Published in final edited form as:

Exp Brain Res. 2016 October ; 234(10): 2841–2847. doi:10.1007/s00221-016-4686-5.

Retention of the spacing effect with mental practice in hemiparetic stroke

Stephen J. Page¹, Erinn M. Hade², and Juan Pang²

Stephen J. Page: Stephen.Page@osumc.edu

¹B.R.A.I.N. Laboratory (Better Rehabilitation and Assessment for Improved Neuro-recovery), School of Health and Rehabilitation Sciences, The Ohio State University, 453 West Tenth Avenue, Suite 443, Columbus, OH 43210, USA

²Center for Biostatistics, Department of Biomedical Informatics, College of Medicine, The Ohio State University, Columbus, OH 43210, USA

Abstract

Mental practice (MP) is a promising adjuvant to physical practice that involves many of the same mechanisms and takes on many of the same properties as physical practice. This study compared efficacy of a “massed” MP regimen versus a “distributed” MP regimen on upper extremity (UE) motor impairment and functional limitation. Twenty-seven chronic stroke survivors were administered the UE section of the Fugl-Meyer (FM) and Action Research Arm Test (ARAT), followed by standardized physical practice and MP regimens. One group was administered “massed” MP (60 min of MP during a single daily session) and a second group administered distributed MP (20 min of MP occurring three times/day). After intervention, changes in FM and ARAT scores of subjects in the distributed condition were significantly higher than those of subjects in the massed condition (FM 3.65, 95 % CI 0.82–6.49, p value = 0.01; ARAT 3.95, 95 % CI 1.24–6.67, p value = 0.006). Likewise, at POST 3, subjects in the distributed group showed significantly higher change in ARAT scores (ARAT 4.90, 95 % CI 0.57–9.22, p value = 0.03); the change in FM scores at POST 3 was 3.18 points higher among subjects in the distributed condition, but only approached significance (95 % CI –1.27 to 7.63, p value = 0.15). Results suggest that a distributed MP schedule is more efficacious in bringing about paretic UE changes than a massed practice schedule, especially in terms of reducing UE functional limitation.

Keywords

Rehabilitation; Mental practice; Stroke; Motor imagery; Spacing effect; Plasticity

Introduction

Stroke remains a leading cause of adult disability, with most of the expanding stroke survivor population retaining devastating upper extremity (UE) motor deficits (Mayo 2002; Dobkin 2005). Several promising UE rehabilitative therapies have been developed (Wolf et

al. 2006; Page et al. 2007, 2008; Kimberley et al. 2004), with most relying on physical practice administered with assistance of a therapist (Wolf et al. 2006; Page et al. 2007, 2008) and/or devices (Kimberley et al. 2004). However, complete clinical application of these regimens can be elusive due to diminishing therapist contact time, availability, and cost of needed equipment, and/or clients' UE motor impairment levels.

Mental practice (MP) constitutes a departure from the above rehabilitative regimens in that actions are cognitively rehearsed in the absence of voluntary physical movements. MP use elicits the same neural (Nyberg et al. 2006; Sharma et al. 2006) and vegetative (Decety et al. 1991; Fusi et al. 2005) responses elicited by physical practice, and mentally performed movements require similar amounts of time to carry out as physically performance of the same tasks, suggesting that Fitt's law is maintained during MP (Decety and Jeannerod 1995, 1996). Moreover, the addition of MP to physical practice in hemiparetic stroke survivors significantly increases paretic UE use (Page et al. 2005), kinematics (Hewitt et al. 2007), and function (Page et al. 2007, 2001a, b; Page 2000; Crosbie et al. 2004; Dijkerman et al. 2004). Some results suggest that addition of MP does not increase post-stroke outcomes (Letswaart et al. 2011; Bovend'Eerd et al. 2010); however, these studies were conducted in clinical environments, in which lesion sizes and locations, the amount and diversity of adjunctive treatments, and even initial impairment levels were not well controlled or not controlled at all.

