REVIEW PAPER

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Clinical applications and efficacy of mirror neuron function

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ABSTRACT

Mirror therapy aims to restore the function of a disabled body part by using the function of mirror neurons in the brain and mimicking the physiological activity of a healthy body part. Mirror neurons were first discovered in monkeys and later found to exist in humans. The working pattern of "mirror" in the brain is always the same. If one limb moves, the correct part of the brain activates and triggers the mirror neurons responsible for stimulating the other limbs. The therapy uses a box with a mirror on one side to hide the impaired limb.. When a healthy limb moves, the mirror reflects it. The brain perceives it as a movement of an inefficient limb, even though it is only an illusion. It drives the recruitment of neural joints and reconstructs neural pathways. The utilisation of mirror neurons holds significant value in various therapeutic approaches, including rehabilitation, mirror therapy (MT), and observational action therapy (AOT). Moreover, these therapeutic methods have evolved to include virtual reality (VR) based treatments. A significant effect of this treatment was present in phantom limb pain (PLP) and post-stroke syndromes, such as motor aphasia and hemiparesis of the lower or upper limb. There are reports on the use of MT in some mental diseases or in autistic people in learning emotions. This review outlines the current possibilities and hopes for therapies based on mirror neuron functions based on selected cases.

Introduction

Mirror therapy (MT) is a treatment based on the function of mirror neurons in the brain. It helps in the treatment of e.g. phantom limb pain (PLP), complex regional pain syndrome (CRPS) or post-stroke hemiparesis. It creates an illusion of a painless and efficient limb in the place of the disabled one [1].

Action Observation Therapy (AOT) uses a similar mechanism and employs video films of physiological movements and the patient's imitation of them as the stimulation of mirror neurons[2]. The newest technological discovery, virtual reality (VR), is promising [3].

A significant improvement was observed in several disorders caused by cerebral infarction, e.g. the motor function of the upper extremities, walking ability, and apraxia of speech [4–6]. On the other hand, MT conducted in the first four weeks after the stroke provided no favourable results compared to standard protocols[7].

Moreover, MT provided significant recovery of motor function in the treatment of Complex Regional Pain Syndrome (CRPS), which occurs after a stroke[8]. It is also helpful in improving proprioception – the patient's sense of body position and self-movement, which may be impaired after a fracture of the distal radius [9]. MT proved to be valuable in motor dysfunctions, including knee osteoarthritis, Bell's palsy and multiple sclerosis (MS) [10–12].

Both analgesic and functional treatment of phantom pain in patients after amputation are promising applications of MT [13, 14]. Although it seems unable to change muscle elasticity in patients with mutilating injuries [15], its positive influence on pain management remains significant [14]. When compared to traditional methods such as routine physiotherapy, it provides significantly better pain management results [16], especially if combined with other treatment methods [17–19].

The review summarises the clinical applications and efficacy of MT and AOT. This work is a review summarizing the achievements of the last five years based on scientific publications.

Mirror neurons and their function

Mirror neurons are unique nerve cells activated by action and observation [20]. Italian scientists discovered them in the 1990s. Rizzolatti et al. noticed that the same part of the monkey's brain is activated when they perform and observe certain activities. Consequently, scientists proved that the same pattern also occurs in the human brain [21]. However, the mirror function has been proved only for four human brain parts [22]. Those parts are the premotor area, the extra motor area, the primary somatosensory cortex, and the lower parietal cortex. Holz et al. observed the activation of these parts of the brain on the EEG [23]. By comparing the functions of mirror neurons and the parts of the brain that behave like them, we can predict situations where mirror neurons will fire. Researchers studying the human brain mirror neuron function establish that while mirror neuron brain regions may contribute to action identification, identifying intention requires additional recruitment of mentalising brain regions [24]. In his work, Sotaro Shimada points out that the key to understanding how we can understand others is not the mirror neuron system's behaviour but rather the multisensory and sensorimotor integration of our own and others' bodies [25]. Sadeghi et al. demonstrate that although the human mirror neuron system (MNS) can be considered the neural basis of social cognition, it still requires further research. n their work, they note that, for example, to imitate, there is a sensory-motor loop for matching external and internal sensory and motor states, allowing the matching of facial movements to the observed emotions of interaction partners [26]. Ramezankhani et al., in a study analyzing the comparison of executive brain and mirror neuron training strategies for frontal lobe function in boys with behavioural disorders, noted that learning mirror neuron strategies had a positive and significant impact on the function of the frontal lobe and its components [27]. Research on mirror neurons is conducted in many applications, including pilot training for the "pull-up" reaction. In their work, Fabre et al. investigated whether alarms based on a mirror neuron system can benefit flight safety, particularly in high stress[28]. Research into understanding the processes occurring in the areas of mirror neurons and their use in treatment is still developing [24].

