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Review Article

Bilateral Synergy: A Framework for Post-Stroke Rehabilitation

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Abstract

Background: Unilateral stroke produces debilitating deficits in voluntary control in the contralesional arm, and significant motor coordination deficits in the ipsilesional arm. In addition, patients tend to avoid bilateral arm patterns during performance of activities of daily living. Nevertheless, upper extremity physical rehabilitation predominantly focuses on motor training activities with only the paretic arm. This can be limiting because of persistent deficits in the ipsilesional arm, and because of the tendency of patients to avoid spontaneous bilateral arm patterns.

Proposition: Rehabilitation should focus on bilateral training to advance recovery of function in both arms of stroke patients, as well as to facilitate spontaneous bilateral arm use. This paper reviews the rationale for this approach, citing evidence for significant hemisphere specific bilateral motor deficits in stroke patients, which affect both the contralesional and the ipsilesional arm. The rationale for, and advantages of, training both arms simultaneously through bilateral tasks is reviewed. Although bilateral training has been employed to treat stroke patients previously, this has tended to focus on bimanual 'coupling' as a rationale for performing parallel, but not cooperative bilateral tasks. Bilateral synergy provides a more functional framework for structuring post-stroke upper extremity rehabilitation.

Conclusion: Bilateral synergy may be causally linked to spontaneous bilateral arm use, suggesting that rehabilitation should be focused on bilateral cooperative tasks, such as bilateral object transport. Further research is required to determine whether this approach could be efficacious for patients with hemiparesis, and whether both left and right hemisphere strokes can benefit from such intervention.

INTRODUCTION

It has been well-established that unilateral stroke results in sensorimotor deficits in both arms of stroke patients, which is often manifested by hemiparesis and deficits in voluntary control in the contralesional arm [1-6], and also by significant coordination deficits in the ipsilesional arm [7-21]. Nevertheless, the primary goals of upper extremity physical rehabilitation continue to focus on recovery of function in the paretic arm alone [22-28]. This can be limiting, even when contralesional arm control improves, because persistent deficits in the ipsilesional arm can limit both recovery of function and carry-over of training into natural settings [29-31]. Physical rehabilitation should focus on bilateral training to advance recovery of function following stroke. This approach has the advantages of promoting recovery in both arms, and of specific training of bilateral movements, which can directly improve performance on activities of daily living (ADL). Physical rehabilitation could be enhanced by exploiting the cooperative action of both hands during common goal directed activities. Such training should enhance spontaneous use of bilateral patterns, which may be critical in promoting spontaneous use of both arms during ADL and thus requisite to more improvements in functional recovery. This paper presents a rationale for training both the contralesional and ipsilesional arms in physical rehabilitation, for focusing on bilateral tasks, and finally for exploiting cooperative, as opposed to parallel, bilateral tasks to elicit bilateral synergies.

Strong rationale for focusing upper limb rehabilitation on bilateral movements have previously been delineated [29,32-34]. Nevertheless, upper limb physical rehabilitation continues to focus predominantly on movement experiences with the contralesional arm. The rationale for this focus is likely that recovery of bilateral patterns will naturally emerge, when paresis is diminished. Indeed, it is well understood that functional activities of daily living are overwhelmingly dependent on bilateral movements [10]. However, this view fails to recognize that substantial movement deficits also occur in the non-paretic arm. In addition, specific deficits in bilateral coordination have been shown to result from unilateral sensorimotor stroke [30,35-37]. In fact, even patients with mild paresis tend to avoid spontaneous use of the contralesional arm to assist with

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ADL that are normally performed using bilateral arm patterns [10,38]. Thus, specific training in bilateral movements seems to be critical to reestablish spontaneous bilateral arm use during ADL. The following sections will present evidence for bilateral motor deficits in stroke patients, the importance of focusing rehabilitation on both arms, and on bilateral movements.

The hemisphere-specificity of the sensorimotor deficits that result from unilateral stroke appears to result from the lateralized organization of motor functions in the cerebral cortices. Previous research from our laboratory has indicated that two aspects of motor control have become specialized to different hemispheres: The right hemisphere for control of limb impedance, and the left hemisphere for predicting task dynamics [39]. Whereas, the specific processes that have become lateralized remain controversial [18,40-44], the effect of lateralization in motor control processes is that unilateral movements require both hemispheres to contribute their specializations to motor performance. Thus, when one hemisphere is lesioned, hemisphere-specific motor deficits become evident in both arms of stroke patients. This bi-hemispheric control scheme is consistent with neuroimaging studies that have revealed activation in motor cortical areas of both brain hemispheres during unilateral hand and arm movements [45-51].

