Referred Sensation Areas in Bilateral Upper Limb Amputee

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Referred Sensation Areas in Bilateral Upper Limb Amputee

Eugen R. Lontis and Winnie Jensen

Abstract—**Phantom limb pain (PLP) following amputation considerably reduces the quality of life, given a difficult to treat pain of highly variate profile. The loss of sensory input induces a complex pattern of neuroplastic changes of the sensory neural pathways and their central projections. Referred sensation areas (RSAs) may occur on the stump as a consequence of amputation, providing a direct path towards the altered central sensory projections. Modulated electrical stimulation of RSAs was investigated in a long-term experiment in the case of a 62 years-old participant with bilateral upper limb amputation due to traumatic injury. RSAs were investigated using mechanical (vibration and pressure) and electrical stimuli over five sessions within a five weeks period. Further test of sensations induced by steady state and modulated electrical stimuli was performed during additional 4 sessions. Location and features of RSAs were highly dependent on the type of stimulus and time of delivery between sessions.**

Clinical Relevance— **The case study presents a variety of types and locations of the sensation induced by electrical and mechanical stimuli that may eventually be used as artificially generated sensory input as individualized alternative form of therapy for PLP alleviation. Furthermore, possible multichannel stimulus delivery on RSAs on both arms and the cross-over effect of the bilateral amputation in perception of the induced sensation in the opposite phantom hand may be considered in dedicated design of an experimental setup that may possibly help investigation of mechanisms for PLP.**

I. Introduction

Up to 80% of amputees experience phantom limb pain (PLP). Main factors leading to amputation are vascular diseases, trauma, and cancer. Evidence has been presented in the literature supporting both peripheral and central mechanisms responsible for generating PLP, however further investigations are required. Neuroplastic changes affect the sensory neural tracts and their central projections following amputation [1-5]. In the absence of the sensory input, maladaptive cortical plasticity may occur, possibly leading to PLP. Consequently, providing an artificially generated sensory input may reverse this cortical reorganization possibly leading to alleviation of PLP [6-7]. Amputated peripheral nerves may grow to the surface of the stump forming referred sensation areas (RSAs). As such, stimulation of RSAs may provide direct access to the sensory neural pathways that innervated the limb prior to amputation. Stimulation of RSAs may induce sensations in the phantom limb that may be regarded as artificially induced sensory input. The quality and quantity of such sensory input artificially induced by various types of stimuli may vary considerably when compared to that of the lost limb. Various techniques for stimulus delivering on RSAs may improve the quality and quantity of the induced sensory input. As such, modulation of the stimulus and contextual correlation with other sensory modalities may improve transmission, perception, and integration of the artificially generated sensory input providing a higher impact on cortical reorganization and eventually a more efficient form of therapy for PLP. We designed a long-term study over six months aiming to provide music modulated electrical stimulation of RSAs in upper and lower limb amputees. We report in this paper the analysis of RSAs mapped using mechanical stimuli (vibration and light pressure) and test of surface electrical stimulation of the stump in the case of a bilateral upper limb amputee.

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II. Methods

A. Participant Information

A 62 years-old female participated in the experiment. Both hands were amputated two years prior to the experiment, having the right arm amputated approximately 7 cm below the elbow and the left arm amputated approximately 10 cm above the elbow due to a traumatic injury. The protocol was approved by the local ethical committee (Den Videnskabstetiske Komité for Region Nordjylland, N-20190016). The participant received oral and written information and signed an informed consent form. The participant attended five sessions during the phase investigating RSAs over five weeks and four sessions of the following phase investigating steady state and music modulated sensory input induced by electrical stimulation of RSAs. The purpose of the second phase was to identify electrical stimuli that form atoms of a language modulated by features of music (as chosen by the participant) and delivered to the RSAs synchronous with the music. After the ninth session, the participant withdrew from the experiment, missing more than half of the phase investigating and defining the modulated sensory input and the entire therapy phase.

The participant experienced PLP on a VAS scale from 4 to 6, under regular medication with Gabapentin, in form of clamping, pricking, abnormal positions of the phantom hands, significantly affecting the quality of life.

