

Referred Sensation Areas in a Bilateral Toes Amputee

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Abstract—Various mechanisms in generating phantom limb pain (PLP) have been hypothesized in the literature. However, there still is no clear understanding of how PLP develops and why it presents. Amputation leads to permanent anatomical and physiological changes of the neural path previously supplying the brain with sensory input, as well as to formation of referred sensation areas (RSAs) on the stump or its vicinity. Sensations may be evoked in the lost body part upon stimulation of RSAs that may be exploited as artificial sensory input. In this work, we present the analysis of RSA maps from a 45-year-old female with bilateral toes amputation. Maps of the RSAs were identified in eight sessions over 107 days, characterized by dynamics in both location and type of associated evoked sensation. The evoked sensations were reported to be felt like current through and brushing of the phantom toes at low intensities close to the sensation threshold. Sensations evoked by electrical stimuli delivered through electrodes covering one or more RSAs approximated the sensation of summation of sensations evoked by mechanical stimuli (light brushing). No painful evoked sensations were observed.

Clinical Relevance— The technique presented may be further improved by using various profiles for stimulation over a longer period of time for possible efficient PLP treatment with artificially generated sensory input.

I. INTRODUCTION

Vascular diseases (54%), trauma (45%), and cancer (less than 2%) have been reported as the main causes leading to amputations, affecting nearly two million people in the US, with 185,000 additional amputations occurring annually. Phantom limb pain (PLP) occurs in up to 80% of amputees, representing a major debilitating condition affecting the quality of life [1-3]. Painful sensations occur in various intensities according to a time and location dependent profile, specific to each amputee, in the lost or paralysed body part. Published evidence points towards specific peripheral and central mechanisms for different selected cases, however, no consistent explanation for generation of phantom limb pain has yet been agreed upon [4-7]. Changes in the cortex of the brain following amputation have been documented [8]. Brain areas controlling the lost or paralysed limb are invaded by neighbouring brain areas, and as such, there is a mismatch between the cortical ‘map’ and the new physical layout of the body. Therapies alternative to medication exploit these observations attempting to restore brain reorganization to decrease PLP by providing artificially generated sensory

input [9-13]. Referred sensation areas (RSAs) may occur in amputees providing valuable gates to the brain through neural paths supplying the brain with sensory input prior to amputation [11-13]. Various types of sensations may be evoked in the lost or paralyzed part of the body by surface stimulation of RSAs with currents of specific parameters. The quality and quantity of the artificially generated sensory input may represent the key attributes of the artificially generated sensory input to be considered when designing paradigms for PLP therapy. However, no consistent knowledge on which type of sensations may be effective in affecting the cortical plasticity and the strategy for applying sensory feedback exist today.

In the EU project EPIONE, we hypothesized that natural sensory feedback related to the missing limb may create appropriate sensations, restore cortical organization and thereby modulate the phantom limb pain perception [9-13]. We defined appropriate sensations as meaningful and clearly defined sensations not inducing discomfort. In our group, we focused on delivering surface electrical stimulation through the RSAs. In spite of the possible advantages of using the RSAs to deliver sensory feedback, it has also been shown that chronic pain patients can experience shifts in the RSA location over time and the type of sensation generated [11-15]. A better understanding of the relationship between stimulus and evoked sensations associated RSAs over time is therefore needed to optimize and individualize a protocol for delivering sensory feedback for pain relief in the future. In the present work, our aim was to characterize features of RSAs in order to select a sensory feedback paradigm in a case study.

II. METHODS

A. Subject Information

A 45-year old female participated in an experiment at Aalborg University under the common clinical protocol as defined by the EPIONE consortium [9]. The protocol was approved by the local ethical committee (Den Videnskabsstetiske Komité for Region Nordjylland, N-20140061). The subject received oral and written information and signed an informed consent form. The subject completed all sessions of the basis and therapy phases according to the protocol, spanning over 50 days (phases basis of 6 sessions over 18 days and therapy of 11 sessions over 22 days, with 11 days of break between these two phases). The basis phase consisted of mapping of RSAs and test of electrical stimulation. The therapy phase consisted of partial RSAs

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Figure 1. Mapping of RSAs on session/day 7/29, 13/42, and 19/107 on the first, second, and third rows respectively. From the basis phase, RSAs maps increased in size from a few areas around the root of the toes up to 22 areas in lateral and proximal directions along the foot (Table 1). Colors correspond to toes where sensation was evoked (blue – toe 1, red – toe 2, green – toe 3, black – toe 4, and violet – toe 5). On the bottom row, electrodes placement for the four channels during session 13, according to investigation of the RSAs maps determined on basis phase, is illustrated.

mapping (i.e. performed on sessions 7 and 13 only), characterization of evoked sensation (e.g. sensory and discomfort thresholds and type and location of the evoked sensation, sessions 7-11), as well as delivery of selected stimuli of up to two hours per session (sessions 12-17). An outcome phase followed three weeks after the therapy phase. Phantom limb pain experienced within the 24-hour period prior to each session was evaluated using the 10 point Visual Analogue Scale (VAS, 0 = no pain and 10 = worst pain imaginable). This article presents data on mapping of RSAs.

