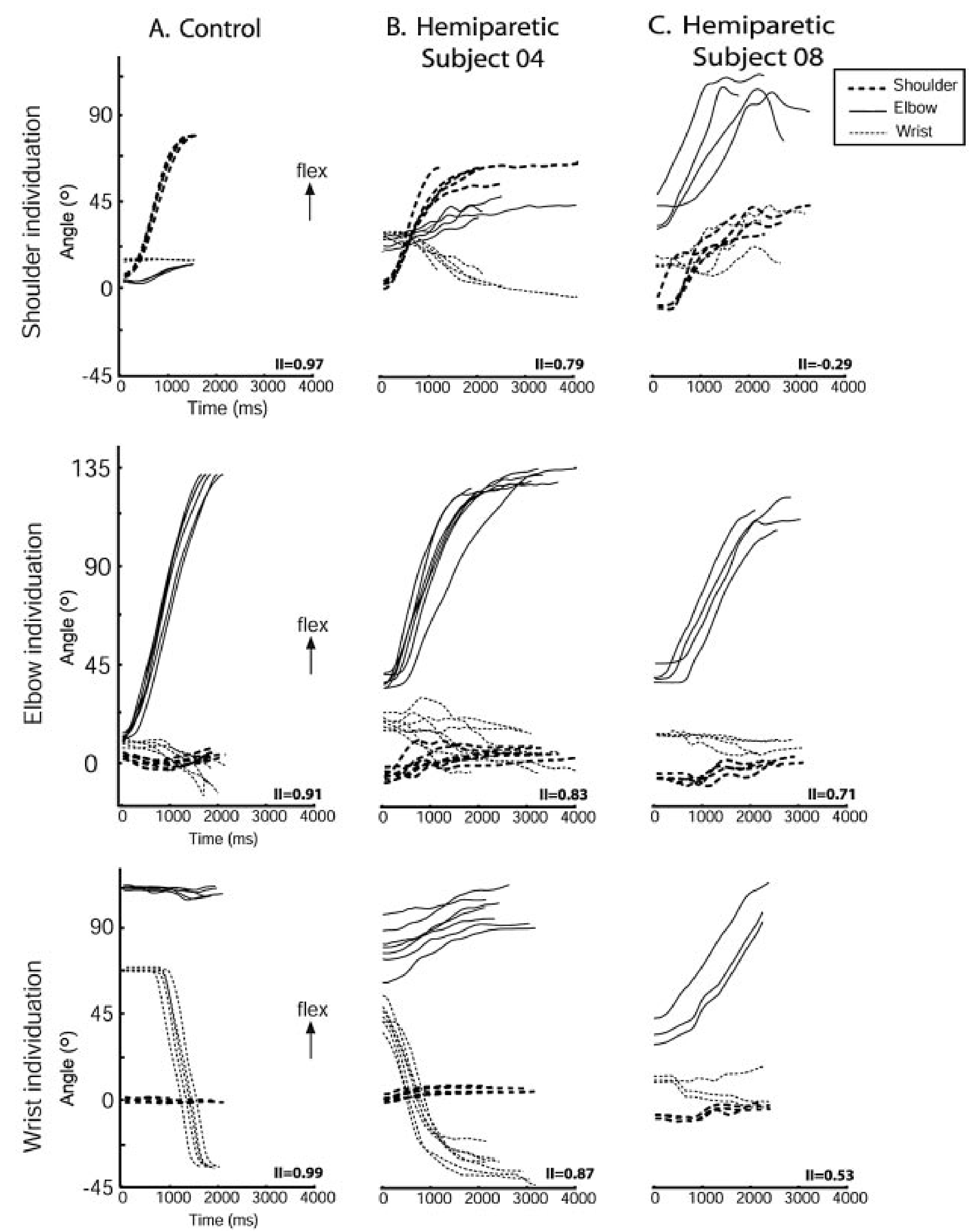

Fig. 4 Shoulder, elbow and wrist individuation movements graphed over time from start of movement to maximum angular excursion in the instructed joint. (**A**) Control. (**B**) Hemiparetic subject 04. (**C**) Hemiparetic subject 08. Bold dashed traces, shoulder angular excursion; narrow solid traces, elbow angular excursion; narrow dashed traces, wrist angular excursion.

months post-stroke for each subject. The individuation index in Table 1 is the average value across the three joints (shoulder, elbow and wrist); we did this to obtain a single index of severity. Likewise, average values of spasticity, strength and sensation measures were calculated. We then determined whether the average individuation index, spasticity score, strength, sensation and months post-stroke were correlated. Table 3 shows correlations for these five variables. Interestingly, we found a significant negative correlation between strength and spasticity (r = –0.70, P = 0.001); this shows that hemiparetic subjects who are weaker are also more spastic. In addition, strength was positively correlated with the individuation index. Though not statistically significant, this finding implies that strength may help individuation and that deficits such as reduced corticospinal tract drive may impair strength and individuation ability, rather than having independent effects. All other measures were poorly correlated with one another.

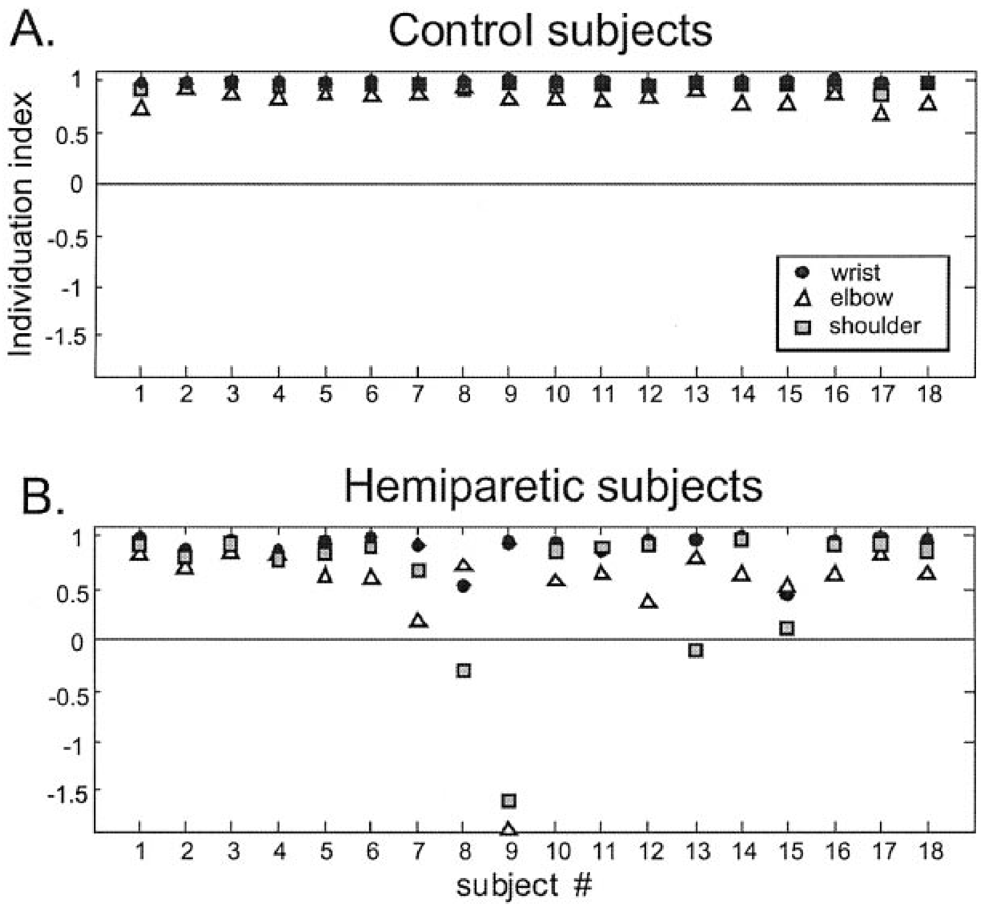

Fig. 5 Individuation index for shoulder, elbow and wrist individuation movements for each subject. (**A**) Control subjects 1–18. (**B**) Hemiparetic subjects 1–18. Solid black circles, wrist individuation index; open triangles, elbow individuation index; grey squares, shoulder individuation index.

What impairments are related to reach performance?

It is not known how individuation, strength, spasticity or sensation impairments are related to functional movements such as a reach. We attempted to identify which of these impairments was most related to specific features of reaching performance of hemiparetic subjects. In a hierarchical regression analysis, reach path curvature was chosen as the dependent variable because it showed great sensitivity to differences between the control and hemiparetic groups and because it dissociated the results of the overall reaching behaviour better than end point error or velocity. Our analysis shows that the average individuation index explained the greatest portion of the variance in reach path (50%, P = 0.0002); sensation explained a smaller portion of the variance in reach path (33%, P = 0.02); and strength and spasticity were not as strongly related. In this analysis, strength explained an additional 17% (P = 0.10), and spasticity explained an additional 3% (P = 0.52) of the variance in reach path

Although reach path curvature best characterized impaired reaching performance, we also evaluated whether the other measured parameters of end point error and peak velocity were more heavily influenced by strength, spasticity or loss of sensation than by individuation. To do this, we applied the same hierarchical regression analysis using peak velocity and end point error as dependent variables. The results show that peak reaching velocity was influenced most by poor strength (58%, P = 0.005); individuation index, spasticity and sensation were not significant in the model. In contrast, end point error, similar to reach path curvature, was most influenced by individuation index (54%, P = 0.0007); in addition, spasticity explained a smaller portion of the variance (40%, P = 0.003); strength and sensation were not strongly related.

It should also be noted that none of the measured reaching parameters were correlated with the amount of time since stroke. Specific correlation results include: reach path curvature, r = –0.15, P = 0.56; peak velocity, r = –0.08, P = 0.74; and end point error, r = –0.14, P = 0.59.

Discussion

Reaching

Historically, Brunnstrom, Fugl-Meyer, Twitchell and others have observed that hemiparetic subjects often move in synergies and typically have trouble using selective movement patterns (Twitchell, 1951; Brunnstrom, 1966; Fugl-Meyer *et al*., 1975). A synergy movement is defined here as movement of the upper extremity in a relatively fixed pattern when attempting a voluntary movement. Twitchell (1951) specifically noted that flexion movements of the upper extremity were the first voluntary movements to return following a cerebral lesion, and that voluntary movements typically resulted in a whole arm movement with the inability to isolate movements outside of this synergy motion.

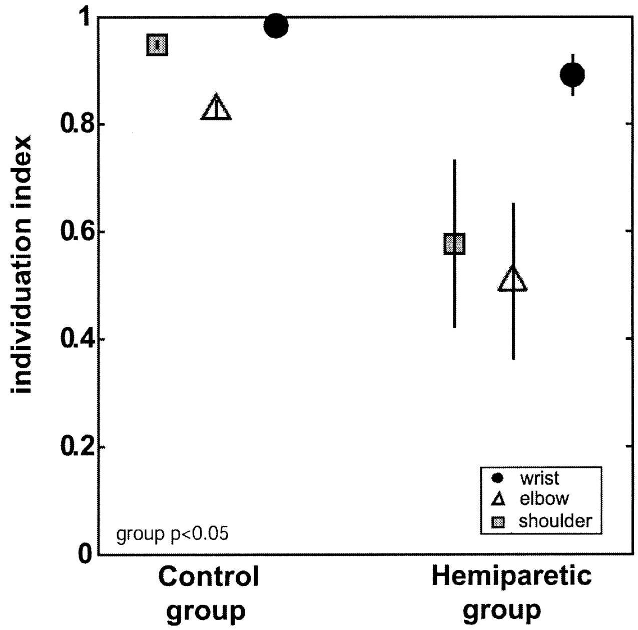

Fig. 6 Mean individuation indices for shoulder, elbow and wrist joints. (**A**) Control group. (**B**) Hemiparetic group. Solid black circles, mean wrist individuation index ± SE; open triangles, mean elbow individuation index ± SE; grey squares, mean shoulder individuation index ± SE.

More recently, studies have shown evidence that hemiparetic subjects activate specific combinations of muscle groups during isometric and planar movement tasks (Beer *et al*., 2000; Dewald and Beer, 2001; Lum, 2003). Lum *et al*. (2003) show an abnormally strong link between flexion of the shoulder and elbow in the paretic arm during an isometric task. They describe strength imbalances in the direction of shoulder and elbow flexion and the resulting synergy pattern. In a separate isometric study, Dewald and Beer (2001) characterized abnormal shoulder–elbow torques and show that an elbow flexion torque is a common secondary torque produced when generating shoulder activity. In a study relating isometric torque patterns to the disturbances in planar arm movements, Dewald *et al*. (2001) provide further evidence for an impaired capacity to generate certain muscle co-activation patterns in the impaired limb. Beer *et al*. (2000) show that hemiparetic patients retain the capacity to modulate the initial direction of a planar arm movement, although these movements were systematically misdirected. Their data suggest that this is due to abnormal spatial tuning of muscle activity specific to the elbow when initiating movements and

Table 2 *Upper extremity active range of motion of the instructed joint during individuation movements*

	Control subjects			Hemiparetic subjects		
	Shoulder flexion	Elbow flexion	Wrist extension	Shoulder flexion	Elbow flexion	Wrist extension
01	54.40	114.12	85.15	68.88	109.49	73.38
02	66.64	116.21	131.45	36.22	80.29	57.8
03	58.49	122.62	106.16	48.26	97.22	85.46
04	56.41	128.49	102.08	53.49	90.28	86.44
05	65.42	122.39	109.27	82.85	48.15	87.72
06	69.72	114.24	97.76	68.82	108.29	91.77
07	66.38	101.96	98.33	58.78	95.05	42.11
08	78.09	93.87	94.02	39.6	71.34	11.23
09	64.51	129.01	103.99	18.21	63.57	0.57
10	75.26	137.82	123.36	53.34	121.17	100.47
11	67.65	122.08	91.66	71.61	144.32	114.67
12	63.31	120.71	103.14	62.09	130.89	94.6
13	73.07	123.53	101.90	41.4	92.81	5.82
14	69.17	129.05	106.29	61.85	121.74	86.89
15	53.99	124.31	94.56	15.59	49.35	9.61
16	60.66	82.66	87.72	72.22	111.9	107.07
17	53.22	110.82	87.89	37.89	5.13	93.57
18	74.07	142.75	113.91	69.83	98.57	65.54
Mean	65.03	118.70	102.15	53.39	91.09	67.48
(SD)	(7.62)	(14.67)	(12.13)	(18.85)	(34.03)	(37.52)

Range of motion of the instructed joint, measured from start of movement to maximum angular excursion during the individuation movement.

Table 3 *Correlations*

Strength and spasticity	$r = -0.70$*
Strength and individuation index	$r = 0.53$
Strength and sensation	$r = -0.06$
Strength and months post-stroke	$r = 0.12$
Spasticity and individuation index	$r = -0.39$
Spasticity and sensation	$r = -0.06$
Spasticity and months post-stroke	$r = 0.02$
Individuation index and sensation	$r = -0.03$
Individuation index and months post-stroke	$r = 0.13$
Sensation and months post-stroke	$r = -0.05$

*$P = 0.001$.

results in impaired multijoint control. Overall, these studies point to a specific problem in coordinating appropriate torques at the shoulder and elbow leading to the use of synergy patterns during reaching movements.

In our study, we report differential impairments when subjects reach in two directions: up and out. Hemiparetic subjects make straighter (more normal) paths and reach faster when moving up. Reaching up requires flexion at both the shoulder and elbow, which would be easier for hemiparetic subjects to perform given that they produce a somewhat obligatory flexor pattern at these two joints. In contrast, reaching out requires shoulder flexion and elbow extension, so that subjects have to activate shoulder flexor muscles while relaxing elbow flexor muscles. This pattern appears to be more difficult for hemiparetic subjects to use, possibly due to an inability to break out of their flexor synergy. Another possibility is that upper extremity strength was a factor that caused the two types of reaches to look different. Presumably a reach out requires greater strength to control a lever arm that is getting longer as the reach progresses outward, whereas a reach up has less of a strength requirement because the lever arm is shorter. However, strength was not related to reaching path in our regression model.

Individuation

The ability to isolate movement at specific joints is essential for many human behaviours. Few studies have directly examined individuation of joint movements. Hager-Ross and Schieber (2000) showed that when healthy subjects attempt to move a single finger, there is often some motion at adjacent fingers. Movements of the thumb, index finger and little finger typically were more highly individuated than were movements of the middle or ring fingers. They speculate that these differences could be due to long-term motor experiences of subjects, the organization of multitendoned finger muscles and/or differences in the central inputs to spinal motoneuron pools (Hager-Ross and Schieber, 2000). Studies of arm control have tested motions similar to our individuated movements (Almeida *et al*., 1995; Gribble and Ostry, 1999). They find that the non-moving joints are actively stabilized in a predictive manner throughout movement of a single joint. Stabilization is necessary in an individuated movement to offset the forces induced by biarticular muscles and/or to offset the rotational forces that arise due to the motions of linked joints (interaction torques). In this sense, joint individuation is a more global measure of reaching performance relative to measures such as strength, sensation or spasticity. We think that the ability to individuate reflects specific motor control problems essential to a reaching movement.

Control subjects in our study were adept at individuating all upper extremity joint movements, although they performed best at the wrist and worst at the elbow. Wrist individuation might have been best because the mass of the hand is smaller than that of the forearm or upper arm, therefore movement at the wrist requires the least stabilization of proximal joints. As a result, wrist motions produce only small interaction torques at proximal joints (Virji-Babul and Cooke, 1995). In addition, the cross-sectional area and moment arms of wrist muscles are relatively small and cannot influence movement at the elbow to any great extent (Loren *et al*., 1996). Wrist motions may have induced movement at the fingers; however, evaluation of movement at the fingers was not done in this study. It is unclear why the elbow was most difficult to individuate. One possibility is that elbow motion requires control of biarticular muscles, whereas shoulder motion theoretically could be done using monoarticular muscles. However, this explanation does not address the fact that individuated movements at either of these joints would require stabilization of the non-moving joints to offset interaction torques (Almeida *et al*., 1995; Bastian *et al*., 2000). Another possibility may be related to long-term motor experiences of these subjects. For example, in day to day activities, it might be more common to move the shoulder while holding the other arm joints steady and less common to move the elbow while holding the other arm joints steady.

Hemiparetic subjects individuated all joint motions much more poorly than controls. When attempting to move any joint, they typically produced unwanted flexion at the shoulder and elbow. In some cases, these subjects flexed more at the non-instructed versus the instructed joint. Based on the typical clinical presentation of subjects with hemiparesis (distal arm/hand worse than proximal), one might expect that the wrist would have the worst individuation index. This was not the case in our subjects. However, we did not test whether the fingers remained stationary during wrist motion, and it is possible that hemiparetic subjects would show more concurrent wrist–hand motion compared with controls. It should also be noted that hemiparetic subjects' wrist joints showed the greatest reduction in active movement. Thus, in an absolute sense, the hemiparetic subjects were most impaired in moving the wrist. Finally, we did not study how well hemiparetic subjects produce the correct (instructed) movement at an individual joint (e.g. they may abduct when trying only to flex the shoulder). This was beyond the scope of this study, although it is an important issue for future work.

We found no correlation between the individuation index and spasticity; this would suggest that hyperactive stretch reflexes are not the cause of poor isolation of joint movement. In addition, we found poor correlations between the four impairments and months post-stroke, implying that hemiparetic subjects did not tend to improve their reaching ability simply with time since stroke. However, we did find a moderate correlation between the individuation index and strength. Strength deficits in this study could be caused by factors such as reduced corticospinal tract drive and also muscle atrophy. Hemiparetic subjects 09 and 15 are two of the three weakest subjects and have some of the poorest individuation indices (–0.81, and 0.36, respectively). However, this was not true for all subjects. Hemiparetic subject 02 did not follow this pattern (individuation index = 0.79); this subject was also extremely weak but was able to individuate better than subjects 09 and 15. Thus, strength might have affected individuation, but was not the only influence.

Parameters relating to reaching performance

Motor function following stroke historically has been assessed using clinical observations (Twitchell, 1951). Fugl-Meyer *et al*. (1975) developed one of the first systematic means of evaluating motor function in hemiparetic subjects; this system characterizes the quality of movements using a rating scale. Few investigators have attempted to dissociate which of the parameter(s) may be contributing to these movement deficits. In this study, reach path curvature was identified as the variable that best describes reaching performance, since it was a sensitive indicator of differences between control and hemiparetic subjects. Our data show that reaching performance was not correlated with the amount of time since the stroke (i.e. subjects who had more time to relearn or compensate were not necessarily better at reaching). We then determined whether specific impairments, including joint individuation, strength, spasticity and sensation, explain reaching abnormalities in hemiparetic subjects. We found that individuation scores and sensation explained most of the variance in reaching path curvature in hemiparetic subjects. It should be noted that we assessed sensation using monofilaments, which would directly reflect fine touch but not proprioception. We think that it is likely that both sensory modalities were impaired, but we cannot address the relative importance of the two. Further, individuation index and spasticity explain most of the variance in end point error in hemiparetic subjects. This suggests that in addition to making a smooth trajectory to the target (reach path), the end point error associated with a reach is also influenced by individuation ability. Finally, strength is the most influential factor to describe peak velocity, supporting the idea that poor strength leads to slower, although not necessarily poorly individuated, movements.

Conclusions

Our data show that subjects with hemiparesis perform reaching motions directed upward faster and straighter than those directed outward. Hemiparetic subjects tended to produce concurrent flexion motions when attempting any movement, providing one explanation for why they were better at reaching up (requiring shoulder and elbow flexion) versus reaching out (requiring shoulder flexion and elbow extension). Our analyses show that joint individuation deficits are most correlated with abnormal reaching performance, followed by sensory deficits. We conclude that hemiparetic subjects show distinct deficits in joint individuation that reflect a fundamental motor control problem explaining some aspects of voluntary reaching deficits of hemiparetic subjects.

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Sensorimotor Training in Virtual Reality: A Review

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Abstract

Recent experimental evidence suggests that rapid advancement of virtual reality (VR) technologies has great potential for the development of novel strategies for sensorimotor training in neurorehabilitation. We discuss what the adaptive and engaging virtual environments can provide for massive and intensive sensorimotor stimulation needed to induce brain reorganization. Second, discrepancies between the veridical and virtual feedback can be introduced in VR to facilitate activation of targeted brain networks, which in turn can potentially speed up the recovery process. Here we review the existing experimental evidence regarding the beneficial effects of training in virtual environments on the recovery of function in the areas of gait, upper extremity function and balance, in various patient populations. We also discuss possible mechanisms underlying these effects. We feel that future research in the area of virtual rehabilitation should follow several important paths. Imaging studies to evaluate the effects of sensory manipulation on brain activation patterns and the effect of various training parameters on long term changes in brain function are needed to guide future clinical inquiry. Larger clinical studies are also needed to establish the efficacy of sensorimotor rehabilitation using VR approaches in various clinical populations and most importantly, to identify VR training parameters that are associated with optimal transfer into real-world functional improvements.

Keywords

virtual reality; virtual environment; sensorimotor training; rehabilitation

1. Introduction

Virtual reality (VR) can be defined as an approach to user-computer interface that involves real-time simulation of an environment, scenario or activity that allows for user interaction via multiple sensory channels [1]. VR technology, and its application, is rapidly expanding across a variety of disciplines. Virtual environments (VEs) in VR can be used to present richly complex multimodal sensory information to the user and can elicit a substantial feeling of realness and agency, despite its artificial nature [2].

Virtual reality systems are generally classified by the visual presentations they provide to a participant, the presence or absence of somatosensory feedback and the modality used to collect

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data from the participant. Visual stimuli are grouped by the level of immersion. Two-dimensional presentations are considered non-immersive. Three dimensional presentations utilizing stereoscopic projections or displays with a fixed visual perspective are considered semi-immersive. Fully immersive systems allow for changing visual perspective with head movement. There are a myriad of methods of collecting data from a subject. Some systems utilize joysticks, hand controls or steering wheels. Motion tracking systems that utilize video and optoelectronic cameras, electromagnetic and ultrasound sensors, accelerometers and gyroscopes provide kinematic data. Instrumented gloves can add precision to tracking of hand motion. The data collected from these devices is used to control a computerized representation of the user or an avatar that represents their movements and interacts with the VE. Video capture virtual reality (VCVR) is a family of video camera based motion capture systems that record and digitize pictures of participants as they move, and transfer those images into a virtual environment, in real time [3]. These systems differ from other forms of VR in terms of their visual presentation which is a mirror image of the participant. Flicker glasses that display alternating right/left views of the picture or head-mounted visual displays (HMD) may be used for greater immersion (for both gait and upper extremity systems). The most immersive system is the CAVE (University of Illinois at Chicago) which is a room-size, 3D video and auditory system. Finally, newer systems that utilize robots to provide interaction forces between the user and VE are classified as haptic systems. Several systems like GENTLE-S [4], MIT-Manus [5] and PneuWREX [6] can be used to provide haptic effects during upper extremity activities in VEs. LOKOMAT (Hocoma) is a robotic exoskeleton, while CAREN System (Motek) utilizes self-paced motorized treadmills mounted on a 6 degree-of–freedom motion. These systems are designed to facilitate gait training, and both systems can be integrated with VE by presenting virtual locomotion scenarios displayed on a screen in front of the subject. The CAREN system can be combined with a harness for safety or body weight support.

