Influence of combined action observation and motor imagery of walking on lower limb reflex modulation in patients after stroke—preliminary results

Frank Behrendt1,2*, Monika Le-Minh1,3 and Corina Schuster-Amft1,2,4

Abstract

Objective: The combined use of action observation and motor imagery (AOMI) is a promising technique in neurorehabilitation that can be usefully applied in addition to conventional forms of therapy. Previous studies with healthy participants showed that the mere passive observation of walking results in a phase-dependent reflex modulation in the tibialis anterior muscle that resembles the pattern occurring when walking. In patients after stroke, a similar reflex modulation was found in several lower limb muscles during the real execution of walking, but responses were blunted. To clarify whether and how lower limb reflex responses are also modulated in such patients during the combined synchronous observation and imagery of walking, medium-latency cutaneous reflexes from the tibialis anterior muscle were measured. We compared the reflex responses of seven patients after stroke during the AOMI of walking from two different conditions: (a) elicited during the end stance phase and (b) during the end swing phase, both normalized to a baseline condition.

Results: So far, using the identical methodological set-up as in our study with healthy individuals, we could not find any noteworthy reflex response modulation. The study was registered with the German Clinical Trials Register (DRKS00028255).

Trial registration: The study was registered with the German Clinical Trials Register: DRKS00028255.

Keywords: Action observation, Motor imagery, Reflex responses, Stroke, Walking

Introduction

For patients with neurological disorders, action observation (AO) and motor imagery (MI) can be useful and safe tools [1–15]. Compared with either AO or MI applied alone, previous studies with healthy participants revealed a stronger effect when action observation is combined and simultaneously performed with motor imagery (AOMI) [16–23]. There is also first evidence of a beneficial effect of synchronous AOMI in chronic stroke rehabilitation [24].

During AO, the actual execution or during MI of an action, similar premotor and parietal neural structures in the perceiver are recruited [25, 26], thus sharing cortical networks [27]. While this effect has been well studied at the cortical level, we reported on the influence of AO at a more peripheral level of the motor system in individuals without impairment [28, 29]. The phase-dependent reflex behaviour in certain leg muscles that occurs as a result of cutaneous electrical stimulation during walking [30] could be found in individuals who were only passively
sitting and observing the walking movement of another person [28]. Since psychophysiological changes in the peripheral and central systems can occur in a seated viewer compared to an upright observer [31], this result was not necessarily to be expected. In this respect, the seated posture certainly has a strong influence on the accessibility of the motor representation.

However, the data demonstrated that healthy individuals in a seated position watching another person walking, recreate a mental image of the observed gait which they reproduce concurrently in lower limb EMG recordings [32]. As an altered reflex response behaviour during real walking was reported in stroke survivors [33], the aim of the current project was to find out whether modulated, phase-dependent reflex responses during synchronous AOMI [24] of walking could be found in stroke survivors. To the best of our knowledge, no study has yet been conducted on cutaneous reflex responses in post-stroke patients during action observation of walking alone or combined with motor imagery. We hypothesised that there would be a modulation of the reflex responses in the patients according to the gait phases, but that it would be somewhat less pronounced than in the group of healthy individuals in our previous study [28].

**Main text**

**Study population**

Data have been collected so far from seven stroke patients (two women) during their stay in a rehabilitation clinic in Rheinfelden, Switzerland. Patients were enrolled between September 2019 and February 2020. Continuation of the recruitment process was not possible due to the Corona-related restrictions and the subsequent termination of the project. The mean age of the patients (2 females) was 57.29 ± 16.41 years (SD) ranging 26 to 71 years with an average time since the stroke of 42.57 ± 51.14 months (Table 1). Inpatients with a diagnosis of ischaemic or haemorrhagic stroke could be included if they were able to sit independently and scored higher than 19 in the Montreal Cognitive Assessment [34]. They further needed to satisfactorily score in two out of three of the following motor imagery ability instruments: (a) Kinaesthetic and Visual Imagery Questionnaire score of 30/50 [35], (b) Mental rotation >75% [36], and (c) Mental chronometry ratio of 1 ± 0.25 [35]. Exclusion criteria comprised a history of multiple strokes, visual impairment, epilepsy seizures in the last year, other neurological, metabolic or mental disorders and a pacemaker.

