"Latency Of The Perceived Sensation Evoked By Peripheral Nerve Stimulation In People With Lower Limb Amputations"

Breanne Christie, Hamid Charkhkar, Emily Graczyk, Dustin Tyler, Ronald Triolo

Introduction: The application of electrical stimulation to the intact sensory nerves of people with amputations can elicit tactile and/or proprioceptive sensations referred to their missing limb. This restoration of sensory feedback can improve their control over their prostheses and increase feelings of embodiment. To maximize the benefits of sensory feedback, the neural stimulation must temporally align with visual cues from the interaction of the prosthesis with objects. In this work, we examined, for the first time, the subjective temporal synchrony between visual stimuli and sensations elicited via neural stimulation in two human subjects with lower limb amputations. Characterization of this temporal relationship between visual and tactile stimuli in people with amputations is essential in order to incorporate instantaneous sensory feedback into a neuroprosthesis.

Materials and Methods: Two volunteers with unilateral trans-tibial amputations were enrolled in the study. Subject 1 was chronically implanted with three 16-contact composite flat interface nerve electrodes (C-FINEs) on his tibial, fibular, and distal sciatic nerves [1]. Subject 2 had one C-FINE on his tibial nerve and two that were 3 cm apart on the distal sciatic nerve. The subjects performed a visual-tactile simultaneity judgment task. The "tactile" portion of this task involved the use of an external stimulator to deliver pulse trains to a single C-FINE contact at a level higher than the threshold needed to elicit sensation. The delivered pulses were repeated at a frequency of 20Hz and had pulse widths between 160-190μs and pulse amplitudes of 0.7-1.2mA. The "visual" component was a blue LED, whose onset could be controlled in real-time. The delay between the two stimuli, referred to as the stimulus onset asynchrony (SOA), was varied between -500 to +500ms. Positive SOA values refer to cases where neural stimulation occurred before the LED was flashed. For various SOAs, the subjects were asked whether these two stimuli were "synchronous" or "asynchronous." To investigate the temporal relationship, we plotted SOA versus the percentage of "synchronous" responses and fit a Gaussian curve to the results. We analyzed the point of subjective simultaneity (PSS) and just noticeable difference (JND) for each electrode contact [2]. The PSS was the timing delay at which subjects perceived the two stimuli as maximally "synchronous." The JND was the smallest temporal interval that participants could reliably detect. Preliminary simultaneity measurements were taken from four electrode contacts across both subjects.

Results and Discussion: Table 1 displays the PSS and JND values that we found for both participants. The positive PSS values mean that it took longer for participants to process neural stimulation than visual stimuli. The PSS values were also significantly larger than those of able-bodied subjects [3] (t-test, $p<0.05$). This could possibly be due to the fact that they are 48 (S1) and 10 (S2) years post-amputation and may now be biased due to their dependence on vision while operating prostheses. The JND values are not significantly different than those found in able-bodied subjects [4] (t-test, $p=0.14$), which indicates that sensitivity to stimulation-induced sensation is similar to the sensitivity of normal tactile sensation. These conclusions match those found in a visual-tactile simultaneity judgment task done using neural stimulation in people with upper limb amputations [5].

Metric	Subject 1, Ch1	Subject 1, Ch2	Subject 2, Ch1	Subject 2, Ch2
PSS (ms)	+113 (stim first)	+140 (stim first)	+143 (stim first)	+60 (stim first)
JND (ms)	147	131	78	109

Table 1. PSS and JND values for the two contacts tested in both subjects.

Conclusions: We were able to quantitatively examine the temporal synchrony between visual stimuli and sensations elicited via neural stimulation in two human subjects with lower limb amputations. After a prosthesis user sees an object interact with their prosthesis, stimulation should occur within this "synchronous" temporal range. This will maximize the benefits of sensory feedback, allowing for improved prosthesis control and embodiment. This is an important step towards the development of a sensory neuroprosthesis.

Acknowledgements: The authors thank the participating subjects, Courtney Shell, Melissa Schmitt, Dr. Gilles Pinault, and Dr. Clay Kelly. This work was sponsored by the Defense Advanced Research Projects Agency (DARPA) BTO under the auspices of Dr. Doug Weber through the Space and Naval Warfare Systems Center, Grant/Contract No. N66001-15-C-4038.

References: [1] M. Freeberg. *JNE.* 2017. *In Press.* [2] M. Keetels & J. Vroomen. The Neural Bases of Multisensory Processes. Boca Raton (FL): CRC Press/Taylor & Francis; 2012. Chapter 9. [3] V. Harrar & L. Harris. *Experimental Brain Research*. 2005. *166*(3-4), pp.465-473. [4] E. Poliakoff. *Neuroscience Letters.* 2006. *396*(3), pp.207-211. [5] E. Graczyk. *Neural Interfaces Conference Poster*. 2014.