Program Booklet

1st International Conference on

Phantom Limb Pain

Aug 31 - Sep 2, 2021| Gothenburg, Sweden

Contents

Welcome to ICPLP

Individuals who have suffered an amputation face challenges beyond functional disability, most notably, post-amputation pain. Research and clinical innovations on the treatment of post-amputation pain, and in particularly Phantom Limb Pain (PLP), have increased in the past decade resulting in new treatments, basic research findings, and new models that have challenged our understanding of this perplexing condition. Starting on August 31st, 2021, the first International Conference on Phantom Limb Pain (ICPLP) will be held in Gothenburg, Sweden. Prominent researchers from around the world will gather to discuss the potential origins and treatment of PLP in a historical event that brings together professionals from many different disciplines, such as medicine, neuroscience, and engineering.

This first edition of the ICPLP will be centered around three major topics:
- Neural basis of PLP: hypotheses, neurophysiological studies, and modeling.
- Treatments for PLP: surgical, neurostimulation, and non-invasive.
- Epidemiology and phenomenology of PLP: prevalence, comorbidities, and quality of life.

These three topics have convoluted relationships. Current hypotheses on the neural basis of PLP will be confronted with the clinical reality presented by the latest epidemiological studies on the condition. Ideally, treatments should address the underlaying mechanisms of the condition they aim to alleviate. However, this has been rarely the case in treatments for PLP as such mechanism are not yet fully understood. At ICPLP, we aim to ground current treatments and their clinical results on a theoretical framework informed by studies on the neural basis of PLP. Moving forward, ICPLP will allow for the findings from such studies to be used to drive improvements or entirely new treatments that are potentially more efficacious. Basic research and clinical results from such treatments will then support or challenge the hypotheses on the neural basis used to develop them. Agreement on the evidence and studies required to gather such evidence will be sought at ICPLP in panel discussions and workshops.

Originally planned on May 2020, we had to delay this conference two times due to the on-going COVID-19 pandemic. This first edition of ICPLP will be held in a hybrid format (virtually and on-line) with most invited speakers presenting in person. This with the purpose to have more lively panel discussions and further conversations through the conference.

The ICPLP scientific committee was formed by Prof. Herta Flor (University of Heidelberg, Central Institute for Mental Health, Mannheim), Prof. Jack Tsao (University of Tennessee), Prof. Tamar Makin (University College London), and me, Prof. Max Ortiz Catalan (Chalmers University of Technology). We reviewed and accepted 18 abstracts for oral presentations and 16 for poster presentations, and 5 workshops. Abstracts were received from 14 different countries and authors had a variety of backgrounds from medicine to engineering (61% Females).

Although PLP has been studied for over a century, this has been done discontinuously and often in isolation, which can potentially explain why there is currently no scientific meeting or journal dedicated to the topic. This is despite the high prevalence of the condition, and its detrimental effect on those afflicted by it. However, an increased interest can be appreciated by numerous publications on the condition in the past years. As the first international conference dedicated to PLP, ICPLP is now bringing together researchers and clinicians to share a venue for scientific discussion. In addition to lectures, ICPLP will provide venues for discussing current and novel scientific ideas in the form of panel discussions. In addition, practical knowledge will be disseminated in workshops where participants will learn the latest investigational and treatment methods.

In behalf of the organizational and scientific committees, as well as the Center for Bionics and Pains Research, we are looking forward to see you in-person and online in this historical event!

Best Regards,

Max Ortiz C., Ph.D.,

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Center for Bionics and Pain Research,
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13:30-13:50	Opening Ceremony	Prof. Max Ortiz Catalan
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		Per Tenggren
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14:30-15:00	Prof. Jack Tsao	
15:00-15:30	Prof. Max Ortiz Catalan	
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16:00-16:30	Prof. Herta Flor	
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16:00-16:30	Prof. Nadia Bolognini
16:30-17:00	Dr. Robin Bekrater-Bodmann
17:00-17:30	Prof. Steven Prescott
17:30-18.30	Panel discussion
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Tuesday, August 31st

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Invited talks

Fernando Cervero

Emeritus Professor, McGill University, Montreal, Canada
Honorary Professor, The University of Bristol, UK
Past-President, International Association for the Study of Pain (IASP)

Understanding Phantom Limb Pain

Tuesday, Aug 31st
13:55-14:30

Abstract: An important aspect of our knowledge about pain mechanisms is the recognition that the plasticity of the nervous system is a key element in the generation of persistent and chronic pain. We know that pain is a dynamic sensation, and we think that the symptoms associated with pain perception are the consequence of plastic changes along the pain system, from peripheral nerves to the higher centers of the brain.

Phantom limb sensations, including pain, following the amputation of a limb have been attributed to spontaneous nerve activity from the stumps to mirage sensations caused by abnormal brain processing or to a combination of both mechanisms. The main problem when dealing with phantom limb sensations is the lack of relationship between a missing input and a vivid output in the form of a sensory perception of a non-existing body part. These dissociations are a feature of complex brain activity and in the talk, I will show examples of how the brain can ignore or modify a sensory input to provide a sensation that does not mirror the presented input.

Biography: Fernando Cervero graduated in Medicine in 1972 and obtained a PhD in Neuroscience in 1975. Between 1975 and 1994 he held academic and research posts at Edinburgh and Bristol Universities (UK). From 1994 to 2002 he was appointed Professor and Chair of Physiology at Alcala University (Madrid, Spain) and in 2002 moved to McGill University in Montreal (Canada), where he was appointed Director of the Alan Edwards Centre for Research on Pain. He has studied the mechanisms of pain and analgesia using techniques ranging from human psychophysics, to cellular and molecular analysis in experimental animals, with a special interest on the peripheral and spinal mechanisms of visceral pain and on the CNS generation of hyperalgesic states. He is a Past-President of the International Association for the Study of Pain (2012-14), member of the Academia Europaea and Editor-in-Chief of Neurobiology of Pain. He currently lives in the UK.

Changing Notions of Phantom Limb Pain: From Psychiatric Condition to Neurological Condition

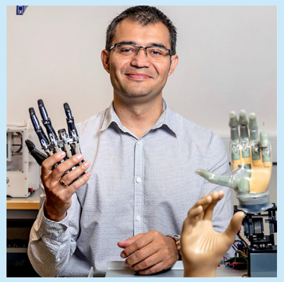
Tuesday, Aug 31st
14:30-15:00

Abstract: This talk will review historical theories about phantom limb pain and present more recent evidence about the nature of this medical condition and discuss contributions of both the peripheral and central nervous system.

Biography: Professor of Neurology, Pediatrics, and Anatomy & Neurobiology at the University of Tennessee Health Science Center, Memphis, TN, USA and Director of the Polytrauma/OIF/OEF Clinic at the Memphis Veterans Affairs Medical Center, a researcher at the Children's Foundation Research Institute at Le Bonheur Children's Hospital, and Fellow of both the American Academy of Neurology and American Neurological Association. Dr. Tsao received his undergraduate degree in biochemistry from Harvard College, a master's degree in biochemistry from the University of Cambridge, England, a doctorate in physiology/pharmacology from the University of Oxford, England, and medical degree from Harvard Medical School. Prior to finishing his medical degree, he was a postdoctoral fellow in the Department of Neurology at Johns Hopkins Hospital. He completed internal medicine internship and neurology residency at the University of California-San Francisco and then began 14 years of active duty service in the United States Navy, where he was first stationed at Naval Hospital Jacksonville, Florida as neurology department head. While there, Dr. Tsao completed a behavioral neurology fellowship at the University of Florida. He was then assigned to the Uniformed Services University of the Health Sciences in Bethesda, MD for 4 years before being selected to become the inaugural Director of Traumatic Brain Injury (TBI) Programs for the United States Navy Bureau of Medicine and Surgery, Falls Church, VA, where he managed Navy and Marine Corps TBI policy and programs for 6.5 years prior to his transfer to the Navy Reserve in 2015. He has published over 100 peer-reviewed articles and book chapters and edited books on TBI and teleneurology. His clinical research is focused on treatments for phantom limb pain in amputees (his research team conducted the first randomized, controlled trial which demonstrated the utility of mirror therapy for treating phantom limb pain), for which he was awarded the 2014 United States Navy Hero of Military Medicine by the Center for Public-Private Partnerships at the Henry M. Jackson Foundation for the Advancement of Military Medicine, and the clinical effects of blast exposure and concussion. He is also a past chairman of both the Government Services Section and the Practice Committee Telemedicine Work Group of the American Academy of Neurology.

Jack Tsao

Professor at University of Tennessee, USA



Max Ortiz Catalan

Professor at Chalmers University of Technology, Gothenburg, Sweden

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Neurogenesis and treatment of PLP

Tuesday, Aug 31st
15:00-15:30

Abstract: Phantom Limb Pain (PLP) can be experienced as the result of different triggering mechanisms such as the excitation of neuromas in the peripheral nerves and maladaptive central changes, and these themselves are underlined by distinct acute and chronic processes. Progress on the surgical treatment of neuromas has made nociceptive induced PLP finally treatable, albeit more randomized clinical trials are required to identify the most effective surgical technique. Conversely, the mechanisms by which PLP persists in the absence of nociceptive input are yet to be understood. After successful results obtained using Phantom Motor Execution (PME), a plasticity-guided therapy, I examined the available PLP models that would explain such seemingly intuitive positive results. Considering previously unaccounted clinical observations, my conclusion was that the original therapeutic value attributed to anthropomorphic visual feedback, and the importance given to the sensorimotor cortex, were potentially misplaced. This led me to propose the Stochastic Entanglement hypothesis (2018) for the origin and treatment of PLP. In this lecture, I will discuss how this hypothesis provides a theoretical basis for PME, as well as the latest clinical evidence on PME as a treatment of PLP. I will describe the Stochastic Entanglement hypothesis relating the undesired coupling of pain and sensorimotor neural circuits, and how clinical observations support and challenge this and other contemporary ideas. Furthermore, I will present how the Stochastic Entanglement hypothesis gave rise to a new treatment method that has the potential to be more effective than PME, namely, Mindful SensoriMotor Therapy (MiSMT).

Biography:Prof. Max Ortiz Catalán, Ph.D., is the Founder and Director of the Center for Bionics and Pain Research (@CBPR.se) and the Professor of Bionics at Chalmers University of Technology, Sweden, where he also heads the Bionics Research Unit at the Department of Electrical Engineering. He has received several honors for his work, notably the "Swedish Embedded Award" by the Swedish Electronic Association in 2018, the "Brian & Joyce Blatchford Award" by ISPO in 2017, the "Delsys Prize" by Delsys in 2016, and the "European Youth Award" by the European Council in 2014. His research includes bioelectric signals acquisition electronics (analog and digital); bioelectric signal processing and machine learning algorithms for decoding motor volition and control; neuromuscular interfaces; neurostimulation for sensory feedback; bone-anchored prostheses and osseointegration; and virtual and augmented reality for neuromuscular rehabilitation and the treatment of phantom limb pain..

Phantom limb pain: a dynamic network perspective

Tuesday, Aug 31st
16:00-16:30

Abstract: Functional and structural plasticity in neural circuits has been associated with phantom limb pain. Such plastic changes involve both injury- and use-related alterations including the acquisition of compensatory motor skills and coping with a chronic pain condition. We address how functional changes interrelate with pain symptoms, not only locally within the primary somatosensory and motor cortex but at a network-level. We show the differential contribution of perceptual factors such as embodiment or agency, behavioural factors such as use of a prosthesis or use of the intact limb, prior pain experiences, non-painful phantom sensations including telescoping and referred sensations as well as psychological factors such as anxiety and depression to sensorimotor changes and pain. Peripheral factors can also modulate these central changes. We suggest that both central and peripheral factors interact in a dynamic manner and modulate the phantom pain experience. Ongoing longitudinal studies as well as studies employing evoked phantom pain and virtual reality paradigms seek to differentiate antecedents and consequences of pain and the role of brain regions involved in sensory and affective mechanisms.

Biography: Prof. Herta Flor is a neuroscientist and the scientific director of the Department of Neuropsychology at the University of Heidelberg, Central Institute for Mental Health, Mannheim, Germany. Prof. Flor is distinguished for seminal discoveries in the field of pain and phantom phenomena including the cortical processing of pain-related information in humans. Most of her work on the topic of pain focuses on the role of learning and memory processes and related plastic changes in the brain in the development and maintenance of chronic pain.

Herta Flor

Scientific director of the Department of Neuropsychology at the University of Heidelberg, Central Institute for Mental Health, Mannheim, Germany.

Tamar Makin

Professor at University College London, UK.
Institute of Cognitive Neuroscience
UCL, London, UK

Stability of sensory topographies in amputees

Tuesday, Aug 31st
16:30-17:00

Abstract: Despite its ubiquity, the neural origins of phantom limb pain is still a mystery for both patient, clinicians and scientists. For the past 25 years it has been predominantly held that phantom limb pain results from maladaptive brain plasticity, triggered by the loss of hand representation to the somatosensory cortex. Based on this theory, many contemporary treatments are specifically designed to 'normalise' the sensorimotor representation of the missing hand, thereby reversing maladaptive reorganisation (e.g. via mirror treatment or more recently virtual and augmented reality). In my talk I will provide multiple evidence using functional MRI in amputees to challenge the proposed link between brain plasticity and phantom pain, and instead demonstrate that brain representation of the missing hand persists decades after amputation. I will next explore the idea that brain plasticity can be harnessed to support adaptive

behaviour. I will argue that brain plasticity is best driven by meaningful inputs, and could be exploited for improving rehabilitation using substitution and augmentation devices. This alternative account advocates for radically different treatment opportunities to phantom limb pain which are to date rarely explored.

Biography: Tamar Makin is a Professor of Cognitive Neuroscience at the University College London, UK and leader of the Plasticity Lab www.plasticity-lab.com. Her main interest is in understanding how our body representation changes in the brain (brain plasticity). Her primary model for this work is studying individuals with a hand loss. Tamar graduated from the Brain and Behavioural Sciences programme at the Hebrew University of Jerusalem in 2009. She was then awarded several career development fellowships to establish her research programme on brain plasticity in amputees at the University of Oxford, first as Research Fellow and later as a Principle Investigator. In 2016 Tamar joined the faculty of UCL to continue this work. She is currently supported by the European Research Council (Starting Grant) and the Wellcome Trust (Senior Research Fellow).

Can the link between cortical/peripheral remapping and phantom limb properties help the development of efficient pain relief therapies and near-natural replacement of missing hands?

Tuesday, Aug 31st
17:00-17:30

Estelle Raffin

Scientist at Centre for Neuroprosthetics (CNP), Swiss Federal Institute of Technology (EPFL), Switzerland

Abstract: Limb amputation is characterized by complex and intermingled brain reorganization processes combining sensorimotor deprivation induced by the loss of the limb per se, and compensatory behaviors, such as the over-use of the intact or remaining limb. Associated with this cortical remodeling, approximatively 80% of amputees report the presence of a phantom limb (PL), which corresponds to the persistence of sensory and motor perceptions in the missing limb. It includes different sensory modalities i.e., interoceptive, exteroceptive or proprioceptive, with characteristics such as shortening or referred sensations. Proprioceptive sensations include a general perception of size, shape and position of the PL. PL pain is present in up to 80% of the patients. Often resistant to therapies, PL pain can severely affect quality of life. Another fascinating feature is the residual capacity to evoke movements with the PL, resembling in many dimensions to "real" movements.
In the first part of my talk, I will review somr evidence including our own work, documenting sensorimotor representation plasticity following arm amputation, and the few investigations that attempt to link PL perceptual features and motor behaviors to brain reorganization, forming the grounds to pain relief therapies. Finally, I will talk about the work performed in my current institute, mostly dealing with prosthetics and sensory feedback restitution, trying to improve the efficacy and "life-like" quality of hand prostheses, resulting in a keystone strategy for the near-natural replacement of missing hands and significant pain relief.

Biography: Dr Estelle Raffin seeks to understand the pathophysiological mechanisms underlying impaired sensorimotor functions and recovery of functions using the multimodal integration of neuroimaging techniques with non-invasive brain stimulation. In particular, she studied the neuropsychological status of phantom limb's movements and showed that higher levels of pain and poor voluntary control of the phantom limb were powerful drivers of representational plasticity within the primary motor cortex. Her ultimate goal is to develop novel personalized, neurotechnological interventions tailored to the individual in the aim of enhancing functional recovery in patients or to treat chronic pain after a limb amputation.

Todd Kuiken

Professor at Northwestern University, USA

Targeted Muscle Reinnervation for the treatment of Postamputation Pain

Wednesday, Sep 1st
16:00-16:30

Biography: Dr. Todd Kuiken is Director Emeritus of the Center for Bionic Medicine at the Shirley Ryan AbilityLab in Chicago. Dr. Kuiken is best known for his research in developing a surgical technique called Targeted Muscle Reinnervation (TMR), which is now a standard procedure and has been performed on more than 100 individuals in hospitals worldwide. TMR is used to improve the control of powered arm prostheses and reduce neuroma pain.

Use of Regenerative Peripheral Neve Interfaces (RPNI) for the Prevention and Treatment of Neuroma and Phantom Pain

Wednesday, Sep 1st
16:30-17:00

Paul S. Cederna

Chief, Section of Plastic Surgery
Robert Oneal Professor of Plastic Surgery
Professor of Department of Biomedical Engineering
University of Michigan

Chairman, American Board of

Abstract: It has been 40 years since Luke Skywalker (Star Wars) received a prosthetic hand controlled by his peripheral nerves. Unfortunately, this peripheral nerve interface has not been achieved in reality largely due to the difficulty recording multiple independent efferent motor control signals from a nerve inside a moving arm. The current best option is targeted muscle reinnervation (TMR), which moves divided nerves into alternate muscles that then function as signal amplifiers. This has worked very well and has provided a significant advance to our current approaches for prosthetic control. Our group has taken this strategy one step further by performing regenerative peripheral nerve interfaces (RPNI), which consist of a skeletal muscle graft placed on the end of a surgically subdivided nerve (nerve fascicle) to provide more control signals for dexterous hand motion including individual finger control. The functionally specific individual nerve fascicle is implanted into an autogenous free

skeletal muscle graft. The skeletal muscle graft revascularizes and is reinnervated by the implanted peripheral nerve fascicle to create a functional regenerative peripheral nerve interface (RPNI). The RPNI effectively prevents neuroma formation while at the same time amplifying the neural signals 100-1000 times making highly favorable signal to noise ratios for prosthetic limb control. Interestingly, while developing this novel peripheral nerve interface we have also learned that RPNIs are effective at treating symptomatic neuromas and preventing the formation of neuromas. In this presentation, I will share our last 10 years of research developing RPNIs and discuss our experiences with this approach for both treating symptomatic neuroma and preventing neuroma and phantom limb pain.

Plastic Surgery
Past-President, Plastic Surgery Foundation
Past-President, American Society for Peripheral Nerve
Past-Chairman, Plastic Surgery Research Council

Jaimie Shores

Associate Professor at Johns Hopkins University School of Medicine, USA

Sami Tuffaha

Department of Plastic and Reconstructive Surgery
Johns Hopkins University School of Medicine

Making Sense of the Contemporary Surgical Approaches for Neuroma Prevention and Treatment

Wednesday, Sep 1st
17:00-17:30

Abstract: A number of promising surgical approaches have emerged to treat and prevent painful neuromas, all of which make use of muscle as a target for regenerating axons. The underlying premise is that the axons regenerating from a severed nerve that would otherwise form a neuroma will instead reinnervate the muscle target instead. We will begin by critically evaluating the scientific basis for this hypothesized mechanism of effect as it pertains to the various types of neuropathic pain that manifest from nerve injury. Next, we will consider the fundamental differences between contemporary surgical approaches, including denervation, vascularity, and mode of neurotization of the muscle target. We will conclude by highlighting the utility of each of these approaches in various clinical circumstances that are frequently encountered.

Biography: Jaimie Shores is an Associate Professor of Plastic Surgery and Orthopedic Surgery at Johns Hopkins University School of Medicine. He is a board certified Plastic Surgeon (ABPS) with a certificate of added qualification (CAQ) in surgery of the hand. He specializes in peripheral nerve surgery, hand/wrist surgery, and microvascular reconstruction. He is the hand surgery fellowship program director and clinical director of the Hand and Upper Extremity Transplantation program at Johns Hopkins. He is a member of the Osseointegration Program and he has an interest in the surgical management of peripheral nerve based neuropathic pain in the upper and lower extremities and in amputees. He has ongoing laboratory and clinical research focused on nerve repair/regeneration and vascularized composite allotransplantation.

Dr. Sami Tuffaha is an Assistant Professor of Plastic Surgery, Neurosurgery, and Orthopedic Surgery at Johns Hopkins University School of Medicine and faculty hand surgeon at the Curtis National Hand Center. His clinical practice is largely focused on peripheral nerve surgery and functional reconstructive microsurgery. He leads a basic and translational research program aimed at developing novel therapeutics, devices and surgical approaches to improve functional recovery and prevent neuropathic pain following nerve injury, with ongoing clinical trials arising from work performed in the lab.

Nadia Bolognini

University of Milano-Bicocca & IRCCS Istituto Auxologico Italiano

Noninvasive brain stimulation therapies in phantom limb pain

Thursday, Sep 2nd
16:00-16:30

Abstract: Phantom Pain Limb remains a challenging condition to treat; although many different therapeutic approaches have been developed in the last decades, yet not one is widely accepted, consistently effective or clearly superior to others has been found. This likely because multiple mechanisms, which are still largely unknown, contribute to Phantom Pain Limb. An interesting therapeutic option that has been proposed in recent years is the non-invasive brain stimulation (i.e., transcranial magnetic and electric stimulations), which has been adopted for reducing or even for preventing Phantom Pain Limb. In this talk, I will offer an overview of the current state of art of this line of clinical research, discussing its rational, strength and limits and possible future developments

Biography: Dr. Nadia Bolognini is Associate Professor of Psychobiology and Physiological Psychology and Director of the Master Degree in Psychology at the University of Milano Bicocca (Italy) and Assistant Scientific Director of the Neuropsychology Lab of IRCCS Istituto Auxologico Italiano, a leading Italian institute devoted to both basic and translational research and clinical care and rehabilitation. She is also member of the Milan Center for Neuroscience (https://neuromi.it/). Her research activity focuses on the study of multisensory processing, body and space representations in healthy humans and in neurological diseases. The second main line of research is grounded on the use of non-invasive brain stimulation for tracking and modulating brain plasticity, including the development of transcranial magnetic and electric stimulations as tools for the treatment of Phantom Limb Pain. She has received several honors, among which the Early Career Award by the Italian Society of Psychophysiology & Cognitive Neuroscience (2014) and the Nottola-Mario Luzi Award (2014) under the High Patronage of the President of the Italian Republic for her research achievements on the therapeutic use of the neurostimulation for Phantom Limb Pain.