The subject underwent bilateral toes amputation due to a condition depriving lower limbs of oxygen intake below the ankles, four years prior to participation in this experiment. Sharp and intense phantom limb pain like knife piercing mostly in the third, fourth, and fifth amputated toes, in random order, at a level of 9 to 10 on the VAS scale were reported during periods without medication. Medication decreased the pain level, however with side effects. Stump pain during standing and walking with bare feet felt like going on a beach covered by small, sharp stones but also producing knife like piercing though the sole that was more intense close to site of amputation. No pain was felt when sitting on a chair (i.e. no pressure exerted on the sole). Standing for a few minutes

generated pain of approximately 3 on VAS scale when wearing custom-made shoes and of approximately 8 on VAS scale when standing on bare feet. Walking of up 30 min increased significantly the stump pain even when using special shoes. The subject was prescribed pain medication while she was enrolled in the trials.

B. Reference System and Mapping of RSA

A reference system was defined as the line normal to the projection of a plane normal to the ankle in fully extended position of the foot, crossing the midpoint of the distance between the lateral and medial malleolus (Figure 1). RSAs were estimated as ovals with center defined by projection on and distance to the reference line, as well as orientation given by the angle between the longest axis and the reference line. RSA area was defined by the two axis of the ellipse. Negative and positive values of coordinates for center of the ellipse as well as of values of angles were defined according to lateral and medial sides relative to the reference line and to sides proximal and distal to the crossing point of the reference line.

The starting point for the scanning procedure was at the amputation site, spreading away on the stump, in lines parallel to the reference line covering the entire surface of the foot and

TABLE 1. Characteristics of maps of referred sensation areas evaluated at different sessions/days throughout the experiment, using tactile (brush) and electrical stimuli, for right and left foot. Total area of RSA was expressed in squared centimeters, rounded to nearest integer, based on the ellipse approximating the RSA. Degree of overlap with respect to location of RSA was estimated as the part of the total area of the current RSAs map overlapping with the total area of the previous RSAs map (marked with superscript), expressed in percentage of the total area of the current RSAs map.

Session / day	Number of RSAs	Total area of RSAs	Degree of overlap relative to RSA map of previous session	Sensations evoked by tactile stimulation (brush)	Sensation evoked by electrical stimulation
S1/1	6 <i>right foot</i>	37	-	Current like through T1-T2-T3-T4-T5	<p>Test ES Oval electrode covered one or more RSAs. One electrode was placed at specific location on the foot and the second electrode was placed consecutively at position around the first electrode at distances up to 10 cm. This procedure was repeated several times, within each session, attempting to cover all RSAs. For consecutive sessions the starting point and choice of position of second electrode depended on the current map of RSAs</p> <p>Sensations evoked by ES for some positions for placement of electrodes: <i>Current like through T1 to T5</i></p> <p>Sensations evoked by ES for some positions for placement of electrodes: <i>Only local effect under electrodes</i></p> <p>Single and Multichannel ES Oval electrode covered one or more RSAs. Position of electrodes for four channels (i.e. two electrodes per channel) was fixed, so that the eight electrodes covered most of foot dorsum and part of the foot planum (Figure 1).</p> <p>Sensations evoked by ES for single and multichannel stimulation: <i>Current like through and brush like of T1 to T5</i></p>
	7 <i>left foot</i>	48	-	Current like through T1-T2-T3-T4 Brushing like of T1-T2-T3-T4-T5	
S2/3	6 <i>right foot</i>	62	27% ^{S1}	Current like through T1-T2-T3-T4-T5	
	9 <i>left foot</i>	77	32% ^{S1}	Current like through T1-T2-T3-T4 Brushing like of T1-T2-T5	
S3/7	12 <i>right foot</i>	122	25% ^{S2}	Current like through T1-T2 Brushing like of T1-T2-T4	
	8 <i>left foot</i>	96	17% ^{S2}	Current like through T1-T3-T4 Brushing like of T1-T3-T4	
S4/10	16 <i>right foot</i>	145	37% ^{S3}	Current like through T1-T2-T3-T4-T5 Brushing like of T2-T3-T4-T5	
	10 <i>left foot</i>	104	29% ^{S3}	Current like through T1-T2-T3 Brushing like of T4-T5	
S5/14	22 <i>right foot</i>	173	19% ^{S4}	Current like through T1-T2-T3-T4-T5 Brushing like of T1-T2-T3-T4-T5	
	10 <i>left foot</i>	58	22% ^{S4}	Current like through T1-T2-T4-T5 Brushing like of T1-T2-T3-T4-T5	
S7/29	13 <i>right foot</i>	117	38% ^{S5}	Current like through T1-T2-T3-T4-T5 Brushing like of T1-T2-T3	
S13/42	14 <i>right foot</i>	136	49% ^{S7}	Current like through T1-T2-T3-T4-T5 Brushing like of T1-T2-T3-T4	
S19 /107	11 <i>right foot</i>	124	44% ^{S13}	Current like through T1-T2 Brushing like of T1-T2-T4	
	13 <i>left foot</i>	97	24% ^{S5}	Current like through T1-T3-T4 Brushing like of T1-T3-T4	

