Proceedings of the
8th Graz Brain-Computer Interface Conference 2019 DOI: 10.3217/978-3-85125-682-6-10

COUNT ON IT: DORSOLATERAL PREFRONTAL CORTEX FOR BCI CONTROL IN LOCKED-IN SYNDROME

S. Leinders[1], E.G.M. Pels[1], B.H. Van der Vijgh[1], M.P Branco[1], Z.V. Freudenburg[1], M.J.E. Van Zandvoort[2], E.J. Aarnoutse[1], M.J. Vansteensel[1], & N.F. Ramsey[1]

[1] UMC Utrecht Brain Center, Department of Neurology and Neurosurgery, Utrecht, the Netherlands

[2] Department of Neurology and Neurosurgery, Brain Center Rudolf Magnus, University Medical Center Utrecht, The Netherlands

E-mail: s.leinders@umcutrecht.nl

ABSTRACT: Self-paced Brain-Computer Interfaces (*BCIs*) have traditionally relied on sensorimotor activity for control. Because some individuals with locked-in syndrome (*LIS*) may not be able to control a sensorimotor-based BCI, alternative control strategies should be investigated. As part of the Utrecht NeuroProsthesis project, two individuals with LIS have been fitted with a fully implanted BCI to test feasibility of independent home-use and investigate long term stability of the BCI control features. Neural activity in the UNP system is measured with subdurally implanted electrocorticography electrodes from sensorimotor cortex and left dorsolateral prefrontal cortex (*dlPFC*). Here we present results from the left dlPFC and show for the first time that LIS users are able to reliably activate the left dlPFC at will by mental arithmetic with no training, and that the relevant neural features (high frequency band power) are stable until the last measurement (161 and 61 weeks after implantation, for the two participants). We conclude that dlPFC-based control is a viable control strategy.

INTRODUCTION

Neurodegenerative disease, stroke, or brain injury can lead to locked-in syndrome (*LIS* [1]), characterized by an almost complete paralysis, the inability to speak, and intact cognition. For the subset of LIS people who cannot reliably control traditional augmentative and alternative communication (*AAC*) devices with residual movement [2], Brain-Computer Interfaces (*BCIs*) are the most promising option for self-initiated communication.

Many BCI systems rely on neural activity associated with mental tasks that can be performed at will and in a self-paced manner. Traditionally, self-paced BCI control employs signals measured from sensorimotor areas, allowing people to control a cursor to type [3-8] or control a Windows tablet [9] during research sessions. Moreover, as part of the Utrecht NeuroProsthesis (*UNP*) project, an individual with LIS due to late-stage ALS was able to control commercial AAC software independently and reliably at home [10], without any research staff present, by attempting to move her hand and thereby generate signal changes in the sensorimotor cortex that were converted into brain-clicks.

Although sensorimotor-based BCI has proven its potential to replace lost function, there may be LIS users who cannot reliably control such a BCI. For instance, when paralysis starts at young age, motor imagery may be difficult [11]. Moreover, cortical atrophy due to neurodegenerative disease such as ALS [12] and stroke or injury to specific areas may prevent BCI control based on those areas.

For the subset of LIS people who cannot reliably control a sensorimotor-based BCI, an alternative self-paced control strategy is needed. A promising alternative is to employ signals from the dorsolateral prefrontal cortex (*dlPFC*). First, this region can be activated by a number of self-initiated tasks, such as mental arithmetic [13-15] and random number generation [16-19]. Second, its signals can be measured from the brain surface with electrocorticography (*ECoG),* as demonstrated in an earlier study from our group [15]). In that study, epilepsy patients with temporarily implanted ECoG electrodes over their left dlPFC were able to control a cursor based on high frequency band (*HFB*) power changes generated by mental serial subtraction.

Here, we investigated whether people with LIS are able to reliably activate the left dlPFC. We report data from two participants of the UNP study who were fitted with the fully implantable BCI system.

MATERIALS AND METHODS

Ethics approval: This study was approved by the medical ethics committee of the UMC Utrecht and conducted according to the declaration of Helsinki (2013).

Participants: The first participant (UNP1) was a woman, 58 years old at time of informed consent (September 2015), with late-stage ALS. Her communication was limited to eye tracker control and blinking for yes and no, and later to sporadic eye tracker control, lip twitches for yes and no, and the UNP system for typing. The second participant (UNP4) was a woman who was 39 years old at time of informed consent (August 2017). A brainstem stroke in 2004 left her in a locked-in state. She used head movements for control over a switch and joystick, and for yes and no. Both participants gave informed consent with a dedicated procedure described in [10].

Screening and Implantation: A neuropsychologist tested mental arithmetic skills prior to implantation. A pre-surgical fMRI was done to determine the target locations for electrode placement. Based on the fMRI results, ECoG strips (4 electrodes per strip, diameter 4mm; inter electrode distance 10mm; Resume II ®, Medtronic, off-label use) were implanted subdurally through burr holes. Leads were tunneled and connected to an amplifier-transmitter device (Activa ® PC+s, Medtronic, off-label use), which was implanted subcutaneously under the left clavicle. fMRI and neurosurgery details have been described earlier [10].

