

# Therapeutic Effect of Motor Imagery on Phantom Limb Pain in Upper Limb Amputees. A Systematic Review.

Efecto Terapéutico del Movimiento Imaginado en Dolor  
de Miembro Fantasma en Amputados de Extremidad  
Superior. Una Revisión Sistemática

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## **Therapeutic Effect of Motor Imagery on Phantom Limb Pain in Upper Limb Amputees. A Systematic Review.**

Efecto Terapéutico del Movimiento Imaginado en Dolor de Miembro Fantasma en Amputados de Extremidad Superior. Una Revisión Sistemática

### **ABSTRACT**

**Introduction:** *Phantom limb pain (PLP) is a common pathology in amputees (50-85%), and though the pathophysiology and aetiology of the conditions remain a mystery, evidence points towards a 'multifactorial model', thus being useful motor imagery to access the cortical motor networks to readjust the sensation perceived by the amputee.*

**Objective:** *To conduct a systematic review of the evidence provided by the published literature regarding the therapeutical and especially analgesic effect of motor imagery in patients with upper limb PLP.*

**Methods:** *an initial electronic search was carried out between December 2015 and March 2016 continuing thereafter between June 2016 and August 2016 in the following databases: Medline, PEDro, ENFISPO and Cochrane. A selection was made of different articles that met the established inclusion and exclusion criteria. Inclusion criteria are: studies aimed at patients with PLP of the upper extremity at different stages, who are submitted to a motor imagery physiotherapy intervention, the results to be measured pre- and post- intervention by standardized tests and ,in some cases, with a follow-up assessment.3 studies were included.*

**Results:** *the studies were of small sample size, with different levels of evidence though appropriately covering the amputee population. Different but comparable outcome measures were used and different intervention periods were applied. Statistical analysis was given of the results in each.*

**Discussion:** *These trials seem to provide evidence supporting motor imagery as a viable and beneficial treatment for PLP, though bigger sample sizes are needed to corroborate this.*

**Keywords:** *phantom limb pain, motor imagery, imagined movement, physical therapy.*

### **RESUMEN**

**Introducción:** *El dolor de miembro fantasma es una patología común en pacientes amputados (50-85%), y aunque la patofisiología y la etiología de las condiciones siguen siendo un misterio, la evidencia defiende un 'modelo multifactorial', así siendo útil el movimiento imaginado para acceder a las redes corticales motoras para reajustar la sensación percibida por el amputado.*

**Objetivo:** *realizar una revisión sistemática de la evidencia que aporta la literatura publicada en relación al efecto terapéutico y sobre todo analgésico del movimiento imaginado en pacientes con dolor de miembro fantasma de la extremidad superior.*

**Métodos:** *se realizó una búsqueda electrónica inicial se llevó a cabo entre diciembre del 2.015 y Marzo 2.016, continuando a partir de ahí entre junio del 2.016 y agosto del 2.016 en las siguientes bases de datos: Medline, PEDro, ENFISPO y Cochrane. Se hizo una selección de diferentes artículos que cumplía el criterio de inclusión y de exclusión establecidos. Los criterios de inclusión fueron: estudios enfocados a pacientes con dolor de miembro fantasma de la extremidad superior en diferentes fases, quienes se someten a una intervención fisioterapéutica de movimiento imaginado, siendo los resultados evaluados pre- y post- intervención mediante pruebas estandarizadas, posiblemente con una evaluación tras la intervención. Se incluyeron 3 estudios.*

**Resultados:** *los estudios tuvieron un tamaño de muestra pequeño, con diferentes niveles de evidencia aunque cubriendo adecuadamente la población de amputados. Se utilizaron pruebas de evaluación diferentes pero comparables y los periodos de intervención fueron variados. Se dieron análisis estadísticos.*

**Discusión:** *Estos estudios parecieron aportar evidencia apoyando el movimiento imaginado como un tratamiento viable y beneficioso para el dolor de miembro fantasma, aunque se requiere tamaños de muestra más grandes para poder corroborarlo.*

**Palabras Clave:** *dolor de miembro fantasma, Movimiento imaginado, terapia física.*

## 1. INTRODUCCIÓN

Phantom limb pain (PLP) is pain that is perceived in a region of the body that is no longer present.<sup>1</sup> Such is the earliest concept of PLP, having evolved to be defined as a type of neuropathic pain caused by pathology in the central or peripheral neurones.<sup>2</sup>

PLP is a common pathology in amputees, the most recent literature pointing towards rates of 50% to 85%. Furthermore, those incidence rates have been shown to be independent of gender, age (in adults) and location and level of amputation. Most studies report that the onset of PLP occurs immediately after amputation, within the first 24 hours for about half of the patients and within a week for another 25%.<sup>1</sup>

In addition, the literature has not shown that incidence rates are related to the mechanism of amputation, that is, elective surgical versus traumatic. This is of great consequence to the selection of the patients in the trials, as it covers a much broader variety of patients.

Nevertheless in spite of, or perhaps due to, the irrelevance of the mechanism of the amputation, the pathophysiology and etiology of the conditions remains a mystery. There are various theories which attempt to address the root cause of PLP, though none has proven to be definitive.