B. Reference System and Mapping of RSA

The scanning procedure at the amputation site, spreading proximally on the stump. Tactile stimuli were applied manually with a 5 mm brush with two scans per second. Pressure stimuli were delivered by using a glass ball of 350 mm diameter in circular movement at a rate of approximately

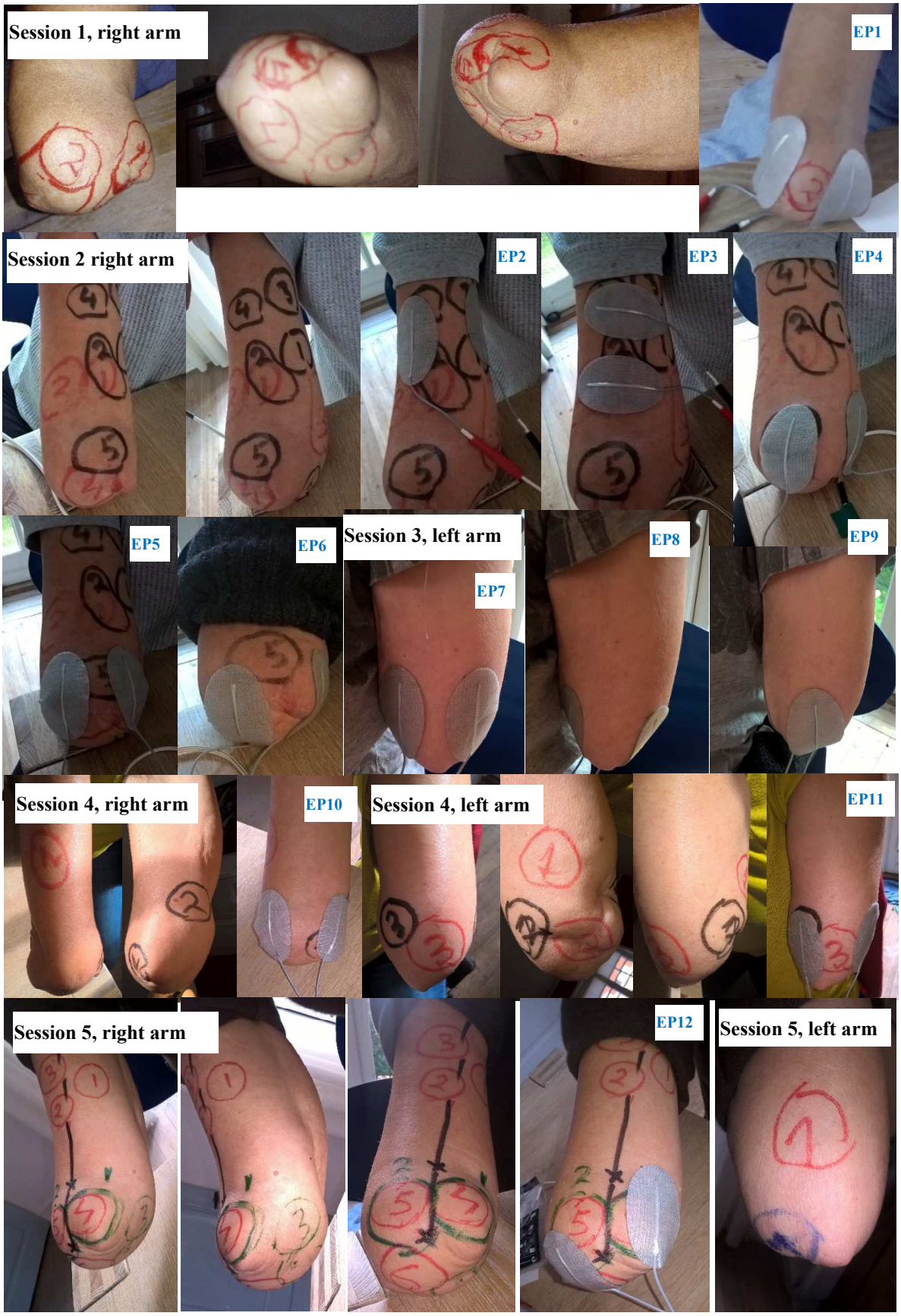

Figure 1. Mapping of RSAs during a five weeks period and placement of electrodes for test with electrical stimuli (EP1-11). Session 1 red color for mapping with glass ball. Sessions 2, 3, and 4 red color for mapping with brush and black for mapping with glass ball. Session 5 red color for mapping with brush and green/blue for mapping with glass ball.

one circular scan per second with lateral shift with a speed similar to that of brush scans. The participant was asked to verbally report on the location, type and intensity of both painful and non-painful sensations evoked in the phantom limb. The participant was additionally asked to score the level of the perceived pain using a VAS score.