Given the preponderance of neurophysiological and evidence supporting MP use, a remaining question is whether the distributed practice effect or "spacing effect"—which is well established to occur when physical practice is administered (Baddeley and Longman 1978)—is also exhibited during MP in stroke survivors. This type of distributed practice regimen increases the practice effect in non-lesioned humans and animals (Letswaart et al. 2011; Sisti et al. 2007), due in part to neural processes such as neurogenesis in animal models (Bovend'Eerd et al. 2010), and increased opportunity for memory consolidation in humans (Nadel and Hardt 2011). Additionally, a number of studies enrolling healthy individuals have reported that randomly practiced, distributed, mental practice of novel tasks significantly increases acquisition (Gabriele et al. 1989; Coelho et al. 2012), and retention of such tasks (Sisti et al. 2007; Debarnot et al. 2015). While MP appears promising for post-stroke survivors, to our knowledge, no study had compared the efficacy of random distributed versus blocked mental practice regimens in this expanding population.

To answer this question, the current study compared efficacy of a "massed" MP regimen versus a "distributed" MP regimen on 27 chronic stroke survivors' UE motor impairment and UE functional limitation. Specifically, a cohort of neurologically stable stroke survivors was administered standardized physical practice and MP regimens that were provided several days/week over a period of 10 weeks. While all aspects of these regimens (e.g., duration, frequency, and movements performed) were held constant, one group of subjects was administered a massed MP regimen (60 min of MP during a single daily session), while a second group was administered a distributed MP regimen (20 min of MP occurring three times/day), both during the ten-week intervention period. While the content and total amount of practice were identical between the groups, the central study hypothesis was that subjects administered MP that used a distributed practice format would exhibit larger score

increases on the Action Research Arm Test (the primary outcome measure) at one week post-intervention (the primary endpoint). That said, in some trials enrolling healthy populations, the benefit of the spacing effect is more apparent in the weeks after training has concluded (e.g., Baddeley and Longman 1978). Thus, our secondary hypothesis was that subjects in the distributed practice group would exhibit larger ARAT score increases at the 3-month post-intervention time point. To our knowledge, this was the first study examining the spacing effect in relation to MP in any neurorehabilitative diagnosis.

Materials and methods

Study design and subjects

This study was a secondary analysis of data collected during several MP efficacy trials approved by the local ethics board. A randomized, single-blinded, pre–post design had been used in each of the trials, in which subjects were tested once prior and twice subsequent to the intervention period, as detailed later in this manuscript. The tester was blinded to subjects' group assignments and the intervention in which they were enrolled.

Subjects had been recruited from local outpatient rehabilitation clinics and stroke support groups and met the following study criteria: inclusion criteria: (a) 10° of active flexion in the paretic wrist, as well as two digits in the more affected hand; (b) one stroke, experienced >3 months prior to study enrollment; (c) a score ≥24 on the Mini-Mental Status Examination; (d) age >18 <75; and (e) discharged from all forms of physical rehabilitation. Exclusion criteria: (a) excessive spasticity in the paretic UE, defined as a score of ≥2 in the paretic elbow, wrist, or fingers as determined by the Modified Ashworth Spasticity Scale (Bohannon and Smith 1987); (b) pain in the paretic UE, as measured by a score ≥4 on a ten-point visual analog scale; (c) participating in any experimental rehabilitation or drug studies; (d) history of a parietal stroke (because some data suggest that ability to estimate manual motor performance through MP is disturbed after parietal lobe damage) (Sirigu et al. 1996).

Instruments

Subjects had been screened using the aforementioned study criteria and had completed consent forms approved by the local ethics board. One week after screening and consenting, the following measures were administered, chosen due to their use in previous MP studies with the stroke population and their responsivity to motor changes in chronic stroke (Van der Lee et al. 2001): (a) To measure paretic UE motor impairment, the UE section of the *Fugl-Meyer Scale (FM)* (Fugl-Meyer et al. 1975) was administered. The FM is organized hierarchically, from having the subject attempt proximal UE movements (e.g., shoulder abduction and internal rotation) to distal UE movements (e.g., mass grasp and pincer grasp). Data arise from a three-point ordinal scale (0 = cannot perform; 2 = can perform fully) applied to each item, and the items are summed to provide a maximum score of 66. (b) To measure paretic UE limitation—our primary study outcome—we administered the *Action Research Arm Test (ARAT)* (Lyle 1981): a 19-item test divided into four categories (grasp, grip, pinch, and gross movement); 16 of the 19 ARAT items measuring distal regions of the arm (e.g., pinching a ball bearing or marble between the thumb and each finger of the affected hand). Each item is graded on a four-point ordinal scale (anchored by 0 = can