The fact that pressure on the amputation stump neuromas provokes PLP (Tinel Sign), and the discovery that neuromas generate ectopic impulse discharge (ectopia), favoured the stump as the pain generator. However, PLP frequently persists despite neuroma infiltration and nerve/plexus block. For this reason, most investigators have abandoned peripheral nervous system (PNS) explanations in favour of the hypothesis that PLP is a consequence of maladaptive cortical plasticity induced by loss of input from the limb.<sup>3</sup>

The same study proposes that ectopic PNS discharge, primarily that originating in dorsal root ganglia (DRG) serving the amputated limb, drives CNS somatic representations to generate a conscious percept of the phantom limb. The fact that stimulating adjacent skin sometimes evokes sensation felt in the phantom probably is due to CNS plasticity and likewise the sense of limb ownership and distortions of the phantom limb with respect to body schema, including telescoping, movement, and unnatural orientations of phantom limbs.

Another study<sup>4</sup> also covers these grounds, stating that early mechanistic theories on PLP localized its source to the stump, postulating that the ectopic discharge of the neuroma were the primary source of pain generation. The study explains that this is an

incomplete explanation. PLP as a centrally maintained phenomenon associated with neuroplastic reorganization of the spinal cord, subcortical brain regions and neocortex has been the generally accepted explanation for some time.

As such, we cannot venture to deny that each and every level of the nervous system plays a role in the mechanisms of PLP, including peripheral nervous system, dorsal root ganglia and cortical reorganization.

The evidence points towards a ‘multifactorial model’, with authors such as Ramachandran and Hirstein suggesting that there are at least 5 different sources that contribute to the PLP experience: residual limb neuromas; cortical remapping; monitoring of corollary discharge from motor commands to the limbs; one’s body image; and vivid somatic memories of painful sensations or posture of the original limb being “carried” over into the phantom. It is perhaps the strongest hypothesis linking phantom limb pain to both cortical and peripheral mechanisms.<sup>1</sup>

We shall take into account the aspect of the central nervous system and the cortical reorganization and neuroplasticity which accompany the amputation, and although phantom pain can also occur in very unique places such as the breast, nose and rectum<sup>1</sup>, we will focus on the part of the body which this intervention can treat, specifically on the upper extremity.

A loose understanding of the theories behind the mechanisms of PLP may aid in comprehending the possible efficiency of the treatment options, although there is no clear consensus on an optimal treatment regimen. The aim of this study is of a specific physiotherapy treatment which intervenes in the cortical control of the hand, thus we shall not venture into the medical field of pharmacologic studies, also as PLP is often resistant to pharmacotherapy; but more into a certain non-traditional therapy for pain.

Aside from those such as transcutaneous electrical nerve stimulation (TENS), deep brain and spinal cord stimulation and acupuncture, there are certain virtual reality and mirror therapies which have been proven to help.

Anecdotal evidence exists to show that visual mirror feedback using mirror therapy reverses cortical reorganisation and potentially alleviates PLP. In recent years, mental visualization of movement alone has been shown to relieve PLP and reverse cortical changes<sup>5</sup>, also known as motor imagery.

Motor imagery refers to mental rehearsal or simulation of a movement without actual body movement and is already widely used in the neurological rehabilitation of stroke and complex regional pain syndrome (CRPS) to potentially improve voluntary control and motor function.<sup>5</sup>

It has been proven through EEG frequency analysis that the neurocognitive mechanisms underlying voluntary action and voluntary inhibition may be central, and do not require either efference to the target body part, or reafference from it. The ability to command voluntary actions, to inhibit them, and to experience conscious volition, all appear to be intrinsic to the brain's cortical motor networks.<sup>6</sup>

As such, it is only logical to access the cortical motor networks as a means to readjust the sensation perceived by the amputee, with the intention of modifying PLP by means of neuroplasticity.

On the one hand, there is recent evidence available studying its effects combined with graded motor imagery<sup>7</sup>, or as a prelude to mirror therapy, yet not as a sole therapeutic method. The purpose of this study is to determine its effect as a single treatment, thus narrowing down the results so as to reach a consensus as to the efficiency of this therapy itself, rather than as a component.

## **2. METHODS**

A systematic review was carried out of randomized controlled trials (RCTs), amongst other studies such as case studies, pilot studies, etc., published between 2006 and 2016, both in English and Spanish, aimed at decreasing the pain and at improving the functionality of the upper extremity in patients who suffer from phantom limb pain (PLP). Studies which included pharmacological treatments, such as opioids, anticonvulsants, nonsteroidal anti-inflammatory drugs, amongst others, were excluded from this review.

With this in mind, we established a series of inclusion and exclusion criterion to define the electronic search; also a search of reference lists of relevant articles and relevant journals was done.

### **- INCLUSION CRITERIA**

The inclusion criteria to be met were the following:

- In terms of the design of the study:
  - > The search consisted of selecting randomised controlled trials (RCTs), pilot studies, case studies, etc. using the CASP (Critical Appraisal Skills Programme) as a tool for critical reading in the case of RCTs and a Questionnaire for case series. Those studies which obtained a minimum score of 6, in a scale of 1-10 (10 being the maximum score), were included in the review, as long as they passed the first three 'screening questions'.



- > Other studies such as clinical guides, systematic reviews, meta-analysis, study protocols, or study design programmes were not included in this systematic review.
- In terms of the participants:
  - > Upper limb amputees.
  - > Patients suffering from phantom limb pain, at any stage: acute, subacute and chronic.
  - > Over 18 years of age.
- In terms of the Intervention:
  - > Studies specifying MI as a primary intervention for PLP management.
  - > Studies with a minimum of 1 week of therapy.
- Outcome Measures and Results

Studies assessing primary outcomes of PLP intensity/severity using standardised self-report pain scales such as the 10-cm visual analogical scale or the numerical rating scale (NRS).