**Set-up**

We used the same set-up, procedure and analysis as in our study with healthy participants [28]. Cutaneous electric stimulation on the foot was applied which can elicit reflex responses in several leg muscles [37]. These responses, starting from about 75–80 ms are known as P2 (medium latency) responses (see Duysens et al. 2004 for a comprehensive description) [38]. Exemplary reflex traces can be found in our previous report.

For displaying human walking, point-light biological motion [39] was used, which was based on 3-D recordings of a real walking movement on a treadmill. The visual stimulus presented a slightly oblique back-view of walking (slanted to the right by 13°) which measured 6 × 15 cm on the 22 ″ TFT display. To ensure that the observers perceived the stimulus as a back-view, the markers were occluded when covered by body parts. This was originally chosen to support a first-person image of the walking movement. The notebook used to present the visual stimulus also triggered the electrical stimulation (Digitimer D57A, Welwyn Garden City, UK). The stimulation electrode (Axelgaard, Fallbrook, CA, USA) was placed at the medial side of the right ankle, where the posterior tibial nerve is closest to the skin [40]. The EMG of the right tibialis anterior muscle was recorded.

**Table 1** Patient characteristics and outcome scores

| ID | Age range | Month post-stroke | Type and site of lesion | KVIQ | MR | MC | FAC | NRR in % during stance phase | NRR in % during swing phase |
|----|-----------|-------------------|-------------------------|------|----|----|-----|-----------------------------|-----------------------------|
| 1  | 65–69     | 3                 | I, right, posterior CR  | 40   | 32 | 1.23 | 5   | 114.7                       | 93.1                        |
| 2  | 65–69     | 14                | I, right, middle CR    | 50   | 31 | 1.02 | 5   | 112.8                       | 122.9                       |
| 3  | 70–74     | 123               | H, right, thalamus and IC | 33  | 27 | 0.49 | 4   | 93.7                        | 99.7                        |
| 4  | 25–29     | 1                 | I, left, middle CR     | 40   | 25 | 0.94 | 5   | 112                         | 110.1                       |
| 5  | 45–49     | 26                | I, right, middle CR    | 28   | 33 | 1.00 | 5   | 67.9                        | 59.2                        |
| 6  | 55–59     | 22                | H, right BG            | 43   | 27 | 0.89 | 5   | 77.2                        | 78.3                        |
| 7  | 70–74     | 109               | I, right BG            | 22   | 27 | 0.87 | 5   | 113.6                       | 110.7                       |

BG basal ganglia, CR cerebral artery, FAC functional ambulation category, H haemorrhagic, I ischemic, IC internal capsule, KVIQ-10 kinaesthetic and visual imagery questionnaire, MC mental chronometry, MR mental rotation, NRR normalized reflex response
at 2000 Hz (Myon, myon AG, Schwarzenberg, Switzerland) using bipolar, amplified surface electrodes with an inter-electrode distance of 21 mm. The surface electrodes were placed at 1/3 on the line between the tip of the fibula and the tip of the medial malleolus according to the SENIAM-guidelines [41]. The recorded signal was band-pass filtered (30–300 Hz), rectified and averaged using Matlab (Mathworks, Natick, MA, USA).

We used the identical set-up with all patients irrespective of the side of lesion. It was originally planned to conduct a subgroup analysis once the sample size was sufficient. However, there is evidence that transcranial magnetic stimulation-evoked potentials are higher in stroke patients on both the affected and unaffected sides during AO [42].

**Procedure**

All patients were invited for a single measurement session. After completion of initial measurements to verify eligibility, patients were asked to sit comfortably on a normal chair in front of the 21.5" TFT monitor that displayed the point-light stimuli and to watch them for 5 min. to get accustomed to the task before the experiment started. They were instructed to remain completely relaxed while observing the visual stimuli attentively and simultaneously imagining the synchronous execution of the observed walking movement [24]. The MI part of the task was performed from an internal perspective with a kinaesthetic mode [43]. The experiment consisted of 39 trials of the visual walking stimulus (26 trials) and a baseline condition (13 trials). In the baseline condition, each of the individual white dots that made up the point-light figure, performed the same movements, i.e. movement trajectories, but in a different, random position on the screen. Thus, no human figure or biological movement could be recognized. All visual trials were presented in random order, each lasting 10 s with a 10-s pause in between, during which a blank screen was shown. The patients were not told that the stimulation was timed with respect to the walking phase. For the presented walking this was either at the end of a stance phase (13 trials) or at the end of a swing phase (13 trials), triggered by the presentation software which was an inhouse programmed application (MotionViewer) using XCode 3.1 and OpenGL.