A technique that has arisen from this data is known as mirror therapy or mirror visual feedback (MVF). The first documented use of magnetic therapy (MT) was for phantom limb pain (PLP)[29]. MT was based on using a box with a mirror on one side. First, the patient with a disabled hand placed their hand in the box. Then, the patient was instructed to place their healthy hand next to the mirror and look into it. Interestingly, this treatment can create an illusion that the hidden, painful limb heals. Another disorder in which MT is helpful is restoring motor skills in post-stroke hemiparesis[30]. The patient observes the limb functioning in the mirror and receives the appropriate visual stimulus. It helps to recruit the premotor cortex during post-stroke rehabilitation. However, Deconinck et al. discovered that the mechanism of resurrecting a paretic limb differs from that in relieving phantom pain [31]. Moreover, research on mirror neurons' role in neuroplasticity is ongoing. The main focus is on motor skills. After MVF, the motor improvement in the paretic limb was due to the plastic change in the primary motor cortex (MI) [32].

Mirror therapy in phantom limb pain (PLP)

Phantom limb pain (PLP) is a type of neuropathic pain that affects the territory of an amputated limb or other surgically removed body parts [33]. Depending on the severity, it can range from a weak, unpleasant sensation to a remarkable pain limiting the quality of life. PLP impedes patient rehabilitation, mental health, and quality of life [34]. However, its prevalence needs to be clarified. It is estimated that PLP of any severity concerns from 49% up to 83% of post-amputation patients [35, 36]. A widely accepted hypothesis considers PLP to be the consequence of postamputation cortical reorganisation [37]. Residual limb pain also called stump pain, occurs in the place of extremity amputation, and often, patients confuse it with PLP [33, 35]. Amputees often describe phantom limb pain episodes as causing tingling, throbbing, electric shock, stabbing, and painful immobility sensations [38]. Treatments for phantom limb pain include pharmacotherapy, physical therapy, nerve blocks, neuromodulation and surgery, as well as mirror therapy [34, 37–39].

The efficacy of MT in PLP treatment is widely discussed and researched. Since PLP is a subjective experience, various assessment tools are utilised to evaluate it. These tools include scales that describe a patient's ability to perform daily activities [40], motor disability and pain score, and the visual analogue scale (VAS), which is one of the most commonly used methods [17, 41–43]. MT decreases PLP over time and can provide the first favourable results after one week of the treatment [36]. A 4-week-long course of MT is sufficient to provide significant results. It leads to over 50% reduction in VAS [17]. What is more, the after-treatment observation shows that the results remain significant for several months [17, 39, 44, 45].

MT can be efficient enough when combined with pharmacological treatment [44]. Simultaneously, it can enhance its effectiveness by incorporating supplementary treatment techniques such as transcutaneous electrical nerve stimulation (TENS) [17]. Both methods are effective, but neither is significantly better than the other in VAS and universal pain score (UPS) [41].

One of the promising aspects of MT in PLP is the possibility of reducing medication intake, which could also lower treatment costs, making it more feasible for patients. While MT proved to be more effective than pharmacological treatment alone [46], other studies question whether it can help significantly reduce drug intake since patients undergoing MT might require even higher doses of analgesics than non-MT patients. Therefore, it is currently undefined if it allows analgesic dose reduction [47]. It was, however, found that MT can help increase shoulder girdle muscle control. Moreover, it significantly reduces disability of patients rated by DASH score [48].

Although promising, MT can be ineffective or cause adverse effects. Some patients report exacerbated PLP or other effects, such as boredom caused by therapeutic methods, cramps or feeling depressed due to the increase of the missing limb awareness [46]. Traditional MT might also be less efficient than the modified versions, such as the illusory touch method. It exploits stroking the patient's healthy limb instead of providing them with illusory movement exercises [49].

MT is effective in 87% of patients, providing the best results in two periods of treatment – one during the first seven sessions and the other from the 14th session onward. Pain intensity influences the time necessary to obtain satisfactory results. There is a tendency for patients with more severe PLP to require more extended treatment in case of VAS > 21mm, reaching over 21 sessions [42].