#### **- EXCLUSION CRITERIA**

- Studies which weren't written in English or in Spanish.
- Studies which weren't developed as a RCT, pilot studies, case studies... such as systematic reviews, meta-analysis... or those which weren't published in the time frame established.
- Studies which look into the efficiency of surgical or pharmacological therapies, looking to diminish PLP.

- Studies which focus on other neurological disorders (such as complex regional pain syndrome or stroke).
- Studies which include a visual feedback as a primary therapy focus such as mirror therapy or virtual reality system.
- Studies which combine motor imagery with other therapies, such as the graded motor imagery method, which includes motor imagery along with left/right discrimination and mirror therapy.

## **- SEARCH STRATEGY**

An initial search was conducted between December 2015 and March 2016, and continued throughout the months of June, July and August of 2016, in the following databases:

- MedLine, through the search engine PubMed
- PEDro
- ENFISPO
- Cochrane

### **1<sup>st</sup> General Search**

#1. “phantom limb” / “phantom”

#2. “phantom limb” AND “imagery”

### **2<sup>nd</sup> Specific Search**

#3. "Imagery (Psychotherapy)"[Mesh] OR "imag\*"[All Fields] OR  
("rehabilitation"[Subheading] OR "rehabilitation"[All Fields] OR

"rehabilitation"[MeSH Terms]) AND "upper extremity"[All Fields] AND "Phantom Limb"[Mesh].

#4. “Motor Imagery”

#5 (((((((((((((((("motor imagery") OR "visual imagery") OR "guided imagery") OR "mental imagery") OR "mental movement") OR "mental representation") OR "movement representation") OR "imagined movement")) AND "phantom limb") OR "pain") OR amput\*)) AND "rehabilitation") OR "therapy") OR "exercise")) AND "upper extremity") OR "upper limb") OR "arm"

#6 (((((((((((("motor imagery") OR "imagined movement") OR "movement representation") OR "therapy") AND "phantom limb") OR "pain") OR amput\*)) AND "upper extremity") OR "upper limb") OR "hand")

#7 “Phantom Limb” AND “Movement Representation”

#8 “Phantom Limb” AND “Exercise”

#9 “Phantom Limb AND “Visual Imagery”

#10 “Phantom Limb AND “Mental Imagery”

#11 “Phantom Limb” AND “Mental Representation”

#12 “Phantom Limb” AND “Imagined Movement”

#13 “Phantom Limb” AND “Pain” AND “Imagery”

Table 1. Summary of the Results Obtained from Each Search

Bases de datos	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13
PubMed	1640	47	24	20	17,305	6,477	6	21	1	4	5	4	4
PEDro	23	5		85				2					
ENFISPO	1	1											
Cochrane	10	11											

First of all, an **initial search** was conducted to gain general knowledge into the subject at hand, including theories and therapies involving PLP and then general information regarding motor imagery.

This initial search was conducted through typing into PubMed, the search engine of Medline, the MeSh terms: “phantom limb”, obtaining 1640 items; yet the same search in PEDro yielded 23 results. In ENFISPO, one article from the term “phantom” appeared (as none appeared for the term “phantom limb”, useful for general knowledge, yet not for the review; and in Cochrane 10 results appeared, none with information on this subject.

Continuing with the gathering of knowledge in PubMed, the MeSh term: “phantom limb” AND “imagery”, obtaining 47 results (the same result in PEDro giving 5 results). Due to the inclusion and exclusion criteria, the “10 years” publication filter was activated, reducing the search to 38 results.

A simple search of “Imagery” was conducted on ENFISPO, as phantom limb yielded nothing previously, which resulted in 1 article and in Cochrane 11, irrelevant to the

review. From this point on, the investigation into these databases, ENFISPO and Cochrane, was abandoned due to lack of relevant articles.

From this initial search, the titles and later the abstracts were screened for relevance. No studies were selected for the review, yet articles were collected to gather information and knowledge.

The difficulty found after investigating studies found in the initial search, was the lack of consensus regarding a common term to define this specific therapy, being valid many terms such as ‘motor imagery’, ‘movement representation’, ‘imagined movement’, etc. Due to this enormous variety of terminology to cover this therapy, several combinations were used to cover all bases regarding this therapy.

Thus, in the **systematic search**, the main issue encountered was the fact that an insufficient number of candidates for the study was found. It was necessary to create a vast search, attempting to span the possibilities wider.

In an attempt to cover more grounds, through the advanced option in Pubmed, search #3 was built.

Through which only 24 results were found, which, after activating the “10 year” filter, was reduced down to 20 results, none of which were valuable for the study.

Parallel to this search, a search on PEDro was conducted with the terms: “motor imagery”, providing 85 results, which were screened through title and abstract and again sought no possible candidates.

The main issue with these searches was the incompatibility with the inclusion criteria, there being many studies including visual feedback or focusing exclusively on other pathologies or solely on lower limb amputees.

As such the search was enlarged, hoping to initially obtain more results and continue to refine. Several searches were conducted along these lines, hoping to cover all bases and possibilities of obtaining all potential studies.

With this in mind, the search #5 was conducted in PubMed, adding a number of filters to include any possible trial into the equation, 17,305 results were obtained. The filters included: clinical studies, clinical trials, controlled clinical trials, observational studies, randomised controlled trials and systematic reviews. The time frame was within the past 10 years and studies on humans only.

This search turned out a ludicrous and unmanageable number of results, nonetheless, it was built with the goal of joining and covering the most important aspects of the review: the intervention itself (motor imagery, visual imagery, etc.), the pathology (phantom limb, amputation, amputees), the field of the science (physiotherapy, as opposed to medical), and the part of the body involved.

