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## Multisensory bionic limb to achieve prosthesis embodiment and reduce distorted phantom limb perceptions

Giulio Rognini<sup>#1,2,3</sup>, Francesco Maria Petrini<sup>#1,4</sup>, Stanisa Raspopovic<sup>#5</sup>, Giacomo Valle<sup>1,4,6</sup>, Giuseppe Granata<sup>7</sup>, Ivo Strauss<sup>1,4,6</sup>, Marco solcà<sup>1,2</sup>, Javier Bello-Ruiz<sup>1,2</sup>, Bruno Herbelin<sup>1,2</sup>, Robin Mange<sup>1,2</sup>, Edoardo D'Anna<sup>1,4</sup>, Riccardo Di Iorio<sup>7</sup>, Giovanni Di Pino<sup>8,9</sup>, David Andreu<sup>10</sup>, David Guiraud<sup>10</sup>, Thomas Stieglitz<sup>11</sup>, Paolo Maria Rossini<sup>7,12</sup>, Andrea Serino<sup>#1,2</sup>, Silvestro Micera<sup>#1,4,6</sup>, Olaf Blanke<sup>#1,2,13</sup>

<sup>1</sup>Center for Neuroprosthetics, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

<sup>2</sup>Laboratory of Cognitive Neuroscience, Brain Mind Institute, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland <sup>3</sup>Laboratory of Robotic Systems, School of Engineering, Ecole Polytechnique Fédérale de Lausanne, Laboratory of Robotic Systems, Switzerland <sup>4</sup>Translational

Neural Engineering Laboratory, Institute of Bioengineering, School of Engineering, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland <sup>5</sup>ETH Zürich, Department of Health Sciences and Technology, Institute for Robotics and Intelligent Systems, TAN E 2, Zürich, Switzerland <sup>6</sup>The Biorobotics Institute, Scuola Superiore Sant'Anna, Pisa, Italy <sup>7</sup>Area of

Neurosciences, Policlinic A Gemelli Foundation, Catholic University of the Sacred Heart, Rome, Italy <sup>8</sup>Neurophysiology and Neuroengineering of Human-Technology Interaction, Campus Bio-Medico University, Rome, Italy <sup>9</sup>Institute of Neurology, Campus Bio-Medico University, Rome, Italy

<sup>10</sup>NRIA Camin team, University of Montpellier – LIRMM 860 Rue Saint Priest, Montpellier, France <sup>11</sup>Laboratory for Biomedical Microtechnology, Department of Microsystems Engineering–IMTEK, University of Freiburg, Freiburg, Germany <sup>12</sup>IRCCS San Raffaele Pisana, Rome, Italy

<sup>13</sup>Department of Neurology, University Hospital of Geneva, Geneva, Switzerland

# These authors contributed equally to this work.

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**correspondence to** Professor Silvestro Micera, Center for Neuroprosthetics, Ecole Polytechnique Fédérale de Lausanne, Lausanne CH-1015, Switzerland; silvestro.micera@epfl.ch.

**Contributors** GR designed the study, performed the experiments, analysed the data and wrote the paper. FMP and SR developed the software for the neural stimulation, contributed to the design of the study, performed the experiments and wrote the paper (GR, FMP and SR equally contributed to the work). GG, RDI, IS, GV and ED collaborated during the development of the neural stimulation software and during the experiment. MS designed, performed and analysed the telescoping experiment. RM developed the augmented reality software and integrated it with the neural stimulation device. JB-R and BH integrated the augmented reality software with the neural stimulation device, contributed to the design of the experiments and performed part of the experiments. GDP selected the patients and collaborated during the experiments. TS developed the TIME electrodes. DA and DG developed the device for the neural stimulation. PMR selected the patients and supervised the experiments. AS designed the study, performed the experiments, analysed the data and wrote the paper. SM and OB designed the study, supervised the experiments and wrote the paper (AS, SM and OB equally contributed to the work). All the authors read and approved the manuscript.

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**Patient consent** Not required.