A reference system was established based on landmarks provided by scars for a given position of the stump (the lack of the bony structures to serve as references imposed a relaxed position of the stump avoiding rotation and compression).

TABLE 1. Location and type of sensation induced by mechanical (tactile – brush and light pressure – glass ball). F1-5 = finger on phantom hand, where F1 is the thumb. RSAs location marked with corresponding color according to Figure 1.

RSA $_{\text{stimulus}}$	***Location and Type of sensation induced in the phantom limb by mechanical stimuli***
Session 1 right arm (sensations induced in right phantom hand)	
^{red}RSA-1$_{glass\text{-}ball}$	F1 (push-pull cyclic movements along finger)
^{red}RSA-2$_{glass\text{-}ball}$	F2, F3 (touch)
^{red}RSA-3$_{glass\text{-}ball}$	F3 (push-pull cyclic movements along finger)
^{red}RSA-4$_{glass\text{-}ball}$	F3, F4, F5 (touch, vibration)
^{red}RSA-5$_{glass\text{-}ball}$	F4 (touch, vibration)
Session 2 right arm (sensations induced in right phantom hand)	
^{red}RSA-1$_{brush}$	F2 (touch)
^{red}RSA-2$_{brush}$	F3 (touch)
^{red}RSA-3$_{brush}$	F5 (touch)
^{red}RSA-4$_{brush}$	Area between wrist and palm (push-pull cyclic movements)
^{black}RSA-1$_{glass\text{-}ball}$	F5 (touch)
^{black}RSA-2$_{glass\text{-}ball}$	F4 (touch)
^{black}RSA-3$_{glass\text{-}ball}$	F5 (touch)
^{black}RSA-4$_{glass\text{-}ball}$	F4 (touch)
^{black}RSA-5$_{glass\text{-}ball}$	F1, F2 (current like sensation)
^{black}RSA-6$_{glass\text{-}ball}$	F5 (touch)
Session 3 left arm	No RSAs identified
Session 4 right arm (sensations induced in right phantom hand)	
^{red}RSA-1$_{brush}$	F1 touches F2 in cyclic movements synchronously with movements of brush
^{black}RSA-1$_{glass\text{-}ball}$	F3, F4 (stretch)
^{black}RSA-2$_{glass\text{-}ball}$	F3, F4 (touch and stretch)
Session 4 left arm (sensations induced in left phantom hand)	
^{red}RSA-1$_{brush}$	F5 (perceives more obvious)
^{red}RSA-2$_{brush}$	Thenar area (touch), F1 (flexes and perceives more obvious)
^{red}RSA-3$_{brush}$	F1, F2 (perceives more obvious)
^{black}RSA-1$_{glass\text{-}ball}$	F4 (perceives more obvious)
^{black}RSA-2$_{glass\text{-}ball}$	Hypothenar area (touch, vibration)
^{black}RSA-3$_{glass\text{-}ball}$	F1 and thenar area (perceives more obvious)
Session 5 right arm (sensations induced in right phantom hand)	
^{red}RSA-1$_{brush}$	F3 (touch)
^{red}RSA-2$_{brush}$	F2 (touch)
^{red}RSA-3$_{brush}$	F1, F2 (touch)
^{red}RSA-4$_{brush}$	Thenar area (touch)
^{red}RSA-5$_{brush}$	F3 (touch)
^{red}RSA-5$_{brush}$	F5 (touch)
^{red}RSA-1$_{glass\text{-}ball}$	Area between wrist and palm (push-pull cyclic movements)
^{green}RSA-2$_{glass\text{-}ball}$	F3, F4 (stretch)
^{green}RSA-3$_{glass\text{-}ball}$	F5 (needles)
^{green}RSA-4$_{glass\text{-}ball}$	F5 (needles)
Session 5 left arm (sensations induced in left phantom hand)	
^{red}RSA-1$_{brush}$	Hypothenar (push-pull cyclic movements)
^{blue}RSA-1$_{glass\text{-}ball}$	F2, F5, F5 root and edge of palm (touch)

C. *Test of Surface Electrical Stimulation*

Electrical stimuli were applied through two oval PALS electrodes (40 x 64 mm). Ramps of increasing bipolar bursts of stimuli (default on - off periods of one second, pulse width Pw between 100 and 400 μs, frequency F between 10 and 120 Hz, and amplitude I between 1 to 80 mA) were delivered in the first phase of the experiment to identify the thresholds of sensation and discomfort as well as the associated type and location of sensation evoked in the phantom hands in the first phase. Steady state (first and second phase, session 3 to 9) and amplitude modulated (second phase, limited test in sessions 8 and 9) stimuli were tested from 500 s up to 1500 s (cycles of 4 s On and 1 s Off). The two electrodes were placed at given positions on the stump (left, right, or both) based on the RSAs mapped with mechanical stimuli during current and former sessions.