This gave a starting point to begin to refine gradually, so the search #6 was conducted and applying the same filters (published in the last 10 years, clinical trials, on humans and including only studies in English and Spanish), 6,477 results were obtained. We can see a reduction in the number of studies yet still not sufficient to screen the titles. This search was abandoned after it was seen that most studies were medical and/or pharmacological and not in the physiotherapy field.

After these searches, more individual and selective searches were performed which, as opposed to amplifying the search, it reduced the options dramatically. As a result, certain searches such as the combination of #7 gave a total number of 6 results, with no filters. None were selected.

From the search #8, 21 results appeared, from which one study was selected. In PEDro, a similar search conducted (phantom exercises) sought two results, which were duplicates from this very same search, one of which was the selected study.

Search #9 only gave one result; #10, 4 results; #11 5 results, none of which were compatible.

Search #12 gave a total of 4 results, from which one article was selected.

A final search with the terms “phantom limb” AND “pain” AND “imagery” was conducted. From 4 results search, the column on the right which showed “Titles with your search terms” was inspected, giving 4 different results, from which one was selected.

These results did not even include any filters, further proving the complication behind the lack of a common terminology for this type of treatment.

Thus, the final number of selected article reached 3.

A manual search through the Journal of Mental Imagery from the following web page: (<http://www.journalofmentalimagery.com/backissues1a.html#36>) sought no useful results in terms of the current focus.

Table 2 contains a summary of all the terms and combinations used in this search.

Table 2. Terms and Combinations for the Search

Bases de Datos	Terms and Combinations Used in the Bibliographic Searches	
	Palabras Clave	Búsquedas
PubMed PEDro ENFISPO Cochrane	<b>Pathology</b>	1 <sup>st</sup> General Search
	1. Phantom Limb	#1. 1
	2. Pain	#2. 1 AND 4
	3. Amput*: Amputee, amputation, etc.	
	<b>Technique</b>	2 <sup>nd</sup> Systematic Search
	4. Imag*: Imagery (Psychotherapy), imagination, etc.	#3 2 OR 14OR 17 AND 1
	5. Motor Imagery	#4 3
	6. Visual Imagery	#5 (5 OR 6 OR 7 OR 8 OR 9 Or 10 OR 11 OR 12) AND (1 OR 2 OR 3) AND (14 Or 13 OR 15) AND (17 OR 16 OR 18).
	7. Guided Imagery	
	8. Mental Imagery	#6 (5 OR 12 OR 11 OR 13) AND (1 OR 2 OR 3*) AND (17 OR 16 OR 19)
	9. Mental Movement	#7 1 AND 11
	10. Mental Representation	#8 1 AND 15
	11. Movement Representation	#9 1 AND 6
	12. Imagined Movement	#10 1 AND 10
	<b>Variable</b>	#11 1 AND 12
	13. Therapy	#12 1 AND 2 AND 4
	14. Rehabilitation	
	15. Exercise	
	<b>Part of the Body</b>	
	16. Upper Limb	
	17. Upper Extremity	
	18. Arm	
	19. Hand	



## METHODOLOGICAL EVALUATION

Of the selected studies, one of them was a randomized controlled trial which was the study of Ülger et al.<sup>8</sup>, and the other two studies were non-controlled clinical case series, one Beaumont et al.<sup>9</sup> and the other MacIver et al.<sup>10</sup> which have a much lower level of evidence. If we are to take into account the strength of evidence basing ourselves on the North of England Evidence Based guideline Development Project, we could say the two RCT studies have a category of evidence of I, and the other two studies of III, considering they were not precisely case-control studies<sup>11</sup>.

Both the internal validity and external validity were taken into account to assess the methodology of the study, through the use of CASP in the case of the randomized controlled trial, the critical appraisal skills programme checking for the trustworthiness, results and relevance of each study, seen in Table 3.

As pertained in the first question of this appraisal tool, the study must address a clearly focused issue. The selected study of a randomized controlled trial which clearly defined the population studied, the intervention given, with a randomised allocation (1<sup>st</sup> and 2<sup>nd</sup> question of CASP). These are the screening questions after which a decision should be made as to include or exclude the study. As such, this study passed this question.

In terms of the third question, it is doubtful as to the blinding of the health workers and study personnel, as due to the very nature of the therapy, it is near impossible to blind the patients, however the assignation of the groups and later assessment can be blinded, which is not left very clear, which only explains that all the assessments were conducted by the same physiotherapist.

As to the fourth question, it is very clear that the groups were similar at the start of the trial, especially when it came to the phantom pain pre-treatment, which is the main

focus of the trial. Nonetheless, it is shown in another table that both groups were also very similar in terms of age, height and weight. A difference which could be taken into account was the time which had passed in months since the amputation, there being a noticeable variation.

Table 3. CASP Appraisal Tool

Question	CASP Assessment of Methodology of the Selected RCTs
	Ülger et al.
1	+
2	+
3	-
4	+
5	-
6	+
7	Phantom sensation, VAS. Phantom Pain, VAS.
8	+
9	+
10	+
11	+
Score	7

*1. Did the trial address a clearly focused idssue? 2. Was the assignment of patients to treatments randomised? 3. Were the patients, health workers and study personnel blinded? 4. Were the groups similar at the start of the trial? 5. Aside from the experimental intervention, were the groups treated equally? 6. Were all of the patients who entered the trial properly accounted for at its conclusion 7. How large was the treatment effect. 8. How precise was the estimate of the treatment effect? 9. Can the results be applied in your context or to the local population? 10. Were all clinically important outcomes considered? 11. Are the benefits worth the harms and costs?*

The group were not treated equally aside from the experimental intervention, as the control group also received a general exercise programme as well as the routine prosthetic training which the experimental group also received; this addition of exercise can give room to error.