Consistent with the idea that both contralateral and ipsilateral hemisphere mechanisms are critical for control of unilateral movements, hemisphere-specific ipsilesional deficits reflect the specializations of each hemisphere for different movement control processes [16,17,52-56]. Not suprisingly, these deficits in motor coordination and learning reflect the functional advantages that were previously reported for the dominant and non-dominant arms of healthy subjects that are associated with handedness [39,57-63]. More specifically, left hemisphere damage is associated with ipsilesional deficits in intersegmental coordination and trajectory smoothness, while right hemisphere damage is associated with deficits in final position accuracy [39]. Other studies have shown that left hemisphere damage produces deficits in the early phase of motion, while right hemisphere damage produces deficits in the later phase, supporting a dissociation between predictive and feedback mediated control processes [17,64]. Desrosiers et al. [21] and Schaefer et al. [53] emphasized the functional importance of these deficits by reporting correlations with deficits in clinical movement evaluations that include simulated activities of daily living. Taken together this research supports a bi-hemispheric model of control, in which each hemisphere contributes specialized processes to each arm. A strong prediction of this model is that hemisphere specific deficits should occur in the contralesional as well as the ipsilesional arms of stroke patients. In support of this prediction, Robertson et al. [65] revealed coordination deficits in both arms of stroke patients with left hemisphere damage that were consistent with previous reports of intersegmental coordination deficits [53]. We recently expanded this support by demonstrating that left hemisphere lesions produce contralesional deficits in directional control and trajectory straightness, whereas, right lesions produce contralesional deficits in movement termination [6]. In summary, there has been substantial support for the idea that the lateralized organization of motor control systems in the brain leads to hemisphere-specific deficits in both arms of stroke patients. These findings support a lateralized, bi-hemispheric model of motor control and emphasize the importance of focusing rehabilitation on both arms of unilaterally lesioned stroke patients.

Bilateral Training in Stroke Rehabilitation

The importance of coordination of the two arms for self care, home, work, and leisure activities is self-evident. The arms engage in an infinite variety of coordinated behaviors that typically involve different actions of each arm, such as slicing bread, washing dishes, buttoning a shirt, and carrying and placing large, heavy, and/or delicate objects. In all of these cases, control of the arms is interactive and coordinated. One might expect such coordination to require devoted neural control mechanisms. In fact, studies in human patients [66], and non-human primates [67] established that damage to supplementary motor area (SMA) specifically disrupts the ability to coordinate the hands, while other studies have identified bilateral-specific neurons in both SMA and primary motor cortex [68-71]. Consistent with these findings, recent studies have indicated limited transfer between unilateral and bilateral conditions [72-74], suggesting that bilateral movement control entails processes that are not shared with unilateral movements. This is of particular importance to physical rehabilitation, given that performance on activities of daily living (ADL) is better predicted by the degree to which stroke patients use both arms to complete the tasks, rather than by the function of either arm alone [10]. The fact that right hemisphere damaged patients tend to avoid bilateral arm use more than the left hemisphere damaged cohort, even when matched for demographic factors, lesion characteristics, and contralesional arm impairment level, suggests that bilateral coordination might also be a lateralized function that is more dependent on right hemisphere mechanisms [38]. However, more research is necessary to test this hypothesis.

Interlimb Coupling: Historically, the vast majority of bilateral studies have focused on the concept of interlimb 'coupling', quantified as a similarity in performance between the arms. This approach, exemplified by the seminal work of Kelso [75], is that control of the two arms can be simplified by "organizing functional groupings of muscles that are constrained to act as a single unit". This constraint is presumably due to a common command signal. Bilateral interference is one example of bilateral coupling, in which a task performed with one hand (i. e. drawing a C shape) seems to interfere with a different simultaneous task performed by the other hand (i. e. drawing a U shape). Ivry and others [76-78] have demonstrated that this is an effect at the cognitive level of task organization that can be mitigated with perceptual cues. Furthermore, other studies have shown that certain bilateral rhythmic motions are more difficult to coordinate than others, including cyclic movements of the arms that have complex temporal relationships. However, these patterns are also easily performed with the advantage of explicit task cues [79], supporting the idea that such 'interference' in performance occurs at the higher levels of task planning, rather than basic sensorimotor processes. Another line of research has shown that performance of synchronous bilateral movements is most symmetric when the biomechanics are similar between the arms [80-82]. A caveate of this approach to assessing bimanual coupling is that the two movement conditions are fundamentally different: If muscle activity is similar, movements that are symmetric with respect to biomechanics will be symmetric with respect to kinematics. Movements that are not mechanically symmetric require different muscle activities for kinematic symmetry. Thus, the idea that interlimb coupling reflects a similarity in the command signals (reflected by muscle activity) is erroneous. If task kinetics are asymmetric, then symmetry in kinematics would require asymmetric muscle activities, a finding that contradicts Kelso's original definition of 'coupling'. Therefore, it is difficult to understand what the empirical findings from this line of research might reveal about neural control. Nevertheless, the general result indicates that interlimb "coupling" is limited to a particular class of bilateral actions, which leaves open the question of how bilateral movements might be coordinated during a more general set of behaviors.

