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From phantom pain to body schema:

Bringing new insight to neuropathic pain through neuro-psychomotor reconstruction of amputees' body schema

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Summary: Phantom limb pain, together with neuropathic pain, is one of the most challenging issues in medicine. Phantom pain is refractory to currently available treatments, with most patients showing minimal if none persistent improvements with frequent severe side effects. The latest neuroscience' researches bring out body schema into the focus of pain by providing a fundamental new understanding of phantom limb phenomenon based on neural plasticity in the cortical areas integrating body schema (=cerebral body representation). Treatment focusing on body representation reorganization might thus positively influence phantom pain.

This project is a continuity of an existing Swiss project which was initiated by the main applicant and funded by multiple Swiss grants, the HES-SO in particular. In this previous project a new phantom limb pain therapy was designed to specifically act on amputees' disturbed body schema which led to start up a pain clinic in Haiti in 2013 in the follow up of the terrible earthquake in Port-au-Prince. Since then, more than two hundred Haitian amputees have reported chronic phantom limb pain recovery after this treatment. Global restructuration of amputees' disturbed body schema, as proposed by the neuro-psychomotor therapy may be thus a straightforward remedy offering a novel non-pharmacological and non-surgical treatment of phantom pain.

These very promising clinical results are nonetheless lacking of scientific proof for their medical significancy to be recognized. Indeed, lack of medical investigations such as functional Magnetic Resonance Imaging (fMRI), Magneto-encephalography (MEG), Motor or Somatosensory Evoked Potentials (MEP or SSEP) or Positron Emission Tomography (PET) scan together with poor research tools available in the country have deeply impacted the possibility to document and validate amputees clinical follow up and recovery. Moreover, Haiti has become nowadays a country very difficult to collaborate with because of political instability and insecurity. Thus, despite the fact that the clinic continues to operate, a new innovation and scientific input is difficult to be achieved in such context. And because amputees are not as common in western countries, it is impossible to recruit in Switzerland a representative sample of participants with same characteristics and inclusion criteria for statistically significant analysis. The question thus remains how to bring Haitian clinical results into the Swiss psychological and medical research field in order to open new phantom limb pain therapy for amputees.

To challenge this issue, a new partnership is suggested with the Saint Joseph University of Beirut. Lebanon is indeed a strategic country for this kind of research linking both a high potential of medical and scientific values together with a large community of amputees due to previous wars and high rate of diabetes in the MENA region. In addition to the financial crisis affecting Lebanon and its impact on medical and pharmaceutic fields, non-surgical and pharmaceutical low-cost therapies are essential to reduce pain symptoms of amputees. Moreover, Lebanon is one of the rare countries in the MENA region displaying a high level of psychomotricity expertise (Bachelor and Master levels) which is shared through a long and strong collaboration with the HETS,

especially with its department of psychomotricity (conventions in annex). Indeed, scientific research is well-developed in Lebanon, both in animal models and Humans, especially in the field of Neuroscience including chronic pain. In fact, the laboratory of research in Neuroscience of the Saint-Joseph University has an expertise in neuropathic pain research and its management. Given all these elements, this project will bring empowerment and sustainability to both countries on the level of phantom pain treatment, neuropathic pain understanding and professionals' education in the neuro-psychomotor therapy.

The aim of this partnership is thus threefold.

1. First, to bring the HETS – filière Psychomotricité clinical results collected in Haiti into the Swiss psychometrician and medical research field with the medical, technical and research skills of our Lebanese partners. This will offer new phantom limb pain therapy for amputees, which low-costs dimension is essential for MENA countries as well as for emerging countries.
2. Second, to give new insights to the understanding of neuropathic pain by exploring the links existing between phantom pain and body schema. In particular, our objective is to better understand how body schema reconstruction affects the cortical correlates of phantom pain and how it may reverse maladaptive functional reorganization of the brain. These findings could lead to new understandings and new considerations about neuropathic pain mechanisms, giving new insights to clinical populations (paraplegic, peripheric nerve lesions, neuroalgodystrophia, stroke, brachial plexus avulsion…), relevant to both western and middle eastern countries.
3. Third, to strengthen the education partnership existing between the department of psychomotricity of both the Swiss HETS and the Lebanese Saint-Joseph University by proposing specific education of neuro-psychomotor therapy at the Master's level thus strengthening the USJ leadership position for psychomotricity in the middle-east region.