**Ethics approval** The experimental procedures were approved by both the Institutional ethics Committees of Policlinic A Gemelli at Catholic University and the IRCCS S raffaele Pisana (rome). Informed consent was obtained from both patients.

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## Introduction

A major goal of neuroprosthetics is to design artificial limbs that are experienced ('embodied') like real limbs. However, despite important technological advances, this goal has not been reached and prosthesis embodiment is still very limited. Differently from our physical body, current bionic limbs do not provide the continuous multisensory feedback required for a limb to be experienced as one's own. Here, we present a novel neuroprosthetic approach that combines peripheral neurotactile stimulation—inducing tactile sensation on the missing limb—and immersive digital technology—providing visual illumination of the prosthetic hand. We tested whether coherent multisensory visuo-tactile neural stimulation (VTNS) induced higher prosthesis embodiment and reduced the distorted perception of the phantom limb (telescoping, ie, the phantom limb is perceived as shorter than the intact limb).

## Methods

Patient 1 and patient 2 are tranSRadial left forearm chronic amputees, who suffered upper limb telescoping. Patients were implanted with transverse intrafascicular multichannel electrodes (TIMEs), which induced the sensation of a vibration in a circumscribed skin region of the finger 2 via medial nerve stimulation in patient 1 (online supplementary figure 1A) and in a skin region of finger 5 via ulnar nerve stimulation in patient 2 (online supplementary figure 1B and material 1). Neurotactile stimulation<sup>2</sup> was coupled with automatised visual illumination of a skin region on the patient's prosthetic hand that corresponded to the somatotopic location of touch sensations experienced on the phantom hand (VTNS; online supplementary video 1, online supplementary figure 1, online supplementary material 1). VTNS was administered in two conditions, either with synchronous visual and neurotactile stimulation or in a control condition of asynchronous stimulation (1.5–2.5s delay).

Prosthesis embodiment was measured via a questionnaire, whereas changes in phantom limb perception were tested via a body landmark task where patients indicated the perceived position of different parts of the phantom limb by moving a ruler in absence of visual stimulation (figure 1B). The experimental procedures were approved by the competent ethical committee.

## Results

### Prosthesis embodiment

In both patients, embodiment ratings based on questionnaires revealed significantly higher scores during synchronous than asynchronous VTNS stimulation ( $p < 0.001$ ; Fisher test; control items for suggestibility were not modulated:  $p > 0.073$ ; figure 1A).

### Reduction of abnormal phantom limb perception: telescoping

During the embodiment-inducing condition, VTNS improved telescoping (online supplementary video 1). Both patients perceived the phantom finger of the stimulated limb in a more distal position as compared with asynchronous stimulation ( $t = 2.13$ ,  $p < 0.01$ , patient

1;  $t=3.6$ ,  $p<0.001$ , patient 2; figure 1C), while there was no change in the perceived elbow position (control) between conditions ( $p=0.76$ , patient 1;  $p=0.099$ , patient 2). Thus, synchronous VTNS increased the perceived length of the phantom hand. Importantly, this effect persisted 10min after VTNS had ended ( $t=1.95$ ,  $p=0.026$ , one-tailed, patient 1;  $t=1.94$ ,  $p=0.029$ , one-tailed, patient 2; figure 1D). See online supplementary material 1 for extended results.

## Discussion

By combining immersive digital technology, neuroprosthetics and paradigms from cognitive neuroscience, in two amputees, we administered direct tactile stimulation to the phantom limb via an intraneural implant into the residual limb nerves. Such stimulation, combined with personalised and coherent visual stimulation using immersive digital technology, VTNS, induced embodiment for the prosthetic hand, and importantly, reduced telescoping of the phantom limb thus improving abnormal phantom limb perceptions.