Interlimb Synergy: Another view of multi-effector coordination has recently been elaborated in the form of movement synergies. According to the 'synergy' view of coordination, the central nervous system organizes sets of effectors (i. e. muscles, limb segments, limbs, etc.), such that the individual effector contributions covary to stabilize task performance. For example, when using both hands to transport a container full of soup, the hands must interact and compensate for one another. If both hands push too hard, the container will collapse, whereas if one hand produces torque about the horizontal axis, the other hand needs to counter this to prevent spills. In short, the two hands must actively compensate for one another's errors to stabilize task performance. This view of coordination has been operationalized in a computational approach advanced by Schoner, Latash, and colleagues in the form of the Uncontrolled Manifold (UCM) Hypothesis [83-87]. The computational details of that approach are beyond the scope of this paper, but the gist of the analysis is demonstrative: The UCM analysis quantifies the variation of the output of each effector at comparable phases across multiple trials. For example, during the performance of a task, such as maintaining an instructed total force with two fingers, each finger produces slightly different forces in different trials. This requires the other finger to compensate for such variations in order to keep total force unchanged between trials. In contrast, if the two finger forces are coupled, or positively covary with one another, task errors would become amplified. UCM analysis quantifies such covariation, relative a manifold corresponding to perfect task performance. Variations orthogonal to the UCM lead to task errors. Substantial evidence has established that during performance of a variety of tasks, variance orthogonal to the UCM is smaller, compared to within the UCM variance [83-87]. This approach provides a convenient perspective for assessment and training of bilateral movements because it is restricted to tasks that require cooperation between the two hands. In order to exemplify the distinction between cooperative and parallel bilateral movements, we next present data on two tasks from our laboratory. Parallel bilateral movements refers to simultaneous movements with both arms, in which task success for one hand does not depend on performance of the other hand, such as when placing two cups on a countertop, one with each hand. Cooperative bilateral movements, in contrast, refers to simultaneous interactive movements, in which task success depends on the cooperative interaction between the hands, such as when placing a single cup, held with both hands, on a countertop.

Tasks: We have designed two virtual transport tasks in order to quantify the effects of task structure on bilateral coordination. Preliminary data in young healthy subjects is presented that differentiates performance on parallel tasks versus cooperative tasks, and exemplifies the importance of bilateral synergy in performance. These tasks are: 1) Parallel Cursor Transport 2) Cooperative Virtual Object Transport. Our experimental setup is depicted in Figure 1, which shows an individual seated in front of a table. The hands rest on the table top between trials, while participants are instructed to lift their hands above the table for the duration of each trial. The task and movement feedback is displayed on a horizontal mirror positioned 35 cm above the table surface. This mirror reflects the stimuli presented on a horizontal, inverted, 55" HDTV display.

Parallel transport (Figure 2): In this task, individuals align two cursors (one for each hand) in start circles at the beginning of trial. After 500 ms, an audio "go" signal is given, when individuals are to move both cursors simultaneously to each of two displayed targets.

Cooperative transport (Figure 3): A single cursor is located with the right and left ends at the same positions as the start positions for Task 1. However, a single cursor is located half way between the hand locations and positioned in a central start circle. The trial can only begin when the hands are symmetrically positioned in the same positions as used for Task 1.

Figure 4 left shows our findings for data calculated at movement end for a representative subject. The location of the left hand final position on an axis perpendicular to the target direction is plotted against the equivalent position for the right hand. If these deviations compensate for one another, the data should fall along a line with a negative slope. For perpendicular

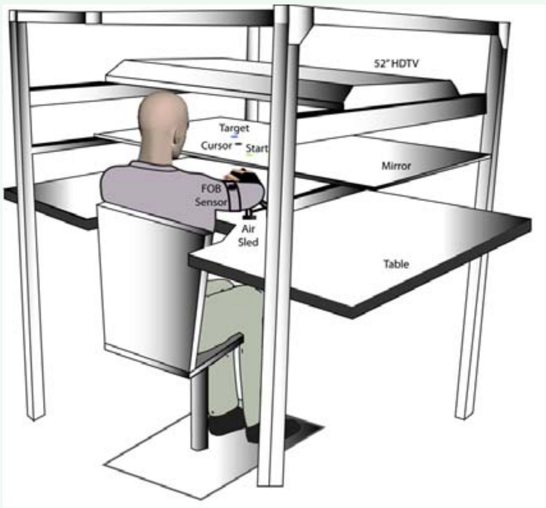

Figure 1 Experimental set-up. Table supports arms between trials. Cursor(s) and target are reflected by mirror in virtual plane of the hands. Flock of Bird (FOB) sensors record 10 degrees of freedom per arm. HDTV positioned above mirror displays task.