1. Introduction

When body integrity is suddenly broken down, as it is the case in amputation, the cerebral representation of one's body (body schema) undergoes a striking reorganization. These dramatic bodily changes generate what is called phantom limb phenomenon referring to the illusory, yet really felt, sensation that the amputated limb continues to be vividly present and preserves most of the time its ability to move.

This very strange sensation that the missing limb survives amputation, immediately follows operation and occurs in all amputees. It is limited to a simple sensation for the majority of children under 4 years and adolescents (Melzack et al., 1997; Muller, 1999; Smith & Thompson 1995). However, more than 80% of adult amputees report it as excruciatingly painful, phantom limb sensation becoming then phantom limb pain (Jensen et al., 1984; Hunter et al., 2008; Schley et al. 2008). Commonly reported sensations are cramps, electric shocks, burning, stabbing or lacerating fleshes in the missing limb. Moreover, some amputees experience their phantom limb as being deformed, paralyzed or twisted in an uncomfortable or even impossible position, thus strongly inhibiting their real functional mobility. People suffering from phantom pain do believe they are getting crazy and some will even commit suicide.

This awkward phenomenon is not an illusion of psychic nature. For the patient, pain is real and is really felt in the amputated limb. Pain may progressively vanish over the first months following amputation (Jensen et al., 1984; Hunter et al., 2008). Yet in 50 up to 60% of amputees, it persists throughout years and usually increases in such an intensity to become intolerable (Casale, 2009; Hunter, 2008 ; Schley, 2008). The more dramatic the context of amputation is, the more prevalent is the phantom pain. In the case of earthquakes, wars or traumatic car accidents, the percentage of amputees suffering from phantom pain may explode up to 80 or even 90% (personal clinic data).

Phantom pain is most of the time refractory to any treatment, being thus a real challenging issue to the medical field. Currently available treatments range from analgesic, antiepileptic and antidepressant medications, to surgical radicotomy or DREZotomy and spinal cord or cerebral stimulation techniques. If some have at first glance shown promise, on the long run they mostly do not show consistent symptoms improvement, long-term efficacy remaining quite low. Moreover, most of these therapeutical approaches are costly and thus only easily available in developed countries. Besides their costs, medication treatments are a constant burden in a lot of cases due to side effects or resistance to drugs over time. On the other hand, surgery, which is particularly invasive (surgical procedure) and sometimes irreversible (less used nowadays), provides only partial relief or may create in some cases new pain problems. Moreover, phantom pain is triggered and exacerbated by cognitive and psychological factors. Social withdrawal is common, depression being the most frequent, yet worst side effect.

To better address the question of treating phantom pain, it is necessary to consider the mechanisms that underlie its production. Recent neuroscience' discoveries bring out **body schema** into the focus of pain. The neuro-anatomical structures involved in the processing of pain are indeed exactly those elaborating cerebral representation of one's body. Such close overlap concerns not only cortical areas contributing to sensory-discriminative features of pain but all areas implicated in the pain perception such as the insula and the anterior cingulate cortex mediating affective features of pain or frontal lobes triggering more cognitive or cultural dimensions. Such close overlaps also exist when considering development. Many clinical examples illustrate how pain and body schema are tied from a developmental point of view, with children suffering from nociceptive alterations presenting highly disturbed body schema.

Yet body schema belongs to the pillar concepts of psychomotricity, a rehabilitation approach linking body, mind and emotion.