Many disciplines of healthcare now rely on VR, such as for training surgeons [7], delivery of cognitive therapy [8], and delivery of post-traumatic stress disorder therapy [9]. The use of VR for sensorimotor training is a promising addition to its already broad utility in healthcare. Initial investigations into this family of approaches to rehabilitation emerged in the mid 1990's. Several reviews summarize the first generation of this research [3,10–13], with more recent systematic reviews examining the clinical efficacy of sensorimotor training in VE for rehabilitating upper extremity function [14] and gait [15] after stroke. This review adds to the existing literature by integrating the above studies with more recent reports, some emanating from our laboratories, that discuss how spatial and temporal manipulations in VR may be used intelligently to enhance sensorimotor training, and how they can be interfaced with robotics for rehabilitation purposes. We conclude with a discussion of the development and efficacy of telerehabilitation applications, which can be interfaced with VR to improve the accessibility of VR to the broader patient population.

2. Why might training in VR be beneficial for restoring neural function?

Recent studies show evidence of the potential of VR-based interventions to benefit patients with disordered movement due to neurological dysfunction. Known neurophysiological and behavioral benefits of movement observation [16–18], imagery [19], repetitive massed practice and imitation therapies [20] in facilitating voluntary production of movement can be easily incorporated into VR to optimize the training experience and allow the clinician to use sensory stimulation through VR as a tool to facilitate targeted brain networks, such as the motor areas, critical for neural and functional recovery. The potential for functional recovery can be optimized by tapping into a number of neurophysiological processes that occur after a brain lesion, such as enhanced potential for neuroplastic changes early in the recovery phase and stimulation of sensorimotor areas that may otherwise undergo deterioration due to disuse. VR may be useful in a number of ways to deal with these processes and potentially trigger compensatory neuroplastic changes.

2.1 Mass practice

Animal and human studies have shown that important variables in learning and relearning motor skills and in changing neural architecture are the quantity, duration and intensity of training sessions. There is evidence to demonstrate that plasticity is “use-dependent” and intensive massed and repeated practice may be necessary to modify neural organization [21–27]. The importance of intensity and repetition has also been confirmed for stroke patients in the chronic phase [28] in the treatment paradigm referred to as constraint-induced-movement-therapy (CIMT). Use-dependent cortical expansion has been shown up to 6 months after 12-days of CIMT therapy in people post stroke [29]. Dependence on existing therapies alone to promote neuroplastic changes might not always be practical. For example, changes at the synaptic level are evident in the rodent brain after the animal is exposed to thousands of repetitions of a given task over a short interval of time, i.e. 12,000 repetitions over 2–3 days [22,30]. In stark contrast, the affected extremity is moved at best 1–2 hours/day in the weeks after stroke [31,32] and as few as 10–20 repetitions per training session in the chronic phase [33]. More than 50% of this time is spent on rehabilitating the lower extremities and balance rather than the hand [34–36]. Use of VR as a training environment may provide a rehabilitation tool that can be used to exploit the nervous systems' capacity for sensorimotor adaptation by providing a technological method for individualized intensive and repetitive training.

2.2 Dynamic and operant conditioning of skill

In addition to the training intensity and volume necessary to induce neural plasticity, sensorimotor stimulation must involve the learning of new motor skills. Empirical data strongly emphasize that learning new motor skills is essential for inducing functional plasticity [30, 37,38], therefore, it appears that critical variables necessary to promote functional changes and neural plasticity are the dynamic and adaptive development and formation of new motor skills. It is believed that adaptive training paradigms that continually and interactively move the subject's performance toward the targeted skill are important to optimize re-learning of motor skills [39]. Once again, VR-based applications can provide adaptive learning algorithms and graded rehabilitation activities that can be methodically manipulated to meet this need.

2.3 VR delivered during critical periods to augment neuroplastic changes

One of the central problems facing patients and clinicians is that most interventions are impractical to deliver to patients at perhaps the most opportune time, that is during the acute phase of stroke when the potential to harness neuroplastic changes is greatest but during which phase the patient is too paretic to perform hand training. If the same principle that is apparent in the developing nervous system of cats applies to the lesioned adult cortex of humans, that lack of stimulation to motor cortex during a critical period leads to lost corticospinal synaptic connections [40] and that stimulation of motor cortical networks during the same critical period can reinstate some of these otherwise lost connections [41],then the acute paretic phase in stroke may perpetuate functional and neural deterioration simply due to absence of cortical stimulation.

The above sections provide an overview of the multifaceted components in skill re-acquisition, such as mass practice, rich environments, and timing of VR delivery that may mediate neuroplasticity following a lesion. The versatility of VR in these respects offers the clinician various ways to modulate brain reorganization. However, perhaps an even more appealing aspect of VR is its versatility in presenting complex sensory stimulation, through a combination of visual, somatosensory (haptic), and auditory feedback. Intelligent manipulation of these parameters may offer the clinician a yet unattained level of control over the therapeutic efficacy of a given intervention. The current state of the art in using these approaches is reviewed below.

3. Effects of visual augmentation on neural circuits

In order to understand the potential of VR to benefit recovery at the functional outcomes level in patient populations, one needs to understand the neural processes that VR may be affecting and, in the case of patient populations, how VR may affect recovery at the neural level. A related and equally important question is whether interacting in VR engages similar neural circuits to those recruited for actions performed in the real-world.

The "wiring" of the brain lends nicely to using visual feedback in VR to augment distributed, but interconnected, cortical regions. For example, retrograde tracer studies show rich intra-hemispheric cortico-cortical connections that link occipital, parietal, and frontal cortices [42–44]. Moreover, single unit recordings demonstrate that a substantial number of motor, premotor, and parietal neurons are modulated by visual information [45–48], suggesting that visual information can provide a potent signal for reorganization of sensorimotor circuits. At the behavioral level, movement errors in the visual domain can influence motor cortical areas during motor learning [49–53] and active / rewarded practice, can be used to reduce movement errors through feedback, and can shape neural activity in motor and premotor areas [50,54]. Finally, even observation of actions (images and video clips), if performed repetitiously and intentionally, can facilitate the magnitude of motor evoked potentials (MEPs) and influence corticocortical interactions (both, intracortical facilitation and inhibition) in the motor and premotor areas [55–58]. This work provides a strong foundation for testing hypotheses on the possible effects that can be produced through visual feedback in VR and opens possibilities for clinical application.

An important consideration in the use of VR as a sensorimotor training tool is the quality of VE rendering compared to what we are used to perceiving in the natural world. In other words, the fidelity of the VR environment may be an important factor in its effectiveness to recruit neural circuits and deliver desirable outcomes at the functional level. Although VE can be used to provide sophisticated visual information to users and elicit a feeling of real presence [2, 59], some work suggests that observation of actions performed by virtual effectors (i.e. the hand) may be less effective in recruiting neural circuits than observation of real hand actions [60]. In a study by Perani, the authors used fMRI to measure the blood oxygen level-dependent (BOLD) signal as subjects observed high-fidelity and low-fidelity renderings of a virtual hand perform a reaching task and compared these conditions with a control in which subjects observed real hand actions. The authors found that both virtual conditions produced significantly smaller activation in the frontoparietal circuit that was recruited in the `real' condition.

However, other evidence suggests that sensorimotor training in VR may actually have similar effects to those noted after real-world training. This evidence comes from several domains. First, studies that have compared the kinematics of movements performed during interaction in a virtual visual environment to those when acting in the real world have found remarkable similarities. For example, healthy subjects responding to targets moving at different velocities exhibit similar movement time, path curvature time, time to peak velocity, and reactions times whether the task is performed in a VE or in the real world [61]. Interestingly, stroke patients' kinematics for reach–to-grasp movements also show similarities in peak wrist velocity, angular shoulder/elbow relationship and maximum grip aperture when acting in the virtual versus a real environment [62].

In two studies performed on persons with stroke, functional improvements following VR training were paralleled by a shift from a predominantly contralesional sensorimotor activation pre-therapy to a predominantly ipsilesional activation post-therapy [63,64]. Similar shifts in hemispheric lateralization are observed after therapy performed in the real world [65,66], suggesting that training an affected limb in VR may tap into similar neural reorganization processes as observed after training in the real world.

Our own work extends this by demonstrating that interacting with virtual representations of ones own hands in VR recruits brain regions involved in attribution of agency [67]. To study such brain-behavior interactions, we integrated our VR system with fMRI and asked thirteen healthy subjects to observe, with the intent to imitate, finger sequences performed by the virtual hand avatar seen in 1st person perspective and animated by pre-recorded kinematic data. These blocks were interleaved with rest periods during which subjects viewed static virtual hand avatars, control trials in which the avatars were replaced with moving non-anthropomorphic objects, or with blocks in which subjects imitated the finger sequence under the above feedback condition. Our data showed a time-variant increase in activation in the left insular cortex for the "observe with the intent to imitate" condition but not in the other conditions. Moreover, imitation with veridical feedback from the virtual avatar (relative to the control condition) recruited the angular gyrus, precuneus, and extrastriate body area, regions which are (along with insular cortex) associated with the sense of agency [68]. Thus, the virtual hand avatars may be useful for sensorimotor training by serving as disembodied tools when observing actions and as embodied "extensions" of the subject's own body (pseudo-tools) when practicing the actions.

The above data inform of potentially useful applications of visual manipulation in VR. For example, intentional observation of movement can be used to stimulate the sensorimotor system without necessitating overt movement itself. Adding more sophisticated manipulations in VR, such as to the color/brightness of objects, their location, form, perspective (1st versus 3rd person), temporal/spatial distortions of the movement trajectory, and feedback replays, can perhaps potentiate these effects in ways that cannot be achieved in the natural world. For example, simulating forward motion by using an optic flow field, and manipulating the speed of the illusory motion during gait training in stroke patients, one can facilitate either faster or slower walking speeds [69].

Another example of a sophisticated VR-based manipulation emerges from an intervention called mirror visual feedback therapy, introduced by Ramachandran and coworkers [70] for amputee and stroke patients. We developed a virtual mirror feedback interface and have used it in conjunction with fMRI to study the effects of this form of visual feedback on neural circuits. In our study [71], a stroke patient performed movements with the unaffected hand that, with the aid of manipulations in the VE, animated either the corresponding or contralateral virtual hand model (in real time). Our findings revealed that activations in the sensorimotor cortex of the affected hemisphere (the "inactive" cortex) were significantly increased simply by providing feedback of the contralateral hand. This effect was also evident in healthy subjects. In a follow up experiment, we measured the MEPs in motor cortex [67], as healthy subjects were exposed to the same feedback conditions as in the fMRI study. Our data indicated that MEPs were substantially increased in both feedback conditions (corresponding and contralateral virtual hand models) but that the MEP amplitude increased by about 8% more in the contralateral relative to the corresponding feedback condition. This is in direct line with similar studies that have used a real, rather than a virtual, mirror feedback setup [72–74] and adds to the body of evidence that suggests that sensorimotor training in VR may have similar effects on neural circuits to real-world training. The advantage of VR, however, is its versatility to allow more control over the type of feedback.

Studies on the use of non-VR presentations of visual stimulation support the possibility of this type of training. A study of horizontally flowing visual information on healthy persons that were stationary produced activation of the visual cortex and a corresponding decrease in the vestibular areas in a PET scan study by [75]. The authors postulated that this was a strategy to resolve the sensory conflict produced by these conditions. Brandt et al. showed activation of adjacent areas of the visual cortex and deactivation of multisensory vestibular centers in a PET scan study of healthy persons in response to large field optokinetic stimuli [76]. Similar findings were described by Konen et al. in an fMRI study of normal responses to optokinetic stimulation and pursuit/scanning type movements [77]. In an fMRI study of persons with chronic bilateral vestibular failure, subject's visual cortex activation was stronger in response to simulated visual motion than in healthy controls. The investigators describe this as an up-regulation of sensitivity to visual stimuli as a compensation for a lack of vestibular information [78]. Each of these studies support the use of visually simulated movement to elicit this functional activation/deactivation pattern when the brain is presented with conflicting information (simulated visual motion in a stationary subject).

4. Visual Feedback Only in VR

The preponderance of evidence for the therapeutic use of VR has come from intervention studies in the stroke patient population. The reason for this is in part attributed to the high prevalence of stroke and the particular challenges that upper extremity movement deficits pose to rehabilitation. Given the above, the following sections are weighted in reviewing VR applications for stroke populations, however, where data is available for other patient populations, we review those as well. Although the evidence generally supports VR's efficacy in retraining upper extremity (UE) function after stroke, the majority of these studies include case studies, small feasibility studies, or studies without strong control groups. Stroke rehabilitation training programs are most effective when requiring practice regimens that both engage and increasingly challenge the patient [79]. VR can aid in this sense by systematically adapting task difficulty to the patient's ability as he/she progresses through training and by providing a motivational factor to encourage longer engagement in the exercises than would otherwise be seen in a real-world environment [80].

Multiple authors describing the training of upper extremity reaching and functional activities in virtual environments have shown that motor skills can be learned through repetitive practice within both immersive and non-immersive and visually simple and complex virtual environments (see [14] for an extensive review). More recent studies have also shown similar results. Stewart et al. [81] describe a VR system that allows subjects to perform complex 3-dimensional tasks involving object manipulation and / or reaching. Following a twelve session intervention with this system, one of the two pilot subjects demonstrated improvements at the impairment and functional level. Piron and colleagues compared a group of subjects less than 3 months after a middle cerebral artery stroke[82]. Twenty-eight subjects performed upper extremity rehabilitation activities in a visual and auditory based, 2-dimensional virtual environment and a second group of 13 subjects performed a comparable volume of conventional upper extremity rehabilitation. The VR rehabilitation group made statistically significant gains on impairment (UE Fugl-Meyer) and functional independence measures (FIM) while the conventional rehabilitation group made smaller, non significant improvements in these measures.

These studies have focused on upper extremity training. Because of fiscal constraints, current service delivery models favor gait-training and proximal arm function [17]. However, the impact of even mild to moderate deficits in hand control effect many activities of daily living with detrimental consequences to social and work-related participation. In our own laboratory, a group of eight subjects with mild to moderate hemiparesis secondary to stroke performed 13 sessions of sensorimotor training in virtual environments that provided rich visual feedback as the subjects played 5 game-like activities targeting independent finger flexion, finger strength, and finger extension speed. Subjects improved in measures of independent finger flexion, finger speed, strength and range of motion measured during training tasks as well as in kinematic measures of reaching and grasping and clinical tests of upper extremity function [83]. The Jebsen Test of Hand Function (JTHF) [84], a timed test of hand function and dexterity, was used to determine whether the kinematic improvements gained through practice in the VE measures transferred to real world functional activities. After training, the average time the subjects needed to complete the six subtests of the JTHF with their hemiplegic hand decreased significantly. In contrast, no changes were observed for the unaffected hand. The subjects' affected hand improved from pre-therapy to post-therapy on average by 12% [85].

We have recently developed a second generation of this system. The piano trainer is a refinement and elaboration of one of our previous simulations [83]. The new version consists of a complete virtual piano that plays the appropriate notes as they are pressed by the virtual fingers. The position and orientation of both hands as well as the flexion and abduction of the fingers are recorded in real time and translated into 3D movement of the virtual hands, shown on the screen in a first person perspective. The simulation can be utilized for training the hand alone to improve individuated finger movement (fractionation), or the hand and the arm together to improve the arm trajectory along with finger motion. This is achieved by manipulating the octaves on which the songs are played. These tasks can be done unilaterally or bilaterally. Other simulations provide practice in the integration of reach, hand-shaping and grasp using a pincer grip to catch and release a bird while it is perched on different objects located on different levels and sections of a 3D workspace.

In addition to upper extremity movement deficits after stroke, spatial neglect is another common syndrome following stroke, most frequently due to damage of the right hemisphere. Up to two-thirds of patients with acute right-hemisphere stroke demonstrate signs of contralesional neglect, failing to be aware of visual, auditory and or tactile stimuli coming from left of their midline in extrapersonal space. Hemispatial neglect has profound effects on the patient's ability to interact with and respond to their environments [86]. VR simulations have been employed with some success in several studies for both the assessment and treatment of visuo-spatial and visuo-motor neglect [87]. With manual exploration tasks, VR applications can detect small variations in performance undetectable by standard paper and pencil tests [88]. Training in VR has shown improvement in learning to cross a busy street, with left to right ratio scores (the ratio of objects seen on left to those seen on right) decreasing [89] and in reaching and grasping activities, where after training patients were able to code objects in the neglected space identically to those presented in their preserved space [90]. However, it was found that only patients without lesions in the inferior parietal/superior temporal regions benefited from this last training paradigm.

VR neglect intervention is not limited to ambulatory patients. Virtual environments have been used to assess spatial attention and neglect in wheelchair navigation. Here the subjects were asked to navigate a virtual path, encountering objects of varying complexity while in a wheelchair [91]. The VR navigation task was shown to have a strong correlation with the live wheelchair navigation task, and was able to detect deficits in mild patients. This implies VR shows promise as an efficient, sensitive measure of assessment and training for spatial neglect.

A patient's gait, or walking pattern, can be significantly altered after a stroke. Virtual realty (VR) offers a variety of methods to assess and improve several aspects of patient gait post-stroke. VR offers significant advantages over the traditional, qualitative, low intensity methods of physical therapy. VR enables the therapist to control duration, intensity, and feedback during specified treatment. The best VE is one that immerses and engages the subject in a realistic manner. To this end several modalities of human-computer interface have been employed [15]. Environments simulating both city and rural landscapes have been used for gait

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rehabilitation after stroke. These environments are used to retrain gait by providing visual cues to augment gait parameters such as stride length and walking velocity, as well as objects in the environment to augment obstacle avoidance. Walking speed is often severely reduced after stroke. Perception of the speed of one's environment has been shown to have an influence on the modulation of walking. Several VR studies have been conducted to quantify this effect. One study used VR to make continuous adjustments to the perception of optic flow speed [92]. Tests showed an inverse relationship between the VR optical flow speed and the walking speed, of patients after a stroke, though the correlation was weaker than that found in healthy subjects. In more recent studies, VE complexity of the city and rural landscapes has grown to include more life-like scenarios of street walking, collision avoidance and park strolling. In a small study, using scenarios of walking in a corridor, a park and across a street, and a motorized treadmill and a 6 dof motion platform, patients benefited from this practice by increasing their walking speed and adapting their gait to the changes in the terrain [93].

4.1 Use of visual feedback in VR to treat Cerebral Palsy

Children with Cerebral Palsy (CP) have difficulty controlling and coordinating voluntary muscle activity. In neuro-rehabilitation, these difficulties combined with the typical mentality of a child, can make this population challenging. Traditional therapies for muscle movement are repetitive and offer very little to keep a young mind occupied. Interactive VEs can provide a much wider array of activities and scenarios for muscle movement. In a selective motor control study of CP patients [94], children were asked to complete several ankle exercises using both video capture based training and conventional programs. While conventional therapy yielded more repetitions of the required exercises, the range of motion and hold time of stretch positions were greater in the VR group, thus the benefit of any movements was much greater during the VR exercises.

Approximately 50% of all children with CP sustain upper-extremity dysfunction to some degree [95]. VR's application extends well into this large area of neuromuscular rehabilitation. We have written above about the motivating advantages to VR. This obviously extends to UE exercises. A recently completed study was able to incorporate commercially available video games into their treatment regimen [95]. The study also revealed that to detect the full benefits of VR in a patient can require more sensitive diagnostic methods than are normally employed in physical and occupational therapy (e.g. Peabody Developmental Motor Scale, QUEST exam).

In addition to measurable changes in physical activity, VR has also shown promise in effecting neuroplasticity in CP patients. fMRI analysis, prior to VR training of the upper extremity of a child with hemiplegic CP, showed predominately bilateral activation of the sensorimotor cortices and ipsilateral activation of the supplementary cortex. After training in a video capture-based VR system, this bilateral activation disappeared and the contralateral sensorimotor cortex was activated [96]. These recorded changes were closely associated with enhanced ability of the subject to perform reaching, dressing, and self-feeding tasks. VR's ability to create widely varying scenarios with a spectrum of difficulty also lends itself to gait training in CP patients [97].

4.2 Use of visual feedback in VR for posture and balance rehabilitation

The appropriate control of posture and balance underlies most functional skills and is achieved through timely integration of sensory information. For fall prevention, this integration requires rapid recalibration of visual, vestibular and somatosensory information. Disorders of the nervous system and aging lead to impairments in this mechanism. VR can be used in several ways to re-train postural control and balance. First, VR can be used to manipulate visual feedback to produce conflicts between visual, somatosensory and vestibular information as a

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way to train different sensory systems. Second, VR feedback can be systematically graded (in terms of speed and complexity) in order to challenge a person's static and dynamic postural control over the course of sensorimotor training.

Small sample investigations on the ability to manipulate visual stimuli in order to evoke conflict between visual, vestibular and somatosensory systems and corresponding changes in vestibular symptoms or postural responses have produced promising results. Scanning in complex visual environments can produce sensory conflict. Whitney et al. found that training in immersive VR may be useful for habituation activities for persons with visual/vestibular impairments. Using an immersive grocery store simulation, a subject with sub acute labyrinthine dysfunction experienced comparable symptoms to those she experienced in a real world grocery store. There was a correlation between the visual complexity of the simulation and her symptoms as well. Interestingly, a second subject with a more chronic lesion had adapted to this conflict and did not experience symptoms in this environment [98].

Immersive VR systems producing flow past a user's peripheral visual fields also produce a sense of motion similar to the optokinetic stimuli described by Brandt and Dieterich [76,78]. The perception of self motion this information creates can be manipulated in VE to elicit specific postural adjustments for training and rehabilitation purposes. In a study on healthy subjects visual stimuli that produced a conflict with simultaneous somatosensory and vestibular signals generated by horizontal motion elicited much stronger postural corrections measured by EMG than those produced by either horizontal motion or simulated visual motion alone [99]. In another study on twelve healthy subjects, center of pressure and perception of vertical measured with a wand in the subjects' hand was collected as subjects were presented with optic flow in three planes (yaw, pitch and roll). The effect of complexity of the visual flow patterns on postural response and perceived vertical was greatest in the roll plane and much less robust in pitch. Responses to varying levels and complexities of visual flow in the pitch plane varied significantly between subjects [100]. A third study by Keshner and colleagues described an increased effect of visually simulated motion on postural responses when subject base of support was decreased, making them more dependent on the erroneous, simulated visual information [101].

Mulavara et al. examined the responses of 30 healthy subjects to linear or rotating patterns of optic flow while walking straight on a treadmill. Subjects demonstrated adaptation to the condition of flow they were presented. Subjects displayed a consistent right bias on an eyes closed stepping task immediately following walking with a right rotating pattern of optic flow, and subjects presented with linear flow in the same plane and direction of their walking displayed no consistent bias [102]. These studies, illustrate the ability of immersive virtual environments to impact the integration of visual, vestibular and somatosensory inputs and subsequent postural responses. The incorporation of this element into rehabilitation programs with the goal of hastening the adaptation process in persons with vestibular pathology and to train postural responses in persons with balance impairments are the logical “next steps” for this line of inquiry.

Several authors discuss the use of balance training interventions using VR in a variety of populations. Oddsson et al. studied balance training in a tilted room environment simulated by lying on a surface that eliminated friction while being presented with virtually simulated immersive visual environments. Healthy subjects trained in the virtual environment made improvements in mediolateral critical time with eyes closed [103]. Training in VR allows for the safe and systematic training of sitting balance in persons with SCI. Kizony et al. studied the feasibility of applying VCVR technology for balance training in persons with paraplegia in a study with 13 subjects. Subjects utilized three 3D simulations, two that involved reaching for moving targets and a third that utilized trunk movement to control a snowboard. Users expressed that they enjoyed utilizing the equipment and reported high levels of presence during the activities. The subjects' scores on the simulations correlated well with their performance on a seated functional reaching task, suggesting that their real world balance and ability to perform the simulations measured a similar construct [104].