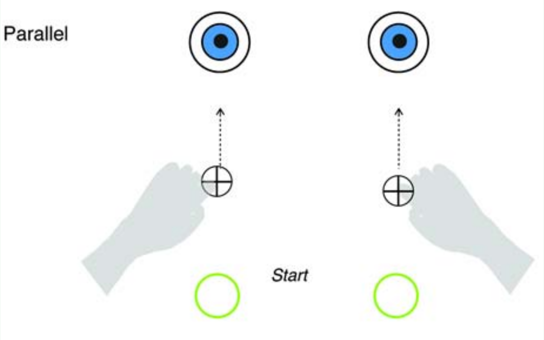

Figure 2 Parallel cursor transport task: Cursors represent position of index finger PIP joint. One start position and target are shown for each hand. Subjects are to perform simultaneous movements to bring each cursor (hand) to each target.

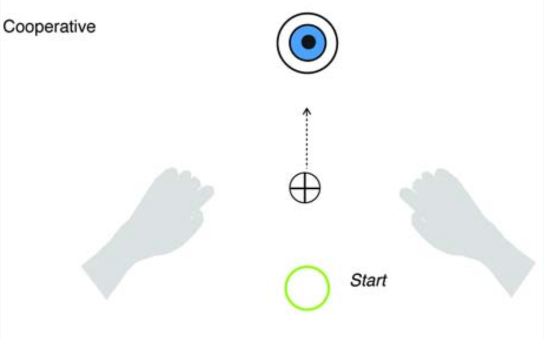

Figure 3 Cooperative virtual object transport: One cursor is shown between the index finger positions. A single start position and target for each trial. Subjects are to bring the cursor from the start position to the target, using both hands.

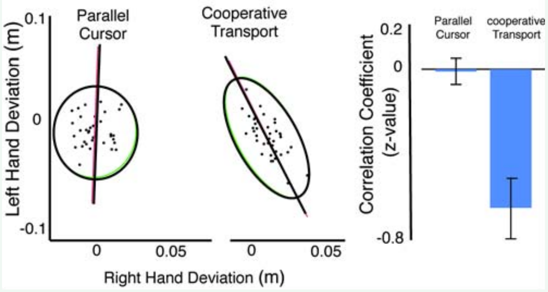

Figure 4 Covariation of position deviations (perpendicular to the target direction) between hands (Left). Right: Correlation coefficients (z-transform) for the data plotted in figure 4 left. Even though the required movements were the same for both tasks, only the cooperative task shows substantial covariation between the hands. This reflects negative covariation that stabilizes task final position errors.

deviations, Task 1 (parallel transport) shows no such covariation between the hands, while the cooperative transport task shows substantial negative covariation. The bar plots indicate the mean ± SE of the Fisher transformed correlation coefficients across all four individuals in two task groups. While the transport task recruits substantial covariation, the parallel cursor task does not. This negative covariation stabilizes cursor location along this axis, and can be considered a synergy that is selectively recruited during the cooperative object transport task. This shows that the nature of the task can elicit different forms of cooperation between the hands. We suggest that bilateral cooperation, in the form of synergy, is a critical component for training bilateral coordination in stroke patients.

SUMMARY AND CONCLUSIONS

Physical rehabilitation has a longstanding tradition of focusing upper limb training on the contralesional, often paretic, arm. There are few clinical or research tools developed for assessing bilateral coordination, or for tracking improvements in bilateral coordination in the clinical or research environments. This is particularly important for right hemisphere damaged patients, as recent research has suggested that right hemisphere stroke is associated with a substantial decrement in spontaneous bilateral arm use, which can be particularly debilitating due to the phenomenon of learned non-use in the contralesional arm [88-91]. This effect can be compounded by the fact that movement practice appears to be the single most critical determinant in motor recovery following stroke [24,92-95], further emphasizing the importance of spontaneous arm use in unsupervised settings. A number of previous intervention studies have shown promising effects of bilateral practice on motor recovery [29-32,96,97]. However, this practice often focuses on bilateral actions that are not cooperative between the hands, such as rhythmic cued movements [36], or robot assisted bilateral reaching [98]. We suggest a causal relationship between bilateral coordination and spontaneous bilateral arm use, and thus propose that rehabilitation protocols should be extended to focus on bilateral cooperative tasks, such as object transport, that elicit covariation between the arms. The concept of bilateral synergy provides a framework for designing tasks and assessing performance during bilateral activities. This framework allows monitoring of bilateral cooperation, rather than similarity in kinematics: If one arm makes tasks errors, the other compensates for these errors. Thus, performance is stabilized by differential actions that are compensatory in nature. This approach should be incorporated into assessment and design of bilateral coordination tasks for patients in both research and clinical settings. Further studies are necessary to determine whether this approach will be efficacious for patients with hemiparesis, and whether left and right hemisphere strokes can benefit from such intervention.