along the leg up to approximately 20 cm above the ankle. Tactile stimuli were applied manually with a brush of 5 mm in diameter. The brush movements had a rate of approximately two scans per second, covering a distance of approximately 20 mm, and a lateral shift with a speed of 5 to 10 mm per second. Mapping of RSAs locations was performed with tactile stimuli during the first five sessions of the basis phase, on sessions 7, 13 of therapy phase, as well as on session 19 of the outcome phase. The patient was asked to verbally report on the location, type and intensity of both painful and non-painful sensations evoked in the phantom limb. The patient was additionally asked to score the level of the perceived pain using a VAS score.

C. Surface Electrical Stimulation

Biphasic, charge-balanced pulse electrical stimuli were delivered through a time-multiplexed 12 channels ISIS neurostimulator, Inomed[®]. The neurostimulator was controlled by a computer through the Psychophysical Platform EPIONE developed at Aalborg University.

During basis phase, test of electrical stimulation was performed by placing two electrodes (i.e. one channel) at positions dependent of the current map of RSAs, attempting to cover all RSAs. For therapy and outcome phase eight electrodes (i.e. four channels) were placed at the same position

for each session, attempting to cover all RSAs, for single and multichannel stimulation. Electrical stimuli were applied through two oval PALS electrodes 40 x 64 mm, for each channel. Ramps of increasing bipolar bursts of stimuli (default on - off periods of one second, pulse width between 200 and 600 μ s, frequency between 10 and 120 Hz, and amplitude between 5 to 60 mA) were delivered to identify the thresholds of sensation and discomfort as well as the associated type and location of sensation evoked in the phantom limb.

During the therapy phase, electrical stimuli were delivered through four channels with electrodes placed on the planum and dorsum of the foot (Figure 1, bottom row).

III. RESULTS

Most of RSAs mapped with tactile stimuli were located on the foot. Few RSAs were found on the leg, just above the ankle. Sensations evoked were felt like current through and brush of specific phantom toes, depending on location of stimulation. Intensity of the evoked sensation was light, close to sensation threshold. In a limited test performed, tactile stimulation of some RSAs after approximately 30 minutes from the initial mapping evoked similar sensation (e.g. current or brush like) in another toe/toes that has/have been previously reported for the corresponding RSA, possibly indicating short-term dynamics of RSAs. Table 1 illustrates evolution of

number of RSAs, their total area, the degree of overlapping from previous session, as well as types of sensations evoked by tactile and electrical stimulation, outlining a consistent type of sensation evoked by both types of stimuli. Dynamics of both location and sensation associated was observed in consecutive sessions. Increase in the area of the foot positively testing for mechanical stimuli with various degrees of overlapping between sessions was observed as well.

The average 24-hours VAS score varied from 6.1 (range 2-8) for pre-therapy sessions to 4.2 (range 2-8) during the first therapy week, 2.7 (range 0-5) during the second therapy week, 3.1 (range 1-5) during the third therapy week, and to 4 (range 3-5) during the fourth therapy week.

IV. DISCUSSION

Tactile and electrical stimulation induced a similar non-painful type of sensations in the phantom toes. The sensations evoked were of low intensity, close to sensation threshold, possibly explaining the dynamics observed in the RSAs map evaluated in consecutive sessions. A tendency of increase in the total area of the foot sensitive to brushing may possibly be explained as well by the learning process experienced by the subject throughout the course of the experiment.

The reference system was found reliable when reporting location, extend, and orientation of RSAs, as well as when reproducing the reference line in consecutive sessions.

The case presented recommends the use of the surface electrical stimulation for generation of sensory input in that the profile of evoked sensations was relatively stable (i.e. no painful sensations were evoked in this case). More intricate profiles for the sensations evoked were previously reported in the cases of arm amputation (following damage of brachial plexus), transpelvic amputation, and transfemoral amputation [11-13] where some of the RSAs identified induced painful sensations upon electrical stimulation.

Positive effect on pain alleviation was reported in the outcome session (day 107), as periods with a pain profile of intensities lower than previously experienced for both phantom and stump pain. Quantification of effects on the pain profile was, however, challenging. The sensory input provided over a relative short period of time competed with the medication intake that the subject continued to follow throughout the course of the experiment. Medication succeeded to hold the pain levels relatively low (e.g. from 6 - 10 down to 0 - 5 on VAS scale), however, with side effects. Furthermore, medium physical activity (e.g. normal walk more than 15 min) induced significant pain increase (e.g. from 0-4 to 3-8 on VAS scale), highly influenced by the type of terrain and of shoes wore at that time.

Further studies are required for a better quantification of efficiency of attempted therapy using sensory input. Design for specific delivery with surface electrical stimulation may include longer periods, several times a day, with various profiles for stimulation. Synchronization of stimuli delivery with more intense physical activity attempting to target failing medication effect on pain alleviation may represent a step forward towards a more effective individualized therapy.

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