Several studies describe simple virtual rehabilitation interventions for persons with other neurologic pathologies. Fulk reported a case utilizing a VR-based balance intervention for a woman with MS. The subject performed a 12 week course of bodyweight supported ambulation training combined with non-immersive balance activities [105]. The subject improved her gait speed, endurance and standing balance measures. Thornton compared VR-based balance interventions and clinical balance activities in a group of patients with traumatic brain injuries. Two groups performed either activity based balance training or balance exercises in a 2 dimensional VR system. VR participants expressed higher degrees of enjoyment, made larger improvements on quantitative measures of balance and scored higher on balance confidence measures [106]. Pavlou et al. performed a comparison of conventional vestibular rehabilitation activities and exposure to visual vestibular conflict produced by an immersive VR system as part of a simulator based treatment that also included rotary chair and other whole body movement simulations. The VR / simulator treatment group made larger changes on posturography tests and larger improvements in symptoms intensity questionnaires than the conventional rehabilitation group [107].

The safety of VE-based balance training also makes it an effective tool for fall prevention interventions in elderly populations. VE can provide distracting environments or additional cognitive tasks, two conditions associated with increased frequency of falls in the elderly. Bisson and colleagues studied two groups of elderly subjects, one that trained on balance activities using visual biofeedback displaying force-plate data and a second performing juggling activities that required lateral reaches in a VCVR environment. Both groups achieved statistically significant improvements in reaction time, and the Community Balance and Mobility Scale [108].

5. Integration of Vision and Haptics in VR

A major development in the use of virtual environments has been the incorporation of tactile information and interaction forces into what was previously an essentially visual experience. Robots of varying complexity are being interfaced with more traditional VE presentations to provide haptic feedback that 1) enriches the sensory experience 2) adds physical task parameters and 3) provides forces that produce biomechanical and neuromuscular interactions with the virtual environment that approximate real world movement more accurately than visual only VE's.

Simple haptic feedback can be utilized to add the perception of contact to skills like kicking a soccer ball or striking a piano key. Lam et al. describe a system that utilized vibratory discs to simulate the feeling of impact during this type of game. The authors cited advanced skill learning in a group of healthy subjects training with added tactile feedback [109]. Adamovich et al. used a force reflecting exoskeleton that simulates contact with piano keys [110]. Collisions with virtual world obstacles can also be used to teach normal movement trajectories such as the action required to place an object on a shelf [68] or step over a curb [111].

Some previous approaches utilized virtual tutors to model ideal trajectories [112,113]. Using haptic obstacles to indirectly shape trajectories may avoid the effects of the explicit, cognitive process associated with presenting a model, into what is usually an implicit process [114]. Further investigations into this potential advantage are necessary because of the significant increases in cost associated with adding haptic effects to virtual rehabilitation applications. Haptic environments can also exert global forces on the user such as antigravity support and viscous stabilization forces. This allows more disabled subjects to exercise reaching and object manipulation in 3D space, which invokes muscular force synergies that are typically used and, advertently, more appropriate neuromuscular feedback as well. Several authors employ these concepts in VR simulations designed to train reaching, grasping, and lifting. Wolbrecht et al. describe a haptic robotic interface that provides anti-gravity assistance as needed to lower functioning persons as they interact with virtual environments. They tested this approach on nine persons with chronic hemiparesis secondary to stroke. As a group these subjects improved on kinematic measures during robotic training and clinical measures of upper extremity function [6]. Our laboratory has investigated the feasibility of this “assist as needed” approach for the arm [68] as well as the hand [110]. Subjects in both studies performed extended training periods in a short period of time without adverse effects and made similar kinematic and real world functional improvements.

Other tasks involve contact and interaction with tools to achieve movement goals. In the real world, object manipulation produces an interaction between user and object that is unique (e.g. the angular momentum of the head of hammer). Haptics can simulate the interaction forces produced by tools in virtual environments. Lambercy et al. describe a haptic knob that can be applied to manipulate objects that vary in size and shape allowing for customization based on therapeutic goals [115]. Haptic forces can also be synchronized with visual feedback to improve a users' sense of agency in the virtual world. In two small studies involving healthy subjects, this feedback combination was found to be more effective for skill learning than visual only feedback in healthy subjects [116,117]. The distortion of forces in a virtual environment is another line of inquiry afforded by haptics. Patton et al. found that haptic forces that augmented the errors of subjects with strokes were more effective in teaching desired trajectories than haptic forces that guided subjects toward these trajectories. These effects were found in simple two dimensional VE [118] and an immersive three dimensional VE [119].

Our laboratory has developed a VR system that utilizes visual and haptic feedback for the sensorimotor training of the hemiparetic upper extremity, specifically to train arm reaching and hand manipulation in three-dimensional space. For the upper arm training, each subject trained using 2 different, 3-dimensional virtually simulated reaching activities over the course of eight or nine sessions. Task one had subjects pick up cups off of a haptically rendered table and place them on haptic shelves. Collisions with the table shelves and other cups were solid, forcing subjects to alter their trajectory to complete the task. Task two required subjects to move through a standardized set of targets with no obstacles. In a group of four chronic stroke subjects [68], subjects demonstrated a 36% improvement in task duration, and a 45% improvement in hand trajectory smoothness on the task with no obstacles. The same subjects demonstrated a 42% reduction in task duration, and a 70% improvement in hand trajectory smoothness during the task that utilized haptic obstacles. These subjects seemed to respond to the independent condition of haptically rendered obstacles with more efficient learning. Future studies of this concept should include a larger sample, generalization testing and measurements of motor control.

For practice in hand manipulation, for patients with greater impairments, the piano trainer (see page 6) can be combined with a force reflecting exoskeleton that can inhibit mass grasp patterns and/or provide for haptically rendered finger tip collisions. In a proof of concept study, three of our subjects utilized the CyberGrasp exoskeleton to facilitate extension of their inactive fingers while utilizing the virtual piano trainer for eight to nine, sixty to ninety-minute sessions. Each of these three subjects were in the chronic stage of their stroke recovery and were classified as level 5 hemiparesis for their arms and level three hemiparesis for their hands using the Chedoke McMaster Stroke Impairment Inventory [120]. Two of the three subjects made improvements in their scores on the Jebsen Test of Hand Function (by 13% and 11 %). It appears that further investigation of this approach for persons with moderate upper extremity hemiparesis is warranted.

It is controversial whether training the upper extremity as an integrated unit leads to better outcomes than training the proximal and distal components separately. Current rehabilitation practice describes the need to develop proximal control and mobility prior to initiating training of the hand. During recovery from a lesion the hand and arm are thought to compete with each other for neural territory. Therefore, emphasizing initial proximal training may actually have deleterious effects on the neuroplasticity and functional recovery of the hand. However, neural control mechanisms of arm transport and hand-object interaction are interdependent. Therefore, complex multisegmental motor training is thought to be more beneficial for skill retention. We used this system to examine the effectiveness of training the hand and arm as a functional unit. The virtual simulations used in this protocol include; 1) a three dimensional pinching task, (the arm transports the hand to the appropriate place to catch a flying bird and the fingers perform a pinching movement to place it on a tree), 2) a pong based game (the arm moves to control the paddle and finger extension engages the paddle allowing participants to compete with a live or computerized opponent, 3) a realistic full sized virtual piano keyboard and 4) a three-dimensional hammering game, in which the arm controls the position of the hammer in 3D space and finger flexion and extension controls the rotation of the hammer as it interacts with the target.

In an ongoing study, a group of 8 subjects with chronic strokes resulting in mild hemiparesis (mean Jebsen Test of Hand Function (JTHF) score = 152), trained for three hours in each of 8 sessions over two weeks using these 4 simulations. Each subject demonstrated improvements in robotically collected kinematics but more importantly, the group demonstrated a mean improvement in JTHF of 21% (SD=15%) and a corresponding improvement in Wolf Motor Function Test Aggregate Time of 24% (SD=11%) (unpublished observations). This data compares quite favorably to a study we published previously [83,121], in which we trained subjects using an earlier iteration of our system practicing tasks that emphasized finger movement only. Eight chronic subjects with a similar level of mild hemiparesis (JTHF pre-test of 140) performed a comparable volume of training resulting in a 10% improvement in JTHF time, approximately half of the improvements experienced by the subjects using our total training approach.

5.1 Use of visual and haptic feedback in VR for gait rehabilitation

Several interesting studies have been generated evaluating the integration of the LOKOMAT, a robotic gait orthosis and virtual environments. Wellner et al. describe a series of experiments manipulating point of view, haptic collisions and augmented auditory feedback with a group of healthy subjects as they step over virtual obstacles with a goal of developing an optimal training program for gait rehabilitation. Subjects in these experiments were more successful when provided with haptic feedback from collisions with the virtual obstacle, and with a lateral view of themselves and their obstacle during training. Furthermore, subjects expressed that auditory feedback that cued them regarding increased gait speed and the distance to approaching obstacles was helpful [111]. Tierney et al. describe the design of a system for the gait rehabilitation of persons with strokes utilizing a partial body weight support system. The authors propose that the normalization of gait speed afforded by BWS gait training, paired with semi-immersive virtual environments simulating real-world ambulation situations may provide more ecologically valid stimuli for gait rehabilitation (unpublished observations).

It is not clear which component of this system provides the positive effects - the robotic assistance or the VR. Mirelman et al. described an additive effect of VR simulations to robotic training for gait when compared to a similar volume of robot-only training [122]. This study compared two groups of subjects with strokes who performed ankle exercises utilizing the

Rutgers Ankle, a six degrees of freedom robot. Nine subjects performed these activities in a VE. Nine more performed the same program receiving knowledge of results and performance feedback from a therapist. VE group subjects made larger improvements in gait speed, six minute walk test and community ambulation distance as measured by a pedometer. All of these comparisons reached statistical significance and were maintained at three month follow-up. Six of the nine subjects in the VE group made improvements in their gait velocity that were large enough to change their functional ambulation category as defined by Perry et al. [123].

5.2 Use of visual and haptic feedback in VR to treat Cerebral Palsy

A critical limitation of the vision-only VR technology for the CP population is the high degree of motor function required to access many formats of this technology. One approach to overcome this issue is the interfacing of virtual environments with robotic assistance to allow participation of more involved patients. To date, only a handful of small studies have utilized interactive haptic environments to train children with CP. Our laboratory has investigated the feasibility of the combination of robotically facilitated movements with rich VE and complex gaming applications. Qiu et al. describe the experience of two children with the NJIT-RVR system. One of the children made a 45° improvement in active supination and the other subject demonstrated clinically significant improvements on the Melbourne Assessment of Upper Extremity Performance after training in VR for one hour per day, 3 days a week for three weeks [124].

One of the important assets of VE systems for the rehabilitation of children is their flexibility. Simple alterations to graphics and sound effects significantly improved time on task and attention levels in the children described above. For example, we have successfully developed and tested a reaching simulation where adults with strokes received adaptable robot assistance during reaching in three-dimensional space presented in stereo [110]. The same activity seemed to be not that interesting for CP children under 10. Adding simple sound and visual effects to the activity (simulating explosions of the target objects) was sufficient to substantially improve attention levels and compliance in this group of 8 children with hemiparetic CP. This flexibility will allow therapists to tailor the presentation of complex interventions to the developmental and cognitive constraints presented by the diverse group of CP patients.

In a recent study, Fasoli et al. (2008) describe a group of 5 to 12 year old children with UE hemiplegia secondary to CP performing16, sixty minute practice sessions in a simple virtual environment with assist as needed robotic facilitation over an eight week period. Each session, consisted of 640 repetitive, goal-directed planar reaching movements. Subjects demonstrated improvements in Quality of Upper Extremity Test and Upper Extremity Fugl-Meyer Assessment scores [125]. Finally, one study was able to use the LOKOMAT gait orthosis in conjunction with VE's to create a realistic haptic world designed to treat children with CP. Simulations utilizing this array included an obstacle course, wading in a stream, crossing a street and performing a virtual soccer activity. To date, proof concept studies performed on healthy subjects utilizing questionnaires have confirmed the realism of these simulations [97]

6. Telerehabilitation

Access to rehabilitation services in rural and other underserved areas is a critical healthcare issue. Telerehabilitation systems (TRS) are one of the approaches being developed to address this issue. Many TRS incorporate some form of VE in their presentation. Several authors have investigated upper extremity interventions utilizing TRS in pilot studies. Two studies examined the efficacy of TRS based interventions for the hemiparetic UE. In one study, impairment level and functional assessments approached statistically significant levels of improvement after TRS training of gross UE movements and finer grasping movements [112]. Carey et al. examined two groups performing finger exercise without direct supervision. The experimental group performed a tracking task presented via a TRS. Controls performed a home exercise program consisting of a similar volume of non-goal oriented finger movements. While clinical testing results were similar for the two groups, fMRI activation during a finger tracking task was higher in the TRS group after training. The results of this study indicate that even the simplest form of interactive visual feedback during sensorimotor training might be beneficial for facilitation of brain activation [126]. Heuser et al. utilized the Rutgers Master II, a haptic glove system, in a thirteen session telerehabilitation intervention that utilized VR simulations for 5 persons post surgery for carpal tunnel syndrome. Three of the five subjects made substantial strength gains measured clinically and all of the subjects expressed satisfaction with their telerehabilitation experience [127].

The studies above begin to establish effectiveness of TRS interventions but do not test for the independent condition of remote supervision. Deutsch et al. examined the effects of utilizing a TRS by having subjects with strokes perform ankle rehabilitation activities in a VE while supervised in person by a therapist. After three weeks of intervention the subjects performed the same protocol with remote supervision by a therapist. The subjects performance and the volume of activity performed during week four, the remote supervision week, was comparable to week three, suggesting that remote monitoring would not detract from the productivity of the session [15].

A study by Piron et al. compared 12 patients with stroke performing a remotely monitored telerehabilitation program for their hemiparetic UE, and another group of 12 subjects with stroke, performing a similar program of real-world UE activity in their homes supervised by a therapist. Both groups made comparable improvements in UE function and untrained reaching kinematics [128]. A second study by Piron et al. (2008) compared two groups of 5 subjects with strokes, one that trained UE movements in a VE while supervised in person by a therapist and a second performing the same VE simulated training program and supervised by a therapist remotely, using video-conferencing equipment. The TRS group in this study made statistically significant improvements in motor performance while the in-person supervision group changes were not statistically significant [129]. While each of these studies cites comparable or superior benefits for TRS, these studies were small indicating a need for further study with larger numbers of patients.

The use of telerehabilitation is in the nascent stage of development and implementation. While the results of these small VR-based studies examining the clinical effectiveness of TRS are promising it is important to note that large studies that have evaluated the cost effectiveness, and practicality of implementation of telerehabilitation services in comparison to hospital based services have shown mixed results [130].

7. Conclusions, limitations, and future directions

Virtual reality technology may be an optimal tool for designing therapies that target neuroplastic mechanisms in the nervous system, allow for mass practice and provide training in complex environments that are sometimes impractical or impossible to create in the natural world. They also allow for access to rehabilitation services through telerehabilitation. Computerized systems are well suited to this and afford great precision in automatically adapting task difficulty based on individual subject's ever changing performance. When virtual reality simulations are interfaced with movement tracking and sensing glove systems they provide an engaging, motivating and adaptable environment where the motion of the limb displayed in the virtual world is a replication of the motion produced in the real world by the subject. Virtual environments can manipulate the specificity and frequency of visual and auditory feedback, and can provide adaptive learning algorithms and graded rehabilitation activities that can be objectively and systematically manipulated to create individualized motor learning paradigms. Thus, it provides a rehabilitation tool that can be used to harness the nervous system's capacity for sensorimotor adaptation.

Virtual rehabilitation for movement disorders has been developing more slowly than virtual technologies in other areas of healthcare. In our opinion there are several factors underlying this trend. System development involves sophisticated interlacing between hardware and software which at the present time is expensive and requires considerable development expertise. The interdisciplinary nature of rehabilitation research also presents challenges. The design of interfaces to accommodate persons with impaired movement requires skills that span orthopedics, neuroscience, biomedical engineering, computer science and multiple rehabilitation disciplines. More studies are emerging to test VR's efficacy in rehabilitation, however, the effectiveness of these studies has not yet reached he higher levels of evidence found in large scale randomly controlled studies. The extent to which repetitive training offers neural and functional benefits beyond the novelty factor as well as the ability to integrate this form of therapy into a clinical setting remains unknown. Finally, and perhaps most important, the full potential of VR will only emerge after we gain a thorough understanding of how various sensory and haptic manipulations in VR affect neural processes. These issues should be a central focus of future investigations.

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The effect of asymmetry of posture on anticipatory postural adjustments

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Abstract

The study investigates the effect of body asymmetry on anticipatory postural adjustments (APAs). Subjects performed a task involving a standard load release induced by a shoulder abduction movement while standing symmetrically or in an asymmetrical stance with either their right or left leg in 45° of external rotation. EMG activities of trunk and leg muscles were recorded during the postural perturbation and were quantified within the time intervals typical of APAs. Anticipatory postural adjustments were observed in all experimental conditions. It was found that asymmetrical body positioning was associated with significant asymmetrical patterns of APAs seen in the right and left distal muscles. These APA asymmetries were dependant upon the side in which the body asymmetry was induced: reduced APAs were observed in the leg muscles on the side of leg rotation, while increased APAs were seen in the muscles on the contralateral side. These findings stress the important role that body asymmetries play in the control of upright posture.

Keywords: Posture; Anticipatory postural adjustments; Human

A large number of individuals with functional and anatomical limitations secondary to stroke, cerebral palsy, cancer, scoliosis, arm or leg amputation, traumatic brain injury, cerebellar disorders, and degeneration or trauma of the lumbar or cervical spine all demonstrate pronounced postural asymmetries. Asymmetry in upright posture is associated with various outcomes such as decreased loading of the affected side in stroke [11], degenerative changes of the hip, knee, and ankle joints and spine, or a leg length discrepancy [14,16]. Other examples of disease-related asymmetries are pelvic tilt, which is common in individuals with hemiparesis, and internal or external leg rotation that is often associated with a stroke or cerebral palsy. It is believed that pronounced body asymmetries attribute to postural imbalance. Thus, experimental data regarding the effect of asymmetry of posture on APAs in these populations would provide valuable information that could be used to refocus conventional rehabilitation strategies. Moreover, the effect of disease-related body asymmetries on anticipatory postural control is mainly unknown. This is probably due to the difficulties that researchers face when studying individuals with pronounced disease-related body asymmetries. For example, unilateral leg amputation does not allow recording EMG activity from both lower extremities or unilateral arm impairment in individuals with stroke makes it harder for them to use both hands to perform experimental tasks. To overcome these difficulties, we studied the anticipatory postural control of healthy subjects who simulated a body asymmetry, 45° of external leg rotation, commonly observed in individuals who have had a stroke. In this study, we used a procedure involving self-induced perturbations that triggered a standard perturbation which was associated with pronounced APAs; this paradigm has been described and studied in detail [6,7].

Six healthy subjects (three female, three male) between the ages of 22 and 27, without any known neurological or muscle disorders, performed motor tasks after giving informed consent approved by the Institutional Review Board of the University of Illinois at Chicago.

The subjects stood barefoot and were instructed to release a 5.0 LB load (dimensions $0.22\,m \times 0.15\,m \times 0.12\,m$) from both hands with their arms extended in front of their bodies using a low-amplitude, fast, bilateral shoulder abduction movement. In the first series, the subjects were required to stand in a symmetrical stance, with their feet parallel and spaced about shoulder width apart (Fig. 1). In the second and third series, the subjects stood in an asymmetrical stance with their left or right leg in 45° of external rotation. To control for possible changes in moments acting on the upper body due to this leg rotation, weight distribution between the left and right legs prior to performing

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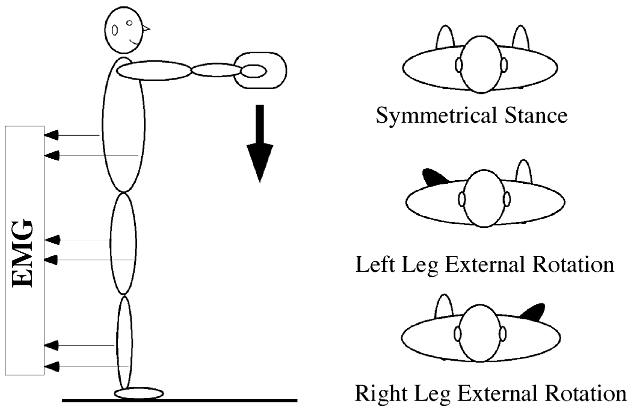

Fig. 1. The schematic representation of the experimental setup. The subjects released a load from both hands with their arms extended in front of their bodies (left), while standing symmetrically or with the right or left leg externally rotated (right).

load-release tasks was measured and subjects were provided with feedback. This was done using a force platform (AMTI OR6) as the subjects placed one foot on a force platform and the second foot on the wooden frame of the same height. Then, the subjects were instructed to maintain similar body weight distribution between the left and right legs, as well as similar trunk position in all experimental series. The same magnitude of perturbation was triggered in all three series due to the fact that the same load was released with the same bilateral arm movements. After the release, the load was caught by a cord attached to the metal frame positioned in front of the subjects. The order of series was randomized.

Electromyograms (EMG) were recorded from the rectus abdominis (RA), erector spinae (ES), rectus femoris (RF), biceps femoris (BF), tibialis anterior (TA), and soleus (SOL) muscles on both the left and right sides with surface electrodes. Signals from a force gauge taped to the load were used for trial alignment. All signals were digitized using 16-bit resolution at 1000 Hz. Data was acquired using LabView program and analyzed off-line (filtering, rectification, alignment, and averaging) with LabView and Matlab software. Anticipatory changes in the EMGs were quantified as integrals from –100 to T_0 ($\int EMG_{100}$) with respect to the first visible deflection of the force gage trace and corrected for background activity. Integrals were further normalized by the maximal absolute value of a given ∫EMG index for a given muscle for each subject across all series. Repeated measures ANOVAs were performed to determine statistical significance of the changes in the integrals of anticipatory EMG activity of postural muscles with different body postures.

Typical APA patterns induced in the series with symmetrical body position included an anticipatory inhibition in the activity of ES, BF, and SOL as well as an anticipatory increase in the activity of the RF and TA muscle approximately 100 ms prior to the perturbation. Fig. 2 shows the normalized ∫EMGs averaged across subjects for the three body positions. There was no statistically significant difference between the left and right ∫EMGs for any muscle in the condition of symmetrical posture ($p > 0.3$). However, when the task was performed in an asymmetrical posture, different patterns of anticipatory activation of the left and right muscles were observed. This could be seen best in the soleus muscle: anticipatory inhibition in the right soleus was observed and a small burst of activity was seen in the left soleus when the left leg was externally rotated. This was then replaced by an anticipatory burst and inhibition of activity in right and left soleus respectively when the right leg was rotated. The changes in the activity of the right and left muscles were statistically significant ($p < 0.01$). A similar but less pronounced dependence of anticipatory ∫EMGs on the side of the asymmetry was observed in TA, RF, and RA. Repeated measures ANOVA demonstrated a statistically significant effect of body side on the anticipatory EMG activities for RA ($F_{1,5} = 11.63$, $p < 0.05$), and a statistically significant effect between the series with different body postures for ES ($F_{2,5} = 4.8$, $p < 0.05$). In addition, there was a statistically significant body posture/body side interaction for RF ($F_{2,5} = 6.65$, $p < 0.05$), SOL ($F_{2,5} = 29.17$, $p < 0.01$), while for TA it was close to being statistically significant ($F_{2,5} = 3.27$, $p = 0.08$).

In everyday life, postural asymmetry can be due to several factors that could be addressed as intrinsic and extrinsic factors. Intrinsic factors include changes in the symmetry of stance due abnormalities such as a stroke-related hemiparesis [22], a leg-length discrepancy [18], or changes in the body configuration associated with performance of a certain task, such as a gait initiation. Postural asymmetry could result in asymmetrical weight-bearing seen in individuals with hemiparesis [11,21,27]. Therefore, postural asymmetry can affect the area of support within which the projection of the center of mass (COM) can move. Extrinsic factors are associated with work conditions in industry, such as lifting from asymmetric positions, or ineffective human environmental designs such as footwear, flooring, chairs, and cushions [2]. Lifting from an asymmetrical body position has been associated with increased moments about the lumbar spine [15] and decreased trunk strength [12]. These different types of body and movement asymmetry allow one to expect varying changes in APAs associated with self-initiated perturbation of body balance. Consequently, it is shown in the literature that asymmetrical motor actions are associated with asymmetrical APA patterns of muscle activity in healthy individuals standing symmetrically [10,23,25].