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REFERENCES

1. Beer RF, Dewald JP, Rymer WZ. Deficits in the coordination of multijoint arm movements in patients with hemiparesis: evidence for disturbed control of limb dynamics. Exp Brain Res. 2000; 131: 305-319.

2. Beer RF, Ellis MD, Holubar BG, Dewald JP. Impact of gravity loading on post-stroke reaching and its relationship to weakness. Muscle Nerve. 2007; 36: 242-250.

3. Dewald JP, Beer RF, Given JD, McGuire JR, Rymer WZ. Reorganization of flexion reflexes in the upper extremity of hemiparetic subjects. Muscle Nerve. 1999; 22: 1209-1221.

4. Dewald JP, Pope PS, Given JD, Buchanan TS, Rymer WZ. Abnormal muscle coactivation patterns during isometric torque generation at the elbow and shoulder in hemiparetic subjects. Brain. 1995; 118 : 495-510.

5. Yao J, Ellis M, Dewald J. Mechanisms and rehabilitation of discoordination following stroke using a cortical imaging method. Conf Proc IEEE Eng Med Biol Soc. 2005; 4: 4138-4141.

6. Mani S, Mutha PK, Przybyla A, Haaland KY, Good DC, Sainburg RL. Contralesional motor deficits after unilateral stroke reflect hemisphere-specific control mechanisms. Brain. 2013; 136: 1288-1303.

7. Podbros LZ, Wyke MA. Laterality differences for speed but not for control in sequential finger tapping. Percept Mot Skills. 1988; 67: 927-933.

8. Wyke M. Effect of brain lesions on the rapidity of arm movement. Neurology. 1967; 17: 1113-1120.

9. Chestnut C, Haaland KY. Functional significance of ipsilesional motor deficits after unilateral stroke. Arch Phys Med Rehabil. 2008; 89: 62-68.

10. Haaland KY, Mutha PK, Rinehart JK, Daniels M, Cushnyr B, Adair JC. Relationship between arm usage and instrumental activities of daily living after unilateral stroke. Arch Phys Med Rehabil. 2012; 93: 1957-1962.

11. Haaland KY, Prestopnik JL, Knight RT, Lee RR. Hemispheric asymmetries for kinematic and positional aspects of reaching. Brain. 2004; 127: 1145-1158.

12. Haaland KY, Schaefer SY, Knight RT, Adair J, Magalhaes A, Sadek J, et al. Ipsilesional trajectory control is related to contralesional arm paralysis after left hemisphere damage. Exp Brain Res. 2009; 196: 195-204.

13. Hermsdörfer J, Laimgruber K, Kerkhoff G, Mai N, Goldenberg G. Effects of unilateral brain damage on grip selection, coordination, and kinematics of ipsilesional prehension. Exp Brain Res. 1999; 128: 41-51.

14. Hermsdörfer J, Ulrich S, Marquardt C, Goldenberg G, Mai N. Prehension with the ipsilesional hand after unilateral brain damage. Cortex. 1999; 35: 139-161.

15. Poole JL, Sadek J, Haaland KY. Ipsilateral deficits in 1-handed shoe tying after left or right hemisphere stroke. Arch Phys Med Rehabil. 2009; 90: 1800-1805.

16. Schaefer SY, Haaland KY, Sainburg RL. Dissociation of initial trajectory and final position errors during visuomotor adaptation following unilateral stroke. Brain Res. 2009; 1298: 78-91.

17. Schaefer SY, Haaland KY, Sainburg RL. Ipsilesional motor deficits following stroke reflect hemispheric specializations for movement control. Brain. 2007; 130: 2146-2158.

18. Wetter S, Poole JL, Haaland KY. Functional implications of ipsilesional motor deficits after unilateral stroke. Arch Phys Med Rehabil. 2005; 86: 776-781.

19. Yarosh CA, Hoffman DS, Strick PL. Deficits in movements of the wrist ipsilateral to a stroke in hemiparetic subjects. J Neurophysiol. 2004; 92: 3276-3285.

20. Jebsen RH, Griffith ER, Long EW, Fowler R. Function of "normal" hand in stroke patients. Arch Phys Med Rehabil. 1971; 52: 170-174 passim.

21. Desrosiers J, Bourbonnais D, Bravo G, Roy PM, Guay M. Performance of the 'unaffected' upper extremity of elderly stroke patients. Stroke. 1996; 27: 1564-1570.

22. Ustinova KI, Feldman AG, Levin MF. Bilateral coupling facilitates recovery of rhythmical movements from perturbation in healthy and post-stroke subjects. Exp Brain Res. 2013; 227: 263-274.

23. Bonifer NM, Anderson KM, Arciniegas DB. Constraint-induced movement therapy after stroke: efficacy for patients with minimal upper-extremity motor ability. Arch Phys Med Rehabil. 2005; 86: 1867-1873.