Robin Bekrater-Bodmann

Department of Psychosomatic Medicine and Psychotherapy, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany

Prosthesis embodiment and phantom limb pain

Thursday, Sep 2nd
16:30-17:00

Abstract:Phantom limb pain (PLP) accounts for a significant reduction in quality of life and is difficult to treat. Prosthesis use has been shown to negatively covary with PLP. There is reason to assume that prosthesis embodiment, that is, the cognitive integration of the prosthetic device into an amputee's body representation, might enhance the positive effects on PLP that are associated with prosthesis use. In the present talk, the recent empirical findings related to prosthesis embodiment are reviewed. Based on research on body perception in non-amputated and amputated individuals, the potential impact of prosthesis embodiment on pain perception in general and PLP in particular is discussed, before the relationship between prosthesis embodiment and PLP is empirically evaluated, using the data of large amputee cohorts. Finally, the clinical implications of the findings are debated.

Biography: Dr. Bekrater-Bodmann received the diploma in Psychology from the Technical University of Braunschweig in 2007. Since 2008 he has been working as a research fellow at the Department of Cognitive and Clinical Neuroscience, Central Institute for Mental Health (CIMH), Mannheim, where he received his doctorate in 2012 from the University of Heidelberg. In 2015, he received the Award for Pain Research from the German Association for the Study of Pain for his participation in research on the neural mechanisms underlying successful mirror therapy for phantom limb pain. In 2016, he became head of the CIMH's research group 'Body plasticity and memory processes'. After a research visit at the Department of Psychology, Royal Holloway, University of London, in 2017, he returned to the CIMH, where he intensified his research on the interaction of body and pain perception. His recent work focused on phantom limb pain and its modulation by the induction of body-related illusions, such as mirror or rubber limb illusion, and he uses neuroimaging and psychophysiological techniques to identify the underlying perceptual mechanisms. In 2018, he was awarded a grant of the German Research Foundation in order to conduct the project 'Phantom body: Neuropsychological mechanisms underlying the perceived unity between the body and the self' in which he currently investigates the interaction between embodied prostheses and clinical markers in lower limb amputees. In the same year, he also received the European Pain Federation – Grünenthal Research Grant (E-G-G 2018) in order to investigate the beneficial effects of embodied prostheses on phantom limb pain.

The role of spike synchrony in tactile perception revealed by kilohertz-frequency spinal cord stimulation

Thursday, Sep 2nd
17:00-17:30

Abstract:Spinal cord stimulation (SCS) is an effective treatment for chronic pain, including phantom limb pain. Conventional SCS (40-60 Hz) reduces pain by engaging inhibitory mechanisms in the spinal dorsal horn via activation of A-beta axons in the dorsal columns. But activating those axons also produces a buzzing sensation, or paresthesia, that can limit the intensity ("dose") of SCS and its analgesic efficacy. Recently developed kilohertz-frequency SCS (kfSCS) produces paresthesia-free analgesia. The absence of paresthesia has been inferred to mean that A-beta axons are not activated, raising questions about how analgesia is produced. Based on electrophysiological studies in rats, we found that A-beta axons are activated by kfSCS but that action potentials (spikes) are not synchronized across axons, unlike conventional SCS, which evokes synchronous spiking. Our experimental data and computational modeling demonstrate that when electrical pulses are delivered at intervals shorter than an axon's refractory period, spikes occur intermittently, in response to only a subset of stimulus pulses; because different axons respond to different pulses, spikes become desynchronized. We speculate that asynchronous spiking in A-beta axons is sufficient to activate inhibitory neurons mediating analgesia whereas synchronous spiking is necessary to activate projection neurons mediating paresthesia. Consistent with this model, cortical recordings show that brain oscillations are altered by conventional SCS but not by kfSCS, though somatosensory evoked potentials are equally attenuated by both forms of SCS. These results have important implications for understanding the neural basis for paresthesia but also have practical implications for choosing SCS parameters to optimize clinical outcomes.

Biography: Dr. Prescott studies how somatosensory information is normally encoded and how disruption of that coding leads to neuropathic pain. His lab combines computational simulations with experimental techniques including in vitro and in vivo electrophysiology, calcium imaging, and optogenetics. Lines of research include how biophysical properties impact neuron coding properties and, in turn, how neuron properties impact network-level phenomena like synchrony. His lab applies information about these fundamental issues to uncover how different forms of spinal cord stimulation (SCS) act to reduce pain, and why some forms of SCS cause paresthesia whereas others do not.

Steven Prescott

Neurosciences & Mental Health, The Hospital for Sick Children
Physiology & Biomedical Engineering, University of Toronto

Workshop proposals

Body illusions for phantom pain relief

Tuesday, Aug 31st
11:15-12:15

Marta Matamala-Gomez[1], Tony Donegan[2], Justyna Swidrak[2,3,4]

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[2] August Pi & Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain
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Conflict of interest: nothing to declare

Description

Body Illusions (BIs) refer to altered perceptual states where the perception of the self-body significantly deviates from the physical body's configuration, for example in aspects like perceived size, shape, posture, location, or sense of ownership [1]. BIs can be triggered through simple experimental manipulations (e.g., through congruent visuo-tactile or visuo-motor sensory stimulation), supporting the overall view that self-body perception is built dynamically on the base of multisensory integration processes and of the prior knowledge and experience we have about our human body [1]. Through BIs, subjects can embody fake body parts or whole fake bodies, which are perceived as belonging to or substituting their physical body [2]. One of the most well-known example of BIs is the rubber hand illusion (RHI) study, in which synchronous visuotactile stimulation of both a rubber hand located within the visual field of the participant, and the participant's real hand, located outside the visual field of the participant, confers an illusion of ownership over the rubber hand [3]. Since this study, many researchers have investigated how to manipulate body perception through the use of fake bodies such as mannequins [4], mirrors [5], virtual reality [6], and 360º video [7]. A number of subsequent studies have focused on chronic pain, with the focus being on the analgesic effects of cross-modal perception (e.g., pain and vision) (for reviews see [8]-[11]). Alterations in body representation have been reported in patients with chronic pain [12]. Some consequences of experiencing body representation alterations include changes in the perception of the size of the painful limb in patients with complex regional pain syndrome [13], or phantom limb sensations in amputees (the persistent feeling that the amputated limb is still there) [14]. In this regard, body ownership illusions have been proposed as an effective tool to modulate the distorted internal body representation of the painful limb as a consequence of a maladaptive cortical plasticity after the injury, such as the telescopic effect in amputees [15], or for modulating the preserved representation of the amputated limb in the area of the brain, which is considered another key factor involved in chronic phantom pain [16]. In detail, it has been shown that through changing the size [17], [18][19], color [20][21], the morphological characteristics of the painful body part [22], or through the movement simulation [5], it is possible to induce pain relief in healthy and clinical populations, and this could also be relevant for phantom pain relief.

Aim of the workshop: The main aim of the present workshop is to provide knowledge about the concept and different types of BIs and how these can be applied for phantom pain relief in amputees.

Topics

- Theoretical background about body illusions:
  - The concept of body illusions.
  - Types of body illusions.
  - Methodology to induce body illusions: fake limb, mirrors, virtual reality, and 360º video.
  - The body in the brain and the concept of body matrix.
  - Use of body illusions for phantom pain relief
- Practicum: Test the induction of body illusions using different set-ups such as a fake limbs, mirrors, virtual reality systems, or 360º video.
- Brainstorming by groups on the topic of how BIs can be integrated with other experimental or clinical techniques (e.g., robotics, brain interfaces, non-invasive brain stimulation, etc.) for phantom pain relief.

References

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Further Reading

Theoretical framework

Moseley, G. L., Gallace, A., & Spence, C. (2012). Bodily illusions in health and disease: physiological and clinical perspectives and the concept of a cortical 'body matrix'. Neuroscience & Biobehavioral Reviews, 36(1), 34-46.

This paper discusses studies in both healthy volunteers and clinical populations that highlight the robust relationship that exists between a person's sense of ownership over a body part, cortical processing of tactile input from that body part, and its physiological regulation. The article proposes that a network of multisensory and homeostatic brain areas may be responsible for maintaining a 'body-matrix'. That is, a dynamic neural representation that not only extends beyond the body surface to integrate both somatotopic and peripersonal sensory data, but also integrates body-centred spatial sensory data.

Ramachandran, Vilayanur S., and Eric L. Altschuler. *"The use of visual feedback, in particular mirror visual feedback, in restoring brain function."* **Brain 132.7 (2009): 1693-1710.**

This article reviews the potential use of visual feedback, focusing on mirror visual feedback, introduced over 15 years ago, for the treatment of many chronic neurological disorders that have long been regarded as intractable such as phantom pain, hemiparesis from stroke and complex regional pain syndrome.

Matamala-Gomez, M., Donegan, T., Bottiroli, S., Sandrini, G., Sanchez-Vives, M. V., & Tassorelli, C. (2019). Immersive virtual reality and virtual embodiment for pain relief. Frontiers in human neuroscience, 13, 279.

This is a review of experimental and clinical studies that have explored the manipulation of an embodied virtual body in immersive virtual reality for both experimental and clinical pain relief. It discusses the current state of the art, as well as the challenges faced by, and ideas for, future research as well as exploring the potentialities of using an embodied virtual body in immersive virtual reality in the field of neurorehabilitation, specifically in the field of pain.

Practical aspects

Donegan, T., Ryan, B. E., Swidrak, J., & Sanchez-Vives, M. V. (2020). Immersive virtual reality for clinical pain: considerations for effective therapy. Frontiers in Virtual Reality, 1, 9.

Immersive virtual reality is transforming medical and psychological research and treatment, including the treatment of clinical pain. This short perspective paper presents some of the methodological difficulties that are rarely discussed in the literature of pain research when using virtual reality. These often-unmentioned problems can confound research investigations or interfere with the therapeutic efficacy in clinical trials.

Clinical Evidence

Ortiz-Catalan, M., Guðmundsdóttir, R. A., Kristoffersen, M. B., Zepeda-Echavarria, A., Caine-Winterberger, K., Kulbacka-Ortiz, K., Widehammar, C., Eriksson, K., Stockselius, A., Ragnö, C., Pihlar, Z., Burger, H., & Hermansson, L. (2016). Phantom motor execution facilitated by machine learning and augmented reality as treatment for phantom limb pain: a single group, clinical trial in patients with chronic intractable phantom limb pain. The Lancet, 388(10062), 2885-2894.

In this study the authors assessed a treatment where the virtual limb responded directly to the myoelectric activity from the stump. A patient with long-term PLP (48 years) performed a series of movements (eight arm movements) with his phantom in AR during 10 min, with the instruction of doing it "as if he still had the missing limb", while EMG information was recorded from the stump. The patient reported gradual reductions on PLP and pain-free periods during the last weeks.

Ortiz-Catalan, M., Sander, N., Kristoffersen, M. B., Håkansson, B., & Brånemark, R. (2014). Treatment of phantom limb pain (PLP) based on augmented reality and gaming controlled by myoelectric pattern recognition: a case study of a chronic PLP patient. Frontiers in Neuroscience, 8.

The study was repeated with fourteen PLP patients and the authors found statistical and clinical improvements after twelve sessions. Phantom limb pain decreased 47% for weighted pain distribution, 32% for the numeric rating scale, and 51% for the pain rating index, comparing results from the first with the last session.

Boesch, E., Bellan, V., Moseley, G. & Stanton, T. (2016). The effect of bodily illusions on clinical pain: a systematic review and meta-analysis, Pain, 157, 3, 516-529.

A systematic review and meta-analysis exploring the evidence for bodily illusions modulating pain. Twenty studies met the inclusion criteria. Risk of bias was high due to selection bias and lack of blinding. There is limited evidence to suggest that bodily illusions can alter pain, but some illusions, namely mirror therapy, bodily resizing, and use of functional prostheses show therapeutic promise.

Herrador Colmenero, L., Perez Marmol, J. M., Martí-García, C., Querol Zaldivar, M. D. L. Á., Tapia Haro, R. M., Castro Sánchez, A. M., & Aguilar-Ferrándiz, M. E. (2018). Effectiveness of mirror therapy, motor imagery, and virtual feedback on phantom limb pain following amputation: A systematic review. Prosthetics and orthotics international, 42(3), 288-298.

Systematic review of the effectiveness of mirror therapy, motor imagery, and virtual feedback for treating phantom limb pain in amputee patients. Twelve studies met the inclusion criteria, no high-quality studies were found, 3 rated as moderate quality and 9 rated as low quality. All studies showed a significant reduction in pain, but there was heterogeneity among subjects and methodologies.

Dunn J, Yeo E, Moghaddampour P, et al. (2017) Virtual and augmented reality in the treatment of phantom limb pain: a literature review. NeuroRehabilitation 40: 595-601.

The only systematic review specifically exploring the use of AR/VR in the treatment of PLP. At the time, no RCTs were identified, and just 6 small prospective case series and 2 qualitative studies. All showed positive results, with minimal adverse effects. However, there was considerable heterogeneous among the interventions and patients (type of injury, time from injury, male vs female). None of the studies were controlled and there was no direct comparison with mirror therapy.

Rothgangel, A., Braun, S., Winkens, B., Beurskens, A., & Smeets, R. (2018). Traditional and aug-

mented reality mirror therapy for patients with chronic phantom limb pain (PACT study): results of a three-group, multicentre single-blind randomized controlled trial. Clinical Rehabilitation, 32(12): 1591-1608.
To date, this is the only high quality randomized controlled trial comparing mirror therapy and augmented reality. 75 unilateral lower limb amputees were randomised to 3 interventions, augmented reality mirror therapy, traditional mirror therapy and sensorimotor exercises for the intact limb. No differences in pain levels between 3 groups at 4 and 10 weeks. At 6 months, traditional MT group PLP duration was significantly improved, but not PLP intensity or frequency. The results do not favour appear to favour MT or augmented reality as a viable treatment for PLP. But subgroup analysis revealed significant effects in females, patients with telescoping and patients with a motor component to their PLP.

Graded Motor Imagery (GMI) and Explain Pain - A physiotherapist's experience of using this concept for treating Phantom Limb Pain over the last 10 years

Wednesday, Sep 1st
9:00-10:30

Kate Lancaster[1]

[1] St Georges NHS Foundation Trust, Queen Mary's Hospital, Roehampton, London, UK

Conflict of interest: Nothing to declare.

Description

I am a specialist physiotherapist in prosthetic rehabilitation and have worked with amputee patients since 2009. I initially felt bewildered in how to manage and treat the majority of my patients who were suffering with phantom limb pain (PLP) as my understanding of complex pain was limited. So when I attended the 2009 British Association of Chartered Physiotherapists in Amputee Rehabilitation (BACPAR) conference and heard for the first time about Explain Pain from the Neuro Orthopaedic Institute (NOI), I felt enlightened and inspired to learn and do more. I then attended the 2 day courses on Explain Pain (2010) and GMI (2011) and again in 2015 to refresh and update. I have been using their treatment concepts to treat and manage PLP since 2010. I have presented at BACPAR study day on Pain Management for Amputees, presented a case study poster at the BACPAR conference 2014 and presented this case study at ISPO international conference in Lyon 2015. I also teach about PLP treatment at our annual 4 day course at Queen Mary's Hospital as well as regularly to students, rotational therapists and registrars.
My treatment and management of amputee patients with PLP has evolved over the years with patient experience and feedback from the patients themselves. PLP remains difficult to treat as each patient is different and so needs an individual approach. There is no one technique.
This workshop will explore the way that we manage and treat PLP at Queen Mary's Hospital, for both primary and established patients using the concepts from NOI – Explain Pain and GMI. It will look into the tools that are used, how they can be adapted for the individual and the variable outcomes that have been achieved and what has influenced these. It will also look at the additional influences that have helped evolve and continue to evolve the treatment of PLP for our patients.

References

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3. Butler D, Moseley GL. The Explain Pain Handbook: Protectometer. Adelaide: Noigroup Publications, 2015
4. Butler D, Moseley GL. Explain Pain Supercharged. Adelaide: Noigroup Publications, 2017

Further reading

Butler D, Moseley GL. Explain Pain Second Edition. Adelaide: Noigroup Publications, 2013
Explain Pain by David Butler and Dr. Lorimer Moseley is an evidence based book designed for therapists, patients and students. It answers the most common questions asked by pain sufferers: 'why do I hurt?' and 'what can I do for my pain?' By understanding why we experience pain and that the amount of pain we experience does not necessarily equate to the amount of damage experienced, we then lose our fear of pain and it has less of a "hold" over us. This then can lead to a pain decrease.

Moseley GL, Butler D, Beames TB, Giles TJ. The Graded Motor Imagery Handbook. Adelaide: Noigroup Publications, 2012
The Graded Motor Imagery Handbook reviews the main principles of pain and provides a guide on how to use GMI as a treatment tool. The book explains each step in detail and helps you to problem solve when treatment does not progress in a smooth linear pattern, exploring options on how to bring the patient back onto the road to recovery. It also provides details on the different tools that can be used and how to use them.

Butler D, Moseley GL. The Explain Pain Handbook: Protectometer. Adelaide: Noigroup Publications, 2015
The Explain Pain Handbook is a book that has been designed specifically with the patient in mind. It explains why we experience pain, why it can become chronic / sensitised and explores the external influences that can impact on our pain experience. The Protectometer is a tool that can be used to explore these external influences further with the patient to then help the patient change negative feelings / experiences into positive ones.

Butler D, Moseley GL. Explain Pain Supercharged. Adelaide: Noigroup Publications, 2017
Explain Pain Supercharged is a more detailed and scientific explanation of pain than the Explain Pain book. It is written principally for clinicians to further improve their knowledge of pain so that they can then help with patients' understanding of pain. To be able to effectively explain pain to patients the clinician needs to have an in depth knowledge of pain and this book provides this with scientific evidence.

Moseley, L. Graded Motor Imagery for Pathological Pain. A randomised controlled trial. Neurology 2006; 67: 2129-2134
51 patients with PLP or CRPS1 were randomly allocated to a GMI treatment group or routine physiotherapy. The paper concludes that GMI reduced pain and disability in these patients, but the mechanisms of the effect was not fully understood.

Limakatso K, Madden V, Manie S, Parker R. The effectiveness in graded motor imagery for reducing phantom limb pain in amputees: a randomised controlled trial. Physiotherapy 109 (2020) 65-74
This is a recent RCT whose protocol is based on Moseley's RCT above, investigating whether GMI treatment is more effective than routine physiotherapy treatment. 21 adults with unilateral UL or LL amputation with self-reported PLP persisting beyond 3 months were randomly assigned to GMI treating group or routine physiotherapy. The participants in the experimental group had significantly greater improvements in pain than the control group at 6 weeks and 6 months post intervention.

Raffin E, Richard N, Giraux P, Reilly K. Primary motor cortex changes after amputation correlate with phantom limb pain and the ability to move the phantom limb. Neuroimage 2016: 130: 134-144
This paper explores the correlation between the reorganisation of primary sensory and motor cortices with PLP. Findings support that there is a positive correlation between cortical reorganisation and chronic PLP and that their finding of "substantial activity in the deprived motor cortex during intact hand movements, which is strongly correlated with the ability to move the phantom, suggests that the synergistic movement of the intact phantom limbs during mirror or imagery therapy might help to shape and reactivate the deprived cortex. This would in turn facilitate voluntary phantom hand movements, protect against reorganisation of the motor cortex contralateral to the amputation and thereby reduce PLP."

Foell J, Bekrater-Bodmann R, Diers M, Flor H. Mirror therapy for phantom limb pain: Brain changes and the role of body representation. European Journal of Pain. 18 (2014) 729-739
This study found that mirror therapy led to a 27% reduction in PLP and that the treatment effects were linked to cortical reorganisation: as PLP reduced, the representation in the somatosensory cortices of both hemispheres became more similar. They also found that the patient's ability to relate to the mirrored limb as their own at the beginning of treatment was predictive of pain relief.

Fuchs X, Flor H, Bekrater-Bodmann R. Psychological factors associated with phantom limb pain: A review of recent findings. Pain Research and Management. 2018 Article ID 5080123, 12 pages. Doi:10.1155/2018/5080123 https://pubmed.ncbi.nlm.nih.gov/30057653/ last accessed on 19/07/2021
This review found that there are bidirectional relationships between stress and PLP, that catastrophising aggravates PLP and that body representation and body perception may be a promising target for treatment of PLP.

Phantom Motor Execution as treatment for Phantom Limb Pain

Wednesday, Sep 1st
11:00-12:30

Corry K van der Sluis[1], Liselotte Hermansson[2,3], Cathrine Widehammar[2,3], Maria Munoz-Novoa[4, 5], Eva Lendaro[4,6], and Max Ortiz-Catalan[4,6,7]

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[2] Department of Prosthetics and Orthotics, Faculty of Medicine and Health, Örebro University, Örebro, Sweden
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[4] Center for Bionics and Pain Research, Mölndal, Sweden.
[5] Center for Advance Reconstruction of Extremities, Sahlgrenska University Hospital, Mölndal, Sweden.
[6]. Department of Electrical Engineering, Chalmers University of Technology, Gothenburg, Sweden.
[7]. Department of Orthopaedics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.

Corresponding author: Max Ortiz-Catalan, maxo@chalmers.se

Topic: Treatment of Phantom Limb Pain

Disclosures
Until 2020, MOC provided consultancy services on PLP for a company that has commercialized a device based on his research.