When it comes to accounting properly for the patient at the conclusion of the trial Ülger gives no reason to believe that there was any abandonment of the participants from the trial, explaining that 20 patients participated in it, and 20 were studied.

In terms of the treatment effect, Ülger claims there being less pain in the experimental group than in the control group ( $p < 0.05$ ), with a clearly specified primary outcome. As such, it can be considered statistically significant and a precise, considering the table described of the comparison of values between pre and post treatment in the groups.

Bearing into account the nature of the pathology and the simplicity of application of the treatment, it can be considered that the results can be applied in my context.

Considering the subjective nature of the issue, it can be said of Ülger that all clinically important outcomes were considered, as the main goal is to reduce pain, which is measured through the VAS. It could have been interesting, although secondary, to study the quality of life.

Lastly, the benefits are worth the harms and costs, as there are no negative repercussions from this therapy and the costs are minimal.

The other two studies were case series (Beaumont et al, and MacIver et al), meaning that the level of evidence was much lower, so needing a validity tool, for which I used the Joanna Briggs Institute Critical Appraisal Tools for use in JBI Systematic Reviews, seen in Table 4.

This checklist consisted of a ten question tool, of which the first question tackled the issue of a clear criteria for inclusion in the case series, which is the case for both Beaumont and MacIver.

The second question in terms of measurement was a pass for both studies considering that the nature of the pathology being entirely subjective and relative to the patients, both applied standardised tools for this type of symptom. This leads to a pass on the third question in terms of the identification.

The fourth, fifth and sixth questions are a fail for both studies, due to the fact that neither detailed the time or completion of recruitment, nor the demographics of the participants.

The seventh question is a pass for both, as both included tables detailing and describing the participants, whereas the eighth question investigates the follow-up, which occurs in Beaumont, yet not in MacIver.

Table 4. Quality Assessment Tool for Case Series Studies

	Quality Assessment Tool for the Case Series selected studies	
	MacIver et al.	Beaumont et al.
1	+	+
2	+	+
3	+	+
4	-	-
5	-	-
6	-	-
7	+	+
8	+	-
9	Not Applicable	Not Applicable
10	+	+
Score	6/10	5/10

*1. Were there clear criteria for inclusion in the case series? 2. Was the condition measured in a standard, reliable way for all participants included in the case series? 3. Were valid methods used for identification of the condition for all participants included in the case series? 4. Did the case series have consecutive inclusion of participants? 5. Did the case series have complete inclusion of participants? 6. Was there clear reporting of the demographics of the participants in the study? 7. Was there clear reporting of clinical information of the participants? 8. Were the outcomes or follow up results of cases clearly reported? 9. Was there clear reporting of the presenting side(s)/clinic(s) demographic information? 10. Was statistical analysis appropriate?*

The Joanna Briggs Institute. Joanna Briggs Institute Reviewers' Manual: 2016 edition. Australia: The Joanna Briggs Institute; 2016.

The ninth question is difficult to assess in general on this subject, as it is a condition in most cases of a traumatic origin, and the adaptability to demographics should not be difficult nor necessary to analyze. Nonetheless, this point was not given. Finally, both studies give an appropriate and detailed analysis of the results

### **3. RESULTS**

In the selected studies, there were different outcome measures used in an attempt to objectify a very individual and subjective symptom: that of pain.

Studies based on the effects of interventions trying to establish causality between pathology and subjective symptoms are problematic because of the difficulty of controlling for the effects of the interventions per se.

As such, three of the studies used a common outcome measure which is that of the 10-cm Visual Analogue Scale, whilst another study used the Numerical Rating Scale. Both reach similar scores due to the same limits, being approximately on a scale with a maximum score of 10. As such, it is understood that they are easily comparable results.

Other outcome measures were not studied in great details as for the intentions of comparison, they are irrelevant. Any important details regarding the results will be explained in the discussion.

#### **CHARACTERISTICS OF THE STUDIES**

In general, the mean age of all participants over the three studies comes to 47,15 years old, starting from 18 years old. The specific age of each participant from the Ülger study is unknown, it reports that the ages range from 30-45, thus making it the study with the youngest participant and MacIver the study with the oldest patient at 75 years old.

In terms of the gender, there is a clear prevalence of males over females, in all studies. It is observed in Ülger with 4 females and 16 males from N=20; in MacIver, 11 males and

2 females from N=13; and in Beaumont that from N=7, all are males. This proves to be studies with more homogenous distribution of gender.

Furthermore, this is also a clear manifestation of extremely low sample sizes, due to a difficulty in recruitment, as the pathology is not very common amongst the general population.

Regarding the cause of amputation, there is a clear predominance of traumatic origin, only one case differed, which was a patient who had been amputated due to bone cancer, in the MacIver study. It is important to bear this into account, as there are reported cases of pre-amputation pain in the other causes of amputation which could be due to different neural pathways, being influenced by different pain mechanisms. As shown, we will delve into the traumatic cases.

The duration of the sessions fluctuates between 30 and 40 minutes daily of the known session times (Beaumont and MacIver, respectively), with the session times of Ülger depending on the disappearance of pain during the exercises. Beaumont reached a total of 20 hours over 8 weeks of daily exercise, and MacIver reached 28 hours of total practise, over 6 weeks. The total time of Ülger sessions is unknown, however it explains participants were to complete the exercise twice daily, reaching a total of 15 repetitions each time for a total of 4 weeks.