TABLE 2. Location and type of sensation induced by electrical stimuli with indication of RSAs identified with mechanical stimuli, possibly affected by electrical stimulation (ramp R and steady state Ss). Placement of electrodes EP1-12 according to Figure 1, where *RSAs were covered by electrodes, **RSAs were partly covered or in-between electrodes.

Location and Type of sensation induced in the phantom limb by electrical stimuli test for given placement of electrodes (EP1-12)
Session 1 right arm (sensations induced in right phantom hand)
EP1: * ^{red}RSA-1, 5$_{glass\text{-}ball}$ and ** ^{red}RSA-2, 4$_{glass\text{-}ball}$
Pw100-F20(R): Palmar Area sensation of bubbling and stretch in F5
Pw200-F20(R): F4, F5 contractions along finger
Pw300-F20(R): F4, F5 strong flexion
Pw100-F60(R): F2, F4, F5 extension
Pw100-F100(R): F2, F3 flexion
Pw300-F100(R): F4, F5 flexion
Session 2 right arm
EP2: ** ^{black}RSA-1, 3, 2, 4$_{glass\text{-}ball}$ and ** ^{red}RSA-1, 2$_{brush}$
EP3: ** ^{black}RSA-1, 3, 2$_{glass\text{-}ball}$, * ^{black}RSA-4$_{glass\text{-}ball}$, ** ^{red}RSA-2$_{brush}$, and * ^{red}RSA-1$_{brush}$
EP4: ** ^{red}RSA-3$_{brush}$, * ^{red}RSA-4$_{brush}$, ** ^{black}RSA-5$_{glass\text{-}ball}$, and * ^{black}RSA-6$_{glass\text{-}ball}$
EP5: ** ^{black}RSA-5$_{glass\text{-}ball}$ and ** ^{red}RSA-3$_{brush}$
EP6: ** ^{red}RSA-3, 4$_{brush}$, and * ^{black}RSA-5, 6$_{glass\text{-}ball}$
No induced sensation observed during test
Session 3 left arm (sensations induced in left phantom hand)
EP7: *no RSAs **no RSAs
Pw100-F100(R): F4, F5 increased awareness
Pw200-F100(R): Palmar edge of phantom hand, contraction in the rhythm of pulse delivery (i.e. on-off sequences of stimulus delivery)
Pw200-F100 (Ss, I of 20 mA): F4, F5 spinning-like sensation felt in approximately last 100 s of the stimulus
Pw300-F100 (Ss, I of 15 mA): F4, F5 spinning-like sensation felt in approximately last 100 s of the stimulus
EP8: *no RSAs **no RSAs
Pw100-F10(R): F2, F5 extension
Pw100-F10 (Ss, I of 68 mA): F2, F4, F5 touch dorsal hand and stretch (very relaxing sensation); after stimulation F2, F4, and F5 still stretched/full extension, before stimulation F2, F4, and F5 were flexed with discomfort/pain
EP9: *no RSAs **no RSAs
Pw100-F20(R): F4, F5 contractions along fingers
Pw200-F10 (Ss, I of 45 mA): phantom hand becomes thinner and larger (telescoping) having fingers gradually disappearing inducing a very relaxed state after stop of stimulus, phantom hand seems easy to rotate mentally (never experienced before)
Pw200-F60(R): F1, F2 touch
Pw200-F60 (Ss, I of 30 mA): pleasant sensation on the stump and all phantom fingers having pleasant flexing activity, after stop of stimulus increased awareness of hand (VAS between 2 to 3, low pain level), during investigation of the stump on the left a much lower pain/discomfort experienced in the right phantom hand