24. Krakauer JW. Arm function after stroke: from physiology to recovery. Semin Neurol. 2005; 25: 384-395.

25. Volpe BT, Ferraro M, Lynch D, Christos P, Krol J, Trudell C, et al. Robotics and other devices in the treatment of patients recovering from stroke. Curr Atheroscler Rep. 2004; 6: 314-319.

26. Page SJ, Elovic E, Levine P, Sisto SA. Modified constraint-induced therapy and botulinum toxin A: a promising combination. Am J Phys Med Rehabil. 2003; 82: 76-80.

27. Vergara-Aragon P, Gonzalez CL, Whishaw IQ. A novel skilled-reaching impairment in paw supination on the "good" side of the hemi-Parkinson rat improved with rehabilitation. J Neurosci. 2003; 23: 579-586.

28. Wolf SL, Blanton S, Baer H, Breshears J, Butler AJ. Repetitive task practice: a critical review of constraint-induced movement therapy in stroke. Neurologist. 2002; 8: 325-338.

29. McCombe Waller S, Whitall J. Bilateral arm training: why and who benefits? NeuroRehabilitation. 2008; 23: 29-41.

30. Summers JJ, Kagerer FA, Garry MI, Hiraga CY, Loftus A, Cauraugh JH. Bilateral and unilateral movement training on upper limb function in chronic stroke patients: A TMS study. J Neurol Sci. 2007; 252: 76-82.

31. Lewis GN, Byblow WD. Neurophysiological and behavioural adaptations to a bilateral training intervention in individuals following stroke. Clin Rehabil. 2004; 18: 48-59.

32. Stewart KC, Cauraugh JH, Summers JJ. Bilateral movement training and stroke rehabilitation: a systematic review and meta-analysis. J Neurol Sci. 2006; 244: 89-95.

33. Latimer CP, Keeling J, Lin B, Henderson M, Hale LA. The impact of bilateral therapy on upper limb function after chronic stroke: a systematic review. Disabil Rehabil. 2010; 32: 1221-1231.

34. Cauraugh JH, Lodha N, Naik SK, Summers JJ. Bilateral movement training and stroke motor recovery progress: a structured review and meta-analysis. Hum Mov Sci. 2010; 29: 853-870.

35. Wyke M. The effects of brain lesions on the performance of bilateral arm movements. Neuropsychologia. 1971; 9: 33-42.

36. Whitall J, McCombe Waller S, Silver KH, Macko RF. Repetitive bilateral arm training with rhythmic auditory cueing improves motor function in chronic hemiparetic stroke. Stroke. 2000; 31: 2390-2395.

37. Rose DK, Winstein CJ. The co-ordination of bimanual rapid aiming movements following stroke. Clin Rehabil. 2005; 19: 452-462.

38. Rinehart JK, Singleton RD, Adair JC, Sadek JR, Haaland KY. Arm use after left or right hemiparesis is influenced by hand preference. Stroke. 2009; 40: 545-550.

39. Mutha PK, Haaland KY, Sainburg RL. The effects of brain lateralization on motor control and adaptation. J Mot Behav. 2012; 44: 455-469.

40. Mieschke PE, Elliott D, Helsen WF, Carson RG, Coull JA. Manual asymmetries in the preparation and control of goal-directed movements. Brain Cogn. 2001; 45: 129-140.

41. Elliott, D., E.A. Roy, D. Goodman, R.G. Carson et al., Asymmetries in the preparation and control of manual aiming movements. Canadian Journal of Experimental Psychology. 1993; 47: 570-589.

42. Elliott D, Carson RG, Goodman D, Chua R. Discrete vs. continuous visual control of manual aiming. Hum Mov Sci. 1991; 10: 393-418.

43. Chua R, Carson RG, Goodman D, Elliott D. Asymmetries in the spatial localization of transformed targets. Brain Cogn. 1992; 20: 227-235.

44. Harrington DL, Haaland KY. Hemispheric specialization for motor sequencing: abnormalities in levels of programming. Neuropsychologia. 1991; 29: 147-163.

45. Caramia MD, Telera S, Palmieri MG, Wilson-Jones M, Scalise A, Iani C, et al. Ipsilateral motor activation in patients with cerebral gliomas. Neurology. 1998; 51: 196-202.

46. Kobayashi M, Hutchinson S, Schlaug G, Pascual-Leone A. Ipsilateral motor cortex activation on functional magnetic resonance imaging during unilateral hand movements is related to interhemispheric interactions. Neuroimage. 2003; 20: 2259-2270.

47. Remy P, Zilbovicius M, Leroy-Willig A, Syrota A, Samson Y. Movement- and task-related activations of motor cortical areas: a positron emission tomographic study. Ann Neurol. 1994; 36: 19-26.

48. Salmelin R, Forss N, Knuutila J, Hari R. Bilateral activation of the human somatomotor cortex by distal hand movements. Electroencephalogr Clin Neurophysiol. 1995; 95: 444-452.