Description
One of the most recently developed treatments for phantom limb pain (PLP) uses motor training and virtual environments in which reality is increased or adjusted. The Phantom Motor Execution (PME) treatment, developed in Sweden by Max Ortiz Catalan and his team, uses phantom exercises in augmented reality to treat PLP (1,2). The patient sees himself through a webcam on a computer screen, where a virtual arm is projected over his stump. The patient has electrodes on his stump, with which he can control the virtual limb using myoelectric pattern recognition. In this way, the patient learns to move his phantom limb and this reduces phantom pain. Recent research into the effectiveness of the PME treatment showed that six months after finishing the treatment participants still had significantly less PLP (2). The effectiveness of the treatment is currently investigated in an international, randomized controlled trial (3). Since this treatment might be an interesting addition to current treatment methods for many rehabilitation teams, we propose a demonstration of the PME treatment. The first part of the workshop will cover theoretical aspects and clinical evidence in support of PME for PLP (4). This will provide a deeper understanding and foundation for the second part of the workshop, where two experienced therapists will demonstrate PME, sharing with the audience their practical insights. Two patients, one with upper limb and one with lower limb amputation, will participate to the demonstration.

References
1: Ortiz-Catalan M, Sander N, Kristoffersen MB, Håkansson B, Brånemark R. Treatment of phantom limb pain (PLP) based on augmented reality and gaming controlled by myoelectric pattern recognition: a case study of a chronic PLP patient. Front Neurosci. 2014 Feb 25;8:24.

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4: Ortiz-Catalan M. The Stochastic Entanglement and Phantom Motor Execution Hypotheses: A Theoretical Framework for the Origin and Treatment of Phantom Limb Pain. Front Neurol. 2018 Sep 6;9:748. doi: 10.3389/fneur.2018.00748. PMID:
30237784; PMCID: PMC6135916.

Further Reading
Theoretical framework

Ortiz-Catalan M. The Stochastic Entanglement and Phantom Motor Execution Hypotheses: A Theoretical Framework for the Origin and Treatment of Phantom Limb Pain. Front Neurol 2018; 9: 1-16.

This paper introduces the Stochastic Entanglement hypothesis regarding the origin of PLP. The current hypothesis for the working mechanism of Phantom Motor Execution (PME) is related to the purposeful engagement of motor neural circuitry affected by the amputation, which in turn results in dissociation from pain processing. Whereas this therapy is focus on motor control, somatosensory circuitry is also engaged while increasing motor dexterity, albeit partially. The initial pathologic association between the sensorimotor circuitry and pain processing is believed to be caused by random and coincidental firing between these networks. This was made possible due to the major perturbation to their normal equilibrium state, which an amputation represents.

Di Pino G, Piombino V, Caracassitti M, Ortiz-Catalan M. Neurophysiological models of phantom limb pain: what can be learned [Internet]. Minerva Anestesiol 2021; 87. Available from:https://www.minervamedica.it/index2.php?show=R02Y2021N04A0481

This paper gives an overview of the current neurophysiological models of PLP, and it's a useful reference to understand the contrast between the Stochastic Entanglement and previous hypotheses on the origin of PLP.

Clinical Evidence

Ortiz-Catalan M, Sander N, Kristoffersen MB, Håkansson B, Brånemark R. Treatment of phantom limb pain (PLP) based on augmented reality and gaming controlled by myoelectric pattern recognition: a case study of a chronic PLP patient. Front Neurosci 2014; 8: 1-22.

This paper describes the first clinical implementation of PME promoted by Myoelectric Pattern Recognition (PMR) and Virtual and Augmented Reality (VR/AR) in Serious Gaming (SG) in a patient with chronic intractable PLP. The study was carried out in 2014 showing encouraging results.

Ortiz-Catalan M, Guðmundsdóttir RA, Kristoffersen MB, Zepeda-Echavarria A, Caine-Winterberger K, Kulbacka-Ortiz K, et al. Phantom motor execution facilitated by machine learning and augmented reality as treatment for phantom limb pain: a single group, clinical trial in patients with

chronic intractable phantom limb pain. Lancet 2016; 388: 2885-94.
This paper presents the results of the first one-arm clinical trial conducted on upper limbs in four independent hospitals. The study showed a reduction of pain of approximately 50% in patients who had suffered PLP for approximately 10 years and who have tried several treatments prior PME. The improvement was observed at the last follow-up six months after.

Lendaro E, Mastinu E, Håkansson B, Ortiz-Catalan M. Real-time classification of non-weight bearing lower-limb movements using EMG to facilitate phantom motor execution: Engineering and case study application on phantom limb pain. Front Neurol 2017; 8
This paper evaluated the application of the treatment in lower limb amputation by demonstration its use on patients with chronic intractable PLP.
Lendaro E, Middleton A, Brown S, Ortiz-Catalan M. Out of the clinic, into the home: The in-home use of phantom motor execution aided by machine learning and augmented reality for the treatment of phantom limb pain. J Pain Res 2020; 13: 195-209.
This paper presents a case series in upper and lower limb amputations, showing the feasibility of this therapy to be conducted unsupervised at home.
Lendaro E, Hermansson L, Burger H, Van der Sluis CK, McGuire BE, Pilch M, et al. Phantom motor execution as a treatment for phantom limb pain: protocol of an international, double-blind, randomised controlled clinical trial. BMJ Open 2018; 8: e021039.
The paper presents the protocol of an international, double-blind, randomized controlled trial (10 hospitals in 8 countries) which is currently being conducted and will be completed by the end of 2021.

Peripheral Nerve Stimulation

Thursday, Sep 2nd
9:30-11:00

Denise Lester MD[1], Douglas Murphy MD[1], Brooke Trainer MD[1], Rob Trainer MD[1]

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Topic: Peripheral Nerve Stimulation For Phantom Limb Pain

Disclosures

- Authors serve as clinical investigators on studies partly sponsored by SPR Therapeutics and have received research related funding by the Hunter Holmes McGuire Research Pilot Grant.
- DL has received a one-time educational stipend for teaching an SPR PNS Course

Description

Up to 85% of individuals undergoing amputation will experience phantom limb pain (PLP) and in most of these cases PLP will either resolve spontaneously or subside significantly [1]. However, in a proportion of this population PLP will persist and cause a troublesome interference in the lives of these individuals. Quality of life will suffer. Consequently, there are many treatments but most of these are not evidence based. Peripheral nerve stimulation has recently offered a means to control pain [2]. There are two basic systems: one that is implanted permanently and one that is temporarily implanted [3]. Temporary implantation would appear more advantageous than permanent implantation in terms of convenience and the risk of infection and other complications. However, does pain relief continue without the device in place? Recently published studies suggest that pain relief will continue after the removal of the device.
The authors have participated in a study that examines the effect of the implantation of the Sprint peripheral nerve stimulation device by SPR therapeutics in the immediate postoperative period following implantation. Results support the conclusion that the device provides pain relief both during the period of implantation and during the period after the device is removed.
The authors propose a workshop that provides attendees with information concerning the research that has been on this method of PLP management as well as a practical experience on implantation. The authors will discuss the hardware, the choice of nerve placement for various levels of amputation, the use of ultrasound in device implantation, post implantation management and the complication risks and their management. Attendees will have a sound basis after this workshop on which to further pursue training so that they can incorporate this system into their practices.

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[2] CA Gilmore, BM Ilfeld , JM Rosenow, S Li, MJ Desai, CW Hunter, RL Rauk, A Nader, J Mak, SP Cohen, ND Crosby, JW Boggs. "Percutaneous 60-day peripheral nerve stimulation implant provides sustained relief of chronic pain following amputation: 12-month follow-up of a randomized, double-blind, pla-

cebo-controlled trial." Reg Anesth Pain Med. 2019 Nov 17. pii: rapm-2019-100937. doi: 10.1136/rapm-2019-100937. [Epub ahead of print]

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Further reading

Theoretical framework

Deer TR, Eldabe S, Falowski SM, Huntoon MA, Staats PS, Cassar IR, Crosby ND, Boggs JW. Peripherally-Induced Reconditioning of the CNS: Proposed Mechanisms for Sustained Relief Following 60-Day Percutaneous PNS Treatment, Journal of Pain Research 2021

Paper on the proposed mechanism of action of PNS. The authors show pathways to peripherally induced reconditioning of the CNS.

Melzack R, Wall PD. Pain mechanisms: a new theory. Science. 1965 Nov 19;150(3699):971-9. doi: 10.1126/science.150.3699.971. PMID: 5320816.

Paper on the proposed mechanism of action of PNS. The landmark paper published in 1965 proposed that non-painful sensory stimuli carried by A-beta large "touch" fibers in the periphery disrupts transmission from small "pain" fibers in the CNS. Though subsequent models and experiments have disputed claims made in this paper, the general ideas put forth in the paper and the experiments they prompted in both animals and patients have transformed our understanding of pain mechanisms.

Nikolajsen L, Jensen TS. Phantom limb pain. Br J Anaesth. 2001 Jul;87(1):107-16. doi: 10.1093/bja/87.1.107. PMID: 11460799.

Paper on the proposed mechanism of action of PNS. The authors discuss the activa-ion of NMDA receptors.

Practical aspects

Visser EJ. Chronic post-surgical pain: Epidemiology and clinical implications for acute pain management, Acute Pain. 2006; 8: 73-81. doi: 10.1016/j.acpain.2006.05.002

Paper indicating the suggested populations for PNS. Certain surgical populations have increased incidence of acute and chronic pain.

Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: Results from a national survey suggest postoperative pain continues to be undermanaged. Anesthesia & Analgesia 2003; 97:534-540.

Peripheral Nerve Catheters or Stimulation? Discussion on Peripheral Nerve Stimulation vs Peripheral Nerve Local Anesthetic Catheters

Clinical evidence

Deer T, Pope J, Benyamin R, Vallejo R, Friedman A, Caraway D, Staats P, Grigsby E, Porter McRoberts W, McJunkin T, Shubin R, Vahedifar P, Tavanaiepour D, Levy R, Kapural L, Mekhail N. Prospective, Multicenter, Randomized, Double-Blinded, Partial Crossover Study to Assess the Safety and Efficacy of the Novel Neuromodulation System in the Treatment of Patients With Chronic Pain of Peripheral Nerve Origin. Neuromodulation. 2016 Jan;19(1):91-100. doi: 10.1111/ner.12381. PMID: 26799373

transcranial Direct Current Stimulation (tDCS): a practical introduction for clinical research

Thursday, Sep 2nd
11:30-12:30

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Conflict of interest: nothing to declare.

Topic: Non-Invasive Brain Stimulation, transcranial Direct Current Stimulation

Description

Non-Invasive Brain Stimulation (NIBS) techniques such as transcranial Direct Current Stimulation (tDCS) have gained popularity in the last decades thanks to their ease of use and promising effects in promoting neuroplasticity [1]. tDCS applications range from basic to clinical research, with such technique being employed in a variety of neurological and neuro-psychiatric conditions [2]. Interestingly, tDCS proved to be effective in modulating various phantom limb phenomena [3], [4].

In this workshop, I will first cover basic technical aspects of tDCS such as current intensity and polarity, stimulation duration, as well as electrodes dimension and montage, considering also its main mechanisms of action. An overview of tDCS applicability in phantom limb pain will be provided. Finally, attendants will be involved in a practical demonstration of a tDCS protocol set-up and administration.

References

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Further reading

Theoretical framework

Nitsche, M. A., & Paulus, W. (2000). Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. The Journal of Physiology, 527(3), 633-639.

oSeminal study demonstrating the use of tDCS to modulate plasticity of the healthy brain, specifically the motor cortex. The study highlights that 1) the stimulation induces after effects lasting several minutes after it ends; 2) these effects depend on stimulation parameters such intensity, duration, and electrodes position; 3) the polarity of stimulation (i.e., the anode vs the cathode on the target area) induces opposite effects on the motor cortex by increasing (anodal stimulation) of decreasing (cathodal stimulation) cortical excitability.

Nitsche, M. A., Liebetanz, D., Schlitterlau, A., Henschke, U., Fricke, K., Frommann, K., ... & Tergau, F. (2004). GABAergic modulation of DC stimulation-induced motor cortex excitability shifts in humans. European Journal of Neuroscience, 19(10), 2720-2726.
The authors show the involvement of GABAergic activity and how it selectively modulates the excitability induced by anodal tDCS by affecting duration and intensity of the after effects.

Monte-Silva, K., Kuo, M. F., Hessenthaler, S., Fresnoza, S., Liebetanz, D., Paulus, W., & Nitsche, M. A. (2013). Induction of late LTP-like plasticity in the human motor cortex by repeated non-invasive brain stimulation. Brain Stimulation, 6(3), 424-432.
The article explores the long-lasting effects of repeated sessions of tDCS and the biological underpinnings of LTP-related mechanisms, mediated by the activity of calcium channels and glutamatergic activity of NMDA receptors.

Lauro, L. J. R., Rosanova, M., Mattavelli, G., Convento, S., Pisoni, A., Opitz, A., ... & Vallar, G. (2014). TDCS increases cortical excitability: direct evidence from TMS-EEG. Cortex, 58, 99-111.
The authors investigate the effect of anodal tDCS by means on of a combined Transcranial Magnetic Stimulation (TMS) and electroencephalography (EEG) approach. They show that tDCS-induced excitability spreads over remote, non-stimulated areas (even the contralateral hemisphere), both during and after the stimulation. The integration of different techniques can provide important information about the effects of brain stimulation.

Kuo, H. I., Bikson, M., Datta, A., Minhas, P., Paulus, W., Kuo, M. F., & Nitsche, M. A. (2013). Comparing cortical plasticity induced by conventional and high-definition 4× 1 ring tDCS: a neurophysiological study. Brain Stimulation, 6(4), 644-648.
tDCS can be applied with increased focality by means of specific electrodes and configurations. In this experimental study on healthy subjects, the authors show that, compared to conventional tDCS (e.g., delivered through 7x5 cm2 or 10x10 cm2 electrodes), 10 minutes of HD-tDCS over the motor cortex can induce plastic changes that peak at 30 min and last more than 2 hours after the stimulation.

Practical aspects
Woods, A. J., Antal, A., Bikson, M., Boggio, P. S., Brunoni, A. R., Celnik, P., ... & Nitsche, M. A. (2016). A technical guide to tDCS, and related non-invasive brain stimulation tools. Clinical Neurophysiology, 127(2), 1031-1048.
Thair, H., Holloway, A. L., Newport, R., & Smith, A. D. (2017). Transcranial direct current stimulation (tDCS): a beginner's guide for design and implementation. Frontiers in Neuroscience, 11, 641.
Two reviews covering practical aspects of transcranial electrical stimulations (tES) experiments implementation (e.g., for how long, at which intensity, control conditions, safety etc.) and integration with other neuroimaging techniques such as EEG and magnetic resonance imaging (MRI).

Da Silva, A. F., Volz, M. S., Bikson, M., & Fregni, F. (2011). Electrode positioning and montage in transcranial direct current stimulation. JoVE (Journal of Visualized Experiments), (51), e2744.
A practical demonstration of conventional tDCS electrodes positioning and montage.

Clinical evidence
Bikson, M., Grossman, P., Thomas, C., Zannou, A. L., Jiang, J., Adnan, T., ... & Woods, A. J. (2016). Safety of transcranial direct current stimulation: evidence based update 2016. Brain Stimulation, 9(5), 641-661.
This review comprehensively summarizes the available evidence about tDCS safety in the healthy population as well as more vulnerable categories, including people with epilepsy, stroke, and mood disorders. Across more than 33,000 sessions of tDCS, the use of conventional protocols in human trials (≤40 min, ≤4 milliamperes, ≤7.2 Coulombs) has not produced any reports of a serious adverse effect or irreversible injury.

Lefaucheur, J. P., Antal, A., Ayache, S. S., Benninger, D. H., Brunelin, J., Cogiamanian, F., ... & Paulus, W. (2017). Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS). Clinical Neurophysiology, 128(1), 56-92.
This review summarizes the evidence about the therapeutic use of tDCS to treat pain, Parkinson's disease, other movement disorders, motor stroke, post-stroke aphasia, multiple sclerosis, epilepsy, consciousness disorders, Alzheimer's disease, tinnitus, depression, schizophrenia, and craving/addiction. Whereas the authors indicate no definite efficacy (Level A) for any treatment, they propose Level B recommendation (probable efficacy) and Level C recommendation (possible efficacy) for a number of neuropsychiatric disorders, including, fibromyalgia, neuropathic pain, depression, and craving.

Pacheco-Barrios, K., Meng, X., & Fregni, F. (2020). Neuromodulation techniques in phantom limb pain: A systematic review and meta-analysis. Pain Medicine, 21(10), 2310-2322.
In this meta-analysis, the authors considered 14 studies - both randomized controlled trials (RCTs) and quasi-experimental (QE) studies - showing, among others, the effect of anodal tDCS over M1 in lowering pain after the stimulation and at one-week follow-up.

Abstracts

Are phantom referred sensations a perceptual consequence of S1 remapping?

Amoruso E.[1], Terhune D.[2], Muret D.[1], Kromm M.[1], Makin T.R[1]

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[2] Department of Psychology, Goldsmiths, University of London, London, United Kingdom

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Format: Oral Presentation

Background and aims

Seminal studies [1,2] have shown that touches on the face can evoke topographically organized sensations on the phantom hand in some amputees (referred sensations). This striking phenomenon has been classically operationalized as the perceptual correlate of the cortical remapping of the face onto the neighboring missing hand territory in the primary somatosensory cortex (S1). However, later studies [3,4] have casted doubt on the validity of the phenomenon as evidence for remapping, by showing that referred sensations can be evoked by touches on many body parts, including those not neighbouring the missing limb cortical representation. Here, we investigate whether reports of referred sensations can be, at least partially, explained by uncontrolled experimental factors, such as demand characteristics and suggestibility, which have recently been shown to account for bodily experiential changes in comparable phenomena (e.g. rubber hand illusion, mirror-touch synesthesia, vicarious pain) [5,6]. To this end, we tested whether reporting feeling referred sensations can be influenced by suggestible instructions in a large sample of amputees and control participants.

Methods

Unilateral upper-limb amputees (N=17), congenital one-handers (N=19), and 20 able-bodied controls (N=20) were repeatedly stimulated with PC-controlled short vibrating trains on both sides of the face, arms, feet. They were asked to report on each trial (120 in total) the occurrence of any dual sensations on the hand(s) (including the phantom in amputees) in a two-alternatives forced choice task. Before starting the experiment, expectations were manipulated by telling all participants that they would receive ‘special’ vibrations (found to be able to evoke dual sensations) intermixed with ‘classical’ vibrations. To further induce suggestibility, they were also told that in half of the trials a visual cue would signal incoming ‘special’ stimuli. In reality, all stimuli were physiologically identical.

Results

Results show that manipulating expectations about the occurrence of the phenomenon are sufficient to induce a significant amount of referred sensations not only in amputees, but also in healthy-bodied participants and congenital one-handers, in which referred sensations have never been reported and should not occur (according to the dominant interpretative theory). Moreover, all groups responded positively to the suggestibility manipulation by reporting significantly more sensations in the trials cued as containing ‘special’ stimuli. Most strikingly, reported referred sensations were not found to be more frequent in amputees than in the other groups. An analysis of the evoking locations revealed a pattern not compatible with the cortical remapping hypothesis, with referred sensations reported not more frequently from stimulation of the face or body-parts ipsilateral to the missing hand.

Conclusions

These findings bring into question the belief that referred sensations, as empirically tested in classical settings, are a phenomenon due to amputation. Referred sensations reports could result from behavioural compliance, task demands (e.g. paying particular attention to the hands could create increased awareness for otherwise irrelevant sensations) or also reflect a non-illusory experience. Importantly, however, by showing that these reports are universal to all tested groups, irrespective of amputation and phantom sensations, our findings generally weaken the hypothesis that referred sensations are a behavioural consequence of post-amputation S1 remapping.

References

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5. Lush, P., Botan, V., Scott, R. B., Seth, A. K., Ward, J., & Dienes, Z. (2020). Trait phenomenological control predicts experience of mirror synaesthesia and the rubber hand illusion. Nature communications, 11(1), 1-10.

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Topics: Referred sensations, plasticity

C.A.L.A. - Computer Assisted Limb Assessment: Visualizing Phantom Limbs and Phantom Limb Pain

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Format: Poster

Background and aims

There is currently no standardized form for documenting the therapeutic assessments of phantom sensation and phantom pain after amputation. Often this is done only on the basis of pain questionnaires or in a completely open manner. While questionnaires such as the Brief Pain Inventory [1] offer an approximate localization of pain by providing a 2D human figure to mark areas of pain, it is not possible to illustrate the deformation and twisting of the phantom limb. Furthermore, these analogue methods make it difficult to quantify the data collected and to monitor their changes over the course of therapy. Body image visualization tools have been popular regarding eating disorders [2-4], the number of tools for the visualization and documentation of phantom sensations, however, is rather limited. Rogers developed a virtual reality tool to be used in therapy that allowed for the visualization of a twisted phantom but did not provide the illustration of deforming sensations or pain [5]. C.A.L.A. aims to provide a digital environment capable of capturing all aspects of the phantom limb during the course of therapy by using a 3D avatar modeled after the patient, and to allow subsequent quantification of the data collected.

Methods

Previously, a prototype had been developed by modifying and extending the Open Source software projects MakeHuman and Blender [6]. Based on this prototype, a first stable version was developed, providing the principal functions of C.A.L.A.: (1) Adapting a 3D avatar for patient self-identification, (2) modeling phantom sensation, (3) adjusting body position, and (4) drawing pain and cramps in the phantom based on the Visual Analogue Scale [7] (see Fig. 1).

C.A.L.A. was evaluated with 20 occupational therapists, physiotherapists and orthopedic technicians who actively work with amputees. After a short introduction, 2 predefined cases had to be modeled, visualizing the appearance and the position of the phantom limb as well as pain and cramps. Thereafter, the usability of C.A.L.A. was evaluated using the System Usability Scale (SUS) [8]. Further questionnaires and semi-structured interviews were used to determine the relevance of the existing functions and to collect additional desirable functions.