Our approach presents several advantages with respect to earlier therapeutic approaches aimed at inducing ownership in amputees,<sup>3–5</sup> as those require the external application of tactile cues on skin regions of the residual limb, which had to be applied manually<sup>3</sup> or via a robotic<sup>5</sup> device as well as the concurrent application of a physical visual stimuli on the prosthetic device.<sup>3–5</sup> This way, such procedures are difficult to apply during continuous prosthetic use in daily-life activities, thus limiting the intensity and duration of the induced prosthesis embodiment and thereby reducing their clinical relevance. Moreover, these previous studies did not test whether embodiment affected phantom limb sensations, that are critical for prosthesis acceptance.<sup>6</sup> Our VTNS stimulation procedure shows that multisensory stimulation necessary to induce prosthesis embodiment does not need to be linked to realistic<sup>4</sup> or functionally relevant interactions<sup>4</sup> as long as VTNS respects the fundamental constraints of embodiment and multisensory integration (eg, synchronous multisensory stimulation).<sup>1</sup>

### Abnormal phantom limb perceptions

Our results reveal another important clinical benefit: the reduction of telescoping. VTNS was able to reshape subjective sensations of upper limb dimensions, as to make it being perceived as more similar to the actual size of the missing limb and the prosthesis. Interestingly, previous research on phantom sensations in a large sample of amputee patients found that prosthesis embodiment sensations are more frequent in patients with an extended phantom as compared with patients with a telescoped phantom.<sup>6</sup>

Two theories have tried to account for cortical reorganisation and phantom sensations following amputation.<sup>7 8</sup> On the one hand, the maladaptive plasticity theory posits that abnormal phantom sensations and phantom pain arise from maladaptive cortical reorganisation, triggered by loss of sensory input,<sup>7</sup> thus associating greater pain with increased local cortical reorganisation. Recent data, on the other hand, suggest that cortical changes following limb amputation may also be due to a combination of loss/altered sensory inputs from the periphery and phantom pain experience, resulting in a maintained brain structural and functional representation of the missing limb in the sensorimotor cortices, but

disturbed long-range connectivity.<sup>8</sup> Our multisensory neuroprosthetic approach might act on either mechanism for the phantom limb syndrome and might be used to reduce telescoping, or in future studies to alleviate phantom pain, if such effects were to be found. Indeed, VTNS provides multisensory coherent bodily stimulation which may target central body representations, but also aims at restoring peripheral inputs from the residual nerves, in turn affecting long-range connectivity. At the moment, it is not possible to determine which mechanism is at the basis of the present effect.

Limitations of our study include the small number of participants tested, and the use of only one measure of embodiment (questionnaire). Future studies investigating prosthesis embodiment in amputees with peripheral neural implants should examine several aspects of embodiment in greater detail. Other limitations are the fact that the experimenters conducting the tests were not blinded to the experimental conditions and that the investigations were only carried out over a limited amount of time (ie, for several hours over different days).

Taken together, our results open up new opportunities to enhance prosthetic acceptance and advance the engineering of personalised artificial limbs that, by providing continuous multisensory feedback, might feel like real limbs.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgements

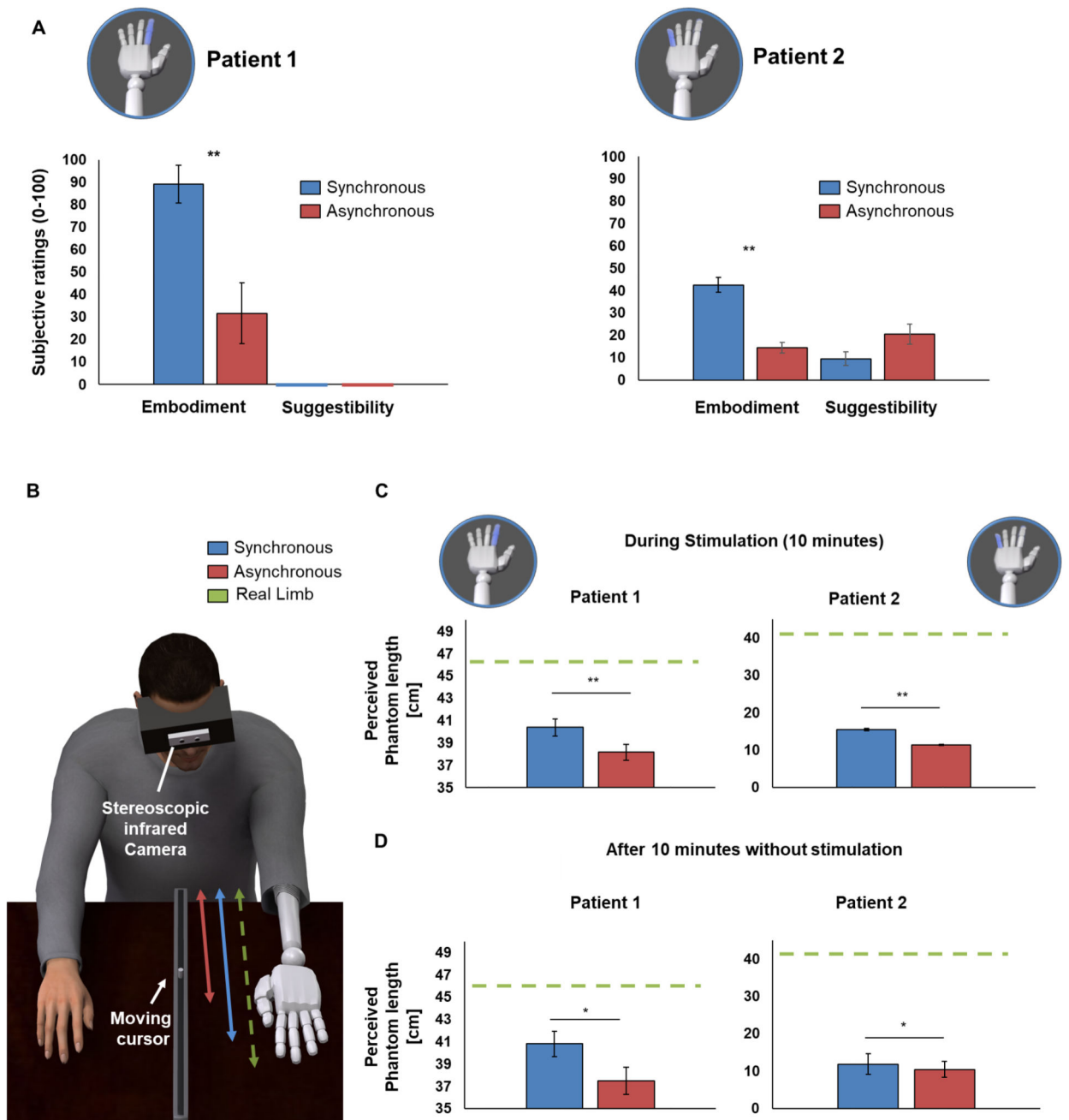
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**Figure 1.**

(A) Prosthesis embodiment. Average ratings of embodiment (Q1–3) and suggestibility items (Q4–5) are shown for all experimental conditions are shown for both patient 1 and patient 2 (see online supplementary material 1). embodiment was highest when VTNS was administered synchronously with illumination of the prosthetic hand (as compared with the asynchronous condition). the synchronous stimulation was characterised by a delay smaller than 10ms between the neurally induced tactile sensation and the visual illumination, whereas in the asynchronous condition the temporal mismatch (1.5–2.5s) between the neural

stimulation and the visual illumination was randomly selected on each trial. In patient 1, suggestibility items were always rated 0 (shown as coloured lines). (B) reduction of abnormal phantom limb perceptions (telescoping). to measure the perceived length of the phantom limb, both patients were asked to operate a movable cursor inside a ruler with their right hand. the difference between the perceived position of this phantom finger and elbow was used to estimate the perceived length (in cm) of the phantom limb (average scores are reported). (C) During synchronous VTNS (blue) both perceived the tip of their phantom finger in a more distal position (vs asynchronous condition;  $p < 0.01$ ; red), compatible with an increase in the perceived length of their phantom limb (B; online supplementary video 2). (D) this condition-specific change in telescoping persisted, in both patients, 10min after VTNS had ended. error bars show Se of the mean. \* $P < 0.05$ ; \*\* $P < 0.01$ . VTNS, visuo-tactile neural stimulation.