49. Singh LN, Higano S, Takahashi S, Kurihara N, Furuta S, Tamura H, et al. Comparison of ipsilateral activation between right and left handers: a functional MR imaging study. Neuroreport. 1998; 9: 1861-1866.

50. Verstynen T, Diedrichsen J, Albert N, Aparicio P, Ivry RB. Ipsilateral motor cortex activity during unimanual hand movements relates to task complexity. J Neurophysiol. 2005; 93: 1209-1222.

51. Nirkko AC, Ozdoba C, Redmond SM, Bürki M, Schroth G, Hess CW, et al. Different ipsilateral representations for distal and proximal movements in the sensorimotor cortex: activation and deactivation patterns. Neuroimage. 2001; 13: 825-835.

52. Schaefer SY, Mutha PK, Haaland KY, Sainburg RL. Hemispheric specialization for movement control produces dissociable differences in online corrections after stroke. Cereb Cortex. 2012; 22: 1407-1419.

53. Schaefer SY, Haaland KY, Sainburg RL. Hemispheric specialization and functional impact of ipsilesional deficits in movement coordination and accuracy. Neuropsychologia. 2009; 47: 2953-2966.

54. Mutha PK, Sainburg RL, Haaland KY. Critical neural substrates for correcting unexpected trajectory errors and learning from them. Brain. 2011; 134: 3647-3661.

55. Mutha PK, Sainburg RL, Haaland KY. Left parietal regions are critical for adaptive visuomotor control. J Neurosci. 2011; 31: 6972-6981.

56. Mutha PK, Haaland KY, Sainburg RL. Rethinking motor lateralization: specialized but complementary mechanisms for motor control of each arm. PLoS One. 2013; 8: e58582.

57. Tomlinson T, Sainburg R. Dynamic dominance persists during unsupported reaching. J Mot Behav. 2012; 44: 13-25.

58. Shabbott BA, Sainburg RL. Differentiating between two models of motor lateralization. J Neurophysiol. 2008; 100: 565-575.

59. Sainburg RL, Duff SV. Does motor lateralization have implications for stroke rehabilitation? J Rehabil Res Dev. 2006; 43: 311-322.

60. Sainburg RL. Handedness: differential specializations for control of trajectory and position. Exerc Sport Sci Rev. 2005; 33: 206-213.

61. Sainburg RL. Evidence for a dynamic-dominance hypothesis of handedness. Exp Brain Res. 2002; 142: 241-258.

62. Przybyla A, Good DC, Sainburg RL. Dynamic dominance varies with handedness: reduced interlimb asymmetries in left-handers. Exp Brain Res. 2012; 216: 419-431.

63. Duff SV, Sainburg RL. Lateralization of motor adaptation reveals independence in control of trajectory and steady-state position. Exp Brain Res. 2007; 179: 551-561.

64. Winstein CJ, Pohl PS. Effects of unilateral brain damage on the control of goal-directed hand movements. Exp Brain Res. 1995; 105: 163-174.

65. Robertson JV, Roche N, Roby-Brami A. Influence of the side of brain damage on postural upper-limb control including the scapula in stroke patients. Exp Brain Res. 2012; 218: 141-155.

66. rust JC. Lesions of the supplementary motor area. Adv Neurol. 1996; 70: 237-248.

67. rinkman C. Lesions in supplementary motor area interfere with a monkey's performance of a bimanual coordination task. Neurosci Lett. 1981; 27: 267-270.

68. Donchin O, Gribova A, Steinberg O, Mitz AR, Bergman H, Vaadia E. Single-unit activity related to bimanual arm movements in the primary and supplementary motor cortices. J Neurophysiol. 2002; 88: 3498-3517.

69. Gribova A, Donchin O, Bergman H, Vaadia E, Cardoso De Oliveira S. Timing of bimanual movements in human and non-human primates in relation to neuronal activity in primary motor cortex and supplementary motor area. Exp Brain Res. 2002; 146: 322-335.

70. Tanji J, Okano K, Sato KC. Neuronal activity in cortical motor areas related to ipsilateral, contralateral, and bilateral digit movements of the monkey. J Neurophysiol. 1988; 60: 325-343.

71. Wiesendanger M, Kaluzny P, Kazennikov O, Palmeri A, Perrig S. Temporal coordination in bimanual actions. Can J Physiol Pharmacol. 1994; 72: 591-594.

72. Nozaki D, Kurtzer I, Scott SH. Limited transfer of learning between unimanual and bimanual skills within the same limb. Nat Neurosci. 2006; 9: 1364-1366.

73. Wang J, Lei Y, Xiong K, Marek K. Substantial generalization of sensorimotor learning from bilateral to unilateral movement conditions. PLoS One. 2013; 8: e58495.