Timms and Carus [50], in 2015, conducted a systematic review of original research specifically examining the use of mirror therapy in patient populations experiencing PLP following unilateral limb amputation. Their research showed that mirror therapy is a promising intervention for PLP. In their conclusions, they noted that regular mirror therapy sessions were required to maintain the effects of the treatment. In turn, Guemann et al. conclusively showed in a 2022 systematic review that MT does not reduce PLP and disability in amputees. They emphasized that a critical issue in this type of research is a large number of patients and high methodological quality [34]. However, Campo-Pietro and Rodríguez-Fuentes [37], in their review, highlighted that MT appears to be effective in relieving PLP by reducing the intensity and duration of daily pain episodes. According to this group of researchers, MT is a practical, simple and inexpensive method of treating PLP. They also noted that the methodological quality of most publications in this field is very limited, highlighting the need for additional high-quality research to develop clinical protocols that could maximize the benefits of MT for patients with PLP.

In the case of PLP, MT achieves almost 87% effectiveness [42]. It can provide satisfactory results as a method added to pharmacological treatment [41], but the most favourable results can be expected when MT is combined with the other treatment methods. It is a promising method, especially in terms of improving daily life activities, allowing reduction of disability and improvement of muscle control [48].

Stroke

Stroke is a frequent and significant cause of critical disability of neurological functions, associated with severe spasticity and hemiparesis. Therefore, every therapy possibility, including MT, is widely studied to find the optimal solution.

As proved by several studies, mirror therapy (MT) was most efficient in upper limb therapy in patients with cerebral infarction. Ehrensberger et al. described their study on 36 patients, which lasted six months and included twelve training sessions. The main questions asked were about the potential outcomes, adverse effects and acceptability of this therapy in patients after stroke. In this randomized assessment, the researchers compared two equal groups of a few parameters, including maximal voluntary isometric elbow extension strength, spasticity, the Chedoke Arm and Hand Activity Inventory Version 8 (CAHAI-8), the ABILHAND questionnaire, and the London Handicap Scale. Both groups consisted of patients who were six months after cerebral infarction. They did not undergo any additional rehabilitation or other illnesses. The results were promising [51]. In another study, the researchers concentrated on associated mirror therapy (AMT). The patients watched hand animation, e.g. rolling or grabbing an object, and simultaneously repeated those actions. The screen was put above patients' hands to give them the impression of two functional limbs. In the study, three types of assessment scores were used: the Fugl-Meyer assessment upper limb subscale (FMA-UL), box and block test (BBT), and functional independence measure (FIM). FMA-AL and FIM showed a statistically significant improvement in motor function in the experimental group compared to the control group. The BBT scores did not differ between these two groups. The number of examined patients was similar to Ehrensberger's. In this version of MT, the improvement of Dexterity was observed [52]. MT also presents some advantages in upper extremity rehabilitation in patients with a stroke compared to bilateral arm training (BAT). The Electroencephalography (EEG) measurements suggest activation of the contralateral sensorimotor cortex by MT [53]. Also, another subtype of MT, task-based mirror therapy (TBMT), is promising in the treatment of subacute stroke patients. The examination covered a couple of various tests (FMA, BRS, MBI, MAS) to assess motor function, daily life activities and spasticity. The results of motor functions of the upper extremity (rated by FMA) were significantly better in the examined group than in the control group [54].

Moreover, MT might be applicable in treating oedema and pain accompanying post-stroke shoulder-hand syndrome. Patients are encouraged to use the previously neglected arm during this therapy, which might enhance blood circulation in this limb. The probable mechanism comprises sympathetic response, vasodilatation and anti-inflammatory activation [55]. However, a blinded, randomised trial by Antoniotti et al. on patients with upper limb hemiparesis showed no evidence of MT efficiency in the first four weeks after the cerebral infarction, raising questions about MT's potential mechanisms, restrictions, and effectiveness [7].

In turn, Wei et al. [56] analyzed whether the use of combined robot-assisted therapy and virtual reality mirror therapy can activate the mirror neuron system and reward circuits to a greater extent. They believe that both RAT and VRMT are promising treatments for improving upper limb motor dysfunction in stroke patients.

MT also seems to be an effective method of rehabilitation of lower limbs. Arya et al. researched MT applicability in the rehabilitation of lower extremities in a group of chronic post-stroke hemiparetic patients. The outcomes were measured in Brunnstrom recovery stages (BRS), Fugl-Meyer assessment lower extremity (FMA-LE), Rivermead visual gait assessment (RVGA), and 10-meter walk test (10-MWT). Except for 10-MWT, the results were significantly better in MT combined with conventional motor therapy than in the control group [5]. In the observation where MT was combined with treadmill training, a significant influence of MT was observed only in ankle plantarflexion muscle tone. The other parameters (10MWT, 6MWT, or FMA-LE) had no statistical difference compared with the placebo [57]. Another variation of MT was added to cross-education and explored in the study on post-stroke patients. The assessment included a modified Ashworth scale (MAS), London handicap sale (LHS), maximal voluntary contraction (MVC), 10-MWT, and timed up and go (TUG), which did not show any significant difference between the groups. The improvement was apparent in walking velocity. No adverse effects were presented [58].