By associating psychomotricity to the latest neuroscience' researches, the main applicant has developed a new phantom limb pain therapy designed to specifically act on amputees' disturbed body schema (Junker-Tschopp & al, 2013, 2015). The strategy ahead was to develop a low-cost therapy improving the rehabilitation of amputees' phantom pain in developing countries such as Haiti. The Swiss Faculty of Psychomotricity (HETS-Geneva) along with the Haitian Faculty of Medicine (FMP-UEH) has opened in October 2013 in Port-au-Prince a new psychomotor rehabilitation center, the CERPA. From a clinical point of view, out of two hundred Haitian amputees, 95% have reported chronic phantom limb pain reduction (pain evaluation NRS scores dropping from ≥ 5 levels) and more than 40% reporting total phantom limb pain recovery (NRS scores equivalent to 0 or 1) after a neuro-psychomotor treatment. **Global restructuration of amputees' disturbed body schema, as proposed by the suggested neuro-psychomotor rehabilitation therapy, may be thus a straightforward remedy offering a novel non-pharmacological and non-surgical treatment of phantom pain.**

These very promising clinical results are nonetheless lacking of scientific proof for their medical significancy to be recognized. Indeed, lack of medical instruments such MRI, MEG, MEP, SSEP or PET scan, together with poor research tools available in Haiti have deeply impacted the possibility to document and validate amputees clinical follow up and recovery. Moreover Haiti has become nowadays a country very difficult to collaborate with because of political instability and insecurity. Thus, despite the fact that the clinic continues to operate, a new innovation and scientific input are difficult to be achieved in such context. And because amputees are not as common in western countries, it is impossible to recruit in Switzerland a representative sample of participants with same characteristics and inclusion criteria for significant statistical analysis.

A new partnership is suggested with the Saint Joseph University of Beirut to bring Haitian clinical results into the Swiss psychological and medical research field. Lebanon is indeed a strategic country for this

kind of research linking both a high potential of medical and scientific values together with a large community of amputees due to previous wars and a high rate of diabetes in the MENA region. In addition to the financial crisis affecting Lebanon and its impact on the medical and pharmaceutic fields, non-surgical and pharmaceutical low-cost therapies are essential to reduce pain symptoms of amputees. Moreover Lebanon is one of the rare countries in the MENA region displaying a high level of psychomotricity expertise (Bachelor and Master level) which is shared through a long and strong collaboration with the HETS, specially with its department of psychomotricity (conventions in annex), as well as high level of scientific research especially in the Neuroscience field. **Given all these elements, this project will bring empowerment and sustainability to both countries on the level of phantom pain treatment, neuropathic pain understanding and professionals' education in the neuro-psychomotor therapy**.

2. Phantom limb pain, brain plasticity and body schema

For many years, the cause of phantom limb pain remained a mystery and the phenomenon was relegated to the psychiatric field. Nowadays, theories involve differentially peripheral, spinal and cortical mechanisms in the nervous system. One explanation of pain, among others, is the presence of peripheral neuromas, which can be documented by ultrasounds, typically triggering pain while pressing through ultrasound probe. Irritation in the severed nerve endings in the residual tissue are thought to send anomalous signals being interpreted by the brain as pain. Imbalance between excitatory and inhibitory pathways in the concerned peripheral nerve also leads to neuropathic pain.

Recent neuroscience' discoveries have provided a fundamental new understanding of phantom limb phenomenon based on neural plasticity in various cortical areas integrating our body schema, in particular the somatosensory and the motor cortex. As first evidenced by Penfield and Rasmussen (1950), there is a complete topographic map of the body on the post-central somatosensory strip (S1) of the parietal lobe (Figure 1A) and on the motor cortex. Because of the loss of sensations following amputation, the somatosensory as well as the motor cortex undergo a striking reorganization (Merzenick & all., 1984; Pons & al. 1991; Ramachandran & Hirstein, 1996). In upper-limb amputation, sensory input from the face originally destinated to go exclusively to the somatosensory face cortical area now also activates cells in the hand area which is then interpreted as arising from the phantom hand (Figure 1A). The two adjacent regions, the stump and the face, progressively invade the deafferented arm region as shown by functional MRI studies (Flor & al, 1998; Flor, 2002) (Figure 1B). This cortical remapping allows phantom limb to exist through the sensations really felt on the face or on the stump. This strong specific correspondence

between the phantom hand and the face/stump may be evidenced by somatotopic referred sensations and maps (Ramachandran & Hirstein, 1996) (Figure 1C).