In order to reliably obtain reflex responses during the experiment, we followed the usual procedure during the preparation phase [34]. During quiet standing, the motor threshold was determined by gradually increasing the stimulus intensity until a visible muscle contraction was elicited in the abductor hallucis which was possible for all included patients. The stimulation intensity was set at 1.5 times the motor threshold.

**Analysis**

Reflex responses elicited by the electrical stimulation [37] were analysed for the three conditions: (a) stance phase, (b) swing phase and (c) baseline by calculating the integral of the root mean square (RMS) of the EMG signal of the time window between 80 and 130 ms from the beginning of the electrical stimulation [44]. For each subject the mean reflex responses for the two walking phases were normalized to the baseline condition. The reflex increase or decrease was defined as the percentage change of the RMS. The data analysis was kept analogous to the established methods for active walking [30, 45, 46].

**Results**

On average, the normalized reflex responses were reduced by 1.2% (±19.5% standard deviation) for the end stance phase condition, and also reduced by 3.7% (±21.7% standard deviation) for the end swing phase (Table 1). The preliminary, paired t-test performed on the normalized responses (Fig. 1) despite the small sample size indicated that there was no modulation (t(6) = 0.65, P = 0.542, d = 0.246). Thus, the evoked EMG responses between the observed and imagined end stance phase and end swing phase did not differ in the stroke patients. In none of the patients, as in our previous study [28], could background muscular activity in the right tibialis anterior muscle be detected, which theoretically could have led to exclusion.

![Fig. 1](image-url) Mean (RMS after rectification) normalized responses of seven stroke patients with standard errors and individual, normalized values. Horizontal grey line: baseline/control condition
Discussion

There is a huge interest in exploiting the positive effect of the observation and mental recreation of motor activities to improve motor function after stroke. These treatment approaches have yielded promising results, suggesting that AO and MI represent valuable additional interventions [10, 14]. However, it might be helpful to better identify those patients for whom AO and MI would be particularly beneficial as for instance the length of time since the stroke and the extent of physical disengagement could play a role. Therefore, the current study aims to understand whether stroke patients, in general, show the same reaction on the muscular level during AO combined with MI.

The preliminary data we collected so far differed from that of healthy, unaffected individuals, as the reflex responses of the stroke survivors were rather similar for all conditions revealing no changed reflex gain according to the phase of the observed and imagined gait cycle. In our earlier study in healthy individuals [28], the difference between the two gait phases was significant, with a modulation difference of more than 30% whereas in the current study we found a difference of only 2.5% in the rather heterogeneous data of the PaS. This deviation occurred even though all stroke patients were able to walk. Zehr and colleagues comprehensively studied the reflex network in stroke survivors during real walking [33]. They examined reflex responses in the more and less affected leg evoked by stimulation at the ankle and wrist during real walking in chronic stroke and found a phase-dependent modulation of cutaneous reflexes in stroke survivors and healthy individuals. Interestingly, responses were blunted in stroke survivors but still present.

Using functional magnetic resonance imaging it could be shown that during AO, as in healthy individuals, a neuronal activation can be found that overlaps with the activation during motor execution for example in premotor, motor and parietal cortical areas [47]. Brunner et al. included subacute stroke survivors who revealed an even increasing activation response in parallel with an improvement of their motor function and according to clinical recovery. This raises the question of whether and how the descending processing might have been affected in the stroke survivors of the current study. In a study investigating the effect of motor imagery on the F-wave elicited from a paretic muscle as a result of stroke, it was suggested that MI could support the process of restoring motor neuron excitability, which is depressed after stroke [48]. Such peripheral changes after stroke might have resulted in an altered modulation of activity in the current study, but can also be positively influenced by AOMI. A further possibility would be to examine corticospinal connections, in particular by measuring the high-frequency, descending waves that occur with transcranial magnetic stimulation, i.e. the D and I-wave [49, 50]. As the I-wave requires the integrity of the cortical grey matter [51], a disrupted grey and white matter network after stroke [52] may also influence a modulation on this level during AOMI.