Results: C.A.L.A. was positively received by the participants to a high degree. The score of the overall usability, assessed with the SUS, reached 74%, ranging in the 2nd quartile and representing high acceptability. The provided functions were considered as useful by most therapists, however, suggestions for improvement were made, such as simplifying the process for adjusting the body position. The evaluation also revealed important future functions for the final version of C.A.L.A., such as the quantification of body position or capturing neuroma pain, and general operational aids which will decisively facilitate practical use in everyday therapy.

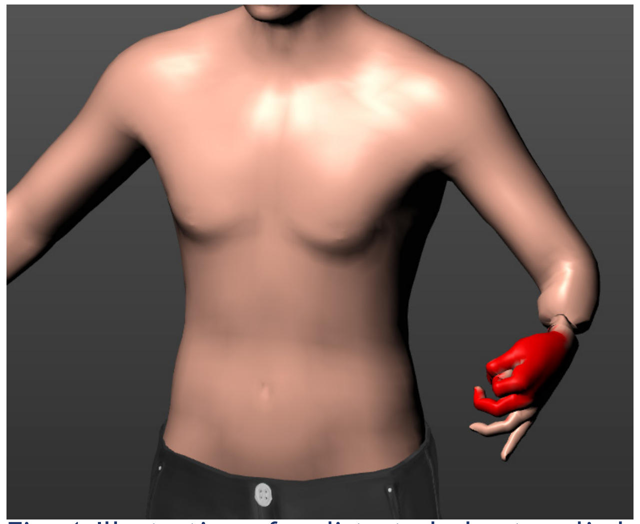

Fig. 1 Illustration of a distorted phantom limb with adjusted body position and marked pain areas.

Conclusions

The use of C.A.L.A. allows a detailed representation of the phantom limb and pain sensation and can moreover be used as a quantitative documentation method. The feedback collected provides important suggestions for further improvement of the usability and functionality. In the next phase of C.A.L.A. an improved final version will be developed and used in a multi-centered, longitudinal study to document the patient population.

References

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Topics: Assessment, Amputations, Phantom Limb Pain, Sensation, Documentation, Software

The multisensory integration between nociception and vision in the rubber hand illusion

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Format: Poster

Body ownership refers to the subjective perception of the body as one's own. This percept depends on the multisensory integration of bodily signals [1]-[3]. The classic way to study body ownership in healthy individuals is to use a perceptual bodily illusion known as the rubber hand illusion (RHI) [1], [4]. In the RHI, a rubber hand in the participant' view is synchronously stroked with the real hand hidden behind a screen. After 10-20s of such stimulation, most participants start to experience the touches as originating directly from the rubber hand and that the rubber hand is part of their body. Previous studies have demonstrated that this illusory percept arises from the integration of vision, tactile and proprioceptive signals [5].
However, little is known about the contribution to nociceptive information for body ownership and the rubber hand illusion, although the subjective experience of such signals give rise to human's conscious experience of pain, which is an essential defense mechanism for protection of bodily self. Furthermore, people who suffer by chronic pain such as the phantom limb pain seem to have distorted body image [6], [7].
Here we investigate the contribution of pure nociceptive signaling to body ownership by introducing the "visuo-nociceptive RHI". To selectively activate nociceptors in the skin, we used a Nd:YAP laser stimulator (Stimul 1340, Deka, 1.34 μm wavelength, 7 ms pulse) that specifically targets C and Aδ fibers. We recruited 90 naïve participants over three separate experiments. In Experiment 1 we investigated the subjective experience of the visuonociceptive RHI with an 8 items questionnaire. We compared a condition with synchronous visual (a brief red light shining on the fake hand) and nociceptive stimulation on the rubber hand with a control condition with this visuo-nociceptive stimulation was asynchronous (the nociceptive input had 1000 ms delay compared to the red light) Experiment 2 used the same two conditions but quantified the illusion objectively with a proprioceptive drift task that registers the changes in hand position sense towards the rubber hand that occurs during the illusion and that is probed by asking the participants to close their eyes and point towards the location of their left index finger with the right index [4], [8]. Finally, in Experiment 3 we manipulated the spatial congruence of the seen and felt orientations of the rubber hand and real hand. In the illusion condition the rubber hand was placed in the same position as the real hand (i.e., 0°) whereas in the control condition the rubber hand was rotated 180°; we used the same proprioceptive drift measure as in experiment 2.
The results of Experiment 1 showed that people rated illusion-related items significantly higher in the synchronous condition than in the asynchronous condition ($p < .01$). In Experiment 2, the proprioceptive drift was significantly higher in the synchronous compared to the asynchronous condition ($p = .01$). Finally, in Experiment 3, the proprioceptive drift was significantly larger in the spatially congruent condition (0°) compared to the spatially incongruent condition (180°) ($p = .001$).
In conclusion, our results suggest that the rubber hand illusion can be triggered by temporally and spatially congruent nociceptive and visual signals and have a bearing on models of body ownership by suggesting an important role for nociception in body perception.

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Microstimulation as a tool to explore sensory percepts elicited by electrical stimulation

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Format: Poster

Background and aims

Most advanced prosthetic limbs are connected to muscular and nervous tissues, enabling intuitive action execution [1] and sensory feedback [2, 3]. Sensory feedback provides tactile information about the contact of the robotic limb with the environment. It enhances the user's experience enabling secure object grasping (e.g. holding an egg without breaking it [2-4]). Restoring sensorimotor loops improves prosthesis embodiment [5] and reduces phantom pain [2, 6]. Only a few studies, including a limited number of amputee individuals, have described the relationship between the parameters of electrical stimulation and the touch percepts elicited [2, 7]. In the present study, we adapted the classic microstimulation technique [8] to study this relationship in a way mimicking the stimulation used in nerve-wired prosthetics, but in a group of non-amputee individuals, as in Oddo, et al. [4].

Methods

36 electrode insertions were conducted on 20 healthy participants. Integrum adapted an electrical stimulator, from the ones used for the prosthetics (current-controlled pulses, amplitude range: 10-500 µA, pulse width: 50-500 µs, frequency range: 1 to 500 Hz). Electrodes were opened to reduce their impedance (from ≈500 KΩ to <20 KΩ). The electrode was inserted near the wrist fold, until reaching the median nerve. Once the nerve was found, the electrode was retracted up to two times to obtain three test locations: 'intraneural, 'epineural', 'extraneural'. At each location, we measured the threshold for sensation (30Hz, pw: 200µs, duration: 500ms). The size, border type, shape, movement, and naturalness of the sensation were evaluated using previous criteria [8]. The area of sensation was drawn on a representative hand. Participants also freely described the sensation evoked. At epineural location, which mimics prosthetic electrode location, other tests were conducted, such as: (1) varying the frequency from 30 to 60Hz, (2) increasing the current by +10 or +20% of threshold, (3) a test of pulse amplitude/width equivalence, (4) a test of two pulse discrimination. Once the three locations were tested, the entire procedure was repeated at a new intraneural location.

Results

The threshold for sensation, as well as the size of the percept, increased with changing location. No effects were revealed for the other variables tested. Verbal descriptions at epineural location revealed that a small oval with a vibrating or tingling sensation dominated the spectrum of sensations. Painful sensations were only reported at intraneural locations. Changing frequency evoked no change in sensation in most participants, while increasing the amplitude systematically increased the area of the percept. Comparing electrical stimulation through pulse amplitude or width modulation at equivalent charges revealed that short pulses were more efficient to evoke a threshold sensation. Finally, the two-pulse discrimination test revealed that pulses were felt as distinct when superior to 9.5 Hz approx., hence a potential useful frequency to evoke continuous sensations under stimulation protocols.

Conclusions

We conclude that using short pulses, at epineural location, modulated in amplitude rather than in frequency, might be the best strategy to evoke useful (rather than natural) sensations. More generally, our work highlights the importance of setting appropriate parameters for sensory feedback, which could strengthen embodiment and reduce phantom limb pain.

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Chronic pain in lower limb amputees and correlation with the use of perioperative epidural or perineural analgesia

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Format: Poster

Background and aims

Chronic post-operative pain is a common complication in patients who undergo amputation surgery and have been distinguished in three main conditions: phantom limb sensation (PLS) is defined as a painless sensation of the missing limb, phantom limb pain (PLP) corresponds to the feeling of pain at the missing limb, and stump/residual limb pain (RLP) which corresponds to pain
at the stump.
The aim of the study was: 1) to investigate the long-term prevalence of PLP, PLS and RLP in patients with lower limb amputation and their correlation with perioperative analgesic treatment with epidural or peripheral nerve block, 2) to evaluate the prevalence of PLS, PLP, RLP and their
correlations with patient age at time of surgery, follow-up, diagnosis, level of amputation (trans-femoral, trans-tibial or hemi-pelvectomy), BMI, drug use and rehabilitation treatment. [1]

Methods

The study lasted for a total of about 20 months. Patient inclusion criteria were: individuals undergoing trans-tibial, trans-femoral or hemi-pelvectomy of any etiology at the Rizzoli Orthopedic Institute between 2008 and 2018. The exclusion criteria were: age <18 years or> 90 years, patients residing abroad and non-ambulatory patients for comorbidity. Patients were enrolled through the Institute's Data Processing Centre and suitable patients were asked to fill out questionnaires including anthropometric data (weight, height), the current use of drugs for the management of pain, any physiotherapy after amputation, the Houghton Scale for prosthetic use and the Prosthetic Evaluation Questionnaire to evaluate the presence of chronic post-surgical pain. [2]

Results

Out of 207 eligible patients, we obtained complete questionnaire data from 79 amputees. Follow up time from amputation was 5.1±2.4 years. The most frequent causes of amputation were musculoskeletal tumors in 28 cases, infectious problems in 29 cases and problems of other nature in the remaining 22 cases. PLS was reported by 68.5% of amputees, PLP by 65.9% and RLP by 53.3%. No correlation was identified between the prevalence of pain syndromes and long-term follow-up, diagnosis, level of amputation, BMI, physiotherapy, and epidural or perineural analgesia. [3]

Conclusions

Data on prevalence of PLP, PLS and RLP is consistent with the literature. No favourable effects in pain reduction in the long term follow up by using peripheral nerve sciatic or femoral or epidural catheters was detected. A more targeted drugs and rehabilitation intervention is desirable to contain these conditions and the consequent disability.

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Topics: Amputation, chronic pain, epidural analgesia, perineural catheters

A novel surgical method based on targeted sensory reinnervation reduces phantom pain and improves prosthetic rehabilitation

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Format: Oral presentation

Background and aims

Phantom and neuroma pain affect a high percentage of amputees and massively impair their quality of life. Treatment of these patients remains challenging and is in most cases limited to symptomatic treatment.

Methods

Between October 2014 and February 2020, four patients underwent Targeted Sensory Reinnervation (TSR), three of them for therapy-refractory phantom pain after either transfemoral or transtibial amputations and one patient for whom TSR was performed prophylactically. TSR is a surgical technique during which a defined skin area is first selectively denervated and then surgically reinnervated by another sensory nerve. In our case, either the area of the lateral femoral cutaneous nerve or the saphenous nerve was reinnervated by the sural nerve. Touching this area of reinnervation is subsequently transmitted via the sural nerve, evoking a sensory feedback which is located on the missing leg. Patients were then fitted with a special prosthetic device capable of transferring the sense of pressure from the sole of the prosthesis to the newly wired skin area.

Results

Pain reduction after TSR was highly significant in all patients. In three patients, permanent pain medication could even be discontinued, in one patient the pain medication has been significantly reduced. Two of the four patients were completely pain-free after the surgical intervention. Due to the sensory feedback system, functional tests showed a significant improvement over conventional prosthesis.

Conclusions

Surgical rewiring of existing sensory nerves by TSR can provide the brain with new afferent signals seeming to originate from the missing limb. These signals help to reduce phantom pain and to restore a more normal body image. In combination with special prosthetic devices, the amputee can be provided with sensory feedback from the prosthesis, thus improving gait and balance.

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Topics: Phantom pain, neuroma pain, amputation, lower limb, TSR

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Correlation between neuromas and phantom limb pain after traumatic hand amputation

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Format: Poster

BackgroundTraumatic amputation of the hand is a devastating and live-changing injury. Irrespective of the cause of amputation, this is followed by different sequels of pain and sensation, either phantom or stump pain. Phantom limb pain and painful sensation at the stump are correlated with symptomatic end neuroma formation.

Aim

To evaluate patients with phantom limb pain and stump pain as a result of neuroma formation after traumatic hand amputation.

Material and Methods

This retrospective study evaluated 6 patients admitted University Clinic for plastic and reconstructive surgery in Skopje , from June 2012 till June 2020, with traumatic hand amputation below the elbow. Patients only with finger amputations were excluded. We analyzed patient demographics, level of amputation and use of prosthesis. Furthermore, we analyzed phantom phenomena and stump pain related with symptomatic neuroma formation detected with ultrasonography.

Results

Five of the patients are male, one female. The average age is 45 years, the youngest being 18 years old. All of the patients experienced phantom sensation. Three patients complained on phantom limb pain and one on stump pain. Two patients were using medication for pain relief. Only two patients are using non-functional rigid prosthetic devices for less than 8 hours a day. Ultrasonography detected painful end neuromas of the median or ulnar nerve in 4 patients that corresponded with the positive Tinel sign on examination.

Conclusion

Phantom phenomena after amputation are limiting everyday activities. Description of the pain and sensations differs between patients, usually depending by their age, profession, social background. Painful neuroma formation prevents the use of prosthetic devices. The results of our study indicate that in the emergency surgery procedures for traumatic amputations, primary treatment of the nerve should be taken in consideration. At transradial level amputations nerves should be located away from the stump and surface so that the neuroma will not prevent use of a prosthesis.

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Topics: Neuromas and Phantom limb pain

A retrospective review of phantom limb pain in patients undergoing lower limb amputations as a result of diabetes

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Format: Poster

Phantom limb pain is a known complication for patients following amputation, with an incidence that has been reported to be in the region of 50-70%. Why it affects some more than others is not well understood nor is the underlying mechanism which drives it. We have observed in our clinical practice that patients undergoing a lower limb amputation which was caused due to complications with diabetes, tended to have less issues with phantom limb pain post operatively. This has previously been investigated by Clark et al (2013) who found no significant difference between the incidence of phantom limb pain in diabetic patients and non-diabetic patients.

We retrospectively reviewed all new lower limb referrals and primary consultations at the Prosthetic Rehabilitation Unit at the Royal National Orthopaedic Hospital, UK, (n=70). Of these 51 met the selection criteria and were split into two groups based on whether diabetes was classified as the cause of their amputation or not. Our review found that in patients where diabetes had been the cause of the amputation only 39% of patients reported phantom limb pain compared with 75% in the group where diabetes did not contribute to their amputation ($p= 0.009$). There was no significant difference between the rate of reporting of phantom limb sensations or residual limb pain ($p= >0.05$). Within the diabetic group however, evidence of peripheral neuropathy was not associated with lower level of phantom limb pain ($p= >0.05$)

These observations are useful when it comes to discussing the risks following amputation with our patients in clinical practice. The effect of diabetes on phantom limb pain may be multifactorial given it has effects on the peripheral and central nervous system and cannot solely be explained by pre-existing neuropathy. As our understanding of the mechanisms of phantom limb pain develops the impact of diabetes on these pathways may be better understood. The results of this study however only represent a snapshot of what is happening with our patients and further work with prospective data collection will be more beneficial in understanding the true effects of diabetes on phantom limb pain.

Reliability of a limb laterality recognition task in people with phantom limb pain.

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Format: Oral Presentation

Background and aims

Phantom limb pain (PLP) is pain perceived as arising from a missing limb and affects up to 80% of amputees. The brain maps that integrate the motor cortices of different bodily regions have been referred to as working body schema (WBS). The WBS may be altered or disrupted in people with PLP and this may play a role in the development and/or maintenance of PLP. Thus, a number of studies have explored WBS using the limb laterality recognition task (LLRT) in this clinical group. The LLRT requires a person to view images of a limb and judge whether they are of a left or right limb. The task is undertaken using implicit motor imagery which is dependent upon the WBS. It is important that any measure demonstrates adequate psychometric properties. Few studies have investigated the reliability of the LLRT in people with PLP. The aim of this study was to quantify the between session test-retest reliability of a LLRT.

Methods

Participants with PLP were recruited from hospitals in the North East of England. After providing written informed consent, two LLRT sessions using E-Prime 2.0 software, were completed, separated by a 7-14 day period. The percentage of correct responses [accuracy] and the speed of identification of correct response [reaction time] were recorded. The systematic and random error between sessions 1 and 2 for the LLRT was quantified using paired t-tests (systematic error), the standard deviation of the differences, the standard error of measurement (SEM), the coefficient of variation, limits of agreement, and a random-error only Intraclass correlation coefficient (ICC). Using the baseline data, a minimal clinically important difference (MCID) was estimated as 8% accuracy and a reaction time of 950 ms (based on 0.5 of the baseline SD). Ethical approval for this study was obtained from the Ethics and Research Governance sub-committee of the School of Health and Life Sciences at Teesside University.

Table 1: Test-retest reliability

	Accuracy (%)	Reaction Time (ms)
Mean session difference (ms)	3.3 (0.2 - 6.3)	250 (-446 - 957)
SD of session differences (ms)	9.0 (7.3 - 11.8)	2073 (1677 - 2716)
SEM (ms)	6.4 (5.2 - 8.3)	1466 (1186 - 1921)
Coefficient of variation (%)	8.0 (6.5 - 10.5)	55 (45 - 73)
Limits of agreement (ms)	17.7 (14.3 - 23.0)	4064 (3287 - 5325)
ICC	0.90 (0.85 - 0.96)	0.60 (0.22 - 0.80)

SEM = standard error of measurement (typical error). ICC = Intraclass correlation coefficient. Values in parentheses are 95% confidence intervals.

Results

Preliminary data from 35 participants were analysed (mean age 56 ±14 years, 26 males and 9 females, all lower limb amputees, 7 bilaterally). The group average PLP intensity score for the previous week was 52/100 recorded using a pain diary. The mean accuracy and reaction time at baseline was 78% (17) and 2774 ms (1900), respectively. The test-retest reliability statistics are presented in Table 1.

Conclusions

The paired t-tests provide evidence of systematic bias for accuracy, likely due to learning effects. Practice sessions should be used to minimize these learning effects. The data shows a greater level of random error for reaction time compared to accuracy. The SEM for accuracy was just below the MCID, while the SEM for reaction time was well above the MCID. The limits of agreements were relatively wide for each measure compared to their respective MCIDs. Thus, clinicians should interpret these measures with a great deal of caution at the individual patient level.

Phantom limb pain and residual limb pain after lower limb amputation - data from the SwedeAmp registry

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Format: Oral Presentation

Background and aims

The Swedish Amputation and Prosthetics Registry for the lower extremity (SwedeAmp) is a national registry aiming to increase knowledge and quality of care for patients undergoing amputations [1]. The aim is to describe patient-reported outcome (PRO) relating to phantom limb pain (PLP) and residual limb pain (RLP) from the database.

Methods

SwedeAmp includes patient-level data, voluntary registered on-line by clinicians using a personal log-in. Data for amputations, prostheses and outcome are included. PRO is recorded at three times points (6, 12, and 24 months after the date of amputation) and include patients with major amputations of which most have attained prosthetic rehabilitation. The two pain questions (PLP and RLP, respectively) concern presence of pain recorded in four levels (No, Yes a little, Yes some, Yes a lot). For those reporting any pain, a follow-up question on treatment follows.

Until 31 December 2020 the registry included 8395 patients with 12078 surgical procedures. Among those, PRO data was recorded for 1648 patients (67% men, mean age 71; 33% women, mean age 77; 81% amputation due to diabetes and/or vascular disease; 74% Transtibial amputation (TTA), 19% Transfemoral amputation (TFA) and 6% Knee disarticulation (KD). The presence of PLP and RLP is reported in patients with a unilateral amputation. In addition, data is reported for the smaller group of patients with recordings at all three time-points and separated into two groups based on amputation level (TTA or KD/TFA).

Results

At 6, 12 and 24 months any PLP was reported by 69% (n=1245), 73% (n=959) and 69% (n=489) and any RLP by 52% (n=1159), 45% (n=884) and 46% (n=446), respectively. A lot of pain was reported among 13-17% (PLP) and 6-8% (RLP). Among those with pain, close to 40% had some kind of pain treatment, 5% did not have treatment, but needed it and close to 60% reported to not need any treatment, regardless of PLP or RLP. Grouped into amputation level longitudinal data showed any PLP in 73, 65 and 65% for TTA (n=190) and 82, 81 and 81% for KD/TFA (n=63), at each time point respectively (Figure 1). Corresponding figures for RLP were 49, 42 and 39% for TTA (n=195) and 61, 39 and 50% for KD/TFA (n=64), respectively.

Conclusions

SwedeAmp data show that PLP is reported among about 70% of the patients with a major amputation and no clear change between time points is indicated. In general, data show more problems with PLP than RLP. In addition, it indicate that patients with a more proximal amputation (KD/TFA) to a higher degree report pain as compared to those with TTA.

To conclude, registry data from SwedeAmp demonstrate that a substantial proportion of patients with a unilateral major lower limb amputation report some degree of PLP and/or RLP and the pain is still present 2 years after the amputation. Registry data from SwedeAmp will in the future enable deeper analyses with regard to PLP/RLP and possible relations to e.g. surgical technique, type of prosthetic supply and quality of life.