Session 4 right arm (sensations induced in right phantom hand)
EP10: ** ^{black}RSA-1, $2_{glass\text{-}ball}$
Pw100-F10(R): F1, F2, F4 contractions along fingers slightly unpleasant with light flexion on F4 F5
Pw100-F60(R): F4 F5 cyclic flexion-extension with palmar hand rotating approx. 90^0 facing upwards, in a relaxed state, very pleasant experience as stimulus increases in intensity
Pw100-F100(R): F3 pleasant pulsing sensation modulated by Ton-Toff pattern of stimulus, a buzzing effect in F4 and F5 was felt close to the end of the stimulus
Pw200-F60(R): unpleasant flexion of fingers
Session 4 left arm (sensations induced in left phantom hand)
EP11: ** ^{red}RSA-3_{brush} and ** ^{black}RSA-2, $3_{glass\text{-}ball}$
Pw100-F100(R); F3, F4 increased flexion
Pw200-F10(R): F4, F5 increased flexion modulated by Ton-Toff pattern of stimulus; after electrical stimulation of left stump the right phantom hand has a less tensed state
Session 5 right arm (sensations induced in right phantom hand)
EP12: ** ^{red}RSA-4, 5, 6_{brush} and ** ^{green}RSA-1, $2_{glass\text{-}ball}$
Pw300-F60 and Pw100-F120(R): F5 tension/contraction along the finger
Pw300-F120(Ss): F5 tension/contraction along the finger that changes to cyclic flexion after 10 min stimulation
Session 5 left arm
No test performed

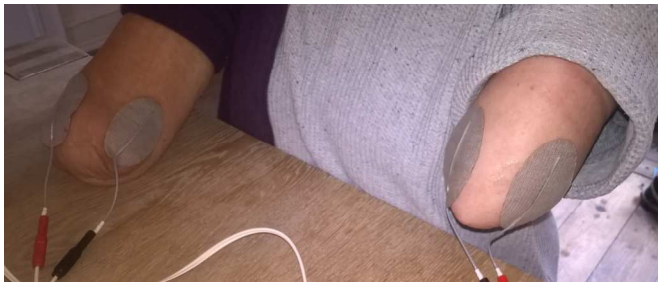

Figure 2. Placement of electrodes in sessions 6 to 9 in the second phase of the experiment.

III. Results

Figure 1 illustrates maps of RSAs investigated using a brush (vibration stimulus) and a glass ball (light pressure) during the five sessions on stump of the right and left arms. The size of the RSAs were circular – oval in shape having typical less than 6 cm in diameter, in a number greatly varying with session (relatively stable within the session) and type of stimulus (brush or glass ball). RSAs were located on an area on the stump within less than 20 cm from the amputation site. The type of sensations induced by mechanical and electrical stimuli are presented in Table 1 and 2, respectively. The participant reported a consistent reduced pain profile on one phantom hand upon focusing on reporting sensation induced by mechanical and electrical stimuli applied on the opposite stump.

Placing one pair of electrodes on each stump (Figure 2) close to the amputation site according to the maps of RSAs and delivering at random a steady state stimulus up to 500 s on one stump at a time induced in approximately 12% of the total numbers of stimulations during the test induced sensation in the opposite phantom hand.

Test of multichannel stimulation (e.g. steady state stimuli delivered simultaneously through the two pair of electrodes, one on each stump, Figure 2) with pulse width of 100 μs and frequency of 60 Hz, current intensity of 25 mA for the right arm and 40 mA for left arm delivered for 25 min during the second phase of the experiment induced a pleasant sense of symmetry (left arm shorter than the right arm gives a sense of asymmetry that balances with this multichannel stimulation). Furthermore, a pleasant small flexion-extension of fingers on both phantom hands was induced as well. Sensation that both arms were more movable/flexible after 25 min multichannel stimulation test was reported in addition to a pleasant sense of sensory experience on both phantom hands. During a very limited test with music energy based modulated stimuli delivered over 500 s on the right stump (no electrodes on the left stump) induced a very dynamic response in both phantom hands.

IV. Discussion

The variety of types and location of the sensation induced by test of electrical stimulation may qualify eventually the sensory input reported in this study for individualized alternative therapy for PLP alleviation. This study reports sensation induced by electrical stimuli applied through a limited number of positions of electrodes, besides those induced by mechanical stimuli. The results show that the sensation induced greatly varies upon the type of the stimulus applied and on position/orientation of electrodes. A more thorough analysis of sensation induced by electrical stimuli on a larger number of electrode position/orientation is required. Bilateral delivery of the sensory input may have a greater impact than the unilateral stimulus delivery. The reported sensation in one phantom hand when delivering stimuli on the opposite stump may be of interest for designing a study evaluating mechanisms for PLP where the added dimension of bilateral vs unilateral sensory delivery may provide additional insight into PLP mechanisms.

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