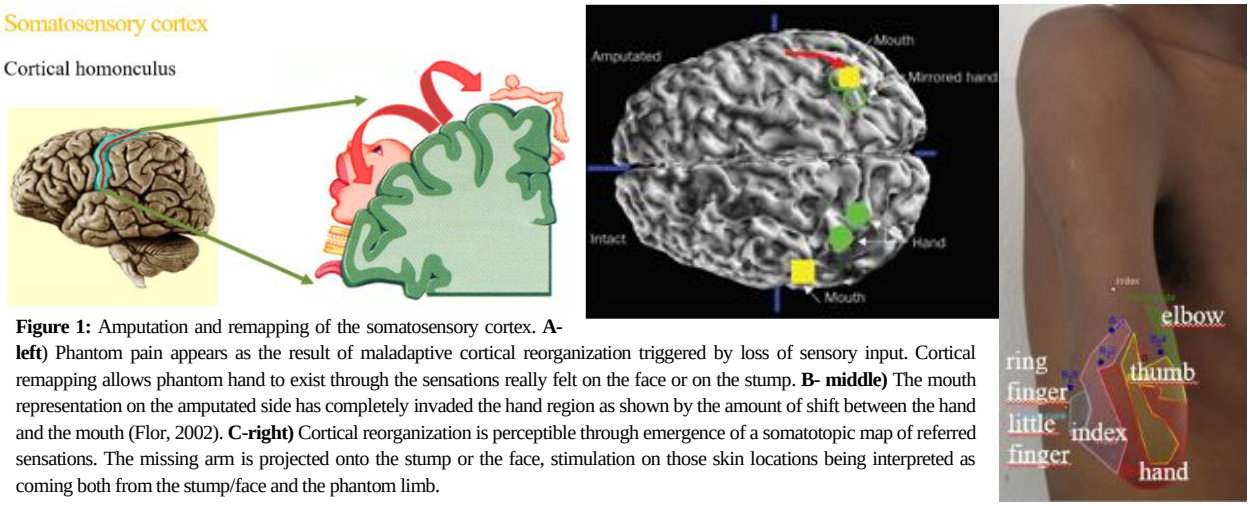

Figure 1: Amputation and remapping of the somatosensory cortex. **A-left**) Phantom pain appears as the result of maladaptive cortical reorganization triggered by loss of sensory input. Cortical remapping allows phantom hand to exist through the sensations really felt on the face or on the stump. **B- middle)** The mouth representation on the amputated side has completely invaded the hand region as shown by the amount of shift between the hand and the mouth (Flor, 2002). **C-right)** Cortical reorganization is perceptible through emergence of a somatotopic map of referred sensations. The missing arm is projected onto the stump or the face, stimulation on those skin locations being interpreted as coming both from the stump/face and the phantom limb.

The phantom limb phenomenon appears as the result of cortical reorganization triggered by loss of sensory input. We know that body schema elaboration is multisensory in nature based on integrative maps of both internal proprioceptive, tactile and vestibular stimulations, together with an external visual image. In the case of amputation, the four sensory modalities are now building up two no-overlapping body-schemas (Figure 2):

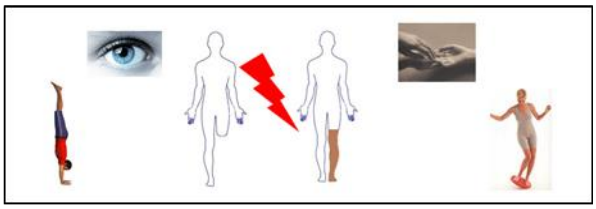

Figure 2 : In the case of amputation, the four sensory modalities elaborating one's body schema, that is proprioception, vision, tact and vestibular system, do not give a coherent body representation. This inconsistency triggers pain.

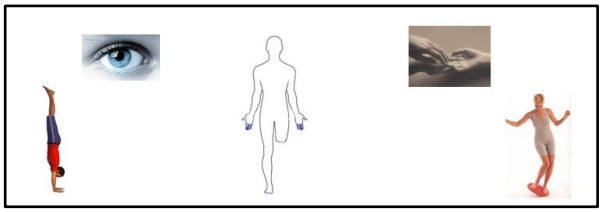

Figure 3 : Reintroducing consistency between the four different sensory maps, by restoring a complete, coherent body schema as proposed by our neuro-psychomotor rehabilitation therapy, allows phantom limb pain to decrease and ultimately to vanish.