Action Observation Therapy (AOT)

Like MT, AOT consists of mirror neurons and motor learning activity. This therapy consists of watching and repeating movies that present a specific movement. In their single-blinded, randomised study, Hsieh et al. [59] assessed three groups of 10 patients. Each group was rehabilitated with the other method: the first with AOT, the second with MT, and the third control group with an active control intervention. The evaluation included upper extremity motor deficits in FMA. The evaluation was based on upper extremity motor deficits in FMA. The results obtained from this therapy were auspicious. AOT presented similar effectiveness to an active control intervention. Nevertheless, the observed group was relatively small, so the following studies are necessary [59]. Another research on AOT also provides evidence of its efficacy in upper limb rehabilitation, evaluated in FMA and Modified Barthel Index (MBI) [4]. In addition, this observation suggests a significant influence of AOT on cognitive function. However, further investigation of AOT's efficacy and applications is needed [4].

Motor aphasia

Motor aphasia is a common form of aphasia wherein patients experience difficulties in naming, spontaneously producing fluent language, and retelling information. There are studies of both MT and AOT applications in motor aphasia after stroke rehabilitation. The treatment includes a unique set of audio and video systems, which guarantees patients the possibility of feedback. Chen et al. [60] explored the usefulness of MT in a group of 30 patients with motor aphasia one week after the acute cerebral infarction. Patients were equally divided into the test group and the control group. All of them presented aphasia according to the Western Aphasia Battery and a damaged left hemisphere in scan imaging. The assessment relied on functional magnetic resonance imaging (fMRI), the modified Rankin scale (mRS), the National Institutes of Health Stroke Scale (NIHSS) and the aphasia quotient (AQ). A significant improvement in the examined group was visible in NIHSS and AQ. Furthermore, fMRI results suggested improvement in the functional connections between lobes of the left hemisphere, which raises more questions about MT's impact [60]. Similarly, in post-stroke patients with aphasia of speech (AOS), AOT possible improvement of speech and perception was observed [6].

Virtual reality

New technological tools involve patients more than standard MT. Game-based virtual reality (VR) with gesture recognition provides similar effects to classical MT in treating upper extremity post-stroke. VR is also a prospective instrument in this group of disorders in addition to occupational therapy [61]. Impressive attempts of VR implementation in upper limb therapy after stroke are made. Systems deliberately designed for this usage enable patients to receive more feedback and do and repeat specified tasks. Already in 2017, Dunn et al. [62] conducted research analyzing the use of VR in PLP therapy. They concluded that many cases analysed were only case studies rather than large groups of patients. They also suggested that although VR has positive effects, these studies need further research. However, later research by Mekbib et al. [3] suggests the effectiveness of these newest training tools in activating mirror neurons and stimulating neuroplasticity. This kind of therapy is a new trend, beautiful for patients. However, the examined groups of patients were relatively small. Thus, the following research is necessary. Also, a systematic review by Hao et al. [63] demonstrated the superior effects of immersive virtual reality on upper limb motor recovery.

Potential areas to conduct more consecutive research, especially on larger groups of patients, arise from the fact that all studies, except Antoniotti [7], suggest a present influence of MT and AOT on improving neurological function in specific disorders.

Bell's palsy

Bell's palsy is a condition involving a rapid and unilateral onset of peripheral paresis/paralysis of the seventh cranial nerve. So far, the cause of this condition remains unexplained [64]. Bell's palsy is a common nerve disorder. The annual incidence of Bell's palsy worldwide is around 11–40 cases per 100,000 people [65]. Different physiotherapy techniques are utilised for treating Bell's palsy, which aims to rebuild regular facial expressions, restore normal strength and function of facial muscles, and decrease all associated symptoms [66]. According to the latest guidelines, corticosteroids are the treatment of choice [67].

It showed that mirror therapy can be helpful in the treatment of Bell's palsy. Martineau et al. [11] named it Mirror Effect Plus Protocol. With a free website – www.webcamtoy.com – patients did some exercises with the healthy part of the face. Then, the computer duplicated this image and showed it as a symmetrical representation of the patient's face [11]. Also, research conducted by the team of Bukhari et al. [65] showed that mirror therapy effectively improves facial symmetry and movements and decreases synkinesis in patients with Bell's palsy.