A larger database would be helpful to determine the influence of the extent of disengagement from physical activity or the duration since stroke. A specification for the current recommendation on the use of AO and MI or AOMI in this regard as an adjunct to physical therapies cannot be made yet. In order to possibly achieve a stronger effect for instance also on lower limb function in gait rehabilitation, it might be helpful to evaluate the combination of AO/MI with repetitive transcranial magnetic stimulation. With regard to the upper extremities, promising results have been reported [53].

Limitations

- Incongruence during motor imagery may have been enhanced as the patients viewed a model walking from a third person perspective but were asked to imagine the movement from a first person, internal perspective.
- Patients were tested for their motor imagery ability in general, but not explicitly asked for the vividness of their image of walking.
- More data is needed to verify the preliminary results and to be able to draw a statistically robust conclusion. A differentiated recommendation which would be transferable to a larger population cannot yet be given.
- The data collected so far reveal a rather large heterogeneity.

Abbreviations
AO: Action observation; AOMI: Combined action observation and motor imagery; MI: Motor imagery; RMS: Root mean square; PaS: Patients after stroke.

Acknowledgements
We thank Marc H. E. de Lussanet from the University of Münster for his support with the presentation software (MotionViewer).

Author contributions
FB designed the study, mainly performed the analysis, was a major contributor in interpreting the results and was the main contributor in writing the manuscript. MLM collected the data and performed parts of the analysis. CSA contributed to the final version of the manuscript. All authors read and approved the final manuscript.
Funding
This research received no external funding.

Availability of data and materials
The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the local ethics committee for Northwest University of Basel, Basel, Switzerland.

The authors declare that they have no competing interests.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
1 Research Department, Reha Rheinfelden, Rheinfelden, Switzerland. 2 Department of Health, Bern University of Applied Sciences, Bern, Switzerland. 3 Department of Health, Bern University of Applied Sciences, Bern, Switzerland. 4 Department of Sport, Exercise and Health, University of Basel, Basel, Switzerland.