Following this theory, phantom pain would be the result of a conflict emerging between 1) the somatosensory and motor maps integrating sensorimotor feeling of the amputated limb through referred sensations and 2) the visual and vestibular maps indicating its absence (the phantom is indeed not visible and has no weight). Therefore reintroducing consistency between these four different sensory maps, by restoring a complete, coherent body schema as proposed by the neuro-psychomotor rehabilitation therapy, allows phantom limb pain to decrease and ultimately to vanish (Figures 2 and 3).

3. The neuro-psychomotor therapy: a therapy specifically designed to act on disturbed body schema

Coordinating psychomotricity with the latest neuroscience' discoveries, this new phantom limb pain therapy is specifically designed to act on amputees' disturbed body schema activating thus neural plasticity.

Cerebral body schema representation is based on a neural network linking sensory, motor, emotional and cognitive areas. Therapy is based on a sensori-motor approach. Visual, tactile, vestibular and proprioceptive sensations are actively explored throughout movement contributing thus to body-schema reconstruction. For example, immersion of the stump in water or sand, or the use of a scarf to move the stump (Figure 3) are situations giving strong sensory information about the new body limits as imposed by amputation. Feeling that body-limits now stop at the stump alleviates immediately the inconsistency between sensory and motor maps. Restoring full coherence within body schema impacts instantly on pain by reducing or even vanishing painful sensations. Yet pain relief is momentary and time is needed for completely and most of the time definitely remapping this body schema representation. Repeating these sensory-stimulation situations over sessions allows new integration of body limits.

Figure 3 : immersion of the stump in water (upper photo) or sand (middle photo) or the use of a scarf (lower photo) gives clear information about the new body limits as imposed by amputation.

Figure 4: Remapping body schema through cognitive and emotional components.

Together with sensory and spatial components, rehabilitation integrates cognitive and emotional factors. Body schema is therefore actively worked both in its limits and in its spatial, cognitive and emotional inscription in the brain (Figure 4). This active remodeling of body schema in the complexity of its dimensions supports the decrease or sometimes disappearance of phantom pains.

More than 200 Haitian amputees have reported chronic phantom limb pain recovery after a neuro-psychomotor treatment. Reduction in phantom pain was significant, independently of the duration since amputation. Amputees suffering from phantom pain for over 20 years did not take longer to recover than other patients. For the great majority (95%), pain tends to reduced (NRS pain scores dropping from ≥ 5 levels) or eventually disappear (40% reporting NRS pain scores equivalent to 0 or 1) in less than three months with two neuro-psychomotor sessions per week. A 6 months follow-up post-therapy does confirm recovery on the long run. Sporadic resurgence of phantom pain may be reported, especially in an emotional context. Yet episodes are no way comparable to the continuous, paroxysmal and intensity components of pain present before therapy. Moreover patients are now able to manage their pain by repeating the learned exercises.

Shrinking of somatotopic maps of referred sensations (Figure 5) was concomitant with decrease in phantom pain intensity, suggesting progressive cortical reorganization of body schema representation. At the end of the therapeutical process, we observe that no pain generally corresponds to the total disappearance of such skin-to-skin mapping.

Figure 5 : Evolution of somatotopic map of referred sensations as measured throughout therapy 1) pre-therapy evaluation [left photo], 2) within the therapeutical process (+32 days) [middle photo], and 3) at the end of therapy (+55 days) [left photo] for an upper-limb traumatic amputated patient.

Our preliminary clinical results support the idea that phantom pain, to some extent, may be reduced and eventually alleviated by approaches such as neuro-psychomotricity **restoring a complete, coherent body schema**.

4. From clinic to research: bringing a new insight into links between phantom pain and body schema

Our clinical results prompt a revisiting of the link between body schema and phantom pain within the research field. Amputation is indeed followed by dramatic changes in the body. Such awkward and unpredictable situation where a limb is present and then suddenly cut off from body integrity would in a sense put the brain in despair to adapt. Maladaptive neural plasticity could thus result in a conflictive situation regarding body schema representation. We suggest that chronic phantom pain is driven by the disorganized state of body schema, pain having a message value! Pain would therefore tell a different, yet much simpler story of what we have been thinking up to now… This hypothesis may explain why chronic phantom pain may be reduced and eventually alleviated by remapping body schema according to the new body limits. The scientific aim of the project is to understand **how body schema reconstruction affects cortical correlates of phantom pain and how it may reverse maladaptive functional reorganization of the brain**.