74. Wang J, Mordkoff JT, Sainburg RL. Visuomotor learning generalizes between bilateral and unilateral conditions despite varying degrees of bilateral interference. J Neurophysiol. 2010; 104: 2913-2921.

75. Kelso JA, Southard DL, Goodman D. On the nature of human interlimb coordination. Science. 1979; 203: 1029-1031.

76. Diedrichsen J, Nambisan R, Kennerley SW, Ivry RB. Independent on-line control of the two hands during bimanual reaching. Eur J Neurosci. 2004; 19: 1643-1652.

77. Hazeltine E, Diedrichsen J, Kennerley SW, Ivry RB. Bimanual cross-talk during reaching movements is primarily related to response selection, not the specification of motor parameters. Psychol Res. 2003; 67: 56-70.

78. Diedrichsen J, Hazeltine E, Kennerley S, Ivry RB. Moving to directly cued locations abolishes spatial interference during bimanual actions. Psychol Sci. 2001; 12: 493-498.

79. Boyles J, Panzer S, Shea CH. Increasingly complex bimanual multi-frequency coordination patterns are equally easy to perform with on-line relative velocity feedback. Exp Brain Res. 2012; 216: 515-525.

80. Treffner PJ, Turvey MT. Symmetry, broken symmetry, and handedness in bimanual coordination dynamics. Exp Brain Res. 1996; 107: 463-478.

81. Swinnen SP, Jardin K, Verschueren S, Meulenbroek R, Franz L, Dounskaia N,. Walter, Exploring interlimb constraints during bimanual graphic performance: effects of muscle grouping and direction. Behav Brain Res. 1998; 90: 79-87.

82. Swinnen SP, Interlimb coordination: neural, dynamical, and cognitive constraints. 1994, San Diego: Academic Press. xxii, 637.

83. Latash ML, Scholz JP, Schöner G. Motor control strategies revealed in the structure of motor variability. Exerc Sport Sci Rev. 2002; 30: 26-31.

84. Tseng Y, Scholz JP, Schöner G. Goal-equivalent joint coordination in pointing: affect of vision and arm dominance. Motor Control. 2002; 6: 183-207.

85. Latash ML, Scholz JF, Danion F, Schöner G. Structure of motor variability in marginally redundant multifinger force production tasks. Exp Brain Res. 2001; 141: 153-165.

86. Scholz JP, Schöner G, Latash ML. Identifying the control structure of multijoint coordination during pistol shooting. Exp Brain Res. 2000; 135: 382-404.

87. Scholz JP, Schöner G. The uncontrolled manifold concept: identifying control variables for a functional task. Exp Brain Res. 1999; 126: 289-306.

88. Taub E, Uswatte G, Mark VW, Morris DM. The learned nonuse phenomenon: implications for rehabilitation. Eura Medicophys. 2006; 42: 241-256.

89. Mark VW, Taub E. Constraint-induced movement therapy for chronic stroke hemiparesis and other disabilities. Restor Neurol Neurosci. 2004; 22: 317-336.

90. Blanton S, Wolf SL. An application of upper-extremity constraint-induced movement therapy in a patient with subacute stroke. Phys Ther. 1999; 79: 847-853.

91. Wolf SL, Lecraw DE, Barton LA, Jann BB. Forced use of hemiplegic upper extremities to reverse the effect of learned nonuse among chronic stroke and head-injured patients. Exp Neurol. 1989; 104: 125-132.

92. Kitago T, Krakauer JW. Motor learning principles for neurorehabilitation. Handb Clin Neurol. 2013; 110: 93-103.

93. Krakauer JW, Carmichael ST, Corbett D, Wittenberg GF. Getting neurorehabilitation right: what can be learned from animal models? Neurorehabil Neural Repair. 2012; 26: 923-931.

94. Raghavan P, Santello M, Gordon AM, Krakauer JW. Compensatory motor control after stroke: an alternative joint strategy for object-dependent shaping of hand posture. J Neurophysiol. 2010; 103: 3034-3043.

95. Krakauer JW. Motor learning: its relevance to stroke recovery and neurorehabilitation. Curr Opin Neurol. 2006; 19: 84-90.

96. Whitall J, Waller SM, Sorkin JD, Forrester LW, Macko RF, Hanley DF, et al. Bilateral and unilateral arm training improve motor function through differing neuroplastic mechanisms: a single-blinded randomized controlled trial. Neurorehabil Neural Repair. 2011; 25: 118-29.

97. Luft AR, McCombe-Waller S, Whitall J, Forrester LW, Macko R, Sorkin JD, et al. Repetitive bilateral arm training and motor cortex activation in chronic stroke: a randomized controlled trial. JAMA. 2004; 292: 1853-1861.

98. Kalveram KT, Seyfarth A. Inverse biomimetics: how robots can help to verify concepts concerning sensorimotor control of human arm and leg movements. J Physiol Paris. 2009; 103: 232-243.

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