perform no part of the test; 3 = performs test normally) for a total possible score of 57. Given the ARAT's focus on functional limitation and paretic UE dexterity—which was the focus of our intervention—the ARAT was identified as our primary outcome measure.

Randomization and intervention

Although enrolled in two separate trials, subjects in each trial reported in this analysis had been randomized to receive up to 60 min of mental practice as an adjunct to a ½-h standardized physical practice regimen. These combined, mental and physical practice sessions were provided 3 days/week, during a 10-week intervention period. Physical practice contents and duration (30 min/day)—as well as mental practice contents and duration (60 min/day as noted above), were held constant. However, subjects assigned to receive mental and physical practice in these trials were randomized to be administered MP that was provided in either (a) a “massed” (60 min of MP all at once) format ($n = 13$), or (b) a “distributed” MP format (MP administered in 20-min increments at three separate time points during the same day) ($n = 14$) in a 1:1 ratio. A computer-generated random numbers table was used to make group allocations.

The physical practice and MP interventions are described elsewhere in detail (Page et al. 2007; Page and Peters 2014). The *physical practice* consisted of individualized, one on one training sessions with a therapist, occurring three times per week, for 10 weeks. The therapy sessions focused on performance of 3–5 common, bilateral and unilateral, UE activities that transferred positively to performance of other activities that stroke survivors often desire to relearn. Activities were graded according to subjects' abilities and progressed to be increasingly difficult during the 10-week regimen and, in some cases, during individual sessions to maximize challenge. Multimodal feedback (verbal, written) conveying knowledge of performance and knowledge of results was used during the therapy sessions, as well as asking subjects regularly to verbally rate self-efficacy and paretic UE use as additional forms of feedback and to instill client insight, as described elsewhere (Page et al. 2013).

Directly after their physical practice sessions, subjects participated in the *mental practice*, either in massed or distributed formats. Individuals randomly assigned to the “massed” MP group were administered a MP audio recording lasting ≈ 60 min in a private room adjacent to the therapy area. Alternatively, subjects randomly assigned to the “distributed” MP group listened to a 20-min version of the MP recording in the adjacent private room, also occurring immediately after therapy. Additionally, subjects in the distributed practice group listened to the same 20-min recording two additional times during the same day, documenting their use in home diaries that were remitted to the study team during each therapy session.

Regardless of the group to which they were assigned, the audio recordings consisted of ≈ 5 , opening minutes of relaxation, asking patients to imagine themselves in a warm, relaxing place (e.g., a beach), and asking them to contract and relax their muscles (i.e., progressive relaxation). This portion of the tapes was followed by suggestions for internal, cognitive polysensory (i.e., using both kinesthetic and visual cues) images (Paivio 1985) related to using the paretic arm in the UE task that had just been physically practiced during the preceding physical practice sessions. Restated, subjects participated in one, chosen UE

functional task (and/or exercises to aid its execution) during a particular physical practice session and mentally rehearsed the same functional task during the ensuing mental practice session. The tape concluded with ≈ 5 min of refocusing into the room.

As with previous MP studies, subjects completed a diary directly after the MP session, in which they verified that they were mentally practicing, the contents of their mental practice sessions, and a scale in which they indicated the proficiency with which they experience mental practice (data from that work will be described in detail in a later paper). Subjects were also visually monitored using a camera system in the room in which they were mentally practicing, and had been told that this was to occur during the consenting process. This was designed both to assure that subjects participated and to provide an inducement to remain participative.