Beaumont considers three phases to the therapy. There is a baseline period, into which the patients were randomly assigned, of 3 weeks (N=2), 4 weeks (N=3), or 5 weeks (N=2), with the aim of ensuring that any changes associated with the introduction of the intervention were not simply due to the amount of time participants had spent in the study group.

After this baseline period, comes a week the first Intervention of active observation both in the laboratory and then at home, to guarantee complete comprehension of the movements and increasing adherence to the therapy. Following this commenced the Intervention 2 consisting of four weeks in which the patients continued the recording of data along with the fulfilment of the exercises.

In the included studies, standardized tests are repeated to assess the results of the different variables, as despite the heretogeneity of the therapies carried out, the aim is to calculate if the proposed treatment is effective within the established parameters, the primary concern being the decrease of PLP, through either the 10-cm VAS or the NRS, both of which work on a scale of 0-10.

Other parameters are considered across all studies. Ülger et al, for example, took into account also phantom sensation; Beaumont covered a number of qualitative results through various questionnaires regarding quality of life and imagery; and lastly MacIver concurs with Beaumont in terms of imagery and quality of life through different questionnaires. These are hard to standardize and also deviate slightly from the main focus of the study.

Going into more details regarding these additional outcome measures, Beaumont created videos of movements, from which they drew scores on a numerical scale (0-10) of Imagery Rating Videos, similar to MacIver's Vividness of Imagery Scale, which however differs in reaching a maximum of 0-6.

With reference to the questionnaires, Beaumont administered the Groningen Questionnaire, to describe individual differences; the West Haven-Yale Multidimensional Pain Inventory Version 3.0 (WHYMPI), covering pain through 9 scales from pain severity to general activity; the Kinesthetic and Visual Imagery

Questionnaire (KVIQ), which measures imagery skills; the Pain Catastrophizing Scale (PCS), to analyze how people tend to perceive their painful situation as a disaster; and finally, the Pain Self-Efficacy Questionnaire (PSEQ), indicating how confident they are in their daily functions.

MacIver, indexed the demographics to record the individuality of each patients; used the PLP Questionnaire; Beck Depression and Anxiety Inventory, to exclude severe anxiety or depression; the Imagery scale mentioned before; and the NRS.

Included in Annexes is Table 5 which summarizes all of the relevant characteristics of the study.

## **SYNTHESIS OF THE RESULTS**

When it came to the treatment program, and the combination with other methods, MacIver developed an intervention program which sought to purely investigate the isolated effects of motor imagery; and on the other hand two studies combined motor imagery with another method of treatment. One included prosthetic training (Ülger), which the control group also received; and another (Beaumont) included a set of movements on videotape designed to teach the patient through observation of said movements, at different speed.

MacIver did delve into the research of fMRI, into which we will not venture, neither in terms of assessment and study design nor in terms of treatment results, as our main focus is on the symptomatic effects and not the physiological ones.

In terms of focusing on the results of the outcome measures, Ülger calculated through the 10-cm VAS the mean scores for both phantom pain and phantom sensation both pre-



and post-treatment in the experimental and the control group. Focusing on phantom pain rather than phantom sensation, due to this being the common factor in all of the studies, we find an important reduction in both experimental and control group, with an added decrease of PLP in the experimental group as opposed to the control group ( $p < 0.05$ ), both in PLP and also phantom sensation. The follow-up in this case was scarce, consisting of a telephone conversation 2 months after discharge, which the study in a general overview claims the patients report a decrease in the frequency of PLP, though there is no quantitative data to back up this statement.

Beaumont required participants to record in a daily diary their average pain also with the 10-cm VAS in two phases, of which Phase B was divided into two Interventions. Hence, in this case we can talk of four frames of time (Baseline up until Intervention 1, Intervention 1, Intervention 2, Follow-Up of 6 months during which the treatment was ceased). When considering the most relevant and comparable results, we will concentrate on the results after Intervention 2, which detail the average pain scores immediately after the treatment has ceased.

With this in mind, we can confirm a significant decrease in pain intensity, showing pain reductions varying from 32% to a maximum of 43% after 8 weeks. Median and range are reported here for Intervention 2: median = 41.7; range = 66.5. It is proven that there is a significant reduction in pain from baseline to Intervention 1 ( $Z = -2.201$ ,  $P = 0.028$ ) and from baseline to Intervention 2 ( $Z = -1.992$ ,  $p = 0.046$ ).

And finally, MacIver et al drew upon the NRS for recording daily pain diaries during three phases: one week following the assessment, the 6 weeks of the intervention and the week prior to the final scan.

In this case, there is also an assessment of a factor other than just purely phantom pain, delving into daily exacerbations of pain and unpleasantness. The mean constant pain intensity which had a score of 7.5 before training (range 3-10, SD 2.3) with a mean unpleasantness score of 5 (range 2-9 SD 1.7); mean number of daily exacerbations was 9 (range 0-43 SD 12.0) at a mean intensity of 6 (range 0-9 SD 2.6) and a mean unpleasantness score of 6 (range 0-9 SD 2.7).

At the end of training in therapy, 9 of the 13 participants had gained >50% pain relief. The most noticeable benefit for the participants was the reduction in the number and severity of exacerbations with six participants free from exacerbations of pain at the end of the study.

As stated when examining the quality of the evidence, there is an inadequate follow-up, posing impossibility for comparison.

As Kern<sup>12</sup> states, the efficacy is optimum at 30% mean difference, as it is considered superior to the maximal placebo effect (<25%) observed in non-pharmacologic randomized double-blind clinical trial conducted on PLP.