Received: 6 December 2021 Accepted: 28 April 2022 Published online: 13 May 2022

References
1. Buccino G, Salocokin A, Small SL. Functions of the mirror neuron system: implications for neurorehabilitation. Cognit Behav Neurol. 2006;19(1):55–63.
2. Mulder T. Motor imagery and action observation: cognitive tools for rehabilitation. J Neural Transm. 2007;114:1265–78.
3. Celnik P, Webster B, Glasser DM, Cohen LG. Effects of action observation on physical training after stroke. Stroke. 2008;39:1814–20.
4. Kim J-Y, Kim J-H, Ko E-Y. The effect of the action observation physical training on the upper extremity function in children with cerebral palsy. J Exerc Rehabil. 2014;10:176–83.
5. Sale P, Ceraudo MG, Franceschini M. Action observation therapy in the subacute phase promotes dexterity recovery in right-hemisphere stroke patients. Biomed Res Int. 2014;2014:457538.
6. Abbruzzese G, Avanzino L, Marchese R, Pelosin E. Action observation and motor imagery: innovative cognitive tools in the rehabilitation of Parkinson’s disease. Park Dis. 2015;2015:124214.
7. Caffarra P, Perini M, Reda V, Barocco F, Michellini G, Spallazzi M, et al. The effectiveness of Action Observation Treatment (AOT) in Alzheimer’s disease: benefit on temporal orientation and visuo-praxic abilities. Alzheimer’s Dement. 2016. https://doi.org/10.1016/j.jalz.2016.06.1221
8. Adams LJ, Smits-Engelsman B, Lust JM, Wilson PH, Steenbergen B. Feasibility of motor imagery training for children with developmental coordination disorder—a pilot study. Front Psychol. 2017;8:1271.
9. Bek J, Gowen E, Vogt S, Crawford T, Poliaeff K. Action observation produces motor resonance in Parkinson’s disease. J Neuropsychol. 2018;12(2):298–311.
10. Borges LR, Fernandes AB, Melo LP, Guerra RC, Campos TF. Action observation for upper limb rehabilitation after stroke. Cochrane Database Syst Rev. 2018. https://doi.org/10.1002/14651858.CD011887.pub2
11. Kim JC, Lee HM. The effect of action observation training on balance and sit to walk in chronic stroke: a crossover randomized controlled trial. J Mot Behav. 2018;50(4):373–80.
12. Buchignani B, Beani E, Pomeroy V, Iacono O, Sicola E, Perazza S, et al. Action observation training for rehabilitation in brain injuries: a systematic review and meta-analysis. BMC Neurol. 2019;19(1):1–6.
13. Oh SJ, Lee JH, Kim DH. The effects of functional action-observation training on gait function in patients with post-stroke hemiparesis: a randomized controlled trial. Technol Heal Care. 2019;27(2):159–65.
14. Silva S, Borges LR, Santiago L, Lucena L, Lindquist AR, Ribeiro T. Motor imagery for gait rehabilitation after stroke. Cochrane Database Syst Rev. 2020. https://doi.org/10.1002/14651858.CD013019.pub2
15. Behrendt F, Zumbrunnen B, Brem L, Suica Z, Gäumann S, Ziller C, et al. Effect of motor imagery training on motor learning in children and adolescents: a systematic review and meta-analysis. Int J Environ Res Public Health. 2021;18(18):9467.
16. Tsukazaki I, Uehara K, Morishita T, Ninomiya M, Funase K. Effect of observation combined with motor imagery of a skilled hand-motor task on motor cortical excitability: difference between novice and expert. Neurosci Lett. 2012;518(2):96–100.
17. Wright DJ, Williams J, Holmes PS. Combined action observation and imagery facilitates corticospinal excitability. Front Hum Neurosci. 2014;8:953.
18. Villiger M, Estévez N, Hepp-Reymond MC, Kiper D, Kollia S, Eng K, et al. Enhanced activation of motor execution networks using action observation combined with imagination of lower limb movements. PLoS ONE. 2013;8(8):e72403.
19. Kondo T, Saeki M, Hayashi Y, Nakayashiki K, Takata Y. Effect of instructive visual stimuli on neurofeedback training for motor imagery-based brain-computer interface. Hum Mov Sci. 2015;43:239–49.
20. Mouthon A, Ruffieux J, Walchli M, Keller M, Taube W. Task-dependent changes of corticospinal excitability during observation and motor imagery of balance tasks. Neuroscience. 2015;303:535–43.
21. Sakamoto M, Muraoka T, Mizuguchi N, Kanosue K. Combining observation and imagery of an action enhances human corticospinal excitability. Neurosci Res. 2009;65:23–7.
22. Wright DJ, McCormick SA, Williams J, Holmes PS. Viewing instructions accompanying action observation modulate corticospinal excitability. Front Hum Neurosci. 2016;10:17.
23. Wright DJ, Wood G, Eaves DL, Bruton AM, Frank C, Franklin ZC. Corticospinal excitability is facilitated by combined action observation and motor imagery of a basketball free throw. Psychol Sport Exerc. 2018;39:114–21.
24. Sun Y, Wei W, Luo Z, Gan H, Hu X. Improving motor imagery practice with synchronous action observation in stroke patients. Top Stroke Rehabil. 2016. https://doi.org/10.1080/10796338.2016.1141472.
25. Fabbri-Destro M, Rizzolatti G. Mirror neurons and mirror systems in monkeys and humans. Physiology. 2008;23:171–9.