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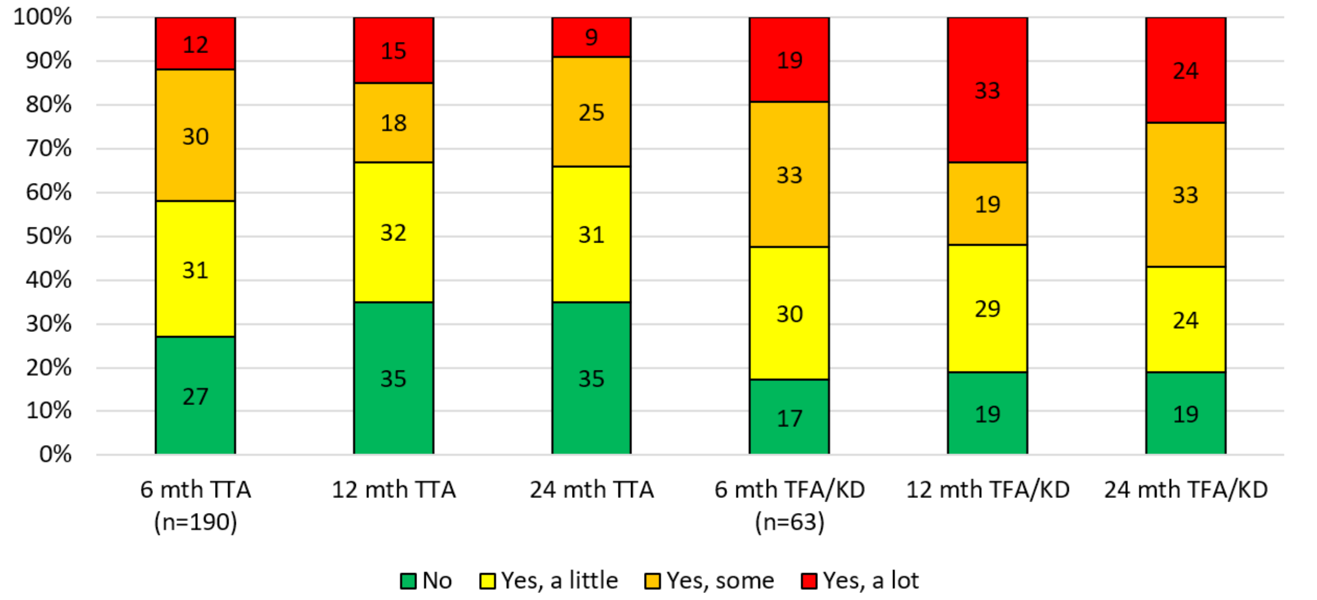

Figure 1: Presence of PLP 6, 12 and 24 months after amputation in the sub-group of patients with unilateral TTA or KD/TFA and with data recorded in SwedeAmp for each time-point.

Effect of Pulse-width Modulated Sensory Feedback on Cortical Excitability

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Format: Poster

Background and aims

Following amputation, almost two-thirds of amputees experience unpleasant to painful sensations in or around the lost limb. While the underlying mechanisms of phantom limb pain (PLP) remains unclear, recent studies have reported that cortical reorganization may play a major role [1]. Some studies also have shown a significant reduction of intracortical inhibition (ICI) in the affected side [2].
Several studies have used transcutaneous electrical nerve stimulation (TENS) as neurorehabilitation for spasticity relief, chronic pain, and temporary PLP relief [3-5]. In EPIONE (an EU project at Aalborg University), application of non-painful, continuous TENS on the residual limb caused significant, but temporary changes in the phantom limb perception and a reduction of PLP up to 40 % [4]. TENS is believed to work by activating the descending pain inhibitory system [6] and possible reversing reorganization at the cortical level [7].
On the other hand, in healthy subjects, changes in the amplitude of motor-evoked potentials (MEPs) have been observed after TENS delivery due to anatomical and functional connections between the primary sensory and motor cortex [8]. Also, it has been reported that changes in MEPs are dependent on the TENS parameters [9].
Recent articles have focused on investigating alternative temporal TENS patterns instead of non-modulated pattern for therapeutic innovation [10]. Pulse width modulated (PWM) TENS is one of the novel approaches tested on patients with back pain [5]. No study to date has investigated the effect of modulated TENS patterns on PLP relief. Our objective was to evaluate the PWM TENS pattern that shows the changes in the CS pathway. In the present work, we focus on healthy subjects; however, our results may lead to the possible enhanced effects on PLP alleviation in amputees in the future.

Methods

A pilot study with two TENS patterns was conducted with; 1) non-modulated TENS (100 Hz rectangular pulses, 1 ms pulse width) and 2) PWM-TENS (100 Hz rectangular pulses, sinusoidally modulated pulse width from 0 to 1 ms). Each pattern was delivered for 20 min with an intensity of 80 % of the discomfort threshold to the left-median nerve of two healthy subjects. The excitability of the CS pathway was measured by averaging the eight MEPs of the target muscle (left abductor pollicis brevis) elicited by TMS pulse with 120 % rest motor threshold intensity for each following time phases; 1) Pre-TENS, 2) Post-TENS (immediately after intervention), and 3) Post30-TENS (30 min after intervention).

Results

The preliminary results showed that both TENS patterns induced changes and increased the excitability of CS pathway, while the non-modulated pattern had a stronger effect on MEPs amplitude (91 % and 35 % increased in MEP amplitude, respectively). Moreover, the enhancement in activity maintained after 30 min, whereas the MEP amplitudes in Post30-TENS became weaker than Post-TENS.

Conclusions

Non-modulated TENS and PWM-TENS applied to the left-median nerve increased the excitability of the CS pathway. Although the results indicated that the two TENS patterns had different power in the enhancement of MEPs amplitude, evaluation of the ICI and cortical map changes may help to further understand the effect of TENS patterns. Besides, a comparative analysis of healthy subjects and amputees is expected to reveal CS markers evoked by the specific types of stimuli that may induce changes in perception of PLP.

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Electroacupuncture for the successful alleviation of phantom limb pain

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Format: Poster

For decades phantom limb pain (PLP) has confounded researchers and practitioners. The debilitating and draining condition, continues to significantly hinder amputees' sleep, quality of life and rehabilitation outcomes. The majority of PLP presents with a similar pattern of neurogenic pain in the phantom limb, however the origin of the pain may be central (neuropathic), local in the residual limb (nociceptive) or from sensitised neuromata in the residual limb (neuroma).

Structural and biomechanical changes take place following transection of nerve fibres, including upregulation of sodium channels, activation of mitogen-activated protein kinases, and altered gene expression, leading to hyperexcitability and spontaneous discharge [1]. Current theories suggest that electroacupuncture (EA) is able to block neurogenic pain by reducing the expression of the voltage-gated sodium channels 1.7 in the dorsal root ganglia [2], by promoting opioids in the spinal cord [3] and reducing the activation of spinal microglia in the spinal cord [4]. Therefore, it is proposed that treating the primary site of injury in peripheral nerves, dorsal root ganglia and spinal cord, with EA is likely to have a positive outcome in an amputees' nociceptive phantom limb pain.

In a case study of a male in his thirties who suffered catastrophic injuries including a high transfemoral amputation as a result of being hit by a car. An EA treatment protocol was followed. Over the course of three months, the EA was effectively able to reduce his pain scores, the intensity, frequency of his PLP, eliminate his use of pharmacological medication and improve his sleep.

Intervention: EA protocol of 2 channels lumbar paraspinals L2-L4 and 1 channel in the residual limb. AS SUPER 4 digital Programme 20, between 2.0 and 3.0mAmps (a strong sensation for the patient) for 40minutes, weekly intervention. There is a positive correlation with high dose acupuncture treatment and positive outcomes [5]. No adverse effects from EA treatment were reported.

This case report is important as it shows for the first time that an easily reproducible EA protocol is effective in reducing nociceptive PLP in amputees, as shown by a significant decrease in all pain scores. Healthcare professionals working with amputees, should consider EA as a therapeutic option for PLP.

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Topics: phantom limb pain, nociceptive pain, electroacupuncture, quality of life.

Towards EEG Signatures of Phantom Limb Pain

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Format: Oral Presentation

Background and aims

People with acquired amputation face often-times the onset of chronic pain, which develops as either residual limb pain, neuroma or nociceptive phantom limb pain (PLP), or neuropathic PLP. (Ortiz-Catalan, 2018)

To date, the pathophysiology giving raise to PLP is still object of debate, with previous literature mainly focusing on whether and how reorganization takes place in the primary somatosensory and motor cortices (Flor et al., 1995; Makin et al., 2013). Striving to understand how changes in somatotopy and mototopy relate to PLP, brain imaging studies have traditionally been conducted with a task-based fMRI approaches which measure the neural activity in an indirect way (Jutzeler, Curt and Kramer, 2015). Yet, little is known about the effect of amputation on the global brain organization and electrophysiological techniques, such as EEG, have not been taken fully advantage of. In this study we analyze the power of spontaneous and ongoing EEG activity as a function of frequency. The rationale for this choice stems from the assumption that brain at rest, in opposition to task-based paradigms, allows to capture dynamics related to the processing of pain which would otherwise be masked by other sensory or cognitive functions processes.

Methods

The study was approved by the ethical committee of Västra Götalandsregionen. A total of 7 adults subjects, 3 women and 4 men between 24 and 57 years of age, were enrolled on a voluntary basis and assigned to one of two groups based on the presence of PLP. The 'no PLP' group was composed of two able bodied subjects and one upper limb amputee. The 'PLP' group was formed by one subject with lower limb amputation and three with upper limb deficiency. During the recording of the EEG signals, subjects rested with their eyes closed sitting comfortably on a chair in a quiet room. EEG was recorded sampling at 2400 Hz in 2 sessions of 7 minutes each, with 63 active electrodes fixed in a cap at the standard 10-20 positions, using an ear-link reference and AFz ground (g.Hlamp, g.tec medical engineering GmbH, Austria).

Data was analysed offline using custom script and EEGLAB (Delorme and Makeig, 2004). The data were re-referenced to the common average reference, filtered with a bandpass IIR filter (-36dB/Octave, 0.5-256Hz) and a notch filter between 48 and 52Hz. EEG data were exported to EEGlab and visually inspected: sequences containing artefacts were visually rejected. Further, independent component analysis was performed using the infomax algorithm as implemented in EEGlab and used to remove eye movements and muscle activity components. A "study" structure was created in EEGlab to calculate and compare the power spectral density on a group level.

Results

Figure 1 shows grand average (plot in black) of the power spectra for the two groups (no PLP on the left and PLP on the right). As the spectra from different channels had similar scale and shape, the data was summarized by averaging all the electrodes for each channel. The aver-

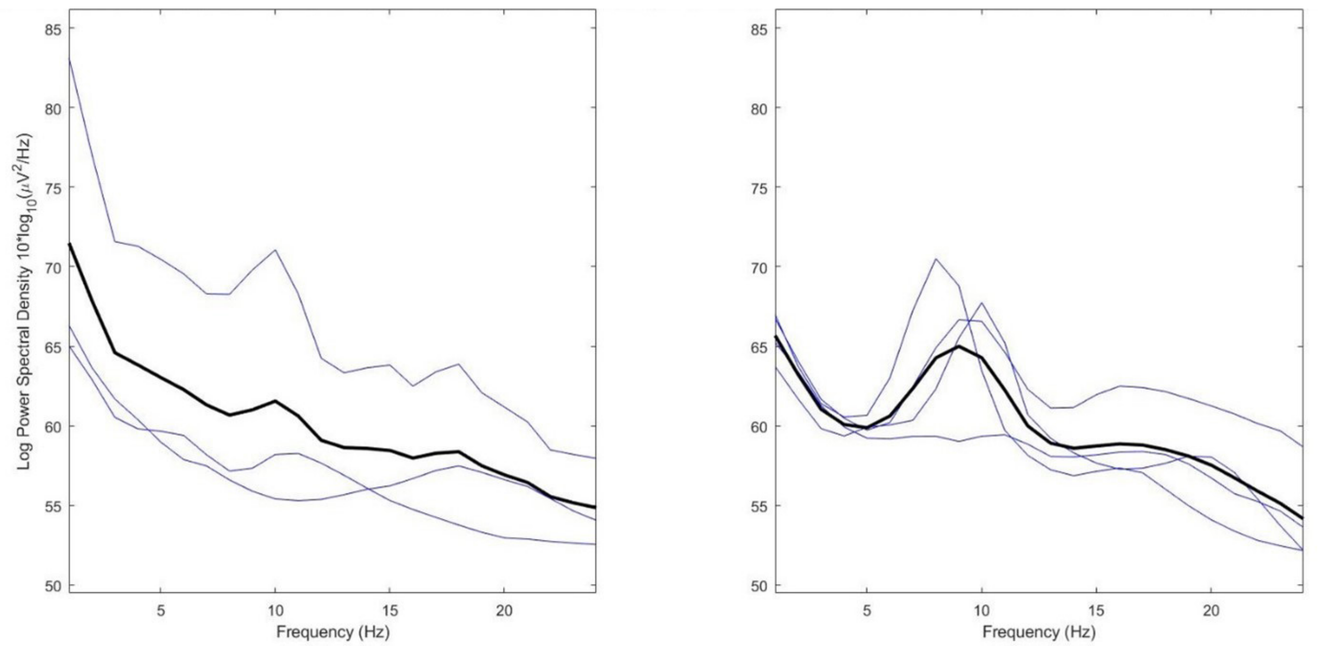

Figure 1: Grand average power spectra. On the left the power spectra of the group without phantom limb pain ('no PLP') on the right side the power spectra of the PLP group. In the 'no PLP' group the curve with the most prominent alpha peak belongs to one of the able-bodied subjects.

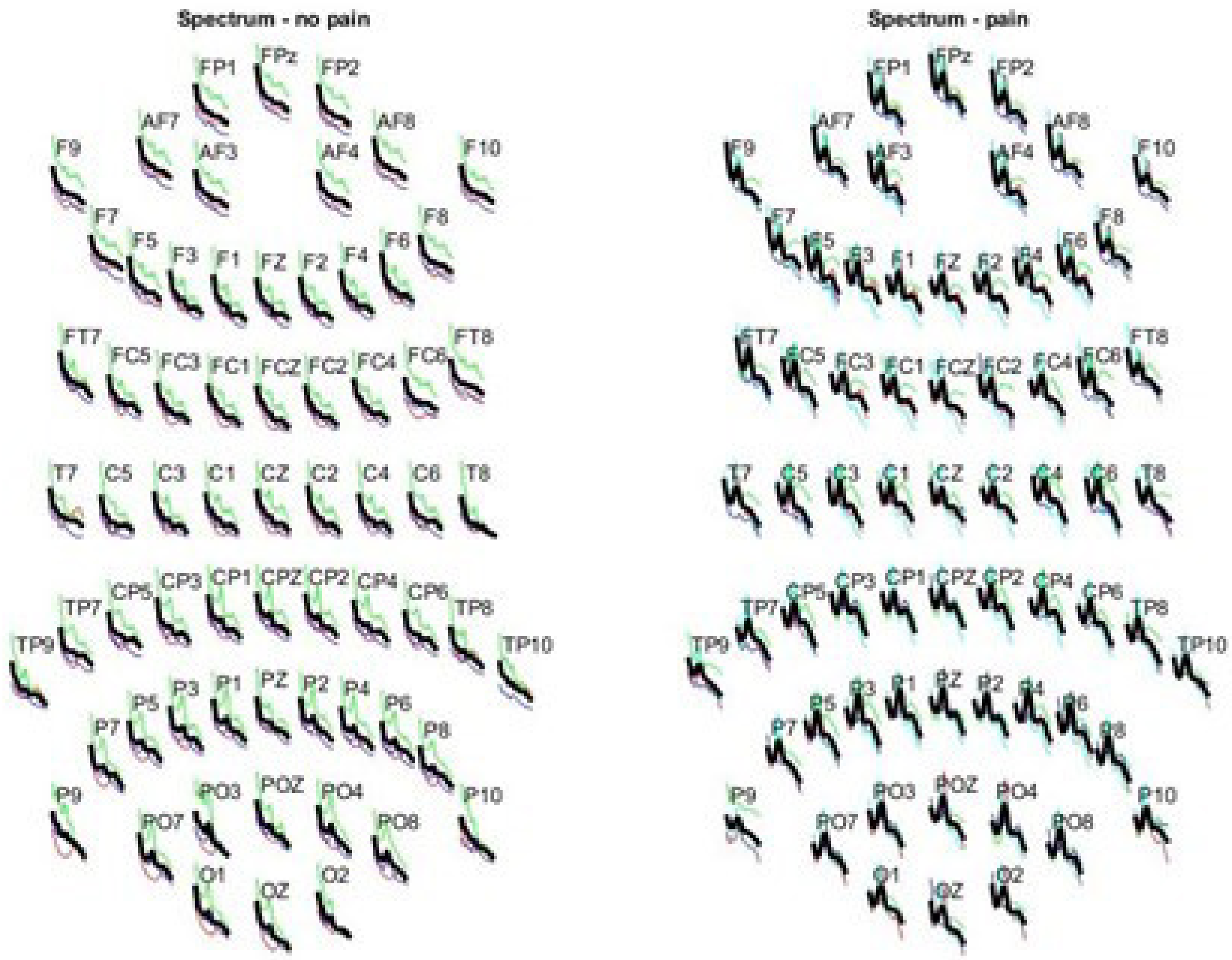

Figure 2: Scalp topography of power spectra averaged over subjects.

ages for individual subjects are shown in blue. Figure 2 shows the topography of the power spectra of every channel averaged over the subjects.

Conclusion

Due to the small size of the sample and to the presence of only one amputee subjects without PLP, it is not possible to draw conclusions of statistical significance. It is however possible to appreciate, that our results point in the same direction of literature on resting state EEG in various chronic pain conditions (Dos Santos Pinheiro et al., 2016). We observe continuous EEG dominated by alpha band oscillation (8-12Hz), widely distributed in the cerebral cortex (Fig.2). Sarnthein et al, (Sarnthein et al., 2006) related this spontaneous alpha oscillation with the concept of thalamocortical dysrhythmia, which could play a role in PLP.
In the future, research on a larger sample while encompassing a more complete repertoire of time-frequency parameters is expected to bring conclusions of statistical valence. The ultimate interest is to identify biomarkers of chronic pain as a treatment target and diagnostic tool.

Additional Notes

The pilot study presented in this abstract used a small sample of 7 subjects. During ICPLP2020 results pertaining to larger dataset (divided in amputees with pain, amputees without pain and able bodied subjects) will be presented.

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Topics: Neural basis of PLP, Electroencephaolography (EEG), neuropathic pain biomarkes

Out of the Clinic, into the Home: The in-Home Use of Phantom Motor Execution Aided by Machine Learning and Augmented Reality for the Treatment of Phantom Limb Pain

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Format: Poster

Background and aims

Phantom motor execution (PME) facilitated by augmented/virtual reality (AR/VR) and serious gaming (SG) has been proposed as a treatment for phantom limb pain (PLP)[1]. Evidence of the efficacy of this approach was obtained through a clinical trial involving individuals with chronic intractable PLP affecting the upper limb [2], and further evidence is currently being sought with a multi-sited, international, double blind, randomized, controlled clinical trial in upper and lower limb amputees [3]. All experiments have been conducted in a clinical setting supervised by a therapist. Here, we present a series of case studies (two upper and two lower limb amputees) on the use of PME as a self-treatment. We explore the benefits and the challenges encountered in translation from clinic to home use with a holistic, mixed-methods approach, employing both quantitative and qualitative methods from engineering, medical anthropology, and user interface design.

Methods

All patients were provided with and trained to use a myoelectric pattern recognition and AR/VR device for PME. Patients took these devices home and used them independently over 12 months. At the end of the treatment period, the research group conducted in-depth, unstructured and non-directive ethnographic interviews lasting from 60-90 mins with each patient in their home environments [4]. In addition, a selfreport questionnaire to identify use preferences was administered. The subjects were also asked openended questions for feedback about possible improvements of the training system. Finally, usage data stored by the training software was gathered and analyzed. The study was approved by the Regional Ethical Review Board in Gothenburg and was carried out in accordance with the relevant guidelines and regulations. All subjects provided their written informed consent to take part in the study and its publication.

Results

We found that patients were capable of conducting PME as a self-treatment and incorporated the device into their daily life routines. Use patterns and adherence to PME practice were not only driven by the presence of PLP but also influenced by patients' perceived need and social context. The main barriers to therapy adherence were time and availability of single-use electrodes, both of which could be resolved, or attenuated, by informed design considerations.

Conclusions

Our findings suggest that adherence to treatment, and thus related outcomes, could be further improved by considering disparate user types and their utilization patterns. Our study highlights the importance of understanding, from multiple disciplinary angles, the tight coupling and interplay between pain, perceived need, and use of medical devices in patient-initiated therapy.

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Topics: Treatment for PLP, phantom limb pain, neuropathic pain, augmented reality, phantom motor
execution, ethnography, user interaction design

An international, double-blind, randomized controlled clinical trial for phantom motor execution as a treatment for phantom limb pain: preliminary results

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Format: Oral Presentation

Background and aims

Despite being a known condition since a long time PLP is still poorly understood. Signs of this lack of understanding are for instance the fact that despite the large number of treatments described in the literature, none of them has proven to be decisively effective and guidelines for treating patients are currently absent [1]. This can be attributed largely to the scarcity of controlled clinical trials (RCTs) on such treatments, which additionally tend also to be of poor quality [2].
More recently, restoration of the control over the phantom limb and the exercise of such control have been hypothesized to reverse brain changes implicated in PLP [3]-[5] and preliminary evidence in support of this hypothesis has been provided by clinical investigations where a myoelectric pattern recognition (MPR) was used as a way to promote Phantom Motor Execution (PME) [6]-[8]. These studies have shown that decoding motor volition, while providing realtime feedback via virtual and augmented reality (VR-AR), is instrumental in facilitating PME, which in turns reengages the motor neural circuitry in the central and peripheral nervous systems, ultimately resulting in PLP reduction. However, previous clinical investigation providing evidence in support of PME as an effective treatment were not RCTs. Hence, they do not ensure in an appropriate way that the effects on pain relief reported are not due to any factor other than the active treatment component (PME). It is therefore necessary to obtain stronger evidence in a way that allows to isolate the effect of PME from contextual factors such as high expectations toward treatment, enthusiasm about a new technology, therapist-patient interactions, decreased negative emotions such as anxiety, to name just a few. For this reason, further evidence is currently being sought with a multi-sited, international, double blind, randomized, controlled clinical trial on both upper and lower limb amputees (Trial registration number NCT03112928) where PME is compared to phantom motor imagery (PMI). In this article we provide an overview of the current status of the RCT which is prospected to be completed by March 2021.