Posttesting

After 10 weeks, all subjects returned to the laboratory, where they were again administered all instruments by an examiner blinded to group assignment. The rater was blinded in that the rater did not know to which group subjects were assigned, or if they even received an intervention. Subjects returned to the same location 3 months later, at which time the same measures were re-administered by the same rater.

Statistical methods

Unadjusted mixed effects regression models, with repeated measures considered for time of assessment for each individual, were first used to test the treatment's effect on changes in FM and ARAT scores at pre-intervention (PRE), at post-intervention (POST), as well as at the 3-month post-intervention visit (POST 3). Adjusted mixed effects regression models for each outcome included adjustment for PRE outcome levels and age. The Kenward–Roger adjustment to the degrees of freedom (Kenward and Roger 1997) was used to control type I error due to a relatively small number of individuals per treatment group. All p values and confidence intervals are presented at the nominal levels and are unadjusted for multiplicity.

Results

Subject demographics

Twenty-seven subjects had been randomized to one of the two treatment regimens [16 males; 23 Caucasian; 16 ischemic strokes; 22 strokes occurring affecting their right, dominant UEs; no pain reported by any subjects (i.e., pain rating = “0”)]. The average age of subjects in the distributed MP condition was significantly higher than subjects in the massed MP condition [66.2 (SD 8.9) years versus 58.5 (SD 7.78) years; average difference 7.73; 95 % CI 1.07–14.39; independent group t test, assuming unequal variance p value = 0.02]. The average time since stroke for subjects in the distributed MP condition was 1041.5 (SD 999.8) days versus 1573.6 (SD 1628.7) days in the massed MP condition (average difference –532.1, 95 % CI –1613.7 to 549.5, p value = 0.32). All subjects had been discharged from all forms of rehabilitative therapy as they had been believed to be neurologically stable and had “plateaued” as ascertained by their therapy personnel. As given in Table 1, the two groups were not statistically different at baseline in their pre-intervention FM and ARAT

scores [baseline FM scores differed by 2.65 points (95 % CI $-5.75, 11.05$, p value = 0.52) between subjects in the distributed condition and subjects in massed conditions; baseline ARAT scores differed by 7.44 points (95 % CI $-4.71, 19.59$, p value = 0.220 between subjects in the distributed vs. massed conditions].

Behavioral outcomes

To investigate differences in score changes from PRE to either POST or POST 3 between the two groups, we included adjustment for PRE scores in the regression models. Models were further adjusted for age at study entry, given that groups differed significantly in age, as noted above. At POST (our primary endpoint), both the change in FM scores and the change in ARAT scores of subjects in the distributed condition were significantly higher than those of subjects in the massed condition (change in FM 3.65, 95 % CI 0.82–6.49, p value = 0.01; change in ARAT 3.95, 95 % CI 1.24–6.67, p value = 0.006). Likewise, at POST 3, subjects in the distributed group showed significantly higher change in ARAT scores (change in ARAT 4.90, 95 % CI 0.57–9.22, p value = 0.03); the change in FM scores at POST 3 was 3.18 points higher among subjects in the distributed condition, but only approached significance (95 % CI -1.27 to 7.63, p value = 0.15). Adjustment for age attenuated these results slightly toward zero; however, effects still remained strong and inference was not greatly altered.

Review of subject diaries revealed only six situations among three different subjects (two from the distributed condition and one from the massed condition) in which the MP regimen was not carried out as instructed. When queried, reasons for this included “lack of time” ($n = 4$) or “I forgot” ($n = 2$).

Discussion

Mental practice (MP) is a promising adjunctive treatment for the growing population of individuals with post-stroke hemiparesis. Moreover, MP is easily administered, requires no specialized equipment or therapist training, and can be used in many clinical or home locations, which constitute advantages over many traditional UE rehabilitative approaches. To optimize MP use, and given that it appears to follow many of the same precepts as physical practice, this study compared the efficacy of massed and distributed MP regimens on paretic UE impairment and functional limitation.