This research issue may be investigated with the help of our Lebanese partner, the Saint-Joseph University of Beirut. The laboratory of research in Neuroscience under the supervision of its director, Joseph Maarrawi , and together with his two colleagues, Hicham Abou Zeid and Sandra Kobaiter Maarrawi, will bring the medical and scientific skills (fMRI and brain morphometry) to scientifically evaluate the cortical correlates of phantom pain when body schema is reconstructed. Moreover, their clinic is following up a large community of amputees making possible the recruitment of a representative sample of

participants (patients and controls) with same characteristics and inclusion criteria for significant statistical analysis. The high level of psychomotricity expertise displayed in the country together with the existing collaboration between the two institutions will offer a good base for the project to be built. Finally, our years-long expertise of somatotopic maps of referred sensations will be brought to Lebanese examination of amputees.

This study aims to determine if body schema reconstruction may reduce and eventually alleviate phantom pain as well as may induce brain plasticity to remap the cortical correlates of phantom pain and pain matrix in general. The research plan will be based on a randomized, controlled, randomized protocol. Two groups of 10 lower limb (at the level of the thigh) amputated patients each will be compared. The first group referred as the experimental group will receive neuro-psychomotor therapy within a test-retest protocol in order to investigate changes in the level of pain and in neural plasticity. The second group, will receive a physiotherapy of the stump, serving thus as a passive control group. Both therapies will be proposed twice à week for a total amount of 36 sessions.

A test-retest (T0-T1-T2) protocol will be applied, test taking place before any treatment, , retest evaluations taking place at the end of therapy (T1) and 4 months later (T2) in order to evaluate stability of results.

5. Research Plan:

Participants: The study will include 20 individuals with traumatic unilateral lower-limb amputation (at thigh level) suffering from chronic phantom limb pain (> 2 years). Age criteria will be 18- up to 70-years-old. Patients with the following conditions will be excluded from the study: 1) patients with associated central or peripheral nervous system damage due to the traumatic accident, 2) patients receiving specific treatments such as transcranial stimulation or psychotherapy, 3) patients having benefited from a neuropathic pain neurosurgical procedure, 4) patients with associated depression or anxiety as measured with Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983), 5) patients with major untreated psychiatric comorbidity, 6) patients with significant untreated dependency on prescription narcotic analgesics or benzodiazepines, 7) patients with unresolved issues of secondary gain, 8) patients with coexisting chronic pain condition or neurological disease 9) claustrophobia or any other MRI contraindication. Patients will be recruited from the pain clinic (Pr Joseph Maarrawi and Dr Hicham Abou Zeid) and referred to the Laboratory of research in Neuroscience- University of Saint-Joseph of Beirut.

Methods: Body schema, phantom limb pain and cortical changes in both the somatosensory and the motor cortex will be assessed through a pre-test/post-test paradigm. Stability of recovery will be estimated by re-testing patients 4 months post therapy. Evaluation will include:

1) Complete medical evaluation including a medical history, a physical examination and an actual record of the ongoing and previous medication
2) Short-Form McGill Pain Questionnaire – Arabic Version (Terkawi et al. 2017)
3) Assessment of pain intensity using the using visual analog scale (VAS) on a ruler with a slide indicator (front: no digits for patient, only line from no pain to worst imaginable pain) read on the reverse by the examiner (0 indicates being pain free and 10 indicates the worst imaginable pain).
   Intensity of pain will be evaluated, before any therapy, at the beginning and at the end of each clinical session, at the end of the protocol and 4 months later.
4) Patient global impression of changes PGIC at the end of the therapy
5) Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) at pre and re-tests
6) Body map on which the patient is asked to draw pain distribution in his real and phantom body (see body scheme file).
7) Somatotopic map of referred sensations (see stump schema p.7).
8) Functional magnetic resonance imaging scan (fMRI): fMRI will be performed before the beginning of the protocol and at the end of therapy. Each patient will undergo an anatomical 3D T1-weighed MRI for Voxel based morphometry (VBM) analysis (structural) and for template images for fMRI,

followed by a fMRI paradigm divided into 3 phases : 1) Motor mapping for hip flexion, knee slight flexion, and ankle flexion/extension of intact and amputee's lower limb (patient will imagine the movement) ; 2) Somatosensory mapping of thigh, leg and foot of intact and amputated lower limb (somatotopic maps) ; 3) Brain response to allodynia (if present) of the stump.