The primary goal of the current study was to find out whether anticipatory postural adjustments were modified in the presence of one of the intrinsic factors, body asymmetry. The experimental paradigm involved self-initiated perturbations performed by healthy subjects simulating a 45° external rotation of a leg, a body asymmetry commonly observed in individuals with hemiparesis as a result of a stroke [11,22]. The results of the experiments showed that an induced body asymmetry has an affect on the organization of anticipatory postural adjustments. In particular, we observed smaller anticipatory EMGs in the muscles on the side that exhibited leg rotation (see for example smaller ∫EMGs in SOL and RA). On the contralateral side, the opposite effect was seen in Sol and RA. Additionally, anticipatory inhibition of RA while standing with the left leg externally rotated was replaced with small anticipatory bursts of activity seen in both, left and right muscles while standing with the right leg rotated. It should be noted that the subjects released the same load in

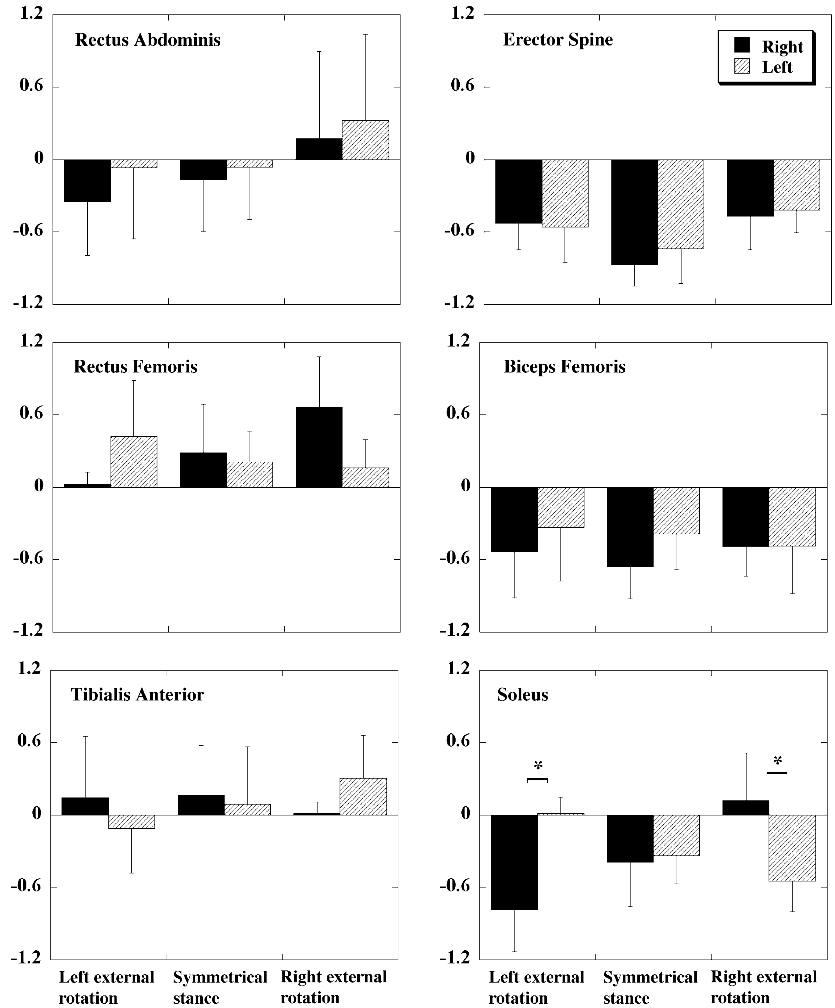

Fig. 2. Normalized ∫EMGs in the leg and trunk muscles for all three body postures averaged across six subjects. Bars show standard deviations. Horizontal axes indicate the body posture while the task of releasing the load was performed: left external rotation and right external rotation, asymmetrical body positions with 45° of external rotation of the leg, and symmetrical stance—regular posture while standing with no leg rotation. Significant differences ($p > 0.001$) between the left and right muscles are indicated with a bracket and a star.

front of them, thus creating a symmetrical body perturbation. As a result, while standing in a symmetrical posture, anticipatory activity in left and right muscles was almost the same and similar to what was previously described in the literature [6,7]. However, in conditions in which the leg was externally rotated, inducing body asymmetry, the same symmetrical perturbations were associated with asymmetrical APAs patterns. Moreover, APAs increased on the side opposite of leg rotation. Thus, suggesting that in the presence of body asymmetry, the CNS adopted a strategy of activating muscles on the contralateral side of the body to compensate for the effects of an additional mechanical constraint.

The asymmetry of APAs has been described in individuals with unilateral hemiparesis [26], individuals with lower leg amputation [8], and in healthy individuals performing unilateral shoulder flexion/extension movements [23,24]. It was also suggested in an earlier study that the role of the distal muscles, controlling the ankle joint, was relatively minor and might involve a fine tuning of the general APA pattern provided mostly by the proximal muscles during fast shoulder movements [5]. However, in the former study, the body posture was symmetrical and the subjects performed bilateral arm movements triggering symmetrical body perturbations. Thus, it is quite possible that in such symmetrical conditions the CNS deliberately uses anticipatory activation of mainly proximal muscles. On the other hand, the current study involving asymmetrical posture showed that distal muscles play an important role in the generation of APAs. It seems that asymmetry-specific anticipatory activation of both, proximal and distal muscles is the strategy that the CNS adopts to compensate for an additional mechanical constraint associated with an experimentally induced asymmetry of the body. Another strategy that the CNS might use to deal with asymmetry of posture, along with associated increased body instability, is anticipatory co-activation of agonist-antagonist muscles leading to increased joint stiffness. We did not observe anticipatory co-activation of muscles in our experiments, however, the literature suggests that individuals with Down syndrome [1] and aged persons [13,17] commonly use co-activation of muscles to help increase body stability. While the above results provide light on anticipatory postural control associated with asymmetry of posture, additional experiments are needed to describe the extent to which the CNS would use APAs in the case of dealing with larger body asymmetries or a combination of asymmetries in posture and motor action, or posture and perturbation.

Furthermore, the results of the current study taken together with the results of APA studies involving asymmetry of posture due to one-leg stance [4,20], lateral leg raising [19], inclined forward standing [3], or with one arm extended to the side [9] suggest the importance of future investigations involving the organization of APAs in the presence of asymmetry. These future studies could provide important information for the facilitation of therapeutic advances focused on an improvement of postural control and a reduction of falls in patients with postural asymmetries.

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Cognitive Load and Dual-Task Performance During Locomotion Poststroke: A Feasibility Study Using a Functional Virtual Environment

Rachel Kizony, Mindy F. Levin, Lucinda Hughey, Claire Perez, Joyce Fung

Background. Gait and cognitive functions can deteriorate during dual tasking, especially in people with neurological deficits. Most studies examining the simultaneous effects of dual tasking on motor and cognitive aspects were not performed in ecological environments. Using virtual reality technology, functional environments can be simulated to study dual tasking.

Objectives. The aims of this study were to test the feasibility of using a virtual functional environment for the examination of dual tasking and to determine the effects of dual tasking on gait parameters in people with stroke and age-matched controls who were healthy.

Design. This was a cross-sectional observational study.

Methods. Twelve community-dwelling older adults with stroke and 10 age-matched older adults who were healthy participated in the study. Participants walked on a self-paced treadmill while viewing a virtual grocery aisle projected onto a screen placed in front of them. They were asked to walk through the aisle (single task) or to walk and select ("shop for") items according to instructions delivered before or during walking (dual tasking).

Results. Overall, the stroke group walked slower than the control group in both conditions, whereas both groups walked faster overground than on the treadmill. The stroke group also showed larger variability in gait speed and shorter stride length than the control group. There was a general tendency to increase gait speed and stride length during dual-task conditions; however, a significant effect of dual tasking was found only in one dual-task condition for gait speed and stride duration variability. All participants were able to complete the task with minimal mistakes.

Limitations. The small size and heterogeneity of the sample were limitations of the study.

Conclusions. It is feasible to use a functional virtual environment for investigation of dual tasking. Different gait strategies, including an increase or decrease in gait speed, can be used to cope with the increase in cognitive demands required for dual tasking.

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Achieving an optimal level of participation in community activities is a main goal of rehabilitation. A common daily activity such as shopping requires the ability to perform 2 or more cognitive and motor activities simultaneously (ie, dual tasking) and to adapt the performance even when unexpected events occur. The paradigm of dual tasking and the effect of a secondary task on balance, gait, and cognitive performance have been examined in healthy and clinical populations in order to understand the role of attention on the maintenance of postural stability and walking. In particular, studies have investigated the "cost" of dual-task performance, usually measured by performance changes in one or both tasks when carried out simultaneously.[1]

Gait and cognitive performance can deteriorate during dual-task performance, especially in people with neurological deficits. Several studies have examined the change in gait or balance parameters while performing a secondary cognitive task[2–4] or the reaction to postural perturbations during performance of another task.[5,6] Dual tasking was found to increase the risk of falling among frail elderly people[7] and, thus, can be used to predict future falls in older adults.[8]

Dual tasking decreases gait speed and stride length during overground walking in people who are survivors of stroke.[4,9] Plummer-D'Amato et al[10] found that in community-dwelling adults who were survivors of stroke, the largest decrease in gait speed occurred during a spontaneous speech task compared with auditory one-back (working memory) and auditory clock (visuospatial) tasks. Canning et al[11] also found that walking performance in survivors of stroke can deteriorate (reduced gait speed, stride length, step length, and cadence) under dual- and triple-task conditions, similar to that observed in elderly people.

Lord et al[12] examined the effect of constraints in the physical environment (clinic, shopping mall, suburban street) and task (no task, stepping over an obstacle, and identifying even and odd numbers) on gait parameters in a cohort of patients with chronic stroke. A significant effect due to environmental context was found on gait speed (eg, patients walked slower within the shopping mall), but there were no significant main effects due to task or interaction effects between task and environment on gait parameters. Although the approach used in that study was novel, the observations should be interpreted with caution because results were reported for only 3 subjects in each of 9 conditions. Controlled studies are needed to determine how the environmental context affects dual tasking, and virtual reality (VR) technology can be used to create simulated functional environments that can be manipulated by the researcher.

Virtual reality refers to the use of interactive simulations created with computer hardware and software to introduce users to opportunities to interact in environments that seem and feel similar to the real world. Users interact, move, and manipulate virtual objects in a way that attempts to "immerse" them within the virtual environment (VE), thereby producing a feeling of "presence" in the virtual world.[13] The rationale for using VR for rehabilitation is based on a number of unique features of this technology.[14,15] One important feature is the ability to manipulate and grade stimulus delivery while measuring changes in performance within the VE. In addition, behavioral changes can be measured by adding other types of technologies such as motion analysis systems. Virtual reality hardware, composed of several types of technologies, facilitates the input and output of information and, when used in combination with programmed VEs, can provide the necessary tools for designing a variety of environments and complex tasks. These tools can enable researchers to analyze task performance in ecologically valid situations similar to real life, yet under experimentally controlled conditions.[15] In the past decade, studies have demonstrated the potential of using VR of various levels of complexity and ecologically valid VEs to study a range of motor and cognitive behaviors following stroke or brain injury.[16–21] Virtual reality also has been used to assess multitasking in people who were healthy[22] and in people with brain injury[23] and stroke.[24]

Most studies that examined dual-task performance have limited ecological validity because the tasks (eg, walking within the laboratory and memorizing a shopping list, walking and counting backward) were not performed within a functional environment or context. Those studies that were done within functional physical environments or VEs focused mainly on cognitive performance and did not examine the performance of an accompanying motor activity. Therefore, the objectives of this study were to test the feasibility of using a virtual functional environment for the examination of dual tasking and to determine the effect of dual tasking within a functional context on gait parameters in people with stroke in comparison with age-matched controls who were healthy. We hypothesized that gait parameters (ie, speed, stride length, and duration and variability of these parameters) would change during dual tasking performed in a functional context. Moreover, we hypothesized that these changes would be greater in people with stroke compared with age-matched controls.

Figure 1.
(A) The virtual reality setup viewed from behind the participant. (B) The virtual grocery aisle.

Method

Participants

A convenience sample of 7 men and 5 women who had a stroke (mean [±SD] age=68.7±6.9 years) were recruited for the study. Five individuals had a left hemispheric stroke, and 7 individuals had a right hemispheric stroke. Participants were included if they were community dwelling, at least 3 months poststroke, able to walk on a self-paced treadmill, and scored at least 25 on the Mini Mental State Examination.[25] Their mean (±SD) overground gait speed during performance of the 10-m walk test was 0.74±0.42 m/s. *Slow walkers* were defined as those individuals in the lower quartile, with an overground gait speed of less than 0.54 m/s. In addition, 4 men and 6 women who were healthy (mean [±SD] age=69.7±7.1 years) were recruited to participate as a control group. Their mean (±SD) overground gait speed during performance of the 10-m walk test was 1.26±0.20 m/s (available for only 8 participants in whom subsequent analyses were done). All participants signed an informed consent form prior to the study.

Instrumentation and Measurement

Virtual reality instrumentation. The instrumentation has been documented previously,[26] where VR technology was used in combination with a self-paced treadmill mounted on a motion platform and a real-time motion tracking system. In that study, the feasibility of using the combined technologies was demonstrated for gait training poststroke, as 2 individuals with chronic stroke were able to adapt and control their gait speed to overcome physical changes in the terrain and in the VE while walking on the treadmill.

In the current study, participants stood or walked on a self-paced, motorized treadmill mounted on a 6-degree-of-freedom motion platform. The VE was rear projected on a 2.44- × 3.05-m screen mounted 1.5 m in front of the end of the treadmill. The treadmill (0.6 × 1.5 m) was custom-built and incorporated a PID servo-controlled motor driven by an algorithm that included the real-time distance acquired by a potentiometer attached to the walking individual, as well as the instantaneous velocity. Thus, the speed of the treadmill was adjusted at will by the moving individual. The participant held with both hands on to a bar that was mounted with linear-bearing sliders on 2 handrails over the treadmill. The handle bar could be pushed up to a predefined point to simulate walking while pushing a shopping cart. A functional VE of a grocery aisle, 16-m long, was created and controlled within the CAREN (Computer Assisted Rehabilitation Environment) system[*27] (Fig. 1). This system synchronized the instantaneous treadmill speed and scene progression such that the participant had control of his movement within the VE. In addition, motion of the body was captured in real-time with a 6-camera Vicon motion analysis system[†] at 100 Hz. Participants walked through the grocery store aisle and selected or "shopped for" items that were placed at the rear of the aisle in front of them, according to the auditory instructions (with different levels of complexity) delivered prior to

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or after gait initiation. "Shopping for" an item consisted of deciding which object to select and then touching it with the hand. There were 4 experimental dual-task conditions: (1) condition 1—shop for one item only (instruction was delivered after gait initiation); (2) condition 2—shop for one item, which was changed to another item after 6 seconds; (3) condition 3—shop for 2 items (instruction was delivered after gait initiation); and (4) condition 4—memorize and shop for a list of 5 items provided prior to gait initiation.

The combination of items for which the participants were asked to shop was randomly changed between repetitions. Two baseline walking and standing conditions (single tasks) were included in which the participant walked through the grocery aisle without instructions (repeated 4–5 times) or shopped for items while standing (repeated 4 times with a different number of items), respectively. Experimental conditions (dual tasks) were grouped into blocks of 4 trials containing one trial of each condition, randomly ordered within each block. Data from 2 to 5 blocks were collected. Data analysis focused on the third walking baseline trial and the second experimental block in order to control for fatigue and learning effects, as well as for adapting to the dual task. Data analysis also focused on "steady-state locomotion" in the middle (60%) of each trial based on the number of strides. The number of strides for analysis varied among the participants depending on their stride length and gait speed and ranged between 6 and 32.

Measurement of gait parameters. For the analysis of gait parameters, a special algorithm (written in MATLAB[‡]) was used to detect critical gait cycle events, based on the foot trajectory in the sagittal plane (using 2 markers on each foot). The algorithm took into account different foot-fall patterns (heel-strike or toe contact) in accurately detecting initial contact (beginning of stance) or toe-off (beginning of swing). The following gait parameters were measured: stride length, stride duration, and cadence. Gait speed was derived from the treadmill motor output acquired by the CAREN system. In addition, the variability of each parameter across multiple strides was measured by the coefficient of variation (CV), defined as a percentage of the standard deviation over the mean. Task completion was measured as the number and type of mistakes that occurred. Mistakes were defined as forgetting an item, selecting the wrong item, or selecting extra items.

Data Analysis

Descriptive statistics were used to describe the performance of the participants for each of the gait parameters. In order to examine how well the self-paced treadmill simulated natural walking, a mixed-model, 2-way, repeated-measures analysis of variance (ANOVA) was used to compare overground and baseline treadmill gait speed. The independent variables were group (between-subject factor: control versus stroke) and condition (within-subject factor: overground versus baseline).

To compare gait parameters between baseline and experimental (dual-task) conditions, taking into account the different locomotor abilities of the participants, mixed-model, repeated-measures analyses of covariance (ANCOVA) were used for each gait outcome measure with the same independent variables (the conditions here were single and dual tasks), but using overground gait speed as a covariate. If there was an interaction between the covariate and group, further analyses were done to compare the different outcomes based on different locomotor abilities (gait speed). *Post hoc* comparisons were used to investigate differences between conditions and groups (Bonferroni correction −.005 for condition). Statistical analyses were performed using SPSS version 15[§] and SAS version 9.1.3[‖] software.

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Results

Participants from both groups were able to walk on the self-paced treadmill and interact within the VE. For 3 participants (2 in the stroke group and 1 in the control group), data from one condition were lost for current analysis due to technical problems, such as a marker falling off while walking. Descriptive statistics for gait parameters at baseline for both groups are presented in the Table.

Gait Speed

In both groups, participants walked significantly faster overground (0.74±0.42 m/s for the stroke group versus 1.26±0.20 m/s for the control group) than on the treadmill (0.51±0.23 for the stroke group versus 0.87±0.13 m/s for the control group; $F_{1,18}$=35.25, P=.0001). The control group walked significantly faster than the

‡ The MathWorks Inc, 3 Apple Hill Dr, Natick, MA 01760-2098.

§ SAS Institute Inc, PO Box 8000, Cary, NC 27513.

‖ SPSS Inc, 233 S Wacker Dr, Chicago, IL 60606.

stroke group in both conditions ($F_{1,18}$=13.47, P=.002).

Analyzing the differences in gait speed between baseline (single task) and experimental conditions (dual tasks) revealed that the direction of change was not consistent, although an overall tendency to increase gait speed during the dual-task conditions was seen. For gait speed, a main effect due to task conditions was found (Fig. 2; $F_{4,70}$=3.83, P=.007). *Post hoc* comparisons showed that participants walked slower at baseline than in condition 1 (t=3.64, P=.0005, 95% confidence interval [CI]=0.05 to 0.18). A similar but nonsignificant change in gait speed was observed between baseline and condition 2 (t=2.57, P=.012, 95% CI=0.02 to 0.15) and between baseline and condition 3 (t=2.76, P=.007, 95% CI=0.03 to 0.15).

The stroke group showed greater variability in gait speed compared with the control group ($F_{1,16}$=7.61, P=.014). The group difference was due mainly to the lower functioning of the participants in the stroke group, who were slow walkers overground (t=−2.63, P=.018, 95% CI=−32.8 to −3.5). Gait speed variability ranged from 20.7% at baseline to 24.3% in condition 2 for the stroke group, as compared with the control group (ranging from 10.1% in condition 3 to 14.7% in condition 1).

Stride Length and Duration

Overall, there was large variability within each group for stride length and duration during single or dual tasking. For stride length (paretic leg of the stroke group and left leg of the control group), a main effect due to group was found (Fig. 3; $F_{1,17}$=5.74, P=.028). The same was found for stride length of the other leg (nonparetic leg of the study group and right leg of the control group) ($F_{1,17}$=5.59, P=.03). The control

Table.
Gait Parameters at Baseline for the Stroke Group and the Control Group

Parameter	Stroke Group (n=12)			Control Group (n=10)		
	X̄	SD	Range	X̄	SD	Range
Gait speed (m/s)	0.51	0.23	0.31–0.92	0.87	0.12	0.68–1.06
Leg[a]						
Stride length (mm)	622	232	324–1,042	1,050	125	841–1,230
Stride duration (s)	1.46	0.27	1.13–1.89	1.33	0.18	0.98–1.54
Cadence (steps/min)	42.3	7.5	31.8–52.9	46.0	7.1	38.9–61.0
Leg[b]						
Stride length (mm)	619	236	250–1,159	1,049	121	841–1,211
Stride duration (s)	1.46	0.28	1.14–1.89	1.33	0.18	0.98–1.54
Cadence (steps/min)	42.3	7.5	31.8–52.7	45.9	7.1	39.0–61.2

[a] Nonparetic leg in stroke group, right leg in control group.
[b] Paretic leg in stroke group, left leg in control group.

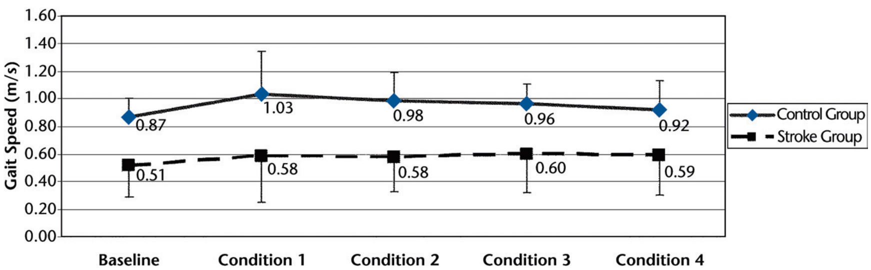

Figure 2.
Means and standard deviations of gait speed in baseline and experimental conditions for the stroke group and the control group. Condition 1=shop for one item only (instruction was delivered after gait initiation); condition 2=shop for one item, which was changed to another item after 6 seconds; condition 3=shop for 2 items (instruction was delivered after gait initiation); and condition 4=memorize and shop for a list of 5 items provided prior to gait initiation.

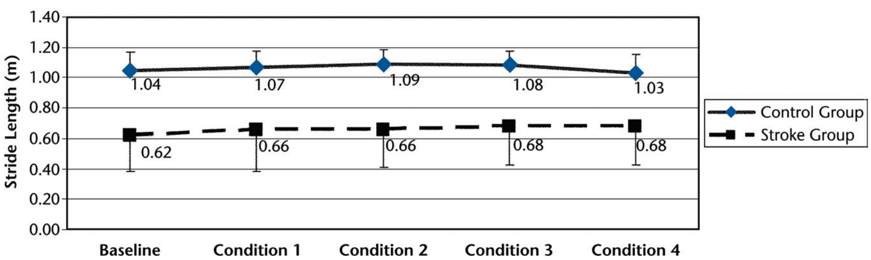

Figure 3.
Means and standard deviations of stride length of the stroke group and the control group across baseline and dual-task conditions (paretic leg for stroke group, left leg for control group). Condition 1=shop for one item only (instruction was delivered after gait initiation); condition 2=shop for one item, which was changed to another item after 6 seconds; condition 3=shop for 2 items (instruction was delivered after gait initiation); and condition 4=memorize and shop for a list of 5 items provided prior to gait initiation.

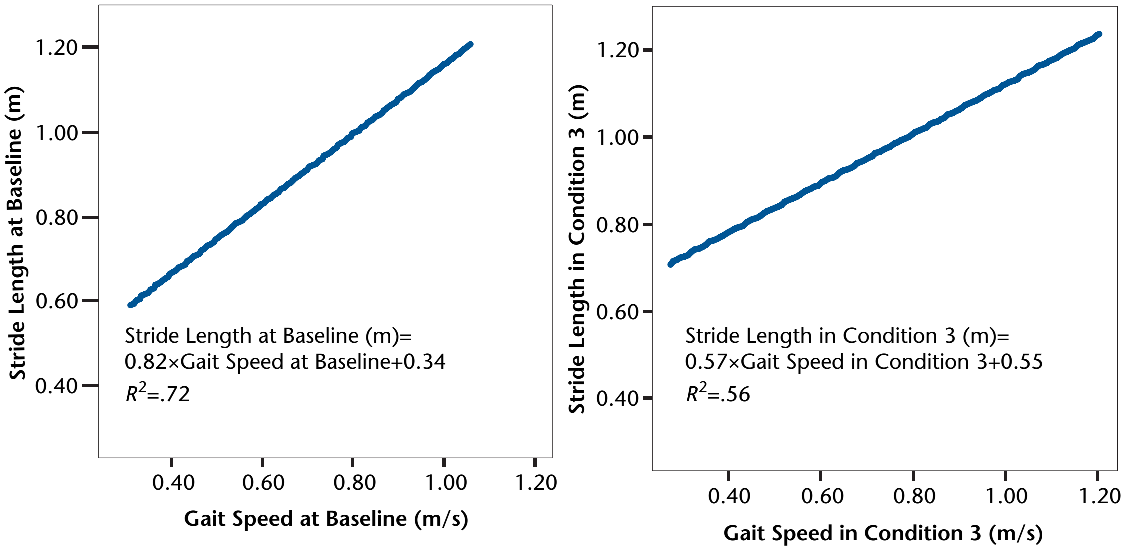

Figure 4.
Illustration of the correlations between stride length and gait speed at baseline and in condition 3 (shop for 2 items; instruction was delivered after gait initiation) in the control group.

group had significantly longer stride lengths across all conditions.