As the table shows, all studies proved to accomplish said scores, the maximum of which was achieved by MacIver et al, with a decrease in pain of >50%; second being Ülger, with 33,7% and lastly Beaumont, with a decrease of 30% at the end of treatment on 4 out of 6 patients.

#### **4. DISCUSSION**

The studies which have been selected for this revision have assessed the benefits of motor imagery which consists in training patients to evoke and control mentally the images and sensations of movements performed with their missing limbs.

Mental Imagery can provide gains in reference to analgesic effects through imagined movements, in some cases observation of movements also, in patients who suffer from phantom limb pain following traumatic amputation.

Other benefits such as reduction of exacerbations of pain and improvement of quality of life have also been taken into consideration.

Ülger describes an important reduction in all subject after four weeks of treatment in both groups, the phantom exercise groups having less pain than the control group. Beaumont et al proved a change in pain ratings (30%) superior to the maximal placebo effect (<25%), which Kern describes, whilst MacIver further surpasses those scores with a gain of >50% pain relief in 9/13 of the participants.

In addition, it also performs a follow-up 6 months after ceasing the therapy at the end of Intervention 2, which reflect scores not significantly different from baseline. When analyzing this, the cessation of the treatment must be considered, possibly requiring a more prolonged intervention. On the other hand, a specific case must be taken into account as one individual out of the six did display a perfect maintenance of the decreased pain scores in the 6 month follow-up, perhaps decreasing said scores even further.

This case is extremely relevant as, despite the fact that the authors did not underline this fact, it was the patient who had suffered the longest duration of PLP by a considerable

difference (27.9 years), the second longest time being 8.4 years. Despite the lengthy duration of baseline phase, baseline scores of pain were quite high even in comparison to the patients who had suffered PLP for less time, and with very few fluctuations during baseline, even considering he was allocated to the extended baseline group (5 weeks). This opens a new line of investigation into the importance of time since commencement of PLP and application of mental imagery; perhaps the attenuation over time of neuroplasticity is an important factor in decreasing PLP through mental imagery.

In terms of pain, MacIver broadens the scope by analyzing the improvement in exacerbations of pain and not simply the intensity of constant pain, proving a noticeable benefit for the patients in the number and severity of exacerbations, with six participants free from exacerbations of pain at the end of the study.

With regards to further outcome measures, Beaumont reports an improvement in imagery, regarding the ability to imagine their phantom limb with four of the six patients perceiving an improved ability to move their phantom limb, which MacIver contradicts with a statistically insignificant improvement of vividness of imagery.

Through the WHYMPI questionnaire, Beaumont suggests that subjects who perceived having control over their life benefited more from the intervention; and through the Groningen Questionnaire, the authors revealed the patients' report of a decrease of the frequency of the suffering associated to their PLP after the Intervention 2.

The included studies did not hold the highest level of evidence, with a pilot RCT which employs a control group and an MI group, and two studies which were clinical case series with low levels of evidence. Beaumont recognises the limitations behind an

absence of a control group or a placebo condition that would have allowed to draw more definitive conclusions about the effectiveness of the intervention.

Aside from the type of studies, the sample size is also an important aspect to take into account, as all were significantly low, leading to the possibility of error due to a lacking external validity. We have to recognise that behind this objective there is a rare clinical population, which leads to difficulties in recruitment and correct randomisation.

Beaumont found that this type of intervention needs time to be integrated and requires active participation to maintain effect, thus underlining the need of a proper continuation of the therapy, along with an adequate follow up.

Though Ülger did make an attempt at a follow-up two months later, no statistical data was provided, simply a report from patients of adherence to the treatment through maintaining the regime. Beaumont's follow-up was discussed previously, yet it defends the need for a maintaining of the treatment.

Some limitations of this review should be considered when investigating the most updated and reliable information on motor imagery in phantom limb patients. Firstly, certain studies were excluded as the main focus was on the upper limb. As such, perfectly valid, interesting and up-to-date articles concentrating solely on lower limb, without including upper limb patients were not available for consideration.

On the other hand, it is very hard to find studies which include motor imagery as an isolated therapy treatment, removing other components such as mirror-therapy, even though through several studies, it has been proven that when included in a varied therapy, it can increase the benefits. Mosely<sup>13</sup> designed a protocol called Graded Motor Imagery, which includes the combination of three phases: limb laterality recognition, imagined movements, and mirrored movements. He reached the conclusion that graded

motor imagery reduces pain and disability in those with phantom limb pain, amongst also in the wider complex regional pain syndrome type I (CRPSI) population and brachial plexus avulsion injury.

In much the same way, a pilot study conducted by Grangeon et al<sup>14</sup> points towards motor imagery having therapeutic benefits if integrated in rehabilitation programs for spinal cord injury, especially on UL function improvement.

As we can see, the target population for motor imagery is far from being limited solely to PLP patients, being applied to a greatly varied scope of patients: stroke, spinal cord injury, CRPSI,...

The need for motor imagery becomes clear through studies such as Malouin<sup>15</sup>, which found that after amputation, patients demonstrate lower motor imagery performance specific to the affected limb. Their findings suggest perceived vividness of body and limb movements to be dependent on imagery experience, and that the ability to generate vivid images of movements can be affected specifically by limb loss or disuse.

In addition, findings suggest that prosthesis use helps in maintaining the mental representation of the missing limb.

This links in with a find by MacIver et al, who found correlation between the hand area activation and contemporaneous pain: and is emphasized by the fact that, with significant pain reduction during the second scanning session, no such abnormal activation was elicited. It concludes that significant associations exist between different types of phantom limb pain and cortical reorganization, and that regularly practiced mental imagery results in pain relief, which is associated with a reduction in cortical reorganization.