Therapies: Amputees suffering from chronic phantom limb pain (> 2 years) will receive neuro-psychomotor therapy (experimental group) and physiotherapy (control group), over 36 sessions, twice a week.

Neuro-psychomotor therapy: Therapy will be based on the neuro-psychomotor approach. Visual, tactile, vestibular and proprioceptive sensations will be actively explored throughout movement contributing thus to body schema reconstruction. Rehabilitation will integrate spatio-temporal together with cognitive and emotional factors. Treatment will include a one-and-half-hour individual session twice a week with two psychomotor therapists specifically educated for this therapy.

Physiotherapy: Therapy will follow the usual treatment proposed to amputees' rehabilitation.

Analysis: the following analysis will be completed with the help of a statistician:

1) Special focus will be given to the actual decrease of pain to better understand to which extent pain is alleviated either by coherent sensorimotor information given by the therapeutical set-up or by learning processes impacting neural plasticity on the sensory and motor cortex as time is needed for neural connections to be reorganized. Results will help draw processes underlying phantom pain.
2) Intensity of pain, as referred by participants will be evaluated throughout therapy sessions using a repeated measures analysis.
3) Associated symptoms (Anxiety and Depression), Patient satisfaction will be evaluated and T0, T1 and T2
4) Medication changes between the beginning and end of therapy and follow-up at 4 months as an indicator of pain relief
5) Superficies of somatotopic maps on body of referred sensations as measured pre- (T0), post- (T1) and 4 months (T2) post-therapy will be extrapolated and contrasted with pain trend
6) Phantom pain intensity will be related with sensory+motor-related functional MRI signal both in the phantom limb area and in the stump area according to the location of referred sensations. The fRMI images will be corrected for motion artifact and smoothed using filters.
7) Pain matrix for allodynia will be compared between T0 and T1
8) Links between body schema and adaptive cortical plasticity will be evaluated through correlation between body (stump) somatotopic maps and fMRI images (cortical maps).

Expected results: We expect that for the experimental group, body schema's remapping driven by the neuro-psychomotor therapy will significantly reduce and even alleviate phantom pain. Moreover, significant differences in pain level and in brain reorganization will be measured between the neuro-psychomotor group and the physiotherapy group.

The main expected result is thus that restoring a complete, coherent body schema as driven by the neuro-psychomotor therapy contributes to reduce and eventually alleviate phantom limb pain. Reduction of pain is expected to be correlated with shrinking of body somatotopic maps and reorganization of both the cortical somatosensory and probably motor cortex as well as cortical pain matrix. Cortical reorganization of body schema will match shrinking of somatotopic map giving thus a new and very simple test to evaluate neural plasticity reorganization within the brain. Finally, we expect that pain will be temporarily alleviated before any structural change in neural network may take place, bringing thus new insight to the understanding of phantom limb pain.

6. Project schedule and milestones

Starting in June 2022, the project will be spread over the next 12 months. As clinical rehabilitation is concerned, sessions take place twice a week and are spread over 36 sessions, twice a week. Research will be carried out throughout the therapy. Testing will be done at the beginning of each rehabilitation session. Project will followed the below schedule:

2022.05	start of the project: recruiting participants, pre-therapy testing: 1) complete medical evaluation, 2) Short-Form McGill Pain Questionnaire 3) HAD questionnaire, 4) VAS.
2022.06 - 2022.11	neuro-psychomotor therapy or physiotherapy depending on the referred group (experimental versus control). At the end of therapy, post-therapy testing
2022.10 - 2023.05	4 months post-therapy testing according to the end of therapy
2023.05 - 2023.06	statistical analysis and results, writing articles

7. Sustainability

The project is sustainable because:

- It is based on a strong partnership with the five applicants and their respective institutions
- The hosting institution, the HETS, will cover the costs of the main applicant's research related salary together with all administration fees.
- The Lebanese partners, will assume full medical evaluation and investigations.
- It is based on a strong clinical experience in the pain treatment of phantom pain in amputees in both countries.
- It is using a well-defined therapy protocol, knowing that 95% of 200 Haitians amputees had reported chronic phantom limb pain recovery after this neuro-psychomotor treatment.
- The proof of a new therapeutical perspective without any harm for the patient (such as side effects of medication, risk of operation), expected long lasting effect would offer a perspective for an up to now insufficiently solved medical problem.
- Relief of pain contributes to a substantial gain in quality of life and can enable social reintegration.
- Based on the record of previous treatment attempts and of current medication compared to treatment costs afterwards. Thus the related-cost effectiveness of the new treatment approach can be estimated.

8. Project's relevance and impact

Relevance of the present study is of clinical, theoretical as much as of professional value. The aim of this partnership is threefold.

1. First, to bring the HETS – filière Psychomotricité clinical results collected in Haiti into the Swiss psychomotor and medical research field with the medical, technical and research skills of our Lebanese partners. This will offer new phantom limb pain therapy for amputees, which low-costs dimension is essential for MENA countries as well as for emerging countries.
2. Second, to give new insights to the understanding of neuropathic pain by exploring the existing links between phantom pain and body schema. In particular, our objective is to better understand how body schema reconstruction affects the cortical correlates of phantom pain and how it may reverse maladaptive functional reorganization of the brain. These findings could lead to new understandings and new considerations about neuropathic pain mechanisms, giving new insights to clinical populations (paraplegic, peripheric nerve lesions, neuroalgodystrophia, stroke, brachial plexus avulsion,…), relevant to both western and middle east countries.

3. Third, to strengthen the education partnership existing between the department of psychomotricity of both the Swiss HETS and the Lebanese Saint-Joseph University by proposing specific education of neuro-psychomotor therapy at the Master's level, thus strengthening the USJ leadership position for psychomotricity in the middle-east region.

By exploring the links existing between phantom pain and body schema, this study may open new insights to the understanding of neuropathic pain. In the recent years, phantom limb pain is widely believed to result from maladaptive cortical plasticity triggered by loss of sensory input. Our clinical experience suggests instead that if phantom limb sensation may indeed arise from neural reorganization taking place in the somatosensory/motor cortex, pain is yet the result of a conflictive situation within body schema integration. According to Hippocrate's first assumption, pain is a message reporting the helplessness situation in which the brain is trapped, not knowing how to resolve the conflict. If verified, this assumption would definitely change both pain representation and pain treatments as medication and surgery seek to switch off the message without responding to it.

We know that body schema representation involves further up cortical structures located specifically in the superior parietal lobe (integrating a multi-sensory and dynamic body schema), and in the supramarginal and angular gyri of the inferior parietal lobe (integrating an auditory map in order to locate the body in space) together with limbic structures such as the right posterior insula which underpins the subjective experience of body-ownership and give a more emotional dimension to body schema. We thus postulate that pain mainly arises from these higher cortical integration centers specifically linked to body schema in space elaboration, emotion coming also in the run.

Thus new understanding of pain will be driven by considering it as a percept with a neural representation organized as a neurotag as it is the case for body schema. Matching pain and body schema according to the cerebral structures participating in their elaboration will give sense to the multi-dimensional features of pain triggering affective, learned, cognitive, cultural or even religious components.

Moreover, bringing Haitian experience into the Swiss psychological and medical research field would have a major clinical relevance. It will indeed offer a new phantom limb pain therapy for amputees in western countries, knowing the tremendous need of effective and sustainable neuropathic pain treatments. Bodily centered psychological therapies will definitely gain new consideration in contrast to surgery or medication treatments. Yet definitive recovery may need to impact all dimensions referring to body schema and to pain, in a way we may say from emotion to cognition!

Last but not least, this study may provide a very simple and low-costing test to differentiate among neuropathic pain mechanisms according to the level of body schema disorganization. Finding a somatotopic map of referred sensations will then attest of a certain degree of body schema disorganization,

thus better orienting pain treatment toward body schema centered therapies. On the contrast, not finding one will then indicate a more appropriate use of medication and/or surgery.

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