While the two groups were closely matched in their pre-intervention FM scores, subjects administered the distributed MP regimen exhibited significantly larger impairment reductions at POST (our primary endpoint). These changes were corroborated by similar trends on the ARAT—our primary outcome measure—that attained statistical significance at both POST and POST 3, with ARAT differences between the distributed and massed practice groups increasing at POST 3. Given these trends on the ARAT, our primary study hypothesis was confirmed. Overall, it appears that distributed mental practice is preferable to optimize motor outcomes in the post-stroke population, as evidenced by the consistently larger magnitude of score changes among subjects administered this type of practice. When comparing Tables 1 and 2, it might appear to the casual reader that the magnitude of ARAT change in the massed group is larger than that in the distributed group. However, the reader

is reminded that Table 1 shows “raw” pre-intervention levels, whereas Table 2 shows adjusted scores. In fact, the massed group’s mean ARAT score only increased by about one point between the pre- and post-intervention periods. This magnitude of ARAT score change in massed condition was decidedly less than that in the distributed condition.

There remain multiple (and sometimes competing) theories accounting for the distributed practice effect in healthy individuals (Cepeda et al. 2006). However, measuring its full impact may sometimes be difficult in clinical populations like stroke, given that there are multiple concurrent events (e.g., therapies and medical events) and conditions that are not present in well-controlled psychological studies studying this phenomenon in healthy, relatively young individuals. For example, in the months after our intervention had concluded, subjects were still enrolled in the study, and several individuals randomized to the distributed condition experienced minor medical events (one fall without hospitalization; one urinary tract infection without hospitalization; two subjects with changes in medication regimens), some of which likely deleteriously affected their outcomes. We believe that the medical nature of this population and the relatively lower level of control that we were able to exert on events occurring in this population during the retention phase may account in part for not seeing uniform score increases during the retention period and, ultimately, our inability to confirm our secondary hypothesis. Additional studies with larger sample sizes may be able to mitigate this concern in the future.

In the current study, subjects participated in MP for either 20 min at a time three times/day (distributed condition), or in a 60-min block. It is worth noting that, from previous experiences incorporating MP using varied dosing schedules in research and clinical contexts, we have found that patients often become disinterested and/or fatigued when concentrating on MP recordings lasting >30 min. This phenomenon is somewhat unique to mental practice, since physical practice is inherently more participatory than mental practice in which one only simulates and imagines physical practice without physical attempts. Thus, a second mechanism responsible for the superiority of distributed MP in this study may be that participants found it easier to concentrate on and adhere to MP programs administered in smaller doses, as opposed to a single, massed dose lasting up to 60 min. While we administered diaries to assure compliance, future researchers may wish to co-administer qualitative measures or “exit interviews” that query subjects’ impressions of different MP durations. In addition to measuring the spacing effect in larger samples of stroke survivors, future researchers may also wish to examine the neural effects associated with the spacing effect in the stroke population. For example, researchers could apply functional magnetic resonance imaging longitudinally during a distributed MP regimen to document cortical changes that co-occur over time with the provision of these versus massed MP treatments. Such information is expected to provide a biological mechanism for the data reported herein, and would likely inform the cost-effective, optimal formatting of such treatments in rehabilitative settings.

Conclusion

MP efficacy is enhanced when provided in a distributed format, as has been shown for decades with physical practice. While this effect was well established and well studied in

relation to physical practice (Letswaart et al. 2011), the impact of varying the scheduling of MP had not been extensively studied, despite the widely accepted promise of MP in neurorehabilitation. For example, our group (Overdorf et al. 2004) administered a standardized MP regimen following either a random or blocked practice schedule to 30 healthy college students, finding no difference between the conditions. Other MP studies have required subjects to alternate between mental and physical practice, simulating a distributed MP condition by interspersing its use with physical practice (for a review see Lotze and Halsband 2006). The spacing effect has also been studied extensively in relation to recall of rote words and facts (Cepeda et al. 2006; Cermak et al. 1996) and has been positively related to physical skill learning and acquisition. To our knowledge, though, this is the first study comparing the efficacy of distributed versus massed *mental* practice in a neurologically impaired population. Since participants were not receiving any other interventions (physical or cognitive) at the time of their participation in this study, were many years post-stroke, and were neurologically stable, it is unlikely that our results were due to chance.