Methods

The RCT is currently taking place in seven counties and it involves nine clinics. Participants are randomly assigned to receive either PME or the PMI in a 2:1 allocation ratio. Power calculations on the primary outcome measure of the RCT, informed by the results of the previous clinical trial [10], have estimated that at least 60 participants were required for a 5% significance level with a two-sided Fisher's non-parametric permutation test. By considering a possible dropout rate of 10%, a total of 66 patients were initially planned. Participants in both arms of the trial receive 15 treatment sessions, after which they are followed up for a period of 6 months. Detailed description of the clinical investigation plan are described elsewhere [9]. Here we present information regarding enrolment and allocation of the patients at the time of writing.
Additionally, we report the results of one of the outcome measures gathered at the end of the 15th treatment session, namely the Patients' Global Impression of Change (PGIC) [10]. The PGIC is a single question used to identify clinically significant change by rating the patient's belief about the efficacy of treatment on a seven-point scale, ranging from a score of 1 'no change (or condition has got worse)' to a score of 7 'a great deal better'. The study is performed in agreement with the Declaration of Helsinki and under approval by the governing ethical committees of each participating clinic.

Results

Table 1 reports the list of countries and clinics taking part to the trial while table two reports the number of patients enrolled per treatment type by each investigation site. One investigation site, the Fysische Geneeskunde en Revalidatie University Hospital Gent (Begium) hasn't enrolled any patients yet due the pending approval from the local ethical committee. Further, The Shirley Ryan Ability Lab in Chicago (IL, United States) joined the trial in a later stage

Country	Investigational site	Experimental	Control
Sweden	Sahlgrenska University Hospital, Gothenburg (SUH)	10	5
	Örebro University Hospital, Örebro (OUH)	5	4
	Rehabcenter Sfären, Bräcke Diakoni, Stockholm (RCS)	5	2
Slovenia	University Rehabilitation Institute, Ljubljana (URI)	5	3
Belgium	Fysische Geneeskunde en Revalidatie University Hospital Gent, Gent (FGR)	-	-
The Netherlands	Department of Rehabilitation Medicine, University Medical Centre Groningen, Groningen (UMG)	13	7
Canada	Institute of Biomedical Engineering, University of New Brunswick, New Brunswick (UNB)	2	1
Ireland	Centre for Pain Research, National University of Ireland, Galway (NUI)	3	0
United States	Shirley Ryan Ability Lab, Chicago, Illinois (SRA)	3	1
Total		46	23

Table 1: List of countries and clinics taking part to the clinical trial. Number of patients enrolled and type or treatment allocated at the time of writing for each investigation sites are also reported.

(after the publication of the protocol). Due to an additional investigation site joining the trial the initial sample sized of 66 has been increased to 80. Figure 1 presents the flow diagram of the progress through the phases of the clinical trial where the number of patients allocated to each arm of the RCT is also reported, together with the number of patients that completed the treatment, the number of patients that dropped out and the number of patients that are currently being treated.
The preliminary results of PGIC questionnaire were analysed based on the portion of patients that completed the treatment and for which these data were available. The mean PGIC score for the experimental treatment group was 4.1 (SD =2.26) while the mean score for the control group was 3.53 (SD =2.00), although the difference was not statistically significant as tested with a two-sample t-test for equal means (p= 0.42).

Conclusions

In this contribution we present some of the preliminary results of a multi-sited, international, double blind, randomized, controlled clinical trial on a non-invasive and non-pharmacological method to treat PLP. The analysis conducted on the PGIC score on the available data revealed no statistical difference between the two groups. Additional results relative to a larger sample of patients will be presented during ICPLP2020.

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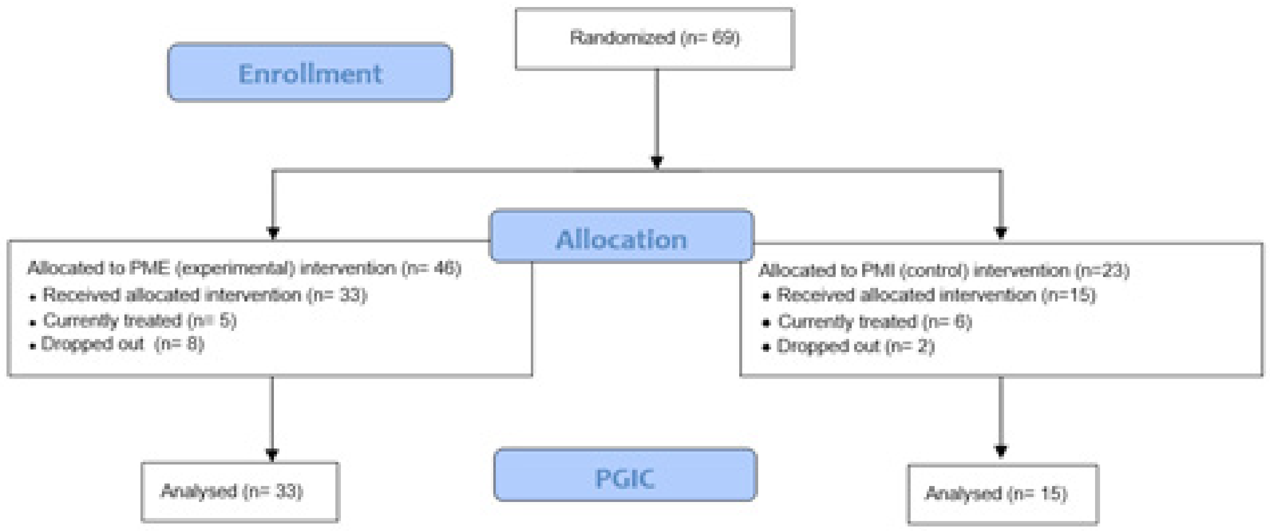

Figure 1: Flow diagram of the progress through the phases of the clinical trial showing to the left the experimental arm of the trial where patients are treated with phantom motor execution (PME), to the right the active control arm where patients are treated with phantom motor imagery (PMI).

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Topics: Treatment for PLP, non-invasive, randomized controlled clinical trial, phantom motor execution

Patients' experiences from a novel treatment of phantom limb pain

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Format: Oral Presentation

Introduction

Phantom limb pain (PLP) is a deteriorating condition that can greatly diminish quality of life. A novel treatment has been developed to relieve the PLP [1, 2]. The Phantom Motor Execution (PME) program uses augmented reality to treat PLP. The patient sees himself through a webcam on a computer screen, where a virtual limb is projected over his stump. The patient has electrodes on his remnant limb, with which he can control the virtual limb. In this way, the patient has the impression that he can actually move his phantom limb. The PME treatment will bring to life areas of the brain that have been inactive, which may have effects on their PLP, phantom sensations, self-agency, daily activities or sleep.The aim was to describe patients' experiences from undergoing phantom motor execution treatment.

Methods

A descriptive, qualitative design was used. Interviews were used to collect data and the framework approach [1] was chosen for analysis. The reporting of the study followed the COREQ checklist [2] to ensure quality. Ethical approval was obtained. Each participant provided written informed consent.
A study specific semi-structured interview guide was developed and translated in Swedish and Dutch. It covers questions about the participants' experiences of phantom limb pain and sensations, and eventual effects in daily life before, during and after treatment. There were also questions about the experiences of the content of the treatment.
Patients with amputation who have undergone the PME treatment in Sweden (n=9) and in the Netherlands (n=12) were recruited for the study. In total 21 patients were included: Mean age 56.7 years, 16 males, 5 upper (all transhumeral) and 16 lower limb amputations (9 transfemoral, 6 transtibial, 1 knee disarticulation), 19 unilateral and 2 bilateral amputations. One month after the last PME treatment, the patients were interviewed by an independent researcher.
Initally a tentative framework following the process described by Gale et al (2013) will be jointly developed by four of the authors. The framework matrix will be applied and data will be charted into it in the respective original language. There will be an openness for revisions of the framework matrix as new content may occur. Before the next step, where data will be interpreted, all text will be translated into English. The interpretation process will be performed in close collaboration between the authors.

Results

Preliminary data show that most participants experienced different degrees of relieve of their PLP due to getting command over their phantom movements and because they learned to relax their phantom limb. A few participants, however, did not experience any change in their PLP. Some participants acknowledged that they were allowed to have a phantom and had learned to perceive it as a positive feeling. Some were able to use the exercises learned during treatment in their home situation without having the PME system, while others were unable to do so without the visual stimulation of the augmented reality. Due to the therapy, the PLP was experienced as less intrusive in daily life. For some the treatment was energy consuming, due to the mental effort that was required to follow the full treatment.

Conclusions

The PME treatment seems to be a promising addition to existing treatments for PLP. Most patients experienced relieve because they learned to get control over their phantom and to regard their PL sensations as positive. However, not all patients experienced a decrease in PLP, so further research is needed to improve the PME treatment in order to be able to help these patients as well.

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The Prevalence and Risk Factors for Phantom Limb Pain in People with Amputations

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Format: Oral Presentation

Background and aims

There are varying reports on the prevalence of phantom limb pain (PLP) - a debilitating and painful condition experienced by amputees in the missing portion of their amputated limb [1]. We have earlier performed a systematic review and meta-analysis of the literature which showed that approximately 63% of people with amputations worldwide are affected by PLP [2]. The prevalence estimates varied significantly between countries. Currently, no studies could be found that were conducted to determine the prevalence of PLP in the African population, and research in this area is indicated to inform us about the prevalence and risk factors for PLP in the African population.
The primary aim of this study is to determine the prevalence of PLP in amputees living in Cape Town, South Africa. The secondary aim of this study is to identify risk factors for PLP in amputees living in Cape Town, South Africa.

Methods.

A cross-sectional study is being conducted at Tygerberg, Victoria and Somerset hospitals. These are tertiary level hospitals based within the Cape Town Metropole. Patients who have undergone limb amputations between January 2017 and February 2020 were identified from the participating hospitals. Identified patients were contacted telephonically to inform them about the study and invite them to participate. Those who consented to participating were screened to confirm the inclusion criteria and reveal the presence of any exclusion criterion. Data on the prevalence and risk factors for PLP were collected immediately using the Brief Pain Inventory and a pre-piloted customised assessment tool from those who met the eligibility criteria [3]. Patients who did not fulfil our eligibility criteria were excluded from the study.

Results.

Our sample size calculation indicated that a sample of 319 participants is required for 95% confidence level [4]. To date, we have collected data on 167 Participants. The prevalence of PLP will be analysed and expressed as a percentage with a 95% confidence interval. The association between PLP and risk factors for PLP (as identified by our systematic review) will be tested using univariate and multivariate logistic regression analyses [5]. Where association is confirmed, the strength of association will be determined by calculating the Odds Ratio [6].

Conclusions.

This study is currently in progress. The complete results of this study will be presented at the 1st international conference on PLP in Gothenburg, Sweden. The results of this study may help to strengthen efforts to optimise recovery from surgery, and to reduce both short-term and long-term suffering and disability in the amputee population. Optimising recovery after surgery and increased knowledge of the risk factors for PLP may result in reduced hospital stay, which in turn may result in reduced health-care costs. Also, increased knowledge of the risk-factors for PLP may yield more effective and targeted post-amputation care, leading to reduced disability, health care utilisation and sick leave due to chronic pain in this population.

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Associated factors of Phantom limb pain: A systematic review and meta-analysis

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Format: Poster

Background and aims
Phantom limb pain (PLP) is a highly prevalent and disabling painful sensation following amputation. To date, the exact physio-pathological mechanisms beneath the genesis of PLP remain unclear. We aim to explore potential associated factors in order to increase comprehension of the underlying mechanisms and enhance the development of effective pain preventive and treatment strategies.

Methods.
A systematic search in Pubmed/MEDLINE, WOS, Embase and PsycInfo was conducted (until December 25, 2020) following the PRISMA guidelines. We included observational studies assessing the frequency of PLP in amputees that provided data for associated factors. Screening and extraction were done by two independent researchers. We calculated odds ratios (OR) using the raw data (2 by 2 tables), then a random-effects model meta-analysis with logarithm back-conversion were performed to calculate the pooled ORs. Pre/perioperative, epidemiological, and clinical associated factors were evaluated.

Results.
We included 31 studies representing 16 360 amputees and 5 982 PLP patients. The assessed factors and pooled estimates are described in Table 1. Female sex, pain prior amputation, general anesthesia, vascular etiology, above knee amputation and comorbidities (phantom limb sensations, residual limb pain, sleep disorders, and depression) were associated with higher odds of PLP. Protective factors were prosthesis use intensity (>8 hours/day) and employment post-amputation.

Conclusions.
We identified a set of factors that underscore the multifactorial etiology of PLP. Besides, we showed potential modifiable factors (anesthesia, prosthesis use, and employment); hence, researchers, clinicians and stake holders could develop interventions to prevent and reduce the appearance of PLP.

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Effects of combined and alone transcranial motor cortex stimulation and mirror therapy in phantom limb pain: A randomized factorial trial

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Format: Oral Presentation

Background and aims

Phantom limb pain (PLP) is a frequent complication in amputees, which is often refractory to treatments. We aim to assess in a factorial trial the effects of transcranial direct current stimulation (tDCS) and mirror therapy (MT) in patients with traumatic lower limb amputation; and whether the motor cortex plasticity changes drive these results.

Methods.

In this large randomized, double-blinded, two-site, sham-controlled, 2x2 factorial trial, 112 participants with traumatic lower limb amputation were randomized into treatment groups (Figure 1). The interventions were active or covered MT for four weeks (20 sessions, 15 mins each) combined with two weeks of either active or sham tDCS (10 sessions, 20 mins each) applied to the contralateral primary motor cortex. The primary outcome was PLP changes on the visual analogue scale at the end of interventions (four weeks). Motor cortex excitability and cortical mapping were assessed by transcranial magnetic stimulation (TMS).

Results.

We found no interaction between tDCS and MT groups (F=1.90, p=0.13). All groups reported analgesic effects. In the adjusted models, there was a main effect of active tDCS compared to sham tDCS (beta coefficient=-0.99, p=0.04) on phantom pain. The overall effect size was 1.19 (95% CI: 0.90, 1.47) (Figure 2). No changes in depression and anxiety were found. We found no difference at follow-up. TDCS intervention was associated with increased intracortical inhibition (coefficient=0.96, p=0.02) and facilitation (coefficient=2.03, p=0.03) as well as a posterolateral shift of the center of gravity in the affected hemisphere (Figure 3). MT induced no motor cortex plasticity changes assessed by TMS.

Conclusions.

We found a short-term statistically significant and clinically important PLP reduction by motor cortex tDCS. These findings indicate that transcranial motor cortex stimulation might be an affordable and beneficial PLP treatment modality.

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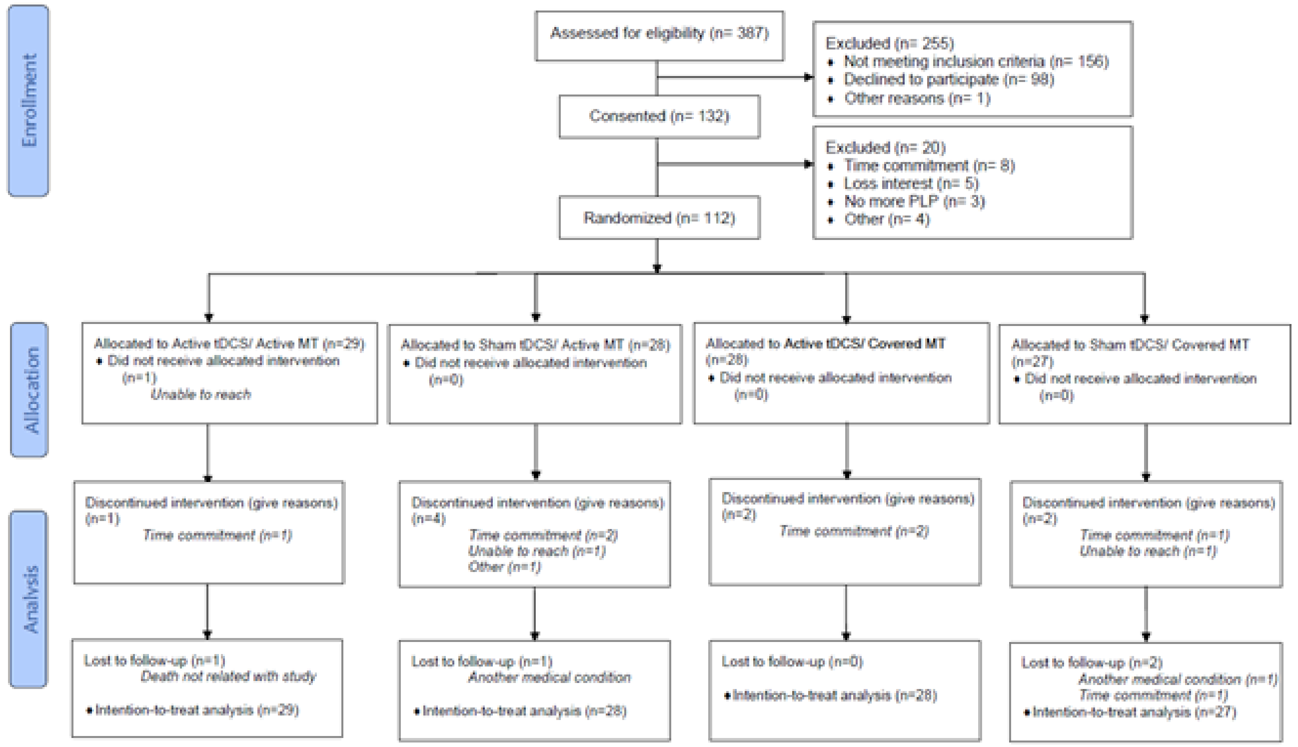

Figure 1. Study Flowchart

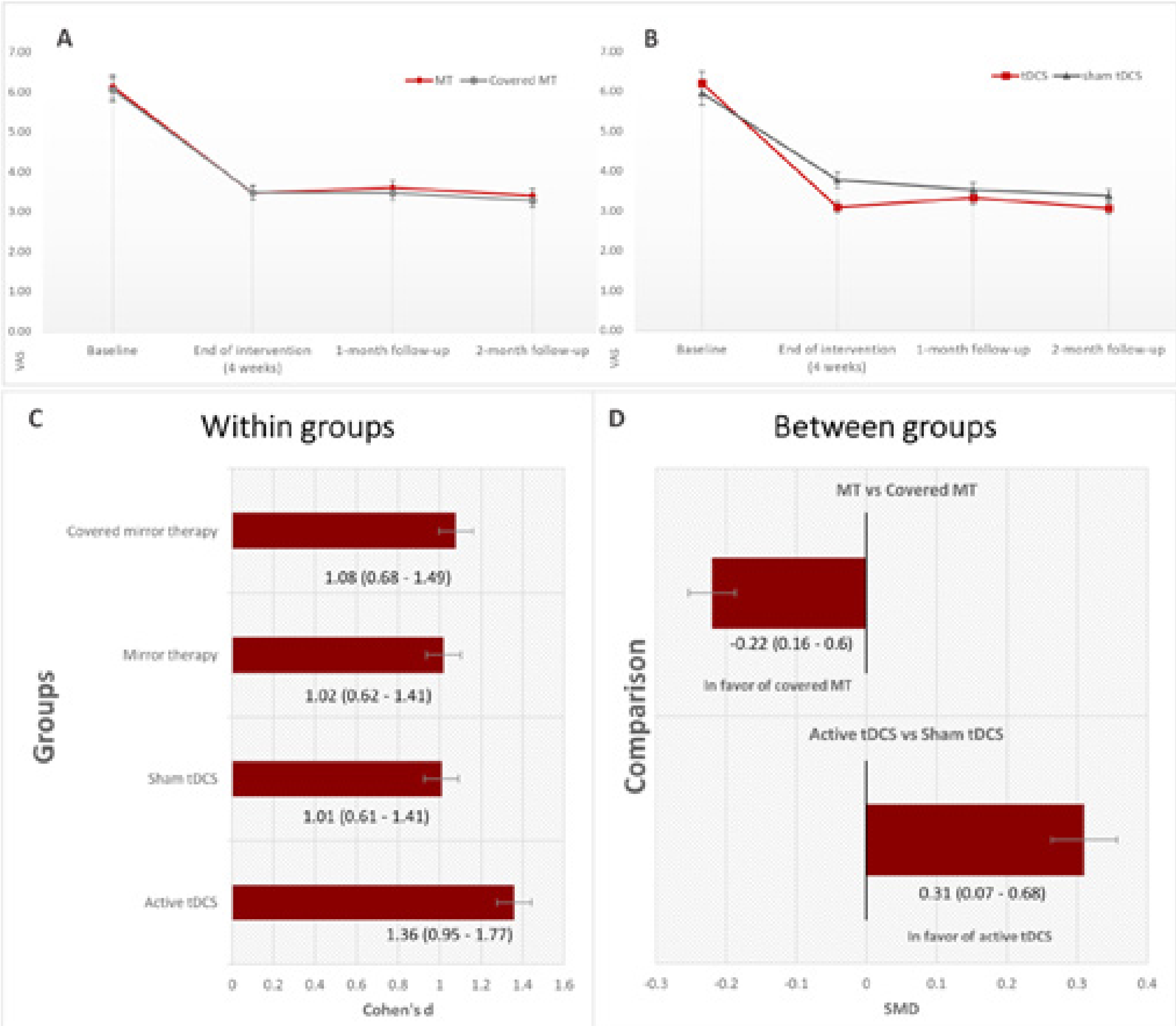

Figure 2. A and B) PLP Longitudinal changes (VAS) per group. We reported raw mean ± Standard errors. The main timepoint was at the end of intervention. Sample sizes at follow-up were: one-month follow-up=91, two-months follow-up=86. C and D) Effect sizes within (Panel C) and between groups (panel D) of different therapies on PLP (ΔVAS). Measures calculated using Cohen's d effect sizes formula and reported with 95% confidence interval. Note = bars represent standard errors.