The team of Martineau et al. [68], in a randomized controlled trial of the effects of the "Mirror Effect Plus Protocol" (MEPP) on overall facial function in acute and severe Bell's palsy, showing that MEPP produces promising long-term results when initiated in the acute phase of moderately severe or complete Bell's palsy. These studies included a group of 40 patients divided into two subgroups. The first group of 20 patients was included in the MEPP program (motor imagery + manipulation + face mirror therapy), and the second group received basic counselling. Both groups met with a physician monthly until the sixth month of treatment and one year after disease onset for evaluation. In turn, the team of Mughal et al. [66] researched to evaluate the effectiveness of facial neuromuscular retraining with or without mirror feedback in patients with Bell's palsy. The patients were divided into two subgroups randomly. Both groups received neuromuscular retraining exercises (NMR), and one also received mirror feedback (MVF). The conclusions were that mirror feedback used in conjunction with NMR was more effective in improving facial symmetry and movement and reducing functional disability than NMR used alone in patients with Bell's palsy.

Based on the results mentioned above, it can be concluded that mirror therapy benefits the group of patients with Bell's palsy.

Complex Regional Pain Syndrome

Complex Regional Pain Syndrome (CRPS) is chronic pain in the extremities and is a complex and multifactorial condition. Despite numerous studies, the current understanding of CRPS needs to be completed [69]. It is described as a burning or drilling sensation and affects deeper layers of tissue. This type of disorder can be associated with trauma, fractures, and even stroke [70]. Additionally, CRPS is associated with cortical reorganization [26, 71]. Larger and higher-quality clinical studies are needed to elucidate this condition's underlying mechanisms further, enabling the development of more precisely targeted therapies [69].

Mirror therapy can be an appropriate solution in rehabilitation [62]. With the use of MT in the post-stroke CRPS, an improvement in the motor function of the limb was observed [73]. Moreover, MT application in post-stroke CRPS provides better results than conventional methods based on single-type rehabilitation without MT [8].

In their meta-analysis of ten systematic reviews, Cuenca-Martínez et al. [74] showed a reduction in pain intensity with the use of manual therapy in patients with complex regional pain syndrome (CRPS) but no significant effect in patients with phantom limb pain (PLP) or post-stroke pain. In the conclusions of their research, they also drew attention to the lack of standardisation of the use of MT and the need for further research in this area. Shafiee et al. [75] team also noted in their review that the use of MT appears to be beneficial for patients, but further research is needed to draw significant conclusions regarding the effectiveness of this method in relieving pain and disability.

MT efficacy in CRPS depends on the duration of symptoms [76]. Mirror therapy would be effective if implemented in early CRPS. "Early" means less than eight months. The longer the CRPS is present, the less plastic the neural pathway becomes.

Other applications

Mirror neurons-based rehabilitation techniques, combined with conventional occupational and physical therapy, can also be a useful approach in hand trauma treatment. Mirror therapy seems effective for hand function recovery, but there is insufficient evidence to recommend its use for motor imagery and action observation [77].

The function of mirror neurons may also be valuable in Parkinson's disease, as shown by an improvement of motor function after a 4-week-long AOT [78]. The visuomotor training strategies such as action observation (AO) and motor imagery (MI) that are based on the activity of the mirror neuron system (MNS) facilitate motor re-learning. Analyzing the current scientific evidence about the effectiveness of MNS's treatments (AO and MI) to treat gait in patients with PD shows that the training with AO and MI are effective in improving disease severity, quality of life, balance, and gait in patients with PD[79].

In 2023 Ortega-Martinez et al. [80] published a paper on a home mirror therapy program for children with unilateral spastic cerebral palsy. In their work, they noted that mirror therapy (MT) could become an accessible, intensive and home-based therapy suitable for children with CP. Their work analysed the therapy results of six children aged 8–12, five days a week, 30 minutes a day. They determined that a home-based mirror therapy program is a safe, cost-effective, and feasible therapy for children with CP if the therapist is engaged in a coaching role throughout the program.

Mirror neurons play an essential role in imitation [22], closely related to the theory of mind and empathy [81]. MT increases the possibility of learning the correct pattern of emotional reaction [27].

Conclusion

MT and AOT are promising tools not only in the therapy of post-stroke patients with various syndromes. However, further research is needed on the broad application of MT and AOT due to the absence of a uniform research protocol. This treatment's appropriate time, frequency, and intensity must be determined. Mirror therapy and other related therapies have a limitation in that they can only benefit individuals who have had unilateral limb amputation. Patients after bilateral amputations lack a healthy, exemplary limb.

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