Since this was the first examination of the spacing effect in the stroke population, and given the promise of MP in people with neurological impairments, future researchers will want to replicate these findings, as well as examining a multitude of distributed strategies to discern which is the most efficacious for clinical use. Future researchers may also wish to examine how rate of motor skill acquisition is mediated by the two conditions. Indeed, a regimen rendering a higher motor skill acquisition rate may accelerate progress in therapies, enabling a more rapid discharge, or, at the very least, allow clinicians to choose to progress tasks or move to other skills to be practiced more quickly. However, the superiority of distributed MP in subacute rehabilitative contexts must first be demonstrated.

Acknowledgments

This work was supported in part by grants from the National Institutes of Health (R21 AT002110-01; KO1 AT002637-05). The authors thank the study coordinators and therapists who assisted with the conduct of this study.

Abbreviations

UE	Upper extremity
ARAT	Action Research Arm Test
FM	Fugl-Meyer Impairment Scale
MP	Mental practice
POST	After intervention
POST 3	3 Months after intervention

References

Baddeley AD, Longman DJA. The influence of length and frequency of training sessions on the rate of learning to type. *Ergonomics*. 1978; 21:627–635.

- Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. *Phys Ther.* 1987; 67:206–207. [PubMed: 3809245]
- Bovend'Eerd TJ, Dawes H, Sackley C, Izadi H, Wade DT. An integrated motor imagery program to improve functional task performance in neurorehabilitation: a single-blind randomized controlled trial. *Arch Phys Med Rehabil.* 2010; 91:939–946. [PubMed: 20510987]
- Cepeda NJ, Pashler H, Vul E, Wixted JT, Rohrer D. Distributed practice in verbal recall tasks: a review and quantitative synthesis. *Psychol Bull.* 2006; 132:354–380. [PubMed: 16719566]
- Cermak LS, Verfaellie M, Lanzoni S, Mather M, Chase KA. Effect of spaced repetitions on amnesia patients' recall and recognition performance. *Neuropsychol.* 1996; 10(2):219–227.
- Coelho CJ, Nusbaum HC, Rosenbaum DA, Fenn KM. Imagined actions aren't just weak actions: task variability promotes skill learning in physical practice but not in mental practice. *J Exp Psychol Learn Mem Cog.* 2012; 38:1759–1764.
- Crosbie JH, McDonough SM, Gilmore DH, Wiggam MI. The adjunctive role of mental practice in the rehabilitation of the upper limb after hemiplegic stroke: a pilot study. *Clin Rehabil.* 2004; 18(1):60–68. [PubMed: 14763720]
- Debarnot U, Abichou K, Kalenzaga S, Sperduti M, Piolino P. Variable motor imagery training induces sleep memory consolidation and transfer improvements. *Neurobiol Learn Mem.* 2015; 119:85–92. [PubMed: 25562401]
- Decety J, Jeannerod M. Mentally simulated movements in virtual reality: does Fitts law hold in motor imagery? *Behav Brain Res.* 1995; 72(1–2):127–134. [PubMed: 8788865]
- Decety J, Jeannerod M. Fitts' law in mentally simulated movements. *Behav Brain Res.* 1996; 72:127–134. [PubMed: 8788865]
- Decety J, Jeannerod M, Germain M, Pastene J. Vegetative response during imagined movement is proportional to mental effort. *Behav Brain Res.* 1991; 42:1–5. [PubMed: 2029340]
- Dijkerman HC, Letswaart M, Johnston M, MacWalter RS. Does motor imagery training improve hand function in chronic stroke patients? A pilot study. *Clin Rehabil.* 2004; 18(5):538–549. [PubMed: 15293488]
- Dobkin BH. Clinical practice. Rehabilitation after stroke. *N Engl J Med.* 2005; 352(16):1677–1684. [PubMed: 15843670]
- Fugl-Meyer AR, Jaasko L, Leyman I, Olsson S, Steglind S. The post-stroke hemiplegic patient. I. A method for evaluation of physical performance. *Scand J Rehabil Med.* 1975; 7:13–31. [PubMed: 1135616]
- Fusi S, Cutuli D, Valente MR, et al. Cardioventilatory responses during real or imagined walking at low speed. *Arch Ital Biol.* 2005; 143(3–4):223–228. [PubMed: 16097499]
- Gabriele TE, Hall CR, Lee TD. Cognition in motor learning: imagery effects on contextual interference. *Human Movement Sci.* 1989; 8:227–245.
- Hewitt TE, Ford K, Levine P, Page SJ. Reaching kinematics to measure motor changes after mental practice in stroke. *Top Stroke Rehabil.* 2007; 14(4):23–29. [PubMed: 17698455]
- Kenward MG, Roger JH. Small sample inference for fixed effects from restricted maximum likelihood. *Biometrics.* 1997; 53:983–997. [PubMed: 9333350]
- Kimberley TJ, Lewis SM, Auerbach EJ, Dorsey LL, Lojovich JM, Carey JR. Electrical stimulation driving functional improvements and cortical changes in subjects with stroke. *Exp Brain Res.* 2004; 154(4):450–460. [PubMed: 14618287]
- Letswaart M, Johnston M, Dijkerman HC, Joice S, Scott CL, MacWalter RS, et al. Mental practice with motor imagery in stroke recovery: randomized controlled trial of efficacy. *Brain.* 2011; 134:1373–1386. [PubMed: 21515905]
- Lotze M, Halsband U. Motor imagery. *J Physiol Paris.* 2006; 99:386–395. [PubMed: 16716573]
- Lyle RC. A performance test for assessment of upper limb function in physical rehabilitation treatment and research. *Int J Rehabil Res.* 1981; 4:483–492. [PubMed: 7333761]
- Mayo N. Activity, participation, and quality of life 6 months poststroke. *Arch Phys Med Rehabil.* 2002; 83(8):1035–1042. [PubMed: 12161823]
- Nadel L, Hardt O. Update on memory systems and processes. *Neuropsychopharmacology.* 2011; 36(1):251–273. [PubMed: 20861829]