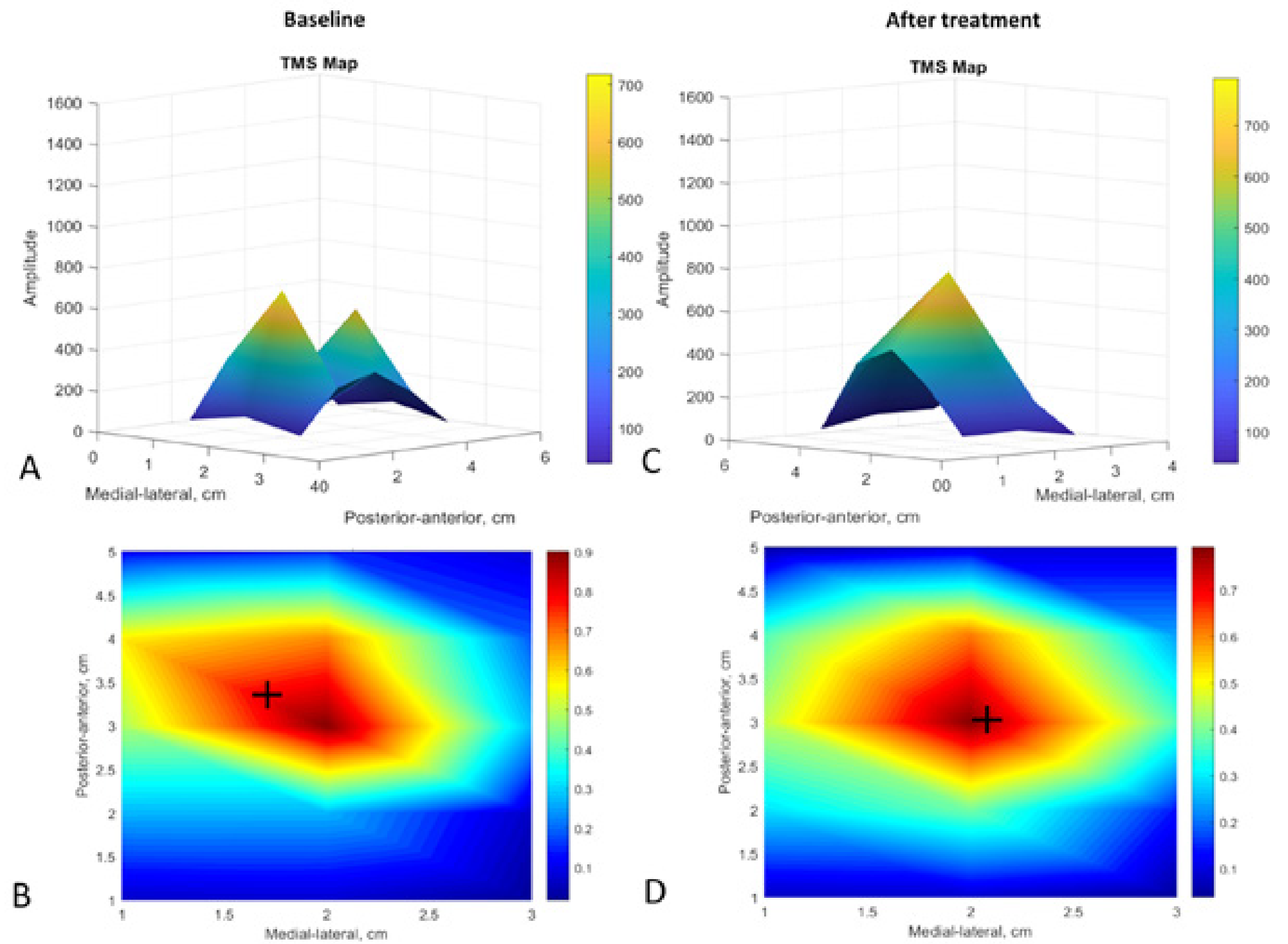

Figure 3. Cortical mapping changes after tDCS in the hand area of the affected hemisphere. At baseline (panels A and B) the cortical representation was disorganized and heterogeneous (panel A) with an anterior and medial center of gravity (COG) (panel B). After tDCS (panels C and D) the cortical representation reorganized, and the COG becomes less anterior (difference=-0.63 cm) and lateral (difference=1.05 cm).

Interplay between innovation and intersubjectivity. How therapists providing Phantom Motor Execution therapy describe and explain change?

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Format: Poster

Background and aims

The effects of Phantom Motor Execution (PME) [1] therapy on pain outcomes is being evaluated in an international randomised control trial [2]. While the focus of this quantitative investigation is on changes in pre-specified health outcomes, pain is not experienced in isolation and may be influenced by processes occurring within an interpersonal context [3]. Apart from an observer being impacted by the pain in others [4], [5], the presence of the other may impact on the experience of pain [3]. How the introduction of a novel rehabilitative tool to this complex scene may influence rehabilitative outcomes has not been extensively examined. This study employed qualitative methodologies to explore subjective perspectives on the PME and elicit the therapists view on how affect, motivation, behaviour, and interpersonal context may have impacted outcomes within the context of a unique and novel rehabilitative process.

Methods

A Framework Method [6] was used to explore therapists` (N=11) subjective experiences of delivering PME treatment, meanings attached to it, and the role of intra- and interpersonal factors that may have mediating effects. Therapeutic alliance was of particular interest in this study. Purposive sampling strategy was used and therapists working with the PME system were recruited. Data was collected with the use of semi-structured, online-based interviews. An interview guide was informed by a framework of contextual factors modulating therapeutic outcomes [7]. A combination of inductive and deductive analytical approaches was used. After developing a working analytical framework, the analysis was completed with the use of NVivo software [8]. Trustworthiness and credibility were ensured by a systematic approach and involvement of a multidisciplinary research team. Standards for Reporting Qualitative Research were used to ensure rigor [9].

Results

In the views of the therapists, the PME therapeutic effects took place within a complex system of interactions between the key actors: therapist, patient, and PME device. This 3-way interaction was identified as an overarching construct tying the four themes together, and formed the context for describing change and an interplay between innovation and intersubjectivity. The perceived therapeutic effects (theme 1) extended beyond those initially hypothesised for the PME therapy [10] and highlighted the need to consider diverse conceptualisations of success and account for surprising effects. Mediating role of the key actors and context (theme 2) were recognised as important by the participants. Therapeutic effects could have been influenced by an array of facilitating and impeding intra- and interpersonal variables. Therapeutic relationship was described in terms of a journey (theme 3) and perceived as both a cause and a consequence of therapeutic effects. Therapists highlighted that the PME rehabilitative context was an opportunity for collaboration, communication, and bonding. Potentials inherent in the system and future directions for PME (theme 4) were highlighted by the participants, with customisation of the system solutions and their enabling aspects being viewed as the strongest points of this novel approach.

Conclusions.

This qualitative investigation pointed to intra- and interpersonal factors that should be considered in clinical implementation of novel rehabilitative tools and their role for therapeutic effects. The need to account for context and intersubjectivity is highlighted and directions for future studies are suggested.

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PhantomAR - Developing a wearable Augmented Reality for treating phantom limb pain

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Format: Oral Presentation

Background and aims

Phantom limb pain (PLP) is a restrictive condition during which patients perceive pain in their non-existent limb, incapacitating them on several levels. Mirror Therapy, during which patients look into a mirror reflecting their healthy limb on their amputated site, has proven to alleviate that pain [1]. Modern methods to address PLP shift the focus on the use of commercial VR and AR systems. VR was already an emerging field with commercial devices for home use such as Oculus Rift or HTC Vive [2]-[4]. Augmented reality (AR) applications typically used cameras to project the augmented image of an able-bodied person onscreen [5], [6]. To further liberate users from a fixed position, PhantomAR aims to leverage the unique capabilities of wearable AR technology and address the limitations of traditional mirror therapy.

Methods

We developed a game-based AR assistive therapy on the Microsoft Hololens 2. The patient's residual limb is augmented by a superimposed virtual arm that can be controlled completely independent from the movements of their healthy limb via EMG electrodes. Patients can manipulate virtual objects using both their healthy limb, and the virtual arm, without being restricted to a sitting position at a table. The patient's upper arm and stump are tracked via gyroscope and accelerometer within two MyoArmbands. The therapy is integrated into a game-based scenario developed together with therapists to stimulate motivation over several therapy sessions. Several parameters for therapy outcome are tracked and can be monitored remotely. 10 able-bodied experts (7 clinicians and 3 engineers), that had one of their hands covered, evaluated the technical characteristics and usability of the PhantomAR prototype with the System Usability Scale (SUS) and a user centered survey.

Results

PhantomAR scored 72.5 in the SUS, representing high usability and acceptability. Wearing the Hololens 2 felt comfortable and users had fun interacting with virtual objects within the actual environment, which were perceived as real. Haptic feedback supported the immersion of grasping objects and controlling the interface was intuitive. However, more feedback mechanisms, apart from haptic feedback on object interactions, should be incorporated. Ownership of the overlaid virtual arm was rated highly, though, agency could still be improved. No cybersickness was reported.

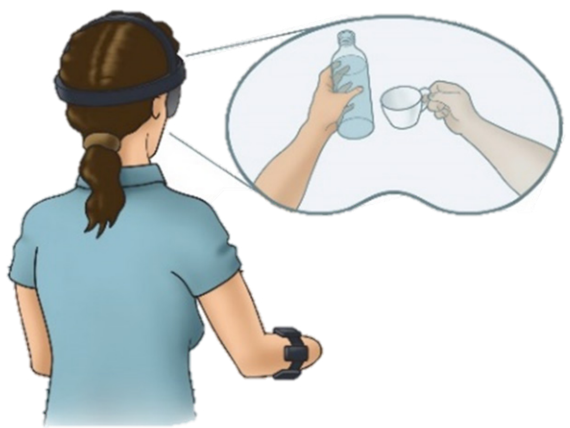

Figure 1 Field of view of a patient interacting with virtual objects.

Conclusion

In an iterative assessment process, we first evaluated the functionality with relevant groups of experts, before piloting the system on patients. Currently, PhantomAR is exclusive to transradial amputees, but in the future we plan extended it to transhumeral amputees as well. With PhantomAR we developed a wearable assistive therapy tool that not only liberates users from a restrictive position at a table, but also allows them to perform bi-manual tasks and freely interact with virtual objects as well as objects found in their actual environment. We expect this type of immersive AR rehabilitation to positively impact outcomes on pain scores, hand/arm functionality, range of motion and motivation to perform therapy even in absence of a therapist.

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Topics: Treatment for PLP, Augmented Reality, Mirror Therapy

Platform combining Transcutaneous Electrical Nerve Stimulation and Virtual Reality for Neuropathy

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Format: Oral Presentation

Background and aims

Pain is not a single dimension phenomena, but rather an outcome of sensory, affective and cognitive processes[1]. In particular, Phantom Limb Pain (PLP) is a chronic pain syndrome which terribly affects the life of many amputees. The responsible mechanisms for this condition are still under investigation, but both peripheral and central nervous processes are considered to play a role[2].

To treat PLP, some approaches target the peripheral nervous system[3], [4]. Transcutaneous electrical nerve stimulation (TENS) is among these and finds its theoretical background in the 'pain-gate' mechanism[5]. However, to obtain effective results with TENS daily sessions for weeks are necessary[6], benefits are not immediate[7] and are often not long-term[8]. This could affect the patients' motivation, which is crucial for positive outcomes[9].

On the other side, others have addressed the central mechanisms of PLP. In particular, given the cortical reorganization found in the sensorimotor cortex (SMC) after an amputation[10], many have used training with visual feedback to revert this maladaptive phenomenon, thanks to a re-established coherence in the limb representation within the SMC[11]. This approach has shown promising results in reducing PLP[11] and the advent of Virtual Reality (VR) has made it easier to manipulate these perceptions.

However, the effectiveness of a technology that targets together central and peripheral contributions of PLP has not been shown yet. We developed a new multimodal platform, combining TENS and immersive VR, hypothesizing that coherent visual-tactile nerve stimulation can positively impact PLP. Before testing this system for PLP, we validated our technology exploring whether it could enhance the naturalness/pleasantness of the TENS and induce embodiment of a virtual leg with synchronous visual stimulation[12] in VR.

Methods

Six healthy subjects participated to this study. First, we performed a calibration to set the stimulation parameters eliciting somatotopic sensations on dorsal and plantar areas of the feet. Four electrodes were placed on the ankle level close to tibial and peroneal nerves. Subsequently, each subject performed three 5-minutes conditions: VR+TENS synchronous (SYNC), VR+TENS asynchronous (ASYNC) and TENS. In VR conditions, subjects were immersed in a beach scenario. In the SYNC condition, the stimulation on their feet had increasing rumps of intensity when the waves were touching their foot. In the ASYNC condition the visuo-tactile stimulations did not match. During TENS condition participants received only stimulation. We replicated this paradigm with two transfemoral amputees. Eliciting somatotopic sensations was not possible due to the amputation level, hence we used a remapped stimulation on their stump.

Results

The calibration results showed that we elicited somatotopic sensations in healthy subjects. SYNC condition resulted in higher pleasantness ($p=0.005$) and naturalness ($p=0.0001$) compared to ASYNC and TENS, while the intensity of the stimulation was perceived similarly in all conditions. Embodiment scores were higher in the SYNC condition ($p=0.01$) compared to ASYNC. Results for amputees showed the same trend as for healthy subjects.

Conclusions

This study showed that combining synchronous electrical stimulation and visual stimuli in VR is able to enhance embodiment of a virtual leg and to increase the pleasantness and naturalness of artificial stimulation. Our results show the feasibility of our system to be tested to treat PLP and other neuropathic conditions.

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Topics: Virtual Reality, Transcutaneous Electrical Nerve Stimulation, Amputation, Embodiment, Neuropathy, Phantom Limb Pain

Filling the gap: mapping the facial homunculus in one-handed individuals and controls

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Format: Oral Presentation

One of the most striking demonstrations of cortical remapping in humans occurs in the primary somatosensory cortex (S1) following upper-limb amputation. Research in amputees has suggested the 'invasion' of the missing hand area by lower face inputs (presumed to be the hands' cortical neighbour) [1]. The proposed consequences of lower-face-to-hand remapping are maladaptive, with the resulting mismatch across bodily inputs thought to underly phantom limb pain (PLP) [2].
However, we have demonstrated that mouth remapping in amputees is smaller than previously thought, with localised shifts that do not encroach the missing hand area [3]. Furthermore, mouth-to-hand remapping is found in individuals with congenital hand loss (hereafter one-handers), who do not experience PLP [4]. In addition, facial topography in humans is currently debated. Contrasting results report either an upright [5], or inverted [6] facial representation. As such, the extent of face-to-hand remapping and its perceptual correlates are unclear.
We aim to fill this gap in the homunculus by investigating the topographic organisation of the face within the sensorimotor cortex. Using univariate and multivariate approaches we first assessed facial topography (e.g. upright verses inverted representation) in two-handed controls. We then examined the extent of face-to-hand remapping in amputees and one-handers. Thirdly, we investigated perceptual correlates by measuring PLP and compensatory behaviour (e.g. using the mouth to open a packet of crisps). We hypothesised that facial remapping co-occurs with compensatory behaviour in one-handers, resulting in an adaptive relationship between remapping and behaviour. Conversely, we hypothesise little evidence for face-to-hand remapping in amputees, with no relationship to behaviour or PLP.
Using fMRI we scanned ~15 amputees, ~20 congenital one-handers and ~20 two-handed controls. We used an active paradigm previously shown to reliably produce finger-selective maps in S1 comparable to passive stimulation [7]. All participants were instructed to move different parts of their face (forehead, nose, lips and tongue), and their thumb (if able). Two independent regions of interest (ROIs) were defined for the sensorimotor hand and face areas using an anatomical atlas.
In controls, using a univariate analysis, we found a facial map with a consistent upright gradient of facial-part selectivity within the sensorimotor cortex (Fig 1). We next used Representational Similarity Analysis [8] to characterise the representational structure within our two ROIs. Preliminary results suggest clear multivariate dissimilarities between face parts (i.e. facial information) within the face ROI in controls bilaterally. These results indicate that this cortical area can distinguish between face movements, validating the use of our active paradigm. Significant facial information was also found in the deprived sensorimotor hand ROI, however, there was no difference between controls and amputees. Data for congenital one-handers is currently being processed for analysis. Correlations between various fMRI remapping (e.g. RSA distances) and behavioural measures will be presented.
These results indicate that the lower face and the hand are not direct cortical neighbours, and leads us to question how much the relative spatial organisation between the face and the hand differs between controls and amputees.

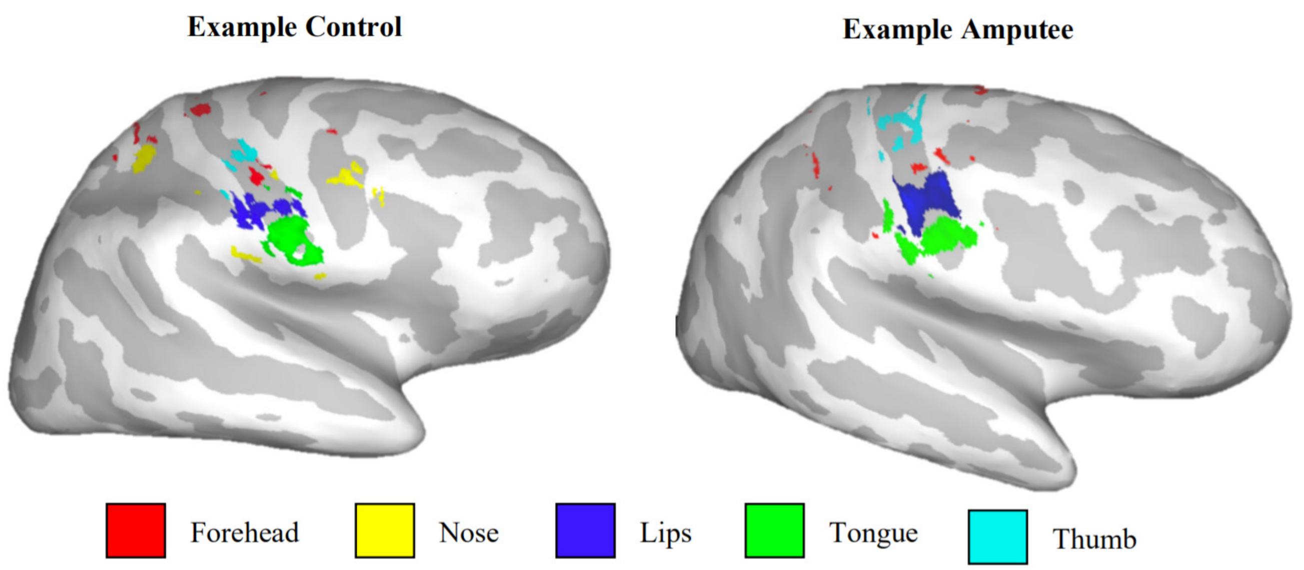

Figure 1. Univariate activity maps (face part > other face parts) in the non-dominant/deprived hemisphere, showcasing an upright facial topography in an example two-handed control (all thresholds Z > 6.1) and acquired amputee (all thresholds Z > 2.3). Non-dominant/phantom thumb activity are contrasted versus rest. All maps initially cluster-based thresholded at Z > 2.3, with a pre-threshold mask of Broadmann areas 1-6 taken from the Harvard Cortical Atlas.

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Phantom limb movements: kinematics and EMG

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Format: Poster

Background and aims

After limb amputation patients experience the possibility to perform movements with their phantom hand [1], [2]. Commonly reported voluntary movements of the phantom arm/hand include reaching out to grab an object, making a fist, and moving one or more fingers individually [3]. However, the nature and mechanisms underlying phantom limb movements remain poorly understood [4]. We report on a series of studies aimed at providing a quantitative analysis of phantom arm movements at the kinematic level and the muscle level.

Methods

Kinematic analysis of phantom movements. The kinematic level refers to the evolution in time of the joint angles and hand configuration. While phantom arm/hand kinematics cannot be tracked directly, phantom trajectory and velocity can be measured indirectly by tracking assimilation/interference effects induced by phantom movements on intact arm movements. We present data showing the potential of this approach ("phantom mocap") for indirectly tracking phantom movement kinematics. Electromyographic analysis of phantom movements. The muscle level refers to the pattern of muscle activity required to produce phantom movements. Using superficial electrodes positioned over the stump (and intact arm), we show the potential of EMG data, in combination with information theoretic approaches [5], to reveal distinctive pattern associated with specific movements of the phantom hand and fingers.

Results

Our results suggest that at both the kinematic level and the muscle level, performed phantom arm movements reflect the operation of the same mechanisms governing execution of intact hand/arm movements.

Conclusions

These results have both theoretical and clinical importance. From a theoretical perspective, they suggest that phantom limb movements are best conceptualized as real movements of a dematerialized arm/hand rather than motor illusions. From a clinical perspective, phantom limb movements may be important for developing new methods that afford more intuitive control over the multiple degrees of freedom of multi-articulate prosthetic hands. An important goal for future research is to determine the exact sequence of operations across kinematic, muscle, and cortical levels that lead to the generation of phantom movements.

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Topics: Phantom motor execution

A four phase therapy concept together with a vibrotactile feedbacksystem reduces phantom pain and improves gait stability

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Format: Poster

Background and aims

By now no holistic treatment and no medical device is found that treats phantom pain by enlarging the embodiment of the user. Often only symptomatic treatments are applied.

Method

An innovative sensory feedback technology is incorporated it in the leg prosthesis, which feeds back information to the brain.
The modular prosthesis system consists of a sensor sock, which detects rolling movement through a set of vibrotactile actuators. The information from the ground is then transmitted non invasive to the nerves of the leg and finally to the brain. As a result, the brain doesn't have to search for the lost limb, the prosthesis is more easily accepted by the body, and the phantom pain goes away. The system is applied together with a four phase therapy concept where in case of phantom and neuroma pain a reconstructive surgery is done first and post-op, the sensory feedbacksystem is applied.