The theory is that mental imagery provides sufficient stimulation of the deafferented neurons and potentially alters reorganisation, which MacIver associates to improving the patient's ability to move their phantom limb, which is shown to occur in Beaumont's study: it accesses not just the motor area, but also the somatosensory area. It reactivates the representation of the missing limb, which may be responsible for the decrease in pain.

Diers<sup>16</sup> reached the conclusion that executed movement shows differential activation for PLP and non-PLP patients, showing that movement and stimulation of one hand also transfer to the other hand, and are in accordance with another finding that mere movement of the intact hand without a mirror also leads to a change in phantom pain and phantom sensation. It expands stating prolonged imagery reduces phantom limb pain and leads to reactivation of the cortical area representing the amputated limb or a symmetrical representation of activity in neighbouring zones. In their study, PLP compared to non-PLP patients showed a lack of activation in MI ipsi- and contralateral to the imagined limb in accordance with other findings.

Brunelli et al<sup>17</sup> described a protocol combining progressive muscle relaxation, motor imagery and a modified set of phantom exercises for lower limb PLP which could not be included in this review due to the nature of the focus on upper limb. Nonetheless, it should be taken into account when considering motor imagery as a feasible therapy for patients. It demonstrated a reduction of phantom limb sensation and reduction of the rate and duration of PLP, though requiring a continuation of treatment throughout a schedule four-week plan, despite possible small effect in the first sessions.

Amongst already well-known types of therapy such as mirror therapy discussed, there are variations which seek to broaden the horizons through virtual reality systems which

provide a computer-generated virtual environment. Osumi et al<sup>18</sup> found that short-term virtual reality rehabilitation successfully and promptly alleviated PLP and simultaneously restored voluntary movements representations of a phantom limb. This directly correlated with the emergence of voluntary movement representation of the phantom limb.

Other psychological method to be contemplated include, for example, Imaginative Resonance Training (IRT) which is an approach based on cyclically evoking and working with the body image of the amputated limb projected against an optically viewed object, e.g. a table-top, near the real body. Meyer et al<sup>19</sup>, reports having achieved a complete elimination of LL PLP after the application of IRT, even 3.5 years after completion of the therapy.

## **CONCLUSION**

Mental imagery, or phantom exercises, are very practical, and do not require any clinical equipment. The fact that this method could be used almost anytime and anywhere as it is a relatively simple and inexpensive method that patients learn quickly, makes it a good potential adjunct to current treatment methods.

It is true that higher levels of evidence are needed, using greater numbers of participants and randomizing the group correctly, however this study sheds light on a need for a continued investigation into this field, as very few updated trials are available for study, yet these previous studies suggest a useful line of investigation.

On the other hand, as mentioned in the case of the patient who had suffered PLP for the longest amount of time, mental imagery may prove more useful in more chronic cases, as neuroplasticity isn't so influenced by recent cortical reorganisation and is more subject to adaptability to the new information provided.



## **ANNEXES**

Table 5. Table 5. Most Relevant Characteristics of the Selected Studies for the Revision

Table 5. Most Relevant Characteristics of the Selected Studies for the Revision						
Author and Year	Study and Duration	Participants	Characteristics	Variables Assessment	Intervention/Number of Sessions	Results
Ülger 2009	RCT Duration: 4 weeks. Follow up: 2 months.	N=20 patients Age: 41.85 y/o Gender: 16 M and 4 F. Time since Amputation: 3 months.	Subacute PLP. Traumatic. Unilateral. UL and LL. Stop taking drugs.	- Phantom pain 10-cm VAS. - Phantom sensation 10-cm VAS.	2 times a day. 7 days a week for 4 weeks. Prosthetic training and phantom exercises.	With a CI of 95% the experimental group showed less pain ( $p<0.05$ ).
MacIver 2008	Case Series. Duration: 8 weeks.	N=13 Age: 52.92 y/o Gender: 11 M and 2 F Time since amputation: 24.54 years.	Mostly traumatic. Unilateral. UL. Chronic PLP of at least 3 years. Stop taking drugs.	- NRS - Clinical interview of Demographics - Phantom Limb Questionnaire - Beck Depression and Anxiety Inventories - Vividness of Imagery Scale - Pain during scanning session (contemporaneous pain)	40 m therapy, 1 per week/fortnight. 6 weeks. Combination of body-scan exercise and imagined movement of and sensation in the phantom limb.	Reduction in pain intensity was significant ( $P<0.0005$ ).
Beaumont (2011)	Case Series. Duration: 6 weeks.	N=6 Age: 52 y/o Gender: 6 M. Time since amputation: 7.58 years.	Chronic PLP, age range 32-65 years. Traumatic. unilateral. UL and LL. Chronic PLP of at least 6 months. Not to modify medication.	- 10-cm VAS - Videos - Imagery Rating Scale - Groningen Q. - West Have-Yale Multidimensional Pain Inventory Version 3.0 - KVIQ - PCS - PSEQ	30 m therapy, 5 days per week. 8 weeks. Combination of active observation and imagined movement.	Significant reduction in pain from baseline to intervention 2 ( $P=0.046$ )

*RCT: randomized clinical trial; M: male; F: female; UL: upper limb; LL: lower limb; PLP: phantom limb pain; VAS: visual analogue scale; CI: confidence interval; NRS: numerical rating scale; KVIQ: kinaesthetic and visual imagery questionnaire; PCS: pain catastrophizing scale; PSEQ: pain self-efficacy questionnaire.*

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