26. Hardwick RM, Caspers S, Eckhoff SB, Swinnen SP. Neural correlates of action: comparing meta-analyses of imagery, observation, and execution. Neurosci Biobehav Rev. 2018;94:31–44.
27. Sharma N, Baron J-C. Does motor imagery share neural networks with executed movement: a multivariate fMRI analysis. Front Hum Neurosci. 2013;7:564.
28. Behrendt F, Wagner H, de Lussanet MHE. Phase-dependent reflex modulation in tibialis anterior during passive viewing of walking. Acta Psychol. 2013;142:343–8.
29. Behrendt F, de Lussanet MHE, Wagner H. Observing a movement correction during walking affects evoked responses but not unperturbed walking. PLoS ONE. 2014;9:e104981.
30. Yang JF, Stein RB. Phase-dependent reflex reversal in human leg muscles during walking. J Neurophysiol. 1990;63:1109–17.
31. Unger J, Andrushko JW, Gates AR, Renshaw DW, Barss TS, Zehr EP, et al. Modulation of the Hoffmann reflex in the tibialis anterior with a change in posture. Physiol Rep. 2019;7:e14179.
32. Behrendt F, de Lussanet MHE, Wagner H. Observing a movement correction during walking affects evoked responses but not unperturbed walking. Front Hum Neurosci. 2013;7:564.
33. Adam TP, Valero-Cabre O, Frank C. Motor cortex lateralization during right-leg walking. J Neurosci. 2006;26:11190–200.
34. Sun Y, Wei W, Luo Z, Gan H, Hu X. Improving motor imagery practice with synchronous action observation in stroke patients. Top Stroke Rehabil. 2016. https://doi.org/10.1080/10796338.2016.1141472.
35. Boltz M, Wirth B, Henricksen SC, Brown B, Schmauss D, Schumacher J, et al. Task-dependent changes of corticospinal excitability during observation and motor imagery of balance tasks. Neuroscience. 2015;303:535–43.
36. Sharma N, Jones PS, Carpenter TA, Baron JC. Mapping the involvement of BA 4a and 4p during motor imagery. Neuroimage. 2008;41(1):92–9.
37. Hugon M. Exteroceptive reflexes to stimulation of the sural nerve in normal man. In: Desmedt JE, editor. New developments in electromyography, clinical neurophysiology. Basel: Karger; 1973. p. 713–29.
38. Duyens J, Bastiaanse CM, Smits-Engelsman BCM, Dietz V. Gait acts as a gate for reflexes from the foot. Can J Physiol Pharmacol. 2004;82:715–22.
39. Johansson G. Visual perception of biological motion and a model for its analysis. Percept Psychophys. 1973;14:201–11.
40. Roby-Brami A, Bussel B. Long-latency spinal reflex in man after flexor reflex afferent stimulation. Brain. 1987;110:707–25.
41. Hermens HJ, Frenkis B, Dissaneth-Klug C, Rau G. Development of recommendations for SEMG sensors and sensor placement procedures. J Electromyogr Kinesiol. 2000;10:361–74.
42. Liepert J, Greiner J, Dettmers C. Motor excitability changes during action observation in stroke patients. J Rehabil Med. 2014;46(5):400–5.
43. Schuster C, Hilfinger R, Amft O, Scheidhauer A, Andrews B, Butler J, et al. Best practice for motor imagery: a systematic literature review on motor imagery training elements in five different disciplines. BMC Med. 2011;9:1–35.
44. Pijnappels M, Van Wezel BM, Colombo G, Dietz V, Duyens J. Cortical facilitation of cutaneous reflexes in leg muscles during human gait. Brain Res. 1998;787:149–53.
45. Duyens J, Trippel M, Horstmann GA, Dietz V. Gating and reversal of reflexes in ankle muscles during human walking. Exp Brain Res. 1990;82:351–8.
46. Duyens J, Tax AA, Murrer L, Dietz V. Backward and forward walking use different patterns of phase-dependent modulation of cutaneous reflexes in humans. J Neurophysiol. 1996;76:301–10.
47. Brunner IC, Skouen JS, Erslund L, Grüner R. Plasticity and response to action observation: a longitudinal fMRI study of potential mirror neurons in patients with subacute stroke. Neurorehabil Neural Repair. 2014;28:874–84.
48. Naseri M, Petroffar P, Ashraf A. Effect of motor imagery on the F-wave parameters in hemiparetic stroke survivors. Ann Rehabil Med. 2015;39(3):401.
49. Zieman U, Rothwell JC. I-waves in motor cortex. J Clin Neurophysiol Off Publ Am Electroencephalogr Soc. 2000;17:397–405.
50. Zieman U. I-waves in motor cortex revisited. Exp Brain Res. 2020;238:1601–10.
51. Di Lazzaro V, Profice P, Ranieri F, Capone F, Dileone M, Oliviero A, et al. I-wave origin and modulation. Brain Stimul. 2012;5(4):512–25.
52. Kessner SS, Schlemm E, Gerloff C, Thomalla G, Cheng B. Grey and white matter network disruption is associated with sensory deficits after stroke. NeuroImage Clin. 2021;31:102698.
53. Noh JS, Lim JH, Choi TW, Jang SG, Pyun S-B. Effects and safety of combined rTMS and action observation for recovery of function in the upper extremities in stroke patients: a randomized controlled trial. Restor Neurol Neurosci. 2019;37:219–30.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:
- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.
Learn more biomedcentral.com/submissions