Results

The pain reduction using a sensory feedbacksystem is highly significant for 2 groups of amputees: A group who had TSR before (indication: the pain was so immanent that a prosthetic care was not possible) as well as a group of user testing the system via an assessment (clinical tests). In both groups also the stability has been improved significantly.

Conclusions

A sensory feedbacksystem has an important role reducing phantom pain for amputees. Together with targeted sensory reinnervation it helps to rise quality of life of amputees dramatically and helps to minimize pain. But also amputees benefit from a feedbacksystem without a surgery to feel the undergroud again and to enlarge the embodiment when a user, integrates a prosthesis much more to the body.

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Changes in brain activity and pain inhibition as possible predictors for phantom limb pain in leg amputees - a longitudinal pilot study

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Format: Oral Presentation

Background and aims

Phantom limb pain (PLP) describes chronic pain that occurs after severe peripheral nerve injury or amputation in the missing body part in up to 80% of amputees [1, 2]. PLP has been associated with cortical reorganization [3]. Additionally, patients suffering from chronic pain show an impaired pain-inhibitory system [4]. However, the causality of the neuronal and perceptual changes regarding PLP is still unclear. Therefore, we aim to examine brain excitability and inhibitory control in 40 leg amputees to determine predictors of phantom limb pain in a longitudinal study.

In this analysis we focus on (1) whether persons with high brain excitability and (2) reduced inhibitory control are more prone to develop phantom limb pain over time.

Methods

So far, we examined five leg amputees (2 women, 3 men, mean age 40.6 years (SD = 9.91) immediately after the amputation and 1 year later, when one participant suffered from phantom limb pain and 4 were pain-free. To assess inhibitory pain control we used stress-induced analgesia (SIA) where stress induction was achieved by exposure to a mental arithmetic task accompanied by white noise [5]. Pain inhibition was determined by comparing pain thresholds as well as pain intensity and unpleasantness ratings of a suprathreshold pain stimulus before and after the stress experience. Pain intensity and unpleasantness were assessed using a numerical rating scale (NRS) ranging from zero to ten.

Brain changes related to the painful heat stimulation were examined during functional magnetic resonance imaging (fMRI) in a block design so far in N = 3 patients (1woman, 2 men, mean age M = 42.3 (SD = 9.5) of whom one person developed no PLP and 2 patients developed PLP. To investigate changes in pain processing after amputation stimulation was applied over the knee of the intact leg and over the groin ipsi- and contralateral to the side of the amputation.

Results

The preliminary results of this study show changes in pain inhibition after amputation. An effect of the stress induction on pain perception (SIA effect) was found at T1. The ratings of pain intensity of the suprathreshold pain stimulus decreased during the stress experience with a ean difference of M = -.9 (SD = 1.95). This SIA effect on intensity was not seen at T2. Additionally, a SIA effect was found in pain thresholds, which increased during the stress experience with a mean difference of M = .5 mA (SD = .09) at T2. Pain threshold as well as suprathreshold pain unpleasantness and intensity were not significantly associated with pain in the early period after amputation nor predictive of later pain.

The changes in brain activity in the course of PLP between the first measurement, early after amputation, and the second follow-up measurement one year after t1 were calculated. The two leg amputees, who reported the development of PLP, showed increased brain activation at T2 compared to T1 in S1 contralateral to the amputation during heat stimulation of the groin of the amputated side. No difference in brain activation in S1 could be found in these patients while they were stimulated on the intact side of the groin. The patient without PLP showed no difference in brain activation in S1 during stimulation, independent of the stimulated region.

Conclusions

In summary, inhibitory pain processes as assessed by SIA were unrelated to phantom pain and its development, although our data are based on a small sample. The results of the longitudinal fMRI data of the leg amputees show changes mainly in the activation of the somatosensory cortex. These results are in accordance with findings of altered activation in S1 in amputees suffering from PLP [6,7]. Larger sample sizes are needed to confirm and extend these preliminary findings.

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Topics: PLP, brain activity, longitudinal changes

"I Did Not Expect the Doctor to Treat a Ghost": Chronic Phantom Limb Pain in Military Amputees, 1914-1985

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Format: Poster

Background and aims

The First World War [FWW] led to the largest amputee cohort in history, with over 41,000 amputee veterans in the UK alone. Current estimates suggest up to 85% of military amputees suffer some form of chronic post amputation pain and applying this estimate to the FWW cohort raises the possibility that up to 33,000 men may have had chronic pain as a result of their injury, in some cases for the rest of their lives. However, this possibility and its potential impact on quality of life has received little attention from academic researchers.
This study is based on a systematic review of the professional medical conversation around chronic post amputation pain, including residual limb, phantom limb and neuropathic pain, in FWW veterans for the years 1914 to 1985. It focuses on the discussion around treatments and aetiologies of phantom limb pain in this cohort, the attitudes of clinicians towards these patients, and investigates how these developed over the 20th century. The results of the review have been linked to medical records held in The National Archives, tracing FWW amputee veterans over the same period, in order to investigate the impact chronic phantom limb pain had on specific individuals in their postwar lives.

Methods

A systematic search of the two principal medical journals in the UK, The Lancet and the British Medical Journal, was carried out for the years 1914 and 1985. Results were screened using Covidence for all references to chronic post amputation pain conditions in FWW ex-servicemen injured as a result of active service. Data were analysed in NVivo.

Results

The search strategy retrieved 9,809 results. Two stages of screening reduced this to 203 relevant articles. Forty-five of these directly related to the aetiology or treatment of phantom limb pain, appearing from 1919 to 1982. The articles reveal the uncertainty around the cause and cure of phantom limb pain from clinicians, and included 12 groups of suggested treatments within six major aetiologies.
The National Archives files were searched for FWW ex-servicemen with chronic post amputation pain and 100 relevant individuals were found. Of these, 8% reported or received treatment for phantom limb pain across the years 1921 to 1982, including one individual who reported phantom limb pain for over 25 years.

Conclusion

A systematic search of the British Medical Journal and The Lancet for the years 1914-1985 retrieved 45 references to conflict-related phantom limb pain in veterans. The data extracted for further analysis included theories on pain aetiology, clinical assessment and attitudes, terminology and patient impact.
This review is part of a wider collaborative project, combining research methods from clinical medicine with the humanities. Despite the century between them, injury patterns and post-acute treatments for amputation in the First world War and the most recent conflicts in Iraq and Afghanistan are remarkably similar and it is hoped the findings of this project will clinically relevant and of use in strategic planning for long-term pain conditions for today's and future blast injury cohorts.

Funding

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A Case Series on Ultrasound-Guided Botulinum Toxin Nerve Blocks for Refractory Phantom Limb and Residual Limb Pain

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Format: Poster

Background and aims

Phantom limb pain (PLP) is a type of neuropathic pain that occurs after amputation. The reported incidence varies from 45-85% of amputees and can be very limiting for some patients.[1] The etiology of PLP is thought to be related to peripheral nerve injury, neuroma formation and cortical reorganization of the central nervous system.[2] There are many treatments for PLP including medications, therapies and injections but it is yet unclear how to best treat refractory PLP.

Methods

This was a case series of two patients with refractory PLP who were treated by the amputee care team at a tertiary academic medical center. Approval for this descriptive study was obtained through the VA Central Institutional Review Board (IRB).

Results

Case #1: A 78-year-old male with type 2 diabetes mellitus and peripheral vascular disease required a left transfemoral amputation due to foot gangrene. 3 years after surgery he began experiencing residual limb pain and PLP up to 10/10, worse at night. He trialed a TENS unit, capsaicin cream, acetaminophen and gabapentin, but his pain was not controlled. He underwent an ultrasound-guided left lateral femoral cutaneous nerve block with 1% lidocaine and depomedrol. He had brief resolution of pain but 3 months later the pain had returned and was rated 10/10. The left lateral femoral cutaneous nerve block was repeated with 50 units of incobotulinumtoxinA and 1% lidocaine. His pain was decreased to 4/10 immediately after injection but lasted only 1 week. He went on to peripheral nerve stimulator placement with improved pain relief.

Case #2: A 69-year-old male with a past medical history of type 2 diabetes mellitus, peripheral vascular disease, and end stage renal disease on dialysis underwent a right transfemoral amputation due to an infected foot wound. One month after surgery he was experiencing significant PLP that limited his progress with therapy, rating the pain 8/10. Multiple medications did not control his pain. He underwent an ultrasound-guided right lateral femoral cutaneous nerve block with 1% lidocaine and 50 units of incobotulinumtoxinA. His pain went down to a 2/10 immediately after the injection. His lowest pain level was 0/10 but in later weeks averaged 5/10.

Conclusions

These cases suggest good support for the role of nerve blocks to reduce or eliminate PLP in individuals with lower limb amputations. The individuals in these cases had failed to respond to other interventions. Botulinum toxin and lidocaine have provided relief that starts relatively quickly and that can continue for up to three months. Furthermore, these nerve blocks have led to the use of peripheral nerve stimulation that has also provided significant relief. No adverse events in this small sample occurred. A case-controlled study with greater numbers of subjects would help to confirm these findings and clarify the most effective implementation of these techniques.

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Topics: phantom limb pain, nerve blocks

Early Experience of Targeted Muscle Reinnervation for Phantom Limb Pain in Lower Limb Amputations

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Format: Poster

Background and aims

Targeted Muscle Reinnervation (TMR) for the management of lower limb phantom and neuroma pain is a new application of an existing technique. Initially developed in the upper limb for myoelectric prostheses control, TMR was also incidentally found to improve pain outcomes. [1]

The technique can therefore be translated into the amputated lower limb where the primary issue is pain. A published RCT has shown improved phantom limb pain in major limb amputees at one year [2], however; little is known about the early post-operative journey after TMR. Introduced as a novel technique at a single centre in early 2019, we present our early experience for TMR use in pain management for lower limb amputee patients.

Methods

Prospective analysis of adult patients undergoing primary or secondary TMR for pain; neuroma, phantom limb pain or chronic pain - performed by a single surgeon. A posterior approach was used; sensory nerves were identified, divided and co-apted onto newly divided motor nerves (identified with nerve stimulator) using nylon microsutures. Standard wound closure.

Primary outcome data: pain scores (visual analogue score, VAS) and quality of life (SF-36). Anaesthesia type, general complications and analgesic use were also noted. “Total Pain Burden” (TPB) assessment was established for assessment of percentage change in pain burden from pre to post-op.

Results

Thirty-three consecutive patients were included: 21 male, 12 female. Four serving military personnel, two veterans and 19 civilians. Average age 49 (14-74). A majority were performed under general or spinal anaesthetic, with one case under local (LA). Twelve trans-femoral, 21 trans-tibial. Of these, six were primary amputations. 100% of patients were pleased they had the surgery and feel their TPB was reduced post-operatively.

Conclusions

Targeted muscle reinnervation has improved pain management in our lower limb amputee patient cohort. Patients should be warned about the potential for pain fluctuations within the post-operative period. Further outcome data for 1 year is awaited. The procedure may be performed under LA in select cases.

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Altered resting-state functional connectivity after sensory feedback training in amputees with PLP

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Format: Oral Presentation

Background and aims

After an amputation, the majority of patients experience phantom limb pain (PLP), a chronic condition difficult to treat. As a promising treatment option, sensory feedback has been suggested to relieve PLP [1]. At the neural level, PLP has also been associated with changes in cortical organization and connectivity [2, 3]. Chronic pain conditions in general have been associated with aberrant activity within nodes of the salience network [4], which includes the anterior cingulate cortex (ACC) and the insula. Consistent with other conditions of chronic pain, PLP has been linked to increased activity in the anterior and posterior cingulate cortex [5]. In this study, we investigated whether reductions in PLP after sensory feedback training would be accompanied by altered functional resting-state connectivity of the somatosensory cortex and brain regions known to be involved in salience detection and pain processing.

Methods

Six upper left-limb amputees with chronic PLP received an intensive treatment directed at controlling phantom-limb movement for 16 days, as previously described [6]. Briefly, muscle contractions at the residual limb were used to provide visual and tactile feedback during phantom movements in order to diminish PLP intensity. Before and after the training period, we collected pain intensity ratings and resting-state functional magnetic resonance imaging data. After showing that the training indeed reduced the pain intensity [6], we now explored changes in resting-state functional connectivity from the baseline to the post-training session. Given the evidence suggesting a central role of the salience network in chronic pain, we focused on changes in connectivity between the sensorimotor and salience network and explored seed-to-voxel connectivity patterns between six nodes of these networks (left lateral, right lateral, and superior node of the sensorimotor network as well as ACC, left, and right anterior insula of the salience network) and the rest of the brain.

Results

The sensory feedback training reduced the pain intensity ratings by on average 25.1%. While no significant network interaction was observed between the sensorimotor and salience network from the pre- to the post-training session, seed-to-voxel connectivity analysis revealed an increased functional connectivity between the ACC and a cluster encompassing parts of the right temporal pole and superior temporal gyrus (i.e. contralateral to the amputation). All other analyses did not yield any significant changes.

Conclusions

To the best of our knowledge, this is the first study analyzing changes in resting-state functional connectivity after a PLP-reduction treatment in amputees. We observed that a reduction of self-reported pain intensity was paralleled by increased resting-state coupling between the ACC, a major node of the salience network, and a cluster located in the temporal lobe, which together are part of an emotional system [7]. This finding may reflect increased interoceptive awareness [8], which has been found to correlate negatively with symptom severity in a number of chronic pain conditions [9]. Also, our findings are in agreement with previously reported changes in gray matter in the ACC and contralateral superior temporal gyrus in amputees reporting high compared to those reporting lower levels of PLP [10].

Acknowledgements

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Topics: phantom limb pain; plasticity; resting-state functional connectivity; salience network

Prostheses with somatosensory feedback reduce phantom limb pain and increase functionality

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Format: Oral Presentation

Background and aims

Phantom limb pain (PLP) is still difficult to treat. Based on ideas to modify cortical reorganization [1,2], we developed prostheses with somatosensory feedback for hand and lower leg [3,4]. The aim was to reduce PLP, increase the functionality of movements with the prostheses, and reduce cortical reorganization.

Methods

18 hand and 14 lower leg amputees were equipped with simple-to-use feedback prostheses. Feedback was provided as electrocutaneous stimulation on the stump with the idea to reduce functional reorganization in the primary somatosensory cortex (S1). Patients received two weeks of intensive training with theses prostheses. We recorded PLP, and functionality of prosthesis use, and assessed cortical reorganization using MEG and fMRI.

Results

We found reduced PLP, increased functional use of prostheses, increased satisfaction with the prostheses both in hand and lower leg amputees. The reduction of PLP was not related to functional reorganization in S1.

Conclusions

The use of prostheses with somatosensory feedback reduces PLP and increases functional use of prostheses. This is an easy-to-use way to reduce PLP.

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Topics: Treatment of PLP – non-invasive; neural basis of PLP – neurophysiological studies

A non-invasive sensory feedback system in hand prostheses used in everyday life

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Format: Oral Presentation

Background and aims

Sensory feedback in hand prostheses is lacking but wished for [1]. Many amputees experience a phantom hand map (PHM) on their residual forearm. When the PHM is touched, it is experienced as touch on the amputated hand [2, 3]. The aim was to evaluate how forearm amputees experienced a non-invasive sensory feedback system that transfer somatotopically matched sensory information via the PHM.

Methods

A longitudinal cohort study including seven forearm amputees. A non-invasive sensory feedback system [4] was used over four weeks in daily life. A mixed method was used for analysis, including quantitative tests and interviews. A directed content analysis with predefined categories: sensory feedback from the prosthesis, agency, body ownership, performance in activity and suggestions for improvements was applied.

Results

The results from interviews showed that sensory feedback was experienced as a feeling of touch which contributed to an experience of completeness. The ability to feel and manipulate small objects was difficult and a stronger feedback was wished for. Phantom pain was alleviated in four out of five patients.

Conclusions

A non-invasive sensory feedback system for hand prostheses was implemented in home environment. The qualitative and quantitative results diverged. The sensory feedback was experienced as a feeling of touch which contributed to a feeling of completeness, linked to body ownership.

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Topics: Sensory feedback, prosthetic hand, phantom hand map

Magnetoencephalographic neurofeedback training to reduce phantom limb pain

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Format: Oral Presentation

Background and aims

Phantom limb pain has been attributed to maladaptive plasticity of the sensorimotor cortex. However, recent findings have raised questions regarding how cortical plasticity affects pain. Our previous study demonstrated that enhanced cortical representation of phantom hand movements induced by neurofeedback was associated with increased pain and suggested that phantom limb pain may be decreased by reducing the cortical representation of the phantom hand movements (1). Here, we developed a novel neurofeedback technique to control a virtual hand image of patients' phantom hands and trained the patients with neurofeedback for three consecutive days to assess the treatment efficacy for reducing pain.

Methods

Participants and preparation

Twelve patients with phantom limb pain (2 amputees and 10 patients with brachial plexus root avulsion) participated in this study at Osaka University Hospital. The study adhered to the Declaration of Helsinki and was performed in accordance with protocols approved by the Ethics Committee of the Osaka University Clinical Trial Centre (No. 13381-6, UMIN000013608).

Stimulation, task and instruction

We first constructed a decoder that classified intact hand movements (grasping and opening) based on patients' cortical motor currents estimated by magnetoencephalographic (MEG) signals using sparse logistic regression. Next, we took 8–10 pictures of the patients' intact hands and flipped them right to left to be used as the controlled image based on the output of the real decoder. Patients were trained for 3 days to control the virtual image of the phantom hand by grasping or opening their phantom hands. For the controls, the same patients engaged with the same hand image, but the image was controlled by randomly changing values.

General procedure and study design

Two training types were randomly assigned to the patients and performed on separate days (a single-blinded, randomized, crossover trial).

Data acquisition

Pain was evaluated using a visual analogue scale (VAS) before and after each training session and for a 17-day follow-up period. The MEG signals were recorded before and after the 3-day training, while the patients attempted to grasp or open their phantom hands.

Data analysis

The VAS scores after day 4 were normalized by the VAS scores before the first day of training. The normalized VAS scores for the real and random trainings among days were compared. The MEG signals during the phantom hand movements were classified using a support vector machine. Ten-fold nested cross-validation was used to evaluate classification accuracy.

Results

VAS scores on day 4 were significantly reduced from the baseline after real training (mean [standard deviation]: 45.3 [24.2] vs 30.9 [20.6], 1/100 mm; $p=0.009$) and differed significantly from the control scores ($p=0.048$). Compared with the scores on day 1, the scores were significantly reduced by 32% on day 4 and by 36% on day 8 after real training. These scores were significantly lower than the control scores ($p<0.01$). The decoding accuracy of the phantom hand was significantly decreased after real training and correlated with pain reduction on day 4 ($R=0.58$).

Conclusions

The 3-day neurofeedback training significantly and sustainably reduced phantom limb pain for 5 days. Neurofeedback training attenuated persistent phantom hand representation, thus decreasing phantom limb pain.

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Topics: MEG, Neurofeedback, motor representation

Sensory Feedback to Investigate and Drive Cortical Plasticity

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Format: Oral Presentation

Background and aims

Amputation of a limb is often followed by intractable phantom limb pain (PLP) that is perceived in the missing amputated limb. While the prevalence of PLP is reported to be as high as 85% of amputees, the underlying mechanisms of PLP are yet not well understood. Previous studies have reported that the functional and structural reorganization of the primary sensorimotor cortex (SI) following amputation is correlated with PLP [1],[2]. Transcutaneous Electrical Nerve Stimulation (TENS) is a popular method in neurorehabilitation for pain and spasticity relief. The delivered electrical current activates the peripheral somatosensory afferents and has shown to decrease both acute and chronic pain [3],[4]. Several clinical studies have illustrated that sensory feedback by electrical stimulation can be mentioned as a type of treatment for temporary PLP reduction [5], [6]. A recent study at Aalborg University (EPIONE project) reported that steadystate surface electrical stimulation delivered to the referred sensation areas of an amputated limb induced significant temporary changes in phantom limb sensation [7]. Our objective was, therefore, to investigate the associated cortical responses following sensory TENS in healthy subjects that may help to better understand the cortical activity in amputees following TENS.

Methods

Forty healthy subjects (20 women; age 26.9 ± 4.3) were randomly assigned to either an intervention group (n=20) or a sham group (n=20). Each experiment session included three phases: T0 (baseline), TENS, and T1 (immediately after intervention). Sensory evoked potentials (SEP) reflect the electrical activity of the brain following various sensory events and SEPs biomarkers as a non-invasive method, have been used to investigate the functionality of the neural pathways [8]. Here, SEPs were recorded in T0 and T1 phases, which consisted of 80 trials. The intervention phase consisted of 20 min of sensory TENS (frequency= 100Hz, pulse width= 1ms) delivered to the attached electrodes on the left-median nerve with intensity at 80 % of the subjective discomfort threshold. Whereas, participants subjected to the sham condition had just one min of sensory TENS with the intensity of the sensation threshold. Continuous EEG data was recorded by a 64-channel system, and amplified using a BrainAmp MR plus amplifiers (Brain Products, GmbH). SEP responses were extracted by segmenting the preprocessed EEG data into 2500 ms epochs (from - 1000 ms to 1500 ms relative to the stimulus onset).

Results

Analyzing brain responses showed that the amplitude of the SEP responses decreased for the N1 and P2 waves following TENS intervention. Also, results from functional power-based onnectivity for Cz and C4 channels in the TENS condition showed that the difference in the correlation coefficient between T1 and T0 was $\Delta R = 0.3$. Whereas results in the sham group showed no significant effect neither in the SEP waves amplitude nor in functional power-based connectivity ($\Delta R = 0.06$).

Discussion and Conclusions

Sensory TENS delivered to the left-median nerve suppressed the N1 and P2 wave and eventrelated synchronization of SEPs. Our results showed that short-term sensory TENS induced quantifiable changes in the electrical activity of the brain. Although the results have demonstrated the influence of sensory TENS on brain activity in the healthy subject, this methodology and biomarkers may be beneficial for the design of possible pain alleviation therapies in the future.

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