There was an overall tendency to decrease stride duration during dual-task conditions; however, there was a main effect only for stride duration variability in the nonparetic leg of the stroke group and right leg of the control group ($F_{4,70}$=2.57, P=.045). *Post hoc* comparisons almost reached significance, showing that stride duration variability tended to be smaller at baseline (4.72%±2.12) compared with condition 1 (6.79%±5.23) (t=2.61, P=.011, 95% CI=0.49 to 3.67). In addition, stride duration variability tended to be greater in condition 1 than in conditions 2, 3, and 4 (t=2.42, P=.018; 95% CI=0.34 to 3.55; t=2.76, P=.007, 95% CI=0.61 to 3.79; and t=1.99, P=.05, 95% CI=0.0001 to 3.21, respectively).

Cadence

An overall tendency to increase cadence during dual-task conditions was seen; however, none of the differences reached significance in either group. In addition, no significant differences were found between groups.

Additional Analysis

In order to better understand the participants' performance during the various dual-task conditions, an ANCOVA was done with performance at baseline as the covariate. An interaction effect between group and stride length at baseline was found for the bilateral stride lengths (left/paretic leg: $F_{1,56}$=8.52, P=.005; right/nonparetic leg: $F_{1,57}$=8.66, P=.005), with greater differences in stride length during dual-task conditions occurring in participants who had shorter strides at baseline (left/paretic leg: t=2.94, P=.008, 95% CI=98.93 to 588.75; right/nonparetic leg: t=2.92, P=.005, 95% CI=93.86 to 575.01). A main effect due to group was found for the left/paretic leg stride length variability ($F_{1,19}$=4.73, P=.042). An interaction effect between group and stride duration at baseline was found for the bilateral stride durations (left/paretic leg: $F_{1,56}$=9.99, P=.003; right/nonparetic leg: $F_{1,57}$=10.30, P=.002). However, *post hoc* analyses revealed no differences based on short or long stride duration.

In addition, for the purpose of explaining the increase in gait speed, Spearman correlations were performed between stride length and duration, cadence, and gait speed. In the stroke group, high correlations (r=.85–.96) were found only between gait speed and stride length of both legs. The correlations did not change between baseline and dual-task conditions. In contrast, as expected in the control group, moderate to high correlations were found between all gait parameters and gait speed. Interestingly, the correlation coefficients between stride length and gait speed decreased from baseline (r=.86 for left leg and .83 for right leg) to dual-task conditions (range between r=.57 to r=.71 in both legs) (Fig. 4).

Completion of Task

The ability to complete the task was determined in comparison with baseline performance (where participants were asked to shop without walking). Overall, the participants in both groups were able to complete the task with only minor mistakes. In the stroke group, 3 participants selected the wrong item once, 1 participant selected an extra item, and 1 participant forgot to select an item. In the control group, 3 participants selected the wrong item once, 2 participants selected an extra item, and 1 participant forgot to select an item.

Discussion and Conclusions

This study showed the potential of using a functional VE to examine dual-task performance during locomotion. The use of the VR setup involving tasks that were context-dependent made it possible to examine performance of dual tasking in an ecologically valid setting. The participants, even those who were lower functioning or slow walkers, were able to walk on the self-paced treadmill and interact with the VE. However, it is important to note that the participants' overground gait speed measured in the physical environment was significantly faster than in the baseline (single-task) condition measured in the VE, in both groups. The decrease in gait speed may have been partly due to having to walk on the treadmill while holding on to the handle of a simulated shopping cart or due to the visual processing required to see the virtual aisle. In addition, the overground and VE conditions may not be strictly comparable because we did not test participants walking overground in a similar aisle pushing a shopping cart. Mean overground gait speed of the stroke group in the current study was similar to that reported for single tasks in previous studies.[10–12,28]

There are a number of potential reasons why there were no significant differences in most gait variables between single- and dual-task conditions in the current study. The results of this study showed large between- and within-subjects' variability in direction and amount of change of gait parameters between single- and dual-task conditions. Although the differences between the conditions in either direction were not always statistically significant, when we examined the relative percentage of change between baseline and experimental conditions, we found that some participants had decreased gait speed during dual-task conditions, whereas other participants had increased gait speed. Thus, the same individual could cope with the increased cognitive load by decreasing gait speed in one condition while increasing it in another. However, despite the large variability, a significant increase in gait speed was found between the single task and one of the dual-task conditions (condition 1—shopping for one item), and a similar trend was found in other dual-task conditions except one (condition 4—memorizing and shopping for a list of 5 items).

These results are in contrast to the findings of other studies that examined the performance of dual tasking in people who had a stroke[4,9,10] or in elderly individuals.[11,29] Those studies showed consistent directions of change in all participants that mostly resulted in decreased gait speed and stride length during dual tasking. In addition, a decrease in gait speed was found in other populations, such as in people with Parkinson disease (PD),[30] in young subjects who were healthy, and in older individuals.[31] The differences may be explained by the fact that the task in the current study was different from that used in other studies; participants were asked to perform a functional task of shopping within the relevant VE of a grocery aisle, while walking on a self-paced treadmill. On one hand, this task was a familiar everyday activity for all of the participants, who probably have developed their own habits and routines.[32] On the other hand, walking on a self-paced treadmill could be perceived by most participants as a novel task in itself, which was reflected by a decrease in gait speed compared with overground walking. These characteristics of the task might have led the participants to use different strategies during dual-task performance, which might explain the inconsistent changes found within- and between-subjects. Within-subject variability was reported by Bock,[33] who examined different dual-task conditions and showed that young and older individuals who were healthy decreased gait speed in a task that required visual processing while walking but not in another task that required memorizing details from a picture. Bock suggested that the visual demand of the secondary task might have affected the cost of dual tasking. In the current study, the visual demands of the secondary task during walking were small, which might explain the lack of a main effect for condition in most of the variables tested.

Two explanations can be found for the strategy of increasing gait speed and stride length during dual-task conditions. Canning[34] found that when subjects with PD were given the instruction to focus on walking and not on a secondary motor task (carrying a tray with glasses), they walked at a speed similar to the single-task condition, and this had no impact on the secondary task. It might be that the participants in the current study, although they were not asked to, prioritized the more novel walking task over the routine shopping task, with the latter task being perceived as easier. Prioritization of gait, especially in novel situations, is considered to be an appropriate strategy.[1]

An alternative explanation can be derived from the motor learning literature. As mentioned previously, the VE treadmill walking task in the current study was new to the majority of the participants. Despite the practice and habituation that were done prior to the beginning of the study and the fact that analysis was performed on the second block of trials, it might be that the participants were in the process of learning this new walking task. One of the principles of motor learning stipulates that an external focus of attention (ie, focusing on the result of the action or on the object) enhances motor learning and performance more than an internal focus of attention (ie, focusing on the movement itself) in adults who are healthy[35] as well as in people with PD.[36] It is possible that some of the participants focused on the shopping task, trying not to forget the items (which were projected on the screen in front of them) they needed to "buy," while knowing that at the end of the aisle, they would need to select the requested items. Therefore, they paid less attention to walking, which became more automatic and thus faster and closer to their overground speed.

Verghese et al[37] reported that when older adults were asked to prioritize a secondary talking task while walking, they decreased their gait speed. Because the paradigm of the current study did not address either of these proposed explanations, future studies should examine the effect of task prioritization as well as the role of motor learning theories in dual tasking. In addition, future studies should investigate whether the increase in gait speed and stride length is an efficient and safe strategy, especially for people who have had a stroke. It might be that, in the event of an unexpected external perturbation, the person who speeds up will not be able to maintain balance, resulting in a fall. As suggested by Kelly et al,[38] the usual finding of a decrease in gait speed during dual tasking might be a mechanism that helps to maintain stability during walking and not necessarily a sign of impaired locomotor control. These authors found that adding a cognitive load to narrow-based walking in elderly people who were healthy resulted in decreased gait speed but did not affect frontal-plane stability.

Overall gait variability did not worsen during dual-task conditions in either group, which may suggest that the participants generally were able to maintain gait stability during dual tasking. Changes in gait parameters and stability often are seen when the walking task and the secondary task are complex and challenging.[1] In the current study, because the feasibility of the setup was being explored, there were no perturbations of the surface or manipulation of the VE, which could add to the complexity of the tasks. This might explain the lack of interference with the cognitive task or absence of interaction effects. The absence of an interaction effect on gait is consistent with previous findings in survivors of stroke who were asked to memorize a shopping list as a secondary task,[4] as well as with similar outcomes when comparing elderly people who were healthy with people with stroke using dual and triple tasks.[11] Our findings, however, were different from those reported by Yang et al,[9] who found greater changes in gait during dual-task conditions that involved a motor task in survivors of stroke, especially those who were least-limited community ambulators, than in elderly individuals who were healthy. Moreover, the interaction found between groups and performance at baseline in our study suggests that the differences were mainly between those participants with stroke who had poorer locomotor abilities at baseline and the control participants.

Finally, all analyses were done using overground gait speed as a covariate. Simple analyses that were done without this variable as covariate did show more significant results. The heterogeneity of this variable in our sample may have under-powered the study, leading to nonsignificant findings. It should be noted that many of the comparisons were significant at a level of $P<.05$, although not significant after applying the strict criterion of $P<.005$ with Bonferroni correction.

In conclusion, the results of the current study showed the potential of using a functional VE for investigating dual-task performance. In addition, the different coping strategies adopted by each individual should be investigated further. However, the results of this study should be interpreted with caution due to the small size and heterogeneity of the study sample, as well as the lack of a more-complex secondary task.

Dr Kizony, Dr Levin, and Dr Fung provided concept/idea/research design. Dr Kizony, Dr Levin, Ms Perez, and Dr Fung provided writing. Dr Kizony, Dr Hughey, Ms Perez, and Dr Fung provided data collection. Dr Kizony, Dr Hughey, and Dr Fung provided data analysis. Dr Kizony and Dr Fung provided project management. Dr Fung provided fund procurement and participants. Dr Levin and Dr Fung provided facilities/equipment and institutional liaisons. Dr Levin provided clerical support. Dr Levin and Dr Hughey provided consultation (including review of manuscript before submission). The authors acknowledge Christian Beaudoin and Valeri Goussev for providing programming and Eric Johnstone for technical support.

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Cognitive Load and Dual-Task Performance During Locomotion Poststroke: A Feasibility Study Using a Functional Virtual Environment

Rachel Kizony, Mindy F. Levin, Lucinda Hughey, Claire Perez, Joyce Fung

Background. Gait and cognitive functions can deteriorate during dual tasking, especially in people with neurological deficits. Most studies examining the simultaneous effects of dual tasking on motor and cognitive aspects were not performed in ecological environments. Using virtual reality technology, functional environments can be simulated to study dual tasking.

Objectives. The aims of this study were to test the feasibility of using a virtual functional environment for the examination of dual tasking and to determine the effects of dual tasking on gait parameters in people with stroke and age-matched controls who were healthy.

Design. This was a cross-sectional observational study.

Methods. Twelve community-dwelling older adults with stroke and 10 age-matched older adults who were healthy participated in the study. Participants walked on a self-paced treadmill while viewing a virtual grocery aisle projected onto a screen placed in front of them. They were asked to walk through the aisle (single task) or to walk and select ("shop for") items according to instructions delivered before or during walking (dual tasking).

Results. Overall, the stroke group walked slower than the control group in both conditions, whereas both groups walked faster overground than on the treadmill. The stroke group also showed larger variability in gait speed and shorter stride length than the control group. There was a general tendency to increase gait speed and stride length during dual-task conditions; however, a significant effect of dual tasking was found only in one dual-task condition for gait speed and stride duration variability. All participants were able to complete the task with minimal mistakes.

Limitations. The small size and heterogeneity of the sample were limitations of the study.

Conclusions. It is feasible to use a functional virtual environment for investigation of dual tasking. Different gait strategies, including an increase or decrease in gait speed, can be used to cope with the increase in cognitive demands required for dual tasking.

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Achieving an optimal level of participation in community activities is a main goal of rehabilitation. A common daily activity such as shopping requires the ability to perform 2 or more cognitive and motor activities simultaneously (ie, dual tasking) and to adapt the performance even when unexpected events occur. The paradigm of dual tasking and the effect of a secondary task on balance, gait, and cognitive performance have been examined in healthy and clinical populations in order to understand the role of attention on the maintenance of postural stability and walking. In particular, studies have investigated the "cost" of dual-task performance, usually measured by performance changes in one or both tasks when carried out simultaneously.[1]

Gait and cognitive performance can deteriorate during dual-task performance, especially in people with neurological deficits. Several studies have examined the change in gait or balance parameters while performing a secondary cognitive task[2–4] or the reaction to postural perturbations during performance of another task.[5,6] Dual tasking was found to increase the risk of falling among frail elderly people[7] and, thus, can be used to predict future falls in older adults.[8]

Dual tasking decreases gait speed and stride length during overground walking in people who are survivors of stroke.[4,9] Plummer-D'Amato et al[10] found that in community-dwelling adults who were survivors of stroke, the largest decrease in gait speed occurred during a spontaneous speech task compared with auditory one-back (working memory) and auditory clock (visuospatial) tasks. Canning et al[11] also found that walking performance in survivors of stroke can deteriorate (reduced gait speed, stride length, step length, and cadence) under dual- and triple-task conditions, similar to that observed in elderly people.

Lord et al[12] examined the effect of constraints in the physical environment (clinic, shopping mall, suburban street) and task (no task, stepping over an obstacle, and identifying even and odd numbers) on gait parameters in a cohort of patients with chronic stroke. A significant effect due to environmental context was found on gait speed (eg, patients walked slower within the shopping mall), but there were no significant main effects due to task or interaction effects between task and environment on gait parameters. Although the approach used in that study was novel, the observations should be interpreted with caution because results were reported for only 3 subjects in each of 9 conditions. Controlled studies are needed to determine how the environmental context affects dual tasking, and virtual reality (VR) technology can be used to create simulated functional environments that can be manipulated by the researcher.

Virtual reality refers to the use of interactive simulations created with computer hardware and software to introduce users to opportunities to interact in environments that seem and feel similar to the real world. Users interact, move, and manipulate virtual objects in a way that attempts to "immerse" them within the virtual environment (VE), thereby producing a feeling of "presence" in the virtual world.[13] The rationale for using VR for rehabilitation is based on a number of unique features of this technology.[14,15] One important feature is the ability to manipulate and grade stimulus delivery while measuring changes in performance within the VE. In addition, behavioral changes can be measured by adding other types of technologies such as motion analysis systems. Virtual reality hardware, composed of several types of technologies, facilitates the input and output of information and, when used in combination with programmed VEs, can provide the necessary tools for designing a variety of environments and complex tasks. These tools can enable researchers to analyze task performance in ecologically valid situations similar to real life, yet under experimentally controlled conditions.[15] In the past decade, studies have demonstrated the potential of using VR of various levels of complexity and ecologically valid VEs to study a range of motor and cognitive behaviors following stroke or brain injury.[16–21] Virtual reality also has been used to assess multitasking in people who were healthy[22] and in people with brain injury[23] and stroke.[24]

Most studies that examined dual-task performance have limited ecological validity because the tasks (eg, walking within the laboratory and memorizing a shopping list, walking and counting backward) were not performed within a functional environment or context. Those studies that were done within functional physical environments or VEs focused mainly on cognitive performance and did not examine the performance of an accompanying motor activity. Therefore, the objectives of this study were to test the feasibility of using a virtual functional environment for the examination of dual tasking and to determine the effect of dual tasking within a functional context on gait parameters in people with stroke in comparison with age-matched controls who were healthy. We hypothesized that gait parameters (ie, speed, stride length, and duration and variability of these parameters) would change during dual tasking performed in a functional context. Moreover, we hypothesized that these changes would be greater in people with stroke compared with age-matched controls.

Figure 1.
(A) The virtual reality setup viewed from behind the participant. (B) The virtual grocery aisle.

Method

Participants

A convenience sample of 7 men and 5 women who had a stroke (mean [±SD] age=68.7±6.9 years) were recruited for the study. Five individuals had a left hemispheric stroke, and 7 individuals had a right hemispheric stroke. Participants were included if they were community dwelling, at least 3 months poststroke, able to walk on a self-paced treadmill, and scored at least 25 on the Mini Mental State Examination.[25] Their mean (±SD) overground gait speed during performance of the 10-m walk test was 0.74±0.42 m/s. *Slow walkers* were defined as those individuals in the lower quartile, with an overground gait speed of less than 0.54 m/s. In addition, 4 men and 6 women who were healthy (mean [±SD] age=69.7±7.1 years) were recruited to participate as a control group. Their mean (±SD) overground gait speed during performance of the 10-m walk test was 1.26±0.20 m/s (available for only 8 participants in whom subsequent analyses were done). All participants signed an informed consent form prior to the study.

Instrumentation and Measurement

Virtual reality instrumentation. The instrumentation has been documented previously,[26] where VR technology was used in combination with a self-paced treadmill mounted on a motion platform and a real-time motion tracking system. In that study, the feasibility of using the combined technologies was demonstrated for gait training poststroke, as 2 individuals with chronic stroke were able to adapt and control their gait speed to overcome physical changes in the terrain and in the VE while walking on the treadmill.

In the current study, participants stood or walked on a self-paced, motorized treadmill mounted on a 6-degree-of-freedom motion platform. The VE was rear projected on a 2.44- × 3.05-m screen mounted 1.5 m in front of the end of the treadmill. The treadmill (0.6 × 1.5 m) was custom-built and incorporated a PID servo-controlled motor driven by an algorithm that included the real-time distance acquired by a potentiometer attached to the walking individual, as well as the instantaneous velocity. Thus, the speed of the treadmill was adjusted at will by the moving individual. The participant held with both hands on to a bar that was mounted with linear-bearing sliders on 2 handrails over the treadmill. The handle bar could be pushed up to a predefined point to simulate walking while pushing a shopping cart. A functional VE of a grocery aisle, 16-m long, was created and controlled within the CAREN (Computer Assisted Rehabilitation Environment) system[*][27] (Fig. 1). This system synchronized the instantaneous treadmill speed and scene progression such that the participant had control of his movement within the VE. In addition, motion of the body was captured in real-time with a 6-camera Vicon motion analysis system[†] at 100 Hz. Participants walked through the grocery store aisle and selected or "shopped for" items that were placed at the rear of the aisle in front of them, according to the auditory instructions (with different levels of complexity) delivered prior to

* MOTEK Medical BV, Keienbergweg 77, 1101GE Amsterdam, the Netherlands.
† Vicon–UK, 14 Minns Business Park, West Way, Oxford OX2 0JB, United Kingdom.

or after gait initiation. "Shopping for" an item consisted of deciding which object to select and then touching it with the hand. There were 4 experimental dual-task conditions: (1) condition 1—shop for one item only (instruction was delivered after gait initiation); (2) condition 2—shop for one item, which was changed to another item after 6 seconds; (3) condition 3—shop for 2 items (instruction was delivered after gait initiation); and (4) condition 4—memorize and shop for a list of 5 items provided prior to gait initiation.

The combination of items for which the participants were asked to shop was randomly changed between repetitions. Two baseline walking and standing conditions (single tasks) were included in which the participant walked through the grocery aisle without instructions (repeated 4–5 times) or shopped for items while standing (repeated 4 times with a different number of items), respectively. Experimental conditions (dual tasks) were grouped into blocks of 4 trials containing one trial of each condition, randomly ordered within each block. Data from 2 to 5 blocks were collected. Data analysis focused on the third walking baseline trial and the second experimental block in order to control for fatigue and learning effects, as well as for adapting to the dual task. Data analysis also focused on "steady-state locomotion" in the middle (60%) of each trial based on the number of strides. The number of strides for analysis varied among the participants depending on their stride length and gait speed and ranged between 6 and 32.

Measurement of gait parameters. For the analysis of gait parameters, a special algorithm (written in MATLAB[‡]) was used to detect critical gait cycle events, based on the foot trajectory in the sagittal plane (using 2 markers on each foot). The algorithm took into account different foot-fall patterns (heel-strike or toe contact) in accurately detecting initial contact (beginning of stance) or toe-off (beginning of swing). The following gait parameters were measured: stride length, stride duration, and cadence. Gait speed was derived from the treadmill motor output acquired by the CAREN system. In addition, the variability of each parameter across multiple strides was measured by the coefficient of variation (CV), defined as a percentage of the standard deviation over the mean. Task completion was measured as the number and type of mistakes that occurred. Mistakes were defined as forgetting an item, selecting the wrong item, or selecting extra items.

Data Analysis

Descriptive statistics were used to describe the performance of the participants for each of the gait parameters. In order to examine how well the self-paced treadmill simulated natural walking, a mixed-model, 2-way, repeated-measures analysis of variance (ANOVA) was used to compare overground and baseline treadmill gait speed. The independent variables were group (between-subject factor: control versus stroke) and condition (within-subject factor: overground versus baseline).

To compare gait parameters between baseline and experimental (dual-task) conditions, taking into account the different locomotor abilities of the participants, mixed-model, repeated-measures analyses of covariance (ANCOVA) were used for each gait outcome measure with the same independent variables (the conditions here were single and dual tasks), but using overground gait speed as a covariate. If there was an interaction between the covariate and group, further analyses were done to compare the different outcomes based on different locomotor abilities (gait speed). *Post hoc* comparisons were used to investigate differences between conditions and groups (Bonferroni correction −.005 for condition). Statistical analyses were performed using SPSS version 15[§] and SAS version 9.1.3[‖] software.

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Results

Participants from both groups were able to walk on the self-paced treadmill and interact within the VE. For 3 participants (2 in the stroke group and 1 in the control group), data from one condition were lost for current analysis due to technical problems, such as a marker falling off while walking. Descriptive statistics for gait parameters at baseline for both groups are presented in the Table.

Gait Speed

In both groups, participants walked significantly faster overground (0.74±0.42 m/s for the stroke group versus 1.26±0.20 m/s for the control group) than on the treadmill (0.51±0.23 for the stroke group versus 0.87±0.13 m/s for the control group; $F_{1,18}$=35.25, P=.0001). The control group walked significantly faster than the

‡ The MathWorks Inc, 3 Apple Hill Dr, Natick, MA 01760-2098.

§ SAS Institute Inc, PO Box 8000, Cary, NC 27513.

‖ SPSS Inc, 233 S Wacker Dr, Chicago, IL 60606.

stroke group in both conditions ($F_{1,18}$=13.47, P=.002).

Analyzing the differences in gait speed between baseline (single task) and experimental conditions (dual tasks) revealed that the direction of change was not consistent, although an overall tendency to increase gait speed during the dual-task conditions was seen. For gait speed, a main effect due to task conditions was found (Fig. 2; $F_{4,70}$=3.83, P=.007). *Post hoc* comparisons showed that participants walked slower at baseline than in condition 1 (t=3.64, P=.0005, 95% confidence interval [CI]=0.05 to 0.18). A similar but nonsignificant change in gait speed was observed between baseline and condition 2 (t=2.57, P=.012, 95% CI=0.02 to 0.15) and between baseline and condition 3 (t=2.76, P=.007, 95% CI=0.03 to 0.15).

The stroke group showed greater variability in gait speed compared with the control group ($F_{1,16}$=7.61, P=.014). The group difference was due mainly to the lower functioning of the participants in the stroke group, who were slow walkers overground (t=−2.63, P=.018, 95% CI=−32.8 to −3.5). Gait speed variability ranged from 20.7% at baseline to 24.3% in condition 2 for the stroke group, as compared with the control group (ranging from 10.1% in condition 3 to 14.7% in condition 1).

Stride Length and Duration

Overall, there was large variability within each group for stride length and duration during single or dual tasking. For stride length (paretic leg of the stroke group and left leg of the control group), a main effect due to group was found (Fig. 3; $F_{1,17}$=5.74, P=.028). The same was found for stride length of the other leg (nonparetic leg of the study group and right leg of the control group) ($F_{1,17}$=5.59, P=.03). The control

Table.
Gait Parameters at Baseline for the Stroke Group and the Control Group

Parameter	Stroke Group (n=12)			Control Group (n=10)		
	X̄	SD	Range	X̄	SD	Range
Gait speed (m/s)	0.51	0.23	0.31–0.92	0.87	0.12	0.68–1.06
Leg[a]						
Stride length (mm)	622	232	324–1,042	1,050	125	841–1,230
Stride duration (s)	1.46	0.27	1.13–1.89	1.33	0.18	0.98–1.54
Cadence (steps/min)	42.3	7.5	31.8–52.9	46.0	7.1	38.9–61.0
Leg[b]						
Stride length (mm)	619	236	250–1,159	1,049	121	841–1,211
Stride duration (s)	1.46	0.28	1.14–1.89	1.33	0.18	0.98–1.54
Cadence (steps/min)	42.3	7.5	31.8–52.7	45.9	7.1	39.0–61.2

[a] Nonparetic leg in stroke group, right leg in control group.
[b] Paretic leg in stroke group, left leg in control group.