- Nyberg L, Eriksson J, Larsson A, Marklund P. Learning by doing versus learning by thinking: an fMRI study of motor and mental training. *Neuropsychologia*. 2006; 44:711–717. [PubMed: 16214184]
- Overdorf V, Page SJ, Schweighardt R, McGrath RE. Mental and physical practice schedules in acquisition and retention of novel timing skills. *Percept Mot Skills*. 2004; 99(1):51–62. [PubMed: 15446630]
- Page SJ. Imagery improves motor function in chronic stroke patients with hemiplegia: a pilot study. *Occup Ther J Res*. 2000; 20(3):200–215.
- Page SJ, Peters H. Mental practice: applying motor PRACTICE and neuroplasticity principles to increase upper extremity function. *Stroke*. 2014; 45(11):3454–3460. [PubMed: 25190436]
- Page SJ, Levine P, Sisto S, Johnston M. Imagery combined with physical practice for upper limb motor deficit in sub-acute stroke: a case report. *Phys Ther*. 2001a; 81(8):1455–1462. [PubMed: 11509075]
- Page SJ, Levine P, Sisto S, Johnston M. A randomized, efficacy and feasibility study of imagery in acute stroke. *Clin Rehabil*. 2001b; 15(3):233–240. [PubMed: 11386392]
- Page SJ, Levine P, Leonard AC. Effects of mental practice on affected limb use and function in chronic stroke. *Arch Phys Med Rehabil*. 2005; 86(3):399–402. [PubMed: 15759218]
- Page SJ, Levine P, Leonard A. Mental practice in chronic stroke: results of a randomized, placebo controlled trial. *Stroke*. 2007; 38(4):1293–1297. [PubMed: 17332444]
- Page SJ, Levine P, Leonard AC, Szaflarski J, Kissela B. Modified constraint-induced therapy in stroke: results of a single blinded, randomized controlled trial. *Phys Ther*. 2008; 88(3):333–340. [PubMed: 18174447]
- Page SJ, Boe S, Levine P. What are the “ingredients” of modified constraint-induced therapy? An evidence based review, recipe, and recommendations. *Restor Neurol Neurosci*. 2013; 31(3):299–309. [PubMed: 23396369]
- Paivio A. Cognitive and motivational functions of imagery in human performance. *J Appl Sport Sci*. 1985; 10(4):22–28.
- Sharma N, Pomeroy VM, Baron JC. Motor imagery: a backdoor to the motor system after stroke? *Stroke*. 2006; 37:1941–1952. [PubMed: 16741183]
- Sirigu A, Duhamel JR, Cohen L, Pillon B, Dubois B, Agid Y. The mental representation of hand movements after parietal cortex damage. *Science*. 1996; 273(5281):1564–1568. [PubMed: 8703221]
- Sisti HL, Glass AL, Shors T. Neurogenesis and the spacing effect: learning over time enhances memory and the survival of new neurons. *Learn Mem*. 2007; 14:368–375. [PubMed: 17522028]
- Van der Lee JH, Beckerman H, Lankhorst GJ, Bouter LM. The responsiveness of the action research arm test and the Fugl-Meyer assessment scale in chronic stroke patients. *J Rehab Med*. 2001; 33:110–113.
- Wolf SL, Winstein CJ, Miller JP, Taub E, Uswatte G, Morris D, Giuliani C, Light KE, Nichols-Larsen D. EXCITE Investigators. Effect of constraint-induced movement therapy on upper extremity function 3 to 9 months after stroke: the EXCITE randomized clinical trial. *JAMA*. 2006; 296(17):2095–2104. [PubMed: 17077374]