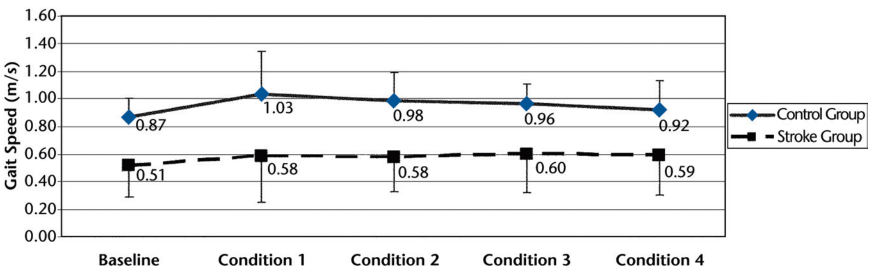

Figure 2.
Means and standard deviations of gait speed in baseline and experimental conditions for the stroke group and the control group. Condition 1=shop for one item only (instruction was delivered after gait initiation); condition 2=shop for one item, which was changed to another item after 6 seconds; condition 3=shop for 2 items (instruction was delivered after gait initiation); and condition 4=memorize and shop for a list of 5 items provided prior to gait initiation.

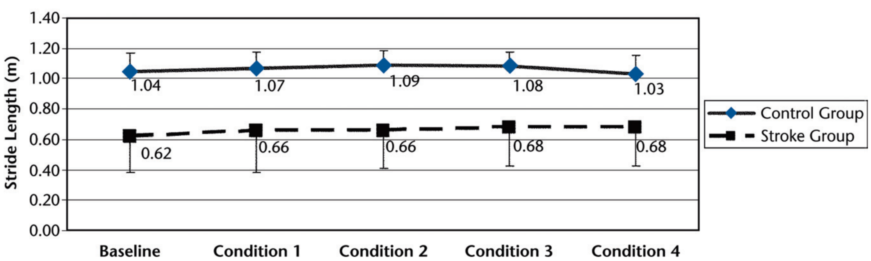

Figure 3.
Means and standard deviations of stride length of the stroke group and the control group across baseline and dual-task conditions (paretic leg for stroke group, left leg for control group). Condition 1=shop for one item only (instruction was delivered after gait initiation); condition 2=shop for one item, which was changed to another item after 6 seconds; condition 3=shop for 2 items (instruction was delivered after gait initiation); and condition 4=memorize and shop for a list of 5 items provided prior to gait initiation.

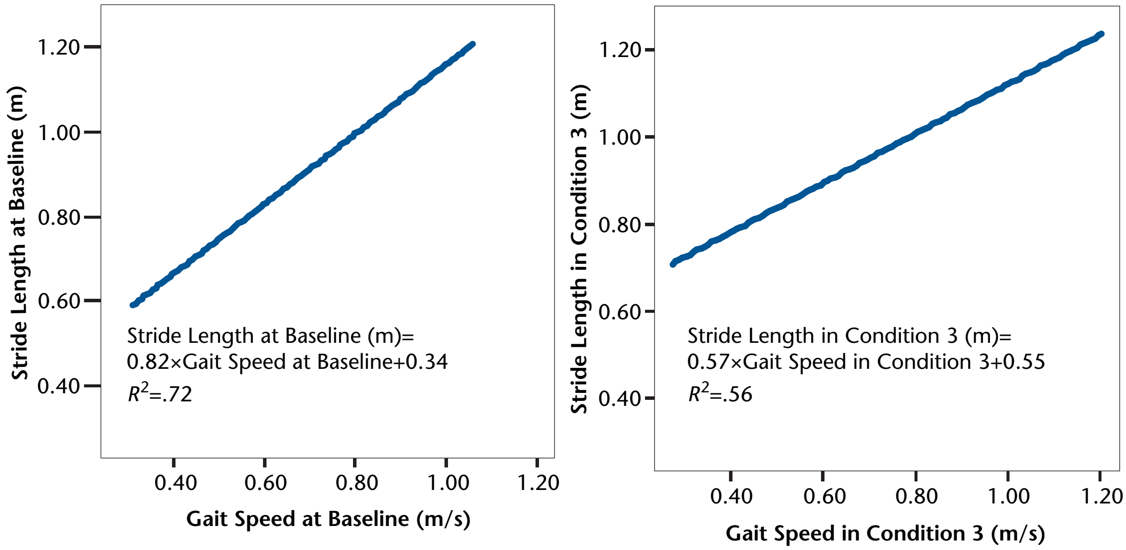

Figure 4.
Illustration of the correlations between stride length and gait speed at baseline and in condition 3 (shop for 2 items; instruction was delivered after gait initiation) in the control group.

group had significantly longer stride lengths across all conditions.

There was an overall tendency to decrease stride duration during dual-task conditions; however, there was a main effect only for stride duration variability in the nonparetic leg of the stroke group and right leg of the control group ($F_{4,70}$=2.57, P=.045). *Post hoc* comparisons almost reached significance, showing that stride duration variability tended to be smaller at baseline (4.72%±2.12) compared with condition 1 (6.79%±5.23) (t=2.61, P=.011, 95% CI=0.49 to 3.67). In addition, stride duration variability tended to be greater in condition 1 than in conditions 2, 3, and 4 (t=2.42, P=.018; 95% CI=0.34 to 3.55; t=2.76, P=.007, 95% CI=0.61 to 3.79; and t=1.99, P=.05, 95% CI=0.0001 to 3.21, respectively).

Cadence

An overall tendency to increase cadence during dual-task conditions was seen; however, none of the differences reached significance in either group. In addition, no significant differences were found between groups.

Additional Analysis

In order to better understand the participants' performance during the various dual-task conditions, an ANCOVA was done with performance at baseline as the covariate. An interaction effect between group and stride length at baseline was found for the bilateral stride lengths (left/paretic leg: $F_{1,56}$=8.52, P=.005; right/nonparetic leg: $F_{1,57}$=8.66, P=.005), with greater differences in stride length during dual-task conditions occurring in participants who had shorter strides at baseline (left/paretic leg: t=2.94, P=.008, 95% CI=98.93 to 588.75; right/nonparetic leg: t=2.92, P=.005, 95% CI=93.86 to 575.01). A main effect due to group was found for the left/paretic leg stride length variability ($F_{1,19}$=4.73, P=.042). An interaction effect between group and stride duration at baseline was found for the bilateral stride durations (left/paretic leg: $F_{1,56}$=9.99, P=.003; right/nonparetic leg: $F_{1,57}$=10.30, P=.002). However, *post hoc* analyses revealed no differences based on short or long stride duration.

In addition, for the purpose of explaining the increase in gait speed, Spearman correlations were performed between stride length and duration, cadence, and gait speed. In the stroke group, high correlations (r=.85–.96) were found only between gait speed and stride length of both legs. The correlations did not change between baseline and dual-task conditions. In contrast, as expected in the control group, moderate to high correlations were found between all gait parameters and gait speed. Interestingly, the correlation coefficients between stride length and gait speed decreased from baseline (r=.86 for left leg and .83 for right leg) to dual-task conditions (range between r=.57 to r=.71 in both legs) (Fig. 4).

Completion of Task

The ability to complete the task was determined in comparison with baseline performance (where participants were asked to shop without walking). Overall, the participants in both groups were able to complete the task with only minor mistakes. In the stroke group, 3 participants selected the wrong item once, 1 participant selected an extra item, and 1 participant forgot to select an item. In the control group, 3 participants selected the wrong item once, 2 participants selected an extra item, and 1 participant forgot to select an item.

Discussion and Conclusions

This study showed the potential of using a functional VE to examine dual-task performance during locomotion. The use of the VR setup involving tasks that were context-dependent made it possible to examine performance of dual tasking in an ecologically valid setting. The participants, even those who were lower functioning or slow walkers, were able to walk on the self-paced treadmill and interact with the VE. However, it is important to note that the participants' overground gait speed measured in the physical environment was significantly faster than in the baseline (single-task) condition measured in the VE, in both groups. The decrease in gait speed may have been partly due to having to walk on the treadmill while holding on to the handle of a simulated shopping cart or due to the visual processing required to see the virtual aisle. In addition, the overground and VE conditions may not be strictly comparable because we did not test participants walking overground in a similar aisle pushing a shopping cart. Mean overground gait speed of the stroke group in the current study was similar to that reported for single tasks in previous studies.[10–12,28]

There are a number of potential reasons why there were no significant differences in most gait variables between single- and dual-task conditions in the current study. The results of this study showed large between- and within-subjects' variability in direction and amount of change of gait parameters between single- and dual-task conditions. Although the differences between the conditions in either direction were not always statistically significant, when we examined the relative percentage of change between baseline and experimental conditions, we found that some participants had decreased gait speed during dual-task conditions, whereas other participants had increased gait speed. Thus, the same individual could cope with the increased cognitive load by decreasing gait speed in one condition while increasing it in another. However, despite the large variability, a significant increase in gait speed was found between the single task and one of the dual-task conditions (condition 1—shopping for one item), and a similar trend was found in other dual-task conditions except one (condition 4—memorizing and shopping for a list of 5 items).

These results are in contrast to the findings of other studies that examined the performance of dual tasking in people who had a stroke[4,9,10] or in elderly individuals.[11,29] Those studies showed consistent directions of change in all participants that mostly resulted in decreased gait speed and stride length during dual tasking. In addition, a decrease in gait speed was found in other populations, such as in people with Parkinson disease (PD),[30] in young subjects who were healthy, and in older individuals.[31] The differences may be explained by the fact that the task in the current study was different from that used in other studies; participants were asked to perform a functional task of shopping within the relevant VE of a grocery aisle, while walking on a self-paced treadmill. On one hand, this task was a familiar everyday activity for all of the participants, who probably have developed their own habits and routines.[32] On the other hand, walking on a self-paced treadmill could be perceived by most participants as a novel task in itself, which was reflected by a decrease in gait speed compared with overground walking. These characteristics of the task might have led the participants to use different strategies during dual-task performance, which might explain the inconsistent changes found within- and between-subjects. Within-subject variability was reported by Bock,[33] who examined different dual-task conditions and showed that young and older individuals who were healthy decreased gait speed in a task that required visual processing while walking but not in another task that required memorizing details from a picture. Bock suggested that the visual demand of the secondary task might have affected the cost of dual tasking. In the current study, the visual demands of the secondary task during walking were small, which might explain the lack of a main effect for condition in most of the variables tested.

Two explanations can be found for the strategy of increasing gait speed and stride length during dual-task conditions. Canning[34] found that when subjects with PD were given the instruction to focus on walking and not on a secondary motor task (carrying a tray with glasses), they walked at a speed similar to the single-task condition, and this had no impact on the secondary task. It might be that the participants in the current study, although they were not asked to, prioritized the more novel walking task over the routine shopping task, with the latter task being perceived as easier. Prioritization of gait, especially in novel situations, is considered to be an appropriate strategy.[1]

An alternative explanation can be derived from the motor learning literature. As mentioned previously, the VE treadmill walking task in the current study was new to the majority of the participants. Despite the practice and habituation that were done prior to the beginning of the study and the fact that analysis was performed on the second block of trials, it might be that the participants were in the process of learning this new walking task. One of the principles of motor learning stipulates that an external focus of attention (ie, focusing on the result of the action or on the object) enhances motor learning and performance more than an internal focus of attention (ie, focusing on the movement itself) in adults who are healthy[35] as well as in people with PD.[36] It is possible that some of the participants focused on the shopping task, trying not to forget the items (which were projected on the screen in front of them) they needed to "buy," while knowing that at the end of the aisle, they would need to select the requested items. Therefore, they paid less attention to walking, which became more automatic and thus faster and closer to their overground speed.

Verghese et al[37] reported that when older adults were asked to prioritize a secondary talking task while walking, they decreased their gait speed. Because the paradigm of the current study did not address either of these proposed explanations, future studies should examine the effect of task prioritization as well as the role of motor learning theories in dual tasking. In addition, future studies should investigate whether the increase in gait speed and stride length is an efficient and safe strategy, especially for people who have had a stroke. It might be that, in the event of an unexpected external perturbation, the person who speeds up will not be able to maintain balance, resulting in a fall. As suggested by Kelly et al,[38] the usual finding of a decrease in gait speed during dual tasking might be a mechanism that helps to maintain stability during walking and not necessarily a sign of impaired locomotor control. These authors found that adding a cognitive load to narrow-based walking in elderly people who were healthy resulted in decreased gait speed but did not affect frontal-plane stability.

Overall gait variability did not worsen during dual-task conditions in either group, which may suggest that the participants generally were able to maintain gait stability during dual tasking. Changes in gait parameters and stability often are seen when the walking task and the secondary task are complex and challenging.[1] In the current study, because the feasibility of the setup was being explored, there were no perturbations of the surface or manipulation of the VE, which could add to the complexity of the tasks. This might explain the lack of interference with the cognitive task or absence of interaction effects. The absence of an interaction effect on gait is consistent with previous findings in survivors of stroke who were asked to memorize a shopping list as a secondary task,[4] as well as with similar outcomes when comparing elderly people who were healthy with people with stroke using dual and triple tasks.[11] Our findings, however, were different from those reported by Yang et al,[9] who found greater changes in gait during dual-task conditions that involved a motor task in survivors of stroke, especially those who were least-limited community ambulators, than in elderly individuals who were healthy. Moreover, the interaction found between groups and performance at baseline in our study suggests that the differences were mainly between those participants with stroke who had poorer locomotor abilities at baseline and the control participants.

Finally, all analyses were done using overground gait speed as a covariate. Simple analyses that were done without this variable as covariate did show more significant results. The heterogeneity of this variable in our sample may have under-powered the study, leading to nonsignificant findings. It should be noted that many of the comparisons were significant at a level of $P<.05$, although not significant after applying the strict criterion of $P<.005$ with Bonferroni correction.

In conclusion, the results of the current study showed the potential of using a functional VE for investigating dual-task performance. In addition, the different coping strategies adopted by each individual should be investigated further. However, the results of this study should be interpreted with caution due to the small size and heterogeneity of the study sample, as well as the lack of a more-complex secondary task.

Dr Kizony, Dr Levin, and Dr Fung provided concept/idea/research design. Dr Kizony, Dr Levin, Ms Perez, and Dr Fung provided writing. Dr Kizony, Dr Hughey, Ms Perez, and Dr Fung provided data collection. Dr Kizony, Dr Hughey, and Dr Fung provided data analysis. Dr Kizony and Dr Fung provided project management. Dr Fung provided fund procurement and participants. Dr Levin and Dr Fung provided facilities/equipment and institutional liaisons. Dr Levin provided clerical support. Dr Levin and Dr Hughey provided consultation (including review of manuscript before submission). The authors acknowledge Christian Beaudoin and Valeri Goussev for providing programming and Eric Johnstone for technical support.

This study was approved by the Review Ethics Board of the Center for Interdisciplinary Research in Rehabilitation.

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Effects of Limb Loading on Gait Initiation in Persons with Moderate Hemiparesis

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Purpose: To examine the immediate effect of symmetrical weight bearing (SWB) on temporal events of gait initiation (GI) patterns and timing and amplitude of lower distal limb muscles activity during GI in persons with hemiparesis. **Method:** The study was a within-subjects design. Twelve persons with hemiparesis were recruited from the Veterans Affairs Brain Rehabilitation Research Center at the Malcom Randall Veterans Affairs, Gainesville, Florida. GI trials were performed from 4 beginning limb-loading conditions presented in a randomized order: (1) GI with the paretic limb during natural (asymmetrical) weight bearing (NWB); (2) GI with the nonparetic limb during NWB; (3) GI with the paretic limb during SWB; and (4) GI with the nonparetic limb during SWB. Temporal events of ground reaction forces (GRFs) and timing and amplitude of distal muscles activity were measured during GI trials in a motion analysis laboratory. **Results:** There were no significant effects of SWB on the temporal events of GRFs and timing and amplitude of distal muscles activity when initiating gait with the paretic limb. Onset of tibilais anterior (TA) muscle was delayed significantly with less amplitude when initiating gait with the paretic limb in both NWB and SWB conditions. However, when initiating gait with the nonparetic limb, TA muscle on the paretic limb was activated normally with greater amplitude in both NWB and SWB conditions. **Conclusion:** Initiating gait with the nonparetic limb as pregait activity may more effectively challenge the dynamic balance for a symmetrical gait pattern than the standard SWB in persons with hemiparesis. **Key words:** *gait initiation, physical therapy, rehabilitation, stroke, symmetry*

Individuals with hemiparesis after stroke frequently have difficulty standing,[1] walking,[2] and moving from sit-to-stand (STS).[3] One reason for these difficulties is the failure to generate adequate limb loading or active weight shift onto the paretic lower extremity.[4] Inability of active weight shift onto the paretic limb induces a heavy limb load on the nonparetic limb while standing, during steady-state walking, and STS.[5-7] As a result, persons with hemiparesis commonly exhibit significant asymmetry during standing and walking,[8,9] with increased body weight bearing through the nonparetic limb.[1,8] Therefore, a common rehabilitation goal for persons post stroke is to decrease the asymmetrical limb loading involving the paretic limb through weight-shifting or weight-bearing training.[1,4,10-12]

Visual or audio signals by instruments have been used in biofeedback therapy to achieve standing symmetry.[13,14] However, it is not known what the net effect of symmetrical weight bearing is in persons with hemiparesis who naturally show an asymmetrical weight bearing during quiet standing. Although stroke rehabilitation programs stressing symmetrical weight bearing result in improved symmetry during static standing, the achievement of more symmetrical limb loading during standing may not be a prerequisite for independent transfer or unsupported walking.[15] Standing asymmetry in persons with hemiparesis is associated with the primary neurological deficits caused by stroke as well as the secondary mechanical load of the distal lower limb[16] due to uneven weight distribution while standing. Accordingly, minimizing the secondary biomechanical effect might be a separate training result independent of the motor recovery of the primary neurological deficits caused by stroke. As examples, Winstein et al[1] indicated that improved static balance while standing was not transferred to the ability of steady-state walking in persons with hemiparesis.

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Rogers et al[6] reported that bending the knee in standing could not be transferred to motor control for the motion of the knee as a component of the walking pattern. Kirker et al[9] showed that a normal pattern of hip muscle activation was identified in stepping, whereas the response of these muscles to a perturbation while standing remained grossly impaired and was compensated by increased activity of the contralateral muscles.

These previous findings support the view that achieving static balance while standing may not be necessary for starting dynamic gait training in persons with hemiparesis. Little attention, however, has been given to validate the clinical assumption that improved weight shift ability onto the paretic limb while static standing would lead to a more symmetrical and effective gait pattern in persons with hemiparesis. Therefore, an examination of the underlying motor control mechanism with respect to symmetrical weight bearing is critically important to understand how biomechanical changes interact with the impaired motor control accompanying a transition movement such as gait initiation (GI) in persons with hemiparesis. GI is known as a well-defined motor task often used to assess the effects of sensorimotor deficits because it involves a stereotyped pattern of muscle activity.[17,18] In addition, GI is a single-axis gross movement in the sagittal plane at the ankle joint, generating momentum to move the body forward like an inverted pendulum.[19,20] The simplicity of this single-axis task affords a salient means to access motor control by minimizing the influence of other joint variables.[18,20,21] The task of GI begins with the inhibition of tonic soleus (Sol)[22] activity followed by the onset of activation of the tibialis anterior (TA) of both the swing and stance limbs.

Figure 1 shows the timing of kinematic and kinetic events during GI. This muscle sequencing pattern is responsible for the movement of the center of pressure (CoP) backward and toward the stance limb, which tends to propel the center of mass forward and toward the stance limb.[17] According to Brunt et al,[17,18] time to onset of electromyography (EMG) activity and force plate recordings, as well as time to swing toe-off, stance heel-off, swing heel strike, and stance toe-off for

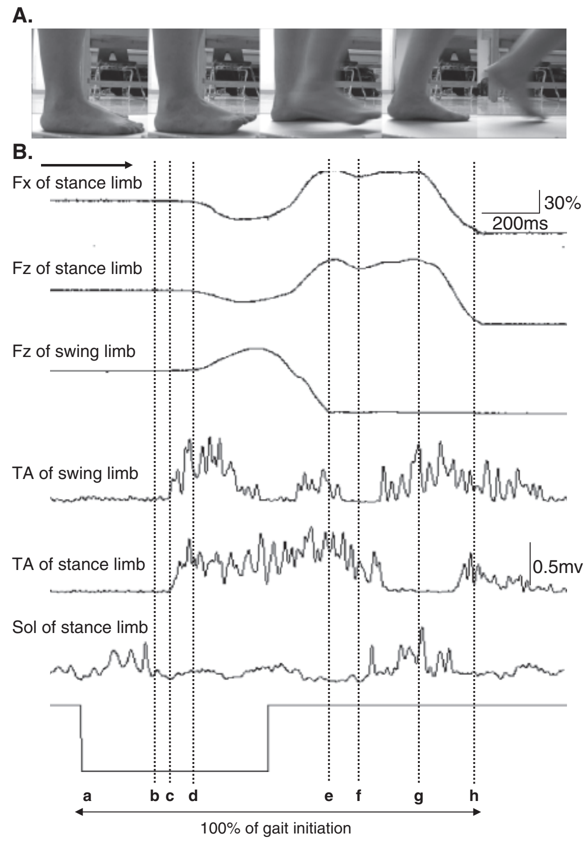

Figure 1. (A) Kinematic representation of the temporal events during gait initiation. (B) Horizontal (Fx) and vertical (Fz) ground reaction force and electromyographic recordings of bilateral tibialis anterior (TA) and soleus (Sol) from a single representative trial of gait initiation in a healthy subject. a. Light signal; b. stance Sol inhibition; c. swing and stance TA onset; d. onset of movement; e. swing limb toe-off; f. stance limb heel-off; g. swing limb heel strike; h. stance limb toe-off. The arrow indicates the direction of movement.

GI, all remain relatively invariant across slow, comfortable, and fast gait velocity in healthy persons. Even in an impaired sensory situation, kinetic temporal parameters are unchanged. Previous studies demonstrated that diminished single-limb postural instability by a tibial nerve block does not influence the change of kinetic temporal parameters during GI.[21] Trimble et al[23] reported that Sol H-reflexes were depressed to 37% of standing values during GI in a peroneal nerve-injured subject, even though no TA activity was observed. This finding is also consistent with the view that reciprocal inhibition of the Sol during GI, which normally involves TA activation, is independent of peripheral sensory input. Therefore, with respect to invariant temporal characteristics during GI, delayed or earlier temporal events during GI could be a biomechanical sign indicating movement compensation or impaired motor control in persons with hemiparesis.

Previous studies in persons with hemiparesis have demonstrated that during GI the magnitude of vertical and horizontal force generation on the ground varied depending on the initial loading when the paretic lower limb executed the first step.[5,6] This finding raises the question of whether weighting shift onto the paretic limb while standing influences the motor pattern of step execution during GI.[7] To investigate the underlying motor control mechanism, the present study examined the immediate effect of natural (asymmetrical) and symmetrical weight bearing on the temporal events of ground reaction forces (GRFs) and on timing and amplitude of lower distal muscle activity during GI in persons with hemiparesis. It was hypothesized that the relative temporal events of GRFs, the timing of TA and Sol muscle activity, and the amplitude of TA would be invariant across limb-loading conditions during GI in persons with hemiparesis.

Methods

Design and participants

The present study was a within-subjects design. Twelve subjects (7 males, 5 females) with unilateral hemiparesis were recruited from the database of the Veterans Affairs Brain Rehabilitation Research Center at the Malcom Randall Veterans Affairs, Gainesville, Florida. Subjects were required to be medically stable, capable of walking at least 5 m at their comfortable speed with guarded assistance, and standing independently for at least 30 seconds. Subjects who had a history of orthopedic or neurological conditions in addition to the stroke were excluded from the study. The ages ranged from 45 to 80 years (60.75 ± 9.85). Stroke duration ranged from 1 to 11 years (5.25 ± 3.14), which allowed time for natural recovery.[24,25] The characteristics of subjects with hemiparesis are presented in **Table 1**. The University of Florida Institutional Review Board and the Veterans Affairs Subcommittee for Clinical Investigation approved this protocol. Each participant provided informed consent before participating in the study.

Table 1. Description of subjects with hemiparesis

Subject	Age, years	Gender	Diagnosis	General locus	Stroke duration, years	CA (with cane, AFO)	FM balance	FM lower extremity score	Gait velocity (m/s)	Natural % BWD (P/NP)
1	56	M	Right infarct	Cerebrum	2	Yes (AFO)	12/14	32/34	0.85	48.9/51.1
2	62	M	Right infract	Cerebrum	9	Yes	11/14	23/34	1.07	46.2/53.8
3	45	F	Left hem	Cerebrum	4	Yes	12/14	27/34	0.9	51.2/48.8
4	61	M	Left hem	Cerebrum	9	Yes	12/14	27/34	1.04	44.1/55.9
5	53	M	Left infract	Brainstem	2	Yes (AFO)	9/14	16/34	0.36	20.4/79.6
6	67	M	Left infract	Cerebrum	3	Yes (cane)	12/14	27/34	0.62	43.5/56.5
7*	67	F	Right infarct	Cerebrum	8	Yes	10/14	32/34	0.82	37.4/62.6
8	64	F	Left infarct	Cerebrum	4	Yes (cane, AFO)	5/14	16/34	0.23	43.1/56.9
9*	80	M	Left infarct	Cerebrum	1	Yes	10/14	31/34	0.96	42.2/57.8
10	71	M	Left infarct	Cerebrum	11	Yes	14/14	32/34	1.25	59.8/40.2
11	51	F	Left infarct	Cerebrum	4	Yes	10/14	15/34	0.68	42.6/57.4
12	52	F	Right infarct	Cerebrum	6	Yes (cane, AFO)	9/14	14/34	0.36	40.8/59.2
Mean (*SD*)	60.75 (9.85)				5.25 (3.14)		10.5 (2.18)	24.33 (6.93)	0.76 (0.3)	43.3(9.3)/ 56.7(9.3)

Note: Subject 7 had second ipsilateral stroke; Subject 9 had a lacunar infarct. Gender: M = male; F = female. CA = community ambulation; AFO = ankle foot orthosis; FM = Fugl-Meyer; BWD = body weight distribution; P = paretic limb; NP = nonparetic limb; Hem = hemorrhage.

Equipment

EMG recording electrodes consisted of 2 silver-silver chloride 1-cm diameter electrodes embedded in an epoxy-mounted preamplifier system (× 35) whose centers were spaced 2 cm apart. Conductive paste was applied to the surface electrodes. After the subject's skin was cleaned with alcohol, surface electrodes were applied to the muscle belly of the TA and Sol of both lower extremities and held in place over the skin by adhesive tape. A reference electrode was attached to the medial aspect of the tibia. Placement of the electrodes was confirmed by the myoelectric signal during isometric muscle contraction. The EMG signals were band-pass filtered (20 Hz to 4 KHz; Therapeutics Unlimited, Iowa City, Iowa) and full-wave rectified online. Final amplification was 10 k. Two force platforms (Advanced Mechanical Technology Inc, Watertown, Massachusetts), embedded in a level walkway (10 m in length and 1.22 m in width), were used to identify the relative temporal events of GRF during GI. Processed EMG and amplified force platform signals were sampled online at a rate of 1000 Hz (BIOPAC System, Goleta, California). F-scan, paper-thin sensors (Tekscan Inc, South Boston, Massachusetts), was placed in the shoes to measure vertical GRF while subjects were standing. F-scan in the shoe system was processed at 120 to 150 Hz to capture foot pressure images. The output from the F-scan system was projected onto a screen at the end of the walk so that subjects received real-time feedback about the weight borne by each lower extremity. This did not interfere with the subject's normal gait.

Procedure

Fugl-Meyer lower extremity and gait velocity

The lower extremity and balance subsections of the Fugl-Meyer motor assessment[26] were performed on the hemiparetic subjects prior to the performance of GI to provide a global indicator of motor impairment. Subjects with hemiparesis donned the standard tennis footwear, and gait velocity was measured by having each subject walk 5 m. The time was measured using a stopwatch. No assistive devices such as a cane or an ankle brace were provided to the subjects to eliminate the effect of those devices during walking.

Symmetrical body weight limb-loading training

Data were recorded prior to GI testing to document the degree of asymmetry achieved. At the beginning of each trial, the subject was asked to watch the screen projected onto the wall in front of him or her that provided immediate feedback concerning the weight distribution or load on each lower limb from the F-scan system (**Figure 2**). Each subject exhibited different limb-loading conditions during natural, quiet standing without visual feedback by the F-scan system. The subject was asked to weight shift to achieve equal weight distribution with visual feedback. The subject practiced the symmetrical position 5 times to gain comfort.

Gait initiation

Next, each subject stood with 1 foot on each force plate, and the starting position was marked by drawing a line at the toe end of the shoe on the force plate. The subject performed the following conditions of limb-loading distribution prior to executing a step in a randomized order: (1) GI with the paretic limb during natural (asymmetrical) weight bearing; (2) GI with the nonparetic limb during natural weight bearing; (3) GI with the paretic limb during symmetrical weight bearing; and (4) GI with the nonparetic limb during symmetrical weight bearing. Subjects began walking at their comfortable speed when they saw a visual cue (light). They were asked to initiate gait as quickly as possible after the visual cue and to return to the marked position after each trial of GI. Subjects completed 5 trials with guarded assistance in each condition. The performance of GI was recorded on videotape. Rest was provided at any point during the testing, if requested. Otherwise, subjects were allowed to sit and rest between test conditions until they were comfortable with proceeding. This experiment took approximately 2 hours.

Data processing

For primary data analysis, the body weight distribution prior to a step execution was

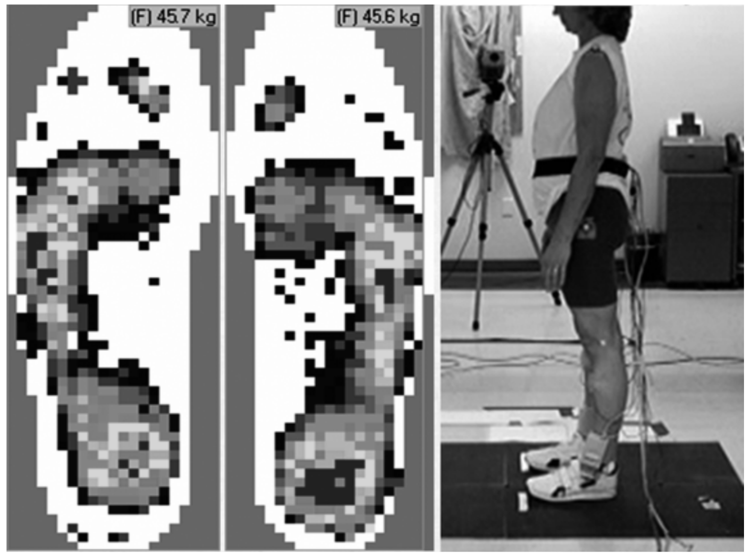

Figure 2. F-scan in the shoe system provides immediate feedback to achieve equal weight distribution while standing prior to executing the first step.

accurately calculated using the F-scan software. The software calibrated each subject's body weight as 100%. The weight distribution, depending on limb-loading conditions, was obtained from the F-scan system. We referred to the GRFs and EMG to determine the relative temporal events of GI. To normalize the temporal parameters of GI according to each subject, we considered the time from the visual cue to stance limb toe-off as 100% of the GI cycle (**Figure 1**). Measured relative temporal parameters included the following: (1) time to TA onset in the swing limb, (2) time to TA onset in the stance limb, (3) time to movement onset, (4) time to swing limb toe-off, (5) time to stance limb heel-off, (6) time to swing limb heel strike, and (7) the interval between Sol inhibition and TA activation on the stance limb.

The onset and offset of muscle activation were determined using an interactive cursor with 1-ms resolution. Onset of muscle activity occurred when the activity level exceeded the mean (the baseline of muscle activity for 30 ms plus 2 *SD*).[27] Offset of muscle activation was defined as when the activity level returned to the mean plus 2 *SD*. The peak TA muscle activity was obtained between visual cue and swing limb toe-off. To normalize the muscle amplitude, we considered the peak value of TA muscle during 1 gait cycle after stance limb toe-off as 100%. The root mean square[28] was used as a smoothing method of the surface EMG.[29] The signal was processed using a moving average of 20 data points.[29]

Data normalization

The Shapiro-Wilk test was used to determine normality of all initial measures of force plates and EMG. Log_{10} transformations were applied to normalize the relative temporal and EMG parameters for the following variables: (1) time to TA onset in the swing limb, (2) time to TA onset in the stance limb, (3) time to swing limb heel strike, (4) the interval between Sol inhibition and TA activation on the stance limb, and (5) peak amplitude of the stance limb TA activity in persons with hemiparesis.

Statistical analysis

Multivariate analysis of variance techniques with 1 fixed factor (limb loading) were used to identify the multivariate effect of loading for dependent variables. A multivariate *F* value was obtained from Wilks lambda. To know exactly which limb-loading conditions means were significantly different from other limb-loading means, we used post hoc univariate *F* tests. The least significant difference (LDS) test was used for multiple comparisons with regard to side of initiation (paretic vs nonparetic) and limb-loading conditions (symmetrical vs natural). The dependent variables were the following parameters: (1) time to TA onset in the swing limb, (2) time to TA onset in the stance limb, (3) time to movement onset, (4) time to swing limb toe-off, (5) time to stance limb heel-off, (6) time to swing limb heel strike, (7) the interval between Sol inhibition and TA activation on the stance limb, (8) peak amplitude of the swing limb TA, and (9) peak amplitude of the stance limb TA during GI. The *P* value of less than .05 was considered to indicate significant differences. All data were analyzed using the Statistical Package for the Social Sciences (SPSS 17 for Windows; SPSS Inc, Chicago, Illinois).

Results

Symmetrical weight bearing prior to GI

The subjects showed an average 43.3 percent body weight (%BW) (±9.3) (Fz) distribution on the paretic limb and 56.7 %BW (±9.3) on the nonparetic limb during quiet natural standing without visual feedback (**Table 1**). Most of the subjects successfully achieved symmetrical body weight limb loading, 50.60 %BW (±5.35) on the paretic limb and 50.42 %BW (±5.40) on the nonparetic limb during the 3 trials in response to verbal instructions and visual weight distribution feedback from F-scan system.

Temporal events of GRFs and timing and amplitude of distal muscles during GI

The multivariate main effect (Wilks lambda) for limb-loading conditions was significant ($F_{24,67}$ = 2.310, P = .004). There were no significant changes on the relative temporal events of GRFs, but timing and amplitude of TA muscle across limb-loading conditions during GI were significant. The univariate main effects were significant for time to TA onset in the swing limb ($F_{3,30}$ = 15.527, P = .000), time to TA onset in the stance limb ($F_{3,30}$ = 2.991, P = .047), and peak amplitude of the swing limb TA ($F_{3,30}$ = 3.755, P = .021). The onset of TA muscle on the paretic side was delayed about 20% GI when the paretic limb was the swing limb compared with TA on the nonparetic side when the nonparetic limb was the swing limb during GI (**Table 2**).

LSD tests showed a significant effect of side of initiation (paretic vs nonparetic) and limb-loading conditions (symmetrical vs natural) during GI. First, with respect to side of initiation, initiating gait with the nonparetic (swing) limb caused the normal timing and greater peak amplitude of TA muscle on the paretic (stance) limb in persons with hemiparesis (P < .05). However, there were no

Table 2. Percentage of gait initiation (GI) cycle of selected temporal events and peak electromyography amplitude of the tibialis anterior (TA)

Limb loading / events	GI with the paretic limb during NWB	GI with the non paretic limb during NWB	GI with the paretic limb during SWB	GI with the non paretic limb during SWB
Swing TA onset (%)*	44.29[a] (15.76)	24.71 (10.91)	46.79[a] (6.39)	28.34 (12.19)
Stance TA onset (%)*	24.60 (13.41)	23.51[a] (10.72)	27.12 (11.31)	27.90[a] (9.54)
Onset of movement (%)	19.42 (4.48)	19.67 (3.62)	22.50 (7.84)	25.45 (4.72)
Swing toe-off (%)	55.48 (5.48)	56.39 (5.09)	57.87 (6.90)	58.57 (4.25)
Stance heel-off (%)	69.76 (2.58)	66.03 (7.67)	69.03 (5.77)	64.97 (7.10)
Swing heel strike (%)	80.98 (3.23)	75.63 (10.20)	81.19 (4.53)	76.86 (9.15)
Sol/TA interval (%)	3.046 (1.26)	3.18 (0.96)	2.72 (0.77)	3.39 (0.82)
Peak amplitude of swing TA (%)*	41.70[a] (25.16)	75.81 (36.35)	43.54[a] (26.32)	75.29 (29.26)
Peak amplitude of stance TA (%)	68.21 (22.90)	73.92[a] (44.53)	79.76 (50.36)	68.40[a] (43.12)

Note: Percent GI is taken from the visual cue to toe-off stance limb; percent of maximum TA activity is taken during 1 gait cycle after stance limb toe-off during GI. NWB = natural weight bearing; SWB = symmetrical weight bearing; Sol = soleus.

[a]The arrow indicates percent GI change of timing and peak amplitude of TA muscle on the paretic limb.

*Statistically significant differences among limb-loading conditions, P < .05.

significant effects of initiating gait with the paretic limb on timing and amplitude of TA muscle on the paretic limb. Second, with respect to limb-loading conditions, initiating with the nonparetic (swing) limb caused a significantly delayed muscle excitation of TA on the paretic (stance) limb while in the symmetrical weight-bearing condition ($P < .05$). However, there were no significant effects of initiating gait with the paretic (swing) limb on timing and amplitude of TA muscle on the paretic (swing) limb while in the symmetrical weight-bearing condition ($P > .05$).

Discussion

The primary finding of this study was that impaired TA muscle on the paretic limb of persons with hemiparesis was activated in a normal sequence of muscle excitation, with greater amplitude when the paretic limb was loaded to allow the nonparetic limb to initiate the first step (**Table 2** and **Figure 3**). In **Figure 3**, the ground reaction force (swing Fz) exhibits an increase with loading in preparation for executing a step. In **Figures 3A** and **3C**, when the subject initiated a step with the paretic limb, the activation pattern of the swing TA is delayed in onset. According to Brunt et al,[17,18] both TA muscles of swing and stance limbs would burst, disrupting balance in preparation of step execution. In **Figures 3B** and **3D** when the subject initiated a step with the nonparetic limb, note the simultaneous burst of TA activity aligned on the arrow. The arrow corresponds to the onset of preparatory movement of the center of pressure for stepping. However, no temporal sign arose on the paretic limb related to GI with the paretic limb while symmetrical weight bearing in the present study. This finding indicates that symmetrical weight bearing in persons with hemiparesis may not affect the temporal events of GI patterns and timing and amplitude of TA muscle activity necessary for GI. Thus, achieving symmetrical weight bearing while static standing may not be a prerequisite for the earlier start of dynamic gait training. Brunt et al[5] reported that the inability to generate forward body progression appears related to the absence of TA activity when movement occurs. Thus, patients with symmetrical limb loading while standing showed increased forward momentum with TA activity on the paretic limb during GI.[5] However, this study showed that improvement of standing symmetry during GI did not induce any adequate muscle activity on the impaired TA muscle for the effective weight shift necessary during GI. This finding indicates the sensory information accompanying symmetrical limb loading while static standing may not link with the central command system to control the motor performance during GI.

This study shows that when initiating gait with the nonparetic (swing) limb, the paretic TA muscle (stance) was activated at the normal relative timing of percent GI cycle (**Figure 3**). In addition, when initiating gait with the nonparetic limb, the amplitude of the TA muscle on the paretic (stance) limb was significantly increased about 27% to 36% compared with the paretic limb as swing limb in both natural and symmetrical limb-loading conditions (**Table 2**). This finding implies that initiating gait with the nonparetic limb might result in more effective backward movement of CoP,[30] which is associated with appropriate timing of the TA muscle on the paretic limb during GI.[31] This study demonstrates that increased amplitude of the TA muscle on the paretic limb was strongly related to the timing of TA muscle activity while initiating the first step with the nonparetic limb during GI. When starting with the nonparetic limb, the CoP must be shifted to the paretic limb, and the paretic limb should play a role as a support limb during GI. Hesse et al[8] indicated that the CoP in persons with hemiparesis was already shifted to the nonparetic limb prior to step execution, whereas CoP is located midway between both feet in healthy people. Although starting GI with the nonparetic limb, the forward momentum was weaker than when starting with the paretic limb,[5,8] and the paretic limb may have a greater potential to be activated for the body forward progression as a support limb.

The relative timing of swing limb heel strike was not altered at all by any limb-loading conditions. Breniere et al[20,32] indicated that the time to first step remained invariant across slow, normal, and fast walking speeds during GI, because during this phase the body behaves as an inverted pendulum

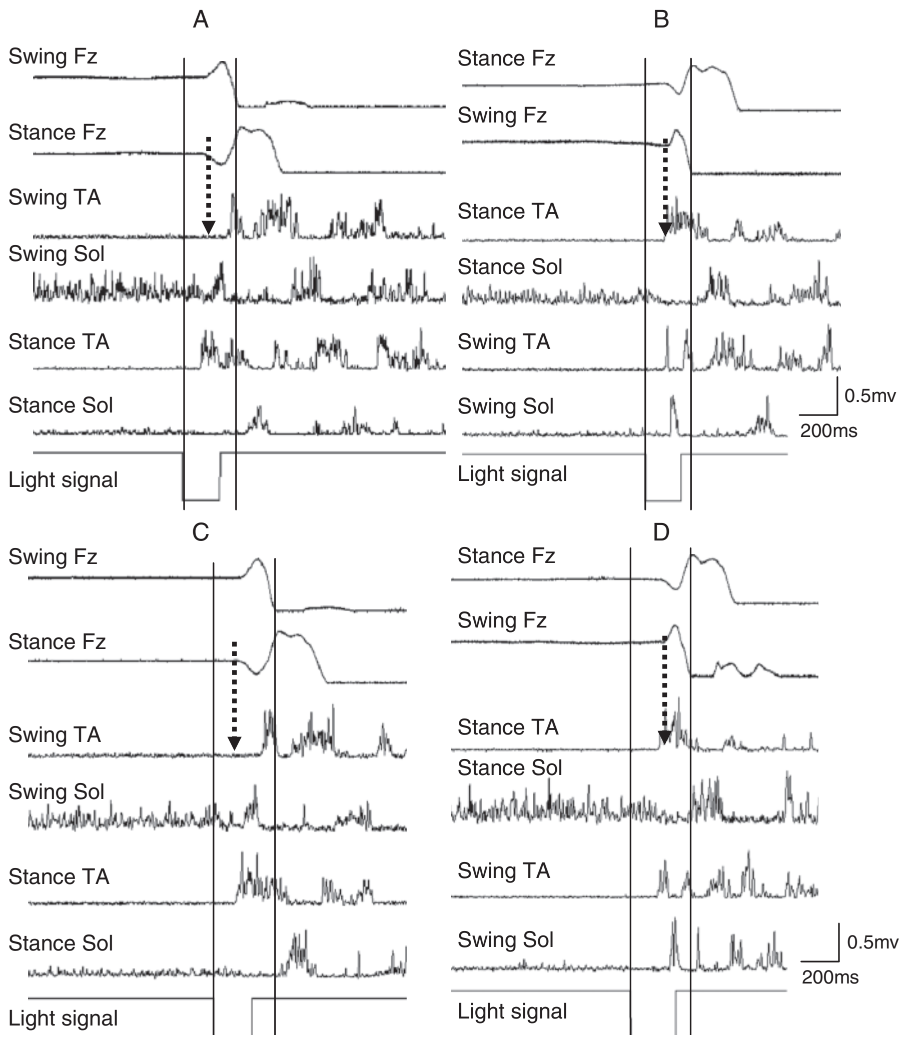

Figure 3. Individual trials from persons with hemiparesis for (A) natural standing position starting with the paretic limb, (B) natural standing position starting with the nonparetic limb, (C) symmetrical limb-loading standing position starting with the paretic limb, and (D) symmetrical limb-loading standing position starting with the nonparetic limb. The arrow indicates the delayed TA (A, C) and presence of TA (B, D). Fz represents vertical ground reaction force. TA = tibialis anterior; Sol = soleus.

and the period of first step might be determined by the biomechanical factors. The relative timing of swing limb heel strike in the present study was similar to the findings of Brunt et al[18] even when comparing an older population (41 to 71 years in this study) with the younger population (18 to 40 years). Thus, time to swing limb heel strike might be an invariant temporal marker determined by the biomechanical factors [20] rather than the central programming of GI.

The interval between Sol inhibition and TA activation during the time from the visual cue to movement onset remained invariant across limb-loading conditions in persons with hemiparesis. When a subject initiates walking,[17] steps over an obstacle,[17] or flexes the knee,[6] the Sol muscle is inhibited bilaterally, and a large burst of TA activity is required to generate the backward movement momentum.[20,33,34] A quick loading of the swing limb and unloading of the stance limb comes with these patterns of muscle activations during GI.[31,34] This sequential synergetic interaction between Sol inhibition and TA activation has been considered a centrally mediated motor program.[31] According to Cordo et al,[35] programmed movement commands determine the temporal sequencing of muscle activity. For instance, the inhibition of tonic Sol followed by the onset of TA represents central programming to execute the step from quiet standing because the interval between Sol inhibition and TA activation remains invariant across intended gait velocities.[30] Crenna et al[30] found that the interval between Sol inhibition and TA activation for all speeds of GI averaged about 100 ms. Brunt et al[17] reported that the interval ranged from 46 to 51 ms regardless of GI speed. This study also showed the interval between Sol inhibition and TA activation ranged from 49 to 61 ms in persons with hemiparesis. Long loop reflexes take more than 100 ms for sensory feedback signals to reach the cortex in the performance of rapid movements.[36,37] This finding suggests that the programming of temporal muscle sequence during GI is independent of peripheral sensory input, depending on limb-loading conditions as well.

Conclusion

According to Hill et al,[38] only 7% of all stroke survivors are able to walk independently in the community. Even among those who achieve independent walking, most of them with residual motor disability are not able, for instance, to walk independently in a crowded shopping center.[39]

Active weight shifting is an important factor in determining the degree of walking ability in persons with hemiparesis. However, this study suggests that symmetrical weight bearing while standing may induce a better postural alignment, but it may not affect the temporal events of GI patterns and timing and amplitude of TA muscle activity necessary for GI. The task of GI requires a transition from a relatively large base of support in bipedal stance to a small base of support in single-limb stance.[40] The body's center of mass moves outside of the base of support during GI. Therefore, initiating gait with the nonparetic limb challenges dynamic balance in a manner similar to the balance required during gait in persons with hemiparesis. As a result, this study suggests that initiating gait with the nonparetic limb as a pregait activity may more effectively challenge the dynamic balance for a symmetrical gait pattern than the standard standing weight shifting in persons with hemiparesis.

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Virtual Reality in Stroke Rehabilitation: A Meta-Analysis and Implications for Clinicians

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Virtual Reality in Stroke Rehabilitation

A Meta-Analysis and Implications for Clinicians

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Background and Purpose—Approximately two thirds of stroke survivors continue to experience motor deficits of the arm resulting in diminished quality of life. Conventional rehabilitation provides modest and sometimes delayed effects. Virtual reality (VR) technology is a novel adjunctive therapy that could be applied in neurorehabilitation. We performed a meta-analysis to determine the added benefit of VR technology on arm motor recovery after stroke.

Methods—We searched Medline, EMBASE, and Cochrane literature from 1966 to July 2010 with the terms "stroke," "virtual reality," and "upper arm/extremity." We evaluated the effect of VR on motor function improvement after stroke.

Results—From the 35 studies identified, 12 met the inclusion/exclusion criteria totaling 195 participants. Among them, there were 5 randomized clinical trials and 7 observational studies with a pre-/postintervention design. Interventions were delivered within 4 to 6 weeks in 9 of the studies and within 2 to 3 weeks in the remaining 3. Eleven of 12 studies showed a significant benefit toward VR for the selected outcomes. In the pooled analysis of all 5 randomized controlled trials, the effect of VR on motor impairment (Fugl-Meyer) was OR=4.89 (95% CI, 1.31 to 18.3). No significant difference was observed for Box and Block Test or motor function. Among observational studies, there was a 14.7% (95% CI, 8.7%–23.6%) improvement in motor impairment and a 20.1% (95% CI, 11.0%–33.8%) improvement in motor function after VR.