Table 1

Subject characteristics

	Overall (N = 27)	Distributed (N = 13)	“Massed” (N = 14)
FM scores, pre-intervention, mean (SD)	28.74 (10.47)	30.12 (9.49)	27.46 (11.52)
ARAT scores, pre-intervention, mean (SD)	20.30 (15.49)	24.15 (13.53)	16.71 (16.80)
Age, mean (SD) (years)	62.22 (9.07)	66.23 (8.89)	58.50 (7.78)
Affected side (%)			
Right	11 (41 %)	6 (46 %)	5 (36 %)
Left	15 (55 %)	7 (54 %)	8 (57 %)
Parallel	1 (4 %)	0 (0 %)	1 (7 %)

Table 2

Group effects on primary outcomes from adjusted models

Outcome	Distributed	"Massed"	Group difference	95 % CI	p value
Mixed models adjusted on pre-intervention outcome levels					
FM scores					
Post-intervention	34.87 (0.99)	31.22 (0.95)	3.65 (1.37)	0.82 to 6.49	0.01
3-Month follow-up	33.42 (1.56)	30.24 (1.48)	3.18 (2.16)	-1.27 to 7.63	0.15
ARAT scores					
Post-intervention	26.12 (0.93)	22.16 (0.91)	3.95 (1.32)	1.24 to 6.67	0.006
3-Month follow-up	26.15 (1.46)	21.24 (1.45)	4.90 (2.07)	0.57 to 9.22	0.03
Mixed models adjusted on pre-intervention outcome levels and age					
FM scores					
Post-intervention	34.86 (1.07)	31.23 (1.03)	3.63 (1.58)	0.39 to 6.88	0.029
3-Month follow-up	33.42 (1.62)	30.25 (1.54)	3.17 (2.30)	-1.56 to 7.89	0.18
ARAT scores					
Post-intervention	25.90 (1.0)	22.38 (0.98)	3.52 (1.50)	0.42 to 6.62	0.028
3-Month follow-up	25.94 (1.50)	21.44 (1.49)	4.50 (2.17)	0.0 to 9.0	0.05

Data presented are least squares means (standard errors) from a mixed model adjusted for PRE levels