Conclusions—VR and video game applications are novel and potentially useful technologies that can be combined with conventional rehabilitation for upper arm improvement after stroke. **(*Stroke*. 2011;42:00-00.)**

Key Words: outcomes ■ randomized controlled trials ■ rehabilitation ■ stroke recovery ■ virtual reality

Stroke is a devastating disease for patients and their families and a leading cause of adult disability. The risk of stroke increases steeply with age; thus, with the aging of the population, an increase in the prevalence of stroke is expected.[1,2] Between 55% and 75% of survivors continue to experience motor deficits associated with reduced quality of life.[3,4] Consequently, with the aging population, more individuals are expected to face the challenge of managing diminished function after stroke.[2,5] Current clinical practice guidelines for stroke rehabilitation are based on increasing evidence from basic science and clinical studies of the remarkable potential for brain remodeling due to neuroplasticity after neurological injury.[4,6,7] Specifically, recent studies have suggested that training has to be challenging, repetitive, task-specific, motivating, salient, and intensive for neuroplasticity to occur.[7] However, current resources are unable to fulfill the intensity requirement for optimizing postinjury neuroplasticity.[8] Although standard rehabilitation (ie, physiotherapy and occupational therapy) helps improve motor function after stroke, only modest benefits have been shown to date. Some of the limitations of conventional rehabilitation approaches are outlined in Table 1.[5,9,10] The head-to-head comparison of conventional rehabilitative approaches (ie, neurodevelopmental techniques, proprioceptive neuromuscular facilitation, or motor relearning) has shown no significant differences between treatment approaches in functional outcomes in stroke survivors.[9,11] The shortage of rehabilitation providers and resources in different regions has limited the provision of adequate and appropriate rehabilitation services to stroke survivors.[5,10] As a result of the limitations of conventional rehabilitation, novel strategies targeting motor skill development and taking advantage of the elements enhancing experience-dependent plasticity[7] have recently emerged, including activities using robotics and virtual reality (VR) technology.[9,12,13]

VR is a computer-based technology that allows users to interact with a multisensory simulated environment and receive "real-time" feedback on performance. VR exercise applications have the potential to apply relevant concepts of neuroplasticity (ie, repetition, intensity, and task-oriented training of the paretic extremity).[9] VR applications range

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Table 1. Limitations of Conventional Rehabilitation[9,11]

Time-consuming
Labor- and resource-intensive
Dependent on patient compliance
Limited availability depending on geography
Modest and delayed effects in some patients
Requires transportation to special facilities
Initially underappreciated benefits by stroke survivors
Requires costs/insurance coverage after the initial phase of treatment

from nonimmersive to fully immersive depending on the degree to which the user is isolated from the physical surroundings when interacting with the virtual environment.[12] Also classified as VR are a variety of nonimmersive video game systems developed by the entertainment industry for home use, making this technology less costly and more accessible to clinicians and individuals. Several of these games have been adopted by clinicians as rehabilitation interventions although they have not been especially designed to meet rehabilitation goals. In the present study, we reviewed the literature and completed a meta-analysis to evaluate the effectiveness of VR applications including commercial video game systems for upper limb functional recovery after stroke.

Methods

We aimed to include articles published in MEDLINE, EMBASE, and Cochrane Review from 1966 to July 2010.

Eligibility Criteria

The search strategy was set to include both clinical trials and observational studies on the use any VR system in the rehabilitation of the upper extremity of patients who had acute, subacute, or chronic stroke.

Exclusion Criteria

Studies were excluded if they were not carried out on humans, the intervention targeted lower extremity rehabilitation, or did not provide information on the outcome of interest. We also excluded case reports or small case series including <3 patients.

Search Strategy

We searched MEDLINE (PUBMED search engine), EMBASE, and the Cochrane library. Search included the following terms: "stroke," "virtual reality," "upper extremity," "upper arm," or "upper limb."

Data Reviews

Two independent reviewers (M.L. and G.S.) screened the retrieved abstracts for eligibility according to their relevance. Inconsistencies were resolved through discussion until a consensus was reached.

Outcome Measures

The primary outcome was improvement of Fugl-Meyer, a measurement of motor impairment. Secondary outcomes included improve-

Table 2. Virtual Reality in Neurorehabilitation of the Upper Extremity After Stroke: Study Characteristics

Author	Design	No.	Age Range, years	Time Since Stroke Onset	Type of VR	Intervention
Holden et al (2002)[15]	Pre/post	9	26–68	>6 mo	Nonimmersive (Virtual teacher)	1 h/d, 3 d a week×20–30 sessions
Boian et al (2002)[16]	Pre/post	4	58–72	1–4 y	Nonimmersive (CyberGlove and a Rutgers Master, Immersion Corp, San Jose, CA	2 h/d, 5 d a week, 3 wk
Piron et al (2003)[17]	RCT	VR=12 CR=12	NA	<3 mo	Nonimmersive (VR Motion, VRmotion Ltd, Padova, Italy)	1 h/d, 5 d a week, 5–7 wk
Piron et al (2005)[18]	Pre/post	50	58 (mean)	>6 mo	Nonimmersive (VR Motion, VRmotion Ltd, Padova, Italy)	1 h/d, 5 d a week, 4 wk
Jang et al (2005)[19]	RCT	VR=5 Control=5	43–68	>6 mo	Immersive (IREX, GestureTek technologies, Toronto, Canada)	1 h/d, 5 d a week, 4 wk
Merians et al (2006)[20]	Pre/post	8	46–81	1–4 y	Nonimmersive (CyberGlove and a Rutgers Master, Immersion Corp., San Jose, CA)	2–2.5 h/d, 13 d, 3 wk
Broeren et al (2007)[21]	Pre/post	5	53–63	>6 mo	Immersive (Reaching APE and Crystal Eyes)	45 min/d, 3 d a week, 5 wk
Fischer et al (2007)[22]	RCT	CO=5 PO=5 Control=5	32–88	1–38 y	Immersive (Glasstrom, Sony Electronics, Tokyo/CAVE, VRCO, Virginia Beach)	60 min, 18 sessions, 6 wk
Yavuzer et al (2008)[23]	RCT	VR=10 Sham VR=10	61 (mean)	<12 mo	Immersive (Playstation EyeToy, Sony Entertainment, Tokyo, Japan)	30 min/d, 5 d a week, 4 wk
Kamper et al (2010)[24]	Pre/post	VR+device=7 VR control=7	54 (mean) 57 (mean)	>6 mo	Non-Immersive (PneuGlove, Vinyl Technology, Inc, Monrovia, CA)	60 min×3 d a week, 6 wk
Yong et al (2010)[25]	Pre/post	16	65 (mean)	< 3 mo	Nonimmersive (Wii, Nintendo, Tokyo, Japan)	30 min×6 sessions within 4 wk
Saposnik et al (2010)[25]	RCT	VR+CR=10 RA+CR=10	41–83	<3 mo	Nonimmersive (Wii, Nintendo, Tokyo, Japan)	60 min×8 sessions within 2 wk

RCT indicates randomized controlled trial; VR, virtual reality; CR, conventional rehabilitation; CO, cable orthosis; PO, pneumatic orthosis; RA, recreational activities.

Table 3. Virtual Reality in Neurorehabilitation of the Upper Extremity After Stroke: Outcome Measures

Author	Time Since Stroke Onset	Total No. of Sessions	Outcome Measures	Findings
Holden et al (2002)[15]	Chronic	20–30 sessions	FM, WMFT	Post-training improvement FM 15%, time improvement in WMFT 24%, improvement in total WMFT 31%
Boian et al (2002)[16]	Chronic	15 sessions	JTHF	Significant improvement in computerized measure of thumb range, finger speed, 23%–28% improvement in JTHF
Piron et al (2003)[17]	<3 months	25–35 sessions	FM, FIM	Improvement in FM 20.2% (VR), 11.3% (control); both groups showed a significant improvement at follow-up
				Improvement in FIM 12.4% (VR), 9.3% (control); both groups showed a significant improvement at follow-up
				No significant difference found in FM and FIM between groups
Piron et al (2005)[18]	Chronic	20 sessions	FM, FIM	Improvement after training FM 15%, FIM 6%, and mean duration of 18% (all $P<0.05$)
Jang et al (2005)[19]	Chronic	20 sessions	FM, BBT, MFT	Improvement in BBT 15.4% (VR) vs 10% (control; $P<0.05$)
				Improvement in FM 13.7% (VR) vs 3.8% (control) ($P<0.05$)
				Improvement in Manual Function test 10% (VR) vs 0% (control)
Merians et al (2006)[20]	Chronic	13 sessions	JTHF	Postintervention improvement in range of motion 19.7% ($P<0.005$), velocity 9.8% ($P<0.007$), and JTHF 15% (0.008); similar degree of improvement were 1 wk postintervention
Broeren et al (2007)[21]	Chronic	15 sessions	Kinematics, BBT, AMPS	Unilateral dexterity improved 11% post-test and 17% at follow-up
				Grip strength: improvement 13%–57% of the mean score compared with a age-/sex-matched healthy control subjects
				No significant difference was observed in BBT and AMPS
Fischer et al (2007)[22]	Chronic	18 sessions	WMFT, FM, BBT	Improvement in WMFT 7.2% (control), 2.2% (CO), 14.1% (PO; $P=0.02$)
				Improvement in FM 12% (control), 14.3% (CO), −5.3% (PO)
				BBT 0→3 (control), 3→5 (CO), 4→3 (PO)
Yavuzer et al (2008)[23]	Subacute/ chronic	20 sessions	Brunnstrom, FIM	Significant difference in the change of motor performance (Brunnstron scale) between groups ($P<0.009$) and FIM self-care ($P<0.001$)
				Improvement in motor performance (baseline to postintervention) within group 47.4% (VR), 3.7% (control)
				Improvement in FIM (baseline to postintervention) within group 20% (VR), 4.2% (control)
Kamper et al (2010)[24]	Chronic	18 sessions	FM, BBT	Improvement in FM 12.2% (VR) vs 16.5% (VR globe; $P<0.05$)
				Improvement in grip strength 12.3% (VR) vs 3.9% (VR globe; $P<0.05$)
				Improvement in BBT 3.9% (VR) vs 20.7% (VR globe; $P<0.05$); similar findings were observed at follow-up 4 wk postintervention
Yong et al (2010)[25]	Subacute	6 sessions	FM, MFT, MAS	Improvement in FM 12.2% ($P=0.007$), Motricity index 6.6% ($P=0.031$), and MAS 20.6% ($P=0.32$)
Saposnik et al (2010)[26]	Subacute	8 sessions	WMFT, BBT, SIS	Improvement within VR group in WMFT (35.5%), BBT (26%), and grip strength (29%)
				Improvement within the control group in BBT (49%) and SIS hand (17%); no improvement observed in WMFT, grip strength; there was a 35% improvement in WMFT (−7; 95% CI −14.5 to −0.2) favoring the VR group after adjustment for differences in baseline characteristics

FM indicates Fugl-Meyer Arm Scale; WMFT, Wolf Motor Function Test; JTHF, Jebsen Test of Hand Function; FIM, Functional Independence Measure; BBT, Box and Blocks Test; MFT, Manual Function Test; AMPS, Assessment of Motor and Process Skills; MAS, Modified Ashworth Scale; SIS, Stroke Impact Scale; VR, virtual acuity; CO, cable orthosis; PO, pneumatic orthosis.

ment in motor function measured as Wolf Motor Function Test (WMFT), Box and Block Test, and Jebson-Taylor Hand Function Test.

Analysis

The Comprehensive-Meta-analysis software package (Biostat Inc 2006) was used for the meta-analysis. Differences in outcomes measures between groups or from baseline are reported in relative terms as provided by the authors or estimated from raw data. We assessed heterogeneity using χ^2 test and I^2.[14] A separate analysis was completed for randomized controlled trials (RCTs) and observational studies due to methodological differences. For RCTs, we evaluated the pooled treatment effect (Mantel-Haenszel OR) by using random-effect models to reduce the effects of heterogeneity between studies. For observational

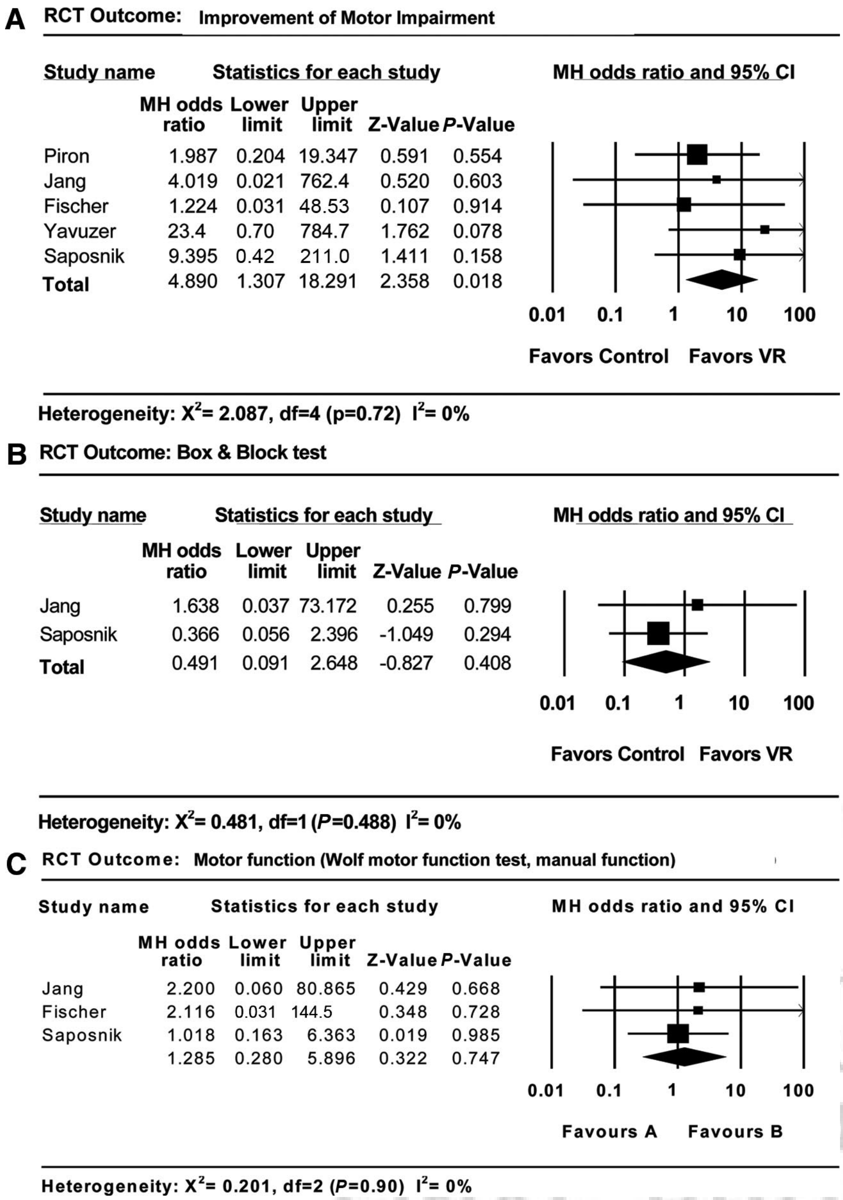

Figure 1. Meta-analysis of RCTs using VR systems in upper extremity impairment (**A**) and motor function (**B, C**). RCTs indicates randomized controlled trials; VR, virtual reality.

studies, we used standardized mean difference and 95% CIs to represent the magnitude of the improvement compared with baseline. For all analyses, $P<0.05$ was considered statistically significant (see details in the Supplement file; http://stroke.ahajournals.org).

Results

There were 35 articles published in Medline combining the selected terms. There were no studies published in EMBASE or in the Cochrane Collaboration. Twelve studies met the inclusion criteria.[15–26] Among them, there were 5 RCTs[18,19,22,23,26] and 7 observational studies with a pre-/postintervention design.[15–17,20,21,23,25] Table 2 summarizes the studies' characteristics and outcomes. Studies included VR (n=9) and commercial video game (n=3) interventions. Only 3 studies targeted patients with acute/subacute stroke[18,25,26]; the remaining 9 included patients with chronic stroke (>6 months). Age ranged from 26 to 88 years old. Two thirds (n=8) of the interventions used nonimmersive VR systems (Virtual teacher, Cyberglobe, VR Motion, Pneumoglobe, Wii). Among the RCTs, there were 3 studies using immersive VR (eg, Glasstrom, IREX, Playstation EyeMotion)[19,22,23] and 2 applying nonimmersive systems (eg, VR Motion, Wii).[18,26]

Interventions were delivered within 4 to 6 weeks in most of the studies (n=9). The duration of the sessions were 1 hour in most of the studies (n=7; range, 30 minutes to 2.5 hours/session). The most commonly used outcome measure was the Fugl-Meyer (n=7) followed by the Box and Block Test (n=4), the WMFT (n=3), and the Functional Independence Measure (n=3). Eleven of 12 studies showed a significant benefit toward VR for the selected outcomes (Fugl-Meyer, WMFT, Functional Independence Measure; Table 3).

At the Body Structure and Function level of the International Classification of Functioning,[27] major outcomes were Fugl-Meyer scores and measures of arm movement speed, range of joint motion, and force. At this level, improvements ranged from 13.7% to 20% compared with 3.8% to 12.2% for control groups. Similarly at the activity level of the Interna-

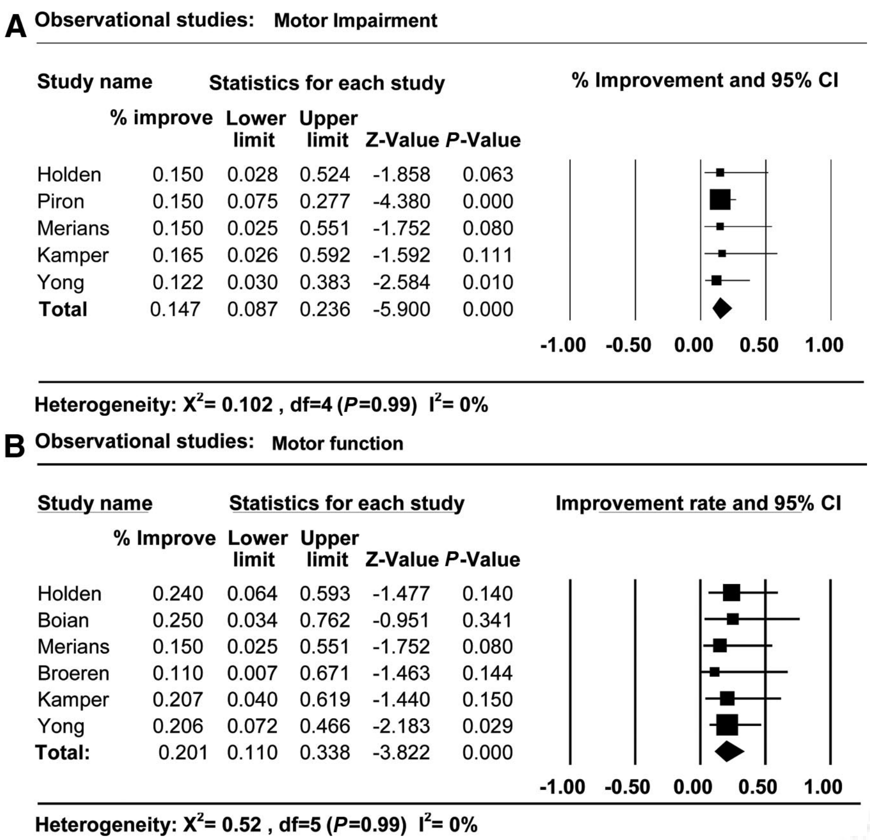

Figure 2. Meta-analysis of observational studies using VR systems in upper limb impairment (**A**) and motor function (**B**). VR indicates virtual reality.

tional Classification of Functioning, outcomes such as WMFT, the Jebson-Taylor Hand Function Test, and the Box and Block Test showed increases of 14% to 35.5% for VR applications compared with 0% to 49% for control groups. After all 5 RCTs were pooled (Figure 1), the effect of VR on motor impairment was OR=4.89(95% CI, 1.31 to 18.3; $P<0.02$; Figure 1A). There was no significant effect on the Box and Block Test (Figure 1B; 2 RCTs; OR, 0.49; 95% CI, 0.09 to 2.65; $P=0.41$) or WMFT (Figure 1C; 3 RCTs; OR, 1.29; 95% CI, 0.28 to 5.90; $P=0.74$). Among observational studies (Figure 2), the effect of VR on motor impairment (percent improvement from baseline) was 14.7% (95% CI, 8.7% to 23.6%; $P<0.001$; Figure 2A) after either type of VR. The effect on motor function (Jebson-Taylor Hand Function Test, WMFT, Motor Activity Scale) was 20.1% (95% CI, 11.0% to 33.8%; $P<0.001$; Figure 2B). The sensitivity analysis using fixed-effect models showed no difference in the significance of the treatment effect for any of the outcomes. There was no evidence of publication bias for the assessed outcomes as per the visual (see Supplemental Figure I) or statistical methods (Egger $P=0.639$).

Discussion

Rehabilitation is an essential component to any program aimed at improving motor function in stroke survivors.[4,11] Novel strategies are becoming available to overcome the modest benefits of conventional rehabilitation.[9,28] The current paradigm for assessing innovative interventions in rehabilitation should include an evaluation of function, activities, and social participation.[27,29] Different tools (eg, scales) are available to assess each domain. In a recent systematic review comparing different approaches in stroke rehabilitation, constraint-induced movement therapy was more effective than conventional rehabilitation in patients within 3 to 9 months from stroke.[9,29] Interestingly, VR applications were not included.[9]

In the present meta-analysis, we found 12 studies and 5 RCTs. Eleven of 12 studies showed a benefit for the primary outcome. There was a significant 4.9 higher chance of improvement in motor strength for patients randomized to VR systems. Formal testing did not identify any substantial heterogeneity among trial findings. Similarly, there was a significant 15% improvement in motor impairment and 20% improvement in motor function outcomes from the pooled observational studies.

There Were No Large Studies Comparing the Benefit of the Combination of Conventional Therapy and VR Technology

In a previous literature review completed in 2007 by members of our group examining studies using VR systems applied to the arm as a rehabilitation strategy after stroke, there were only 5 publications, 2 RCTs and 3 observational studies.[12] Meta-analysis was not completed. Because VR systems are now more available and more widely used, further analysis from the clinician's perspective is warranted.

However, there are several differences in the population target, design, VR systems, and interventions. For example, some studies compared an intervention plus conventional physical therapy versus conventional physical therapy alone, which by necessity allowed for more rehabilitation time in the experimental group.[9] This creates a bias in favor of the new intervention because the intensity and frequency of rehabilitation per se is known to directly and beneficially affect functional outcomes. Moreover, there was a broad variety of outcome measures. Some studies focused on single rather than multiple dimensions (eg, motor impairment, activities, social participation/quality of life). For instance, the main outcome measure was motor function using WMFT or the Box and Block Test in 6 of 12 studies, and only 1 included social participation/quality of life (Stroke Impact Scale). Improvement in activities of daily living (eg, Barthel index; 0/12) or social participation/quality (1/12) of life were not included in the majority of the studies.

The limited number of studies is likely due to the only recent availability of this novel technology and, therefore, subject to potential publication bias. For example, in the 1990s, most VR systems were limited to use in research laboratories. More recently, the entertainment industry has facilitated a significant growth in the number of rehabilitation applications. In fact, 6 of 12 studies included in the present meta-analysis were published in the last 3 years.

What Are the Potential Implications for Clinicians?

Recovery of motor skill depends on neurological recovery, adaptation, and learning new strategies and motor programs.[7,9] VR systems apply relevant concepts for driving neuroplasticity (ie, repetition, intensity, and task-oriented training of the paretic extremity)[9] and lead to benefits in motor function improvement after stroke.[12] This is possible due to cortical reorganization and rewiring in the injured brain (brain plasticity).[6,19] The use of VR showed practice-dependent enhancement of the affected arm through the facilitation of cortical reorganization. This process may be facilitated by the provision of multisensorial (visual, auditory, and tactile) feedback of some VR systems (eg, Wii, Kinect, Playstation).[19] The duration and intensity of the rehabilitation strategy are important factors in its effectiveness.[9] The present analysis suggests that VR and video game applications may be promising strategies to increase the intensity of treatment and to promote motor recovery after stroke. However, not all patients would be eligible for this technology. Most studies included patients with mild to moderate stroke and did not assess the more challenging severely affected patients. Future studies may help determine whether the combination of VR with conventional physical and occupational therapy enhances stroke rehabilitation.

Stroke rehabilitation is rapidly evolving. Novel approaches including the use of VR systems may help improve motor impairment, activities, and social participation. The primary purpose of this review is to present information rather than to offer advice or recommendations. Larger multicenter randomized trials are needed before making conclusions that might influence clinical practice. The completion of well-designed RCTs will ultimately advance knowledge about the optimal rehabilitation strategy for patients with a disabling stroke.

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