Task and Data: After implantation, the participants regularly performed a count task, while the neural signal was recorded with the implanted device. The *count task* was a block-design task, comprising alternating active (mental arithmetic) and rest trials of 15 seconds. During active trials, participants had to perform serial subtraction for the duration of the trial. For UNP1, task length was 2 or 5 minutes, and for UNP4, task length was always 3 minutes. Every trial, UNP1 was presented with a starting number and step size, and UNP4 with just a starting number (i.e. she always used the same step size in one run, which was sometimes adjusted between sessions when she indicated it was getting easier). During research sessions at the homes of the participants, an experimenter administered the count task regularly to 1) test whether the participants could regulate HFB (65-95Hz) power in the left dlPFC using mental arithmetic, and 2) test stability of the neural signal features. All count task data presented here was recorded with the same bipolar pair for each of the participants (bipolar pair selection was based on an initial evaluation of all bipolar combinations, using the count task). Count task data were recorded with the implanted device at a sampling frequency of 200Hz, with a high pass filter of 0.5Hz. For analysis, raw voltage was converted offline into power data for frequencies from 1-100Hz in 1Hz bins. The mean HFB power (65-95Hz) was calculated for each 15 second block. The coefficient of determination (r^2) between those mean values and the block design of the task (a binary array) and the respective p-values were calculated for each run.

RESULTS

UNP1 performed 61 runs of the count task, with the last run recorded 161 weeks after implantation. Mean HFB power correlated significantly with the task in all runs, except for two runs in weeks 41 and 42 (Figure 1A). The average r^2 value was 0.68 ± 0.20.

UNP4 performed 31 runs of the count task and her last run was recorded 61 weeks after implantation. Again, HFB power correlated significantly with the task for all runs (Figure 1B), except in 3 runs in weeks 6, 35 and 50. The average r^2 value was 0.61 ± 0.18.

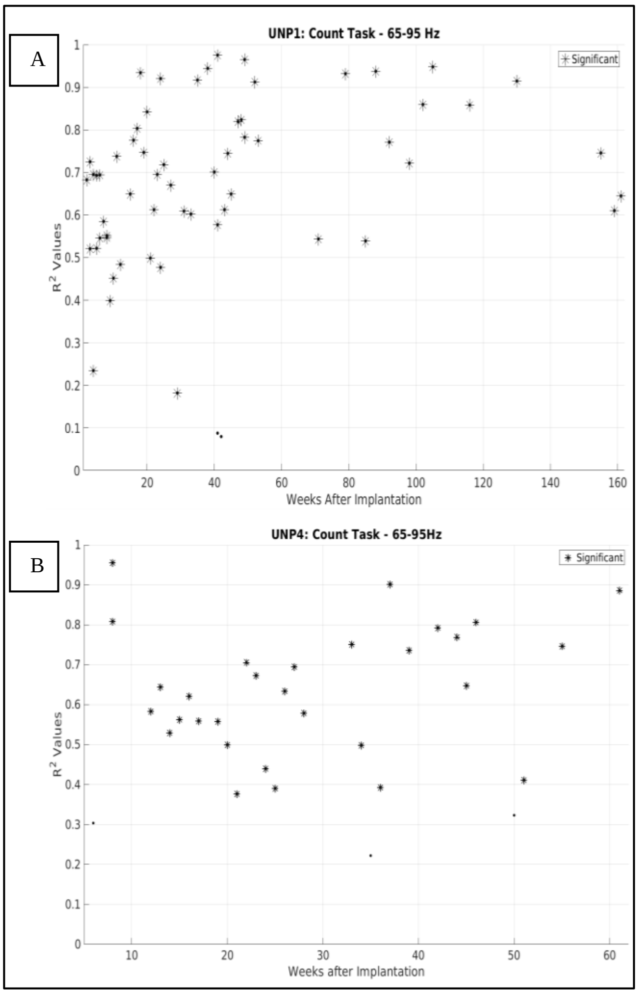

Figure 1: r^2 values calculated between the block-design of the count task and the mean HFB power of active and rest blocks for both participants. X-axis indicates weeks since implantation. Asterisks indicate a significant r^2 value. Due to different task lengths (i.e. sample points), the significance level of r^2 values can differ between sessions or participants (e.g. UNP1 in week 29 was significant, but UNP4 in week 6 was not).

DISCUSSION

Both participants were able to activate their left dlPFC – as measured by HFB power – by mental arithmetic for a period of 161 and 61 weeks (UNP1 and UNP4, respectively). They were able to activate their dlPFC at will from study start, meaning no training was required for volitional HFB power increase with mental arithmetic.

Importantly, for both participants, HFB was not always significantly modulated by the task. Moreover, compared to sensorimotor results from UNP1 [10], count task r^2 values were lower (average sensorimotor r^2 value was 0.89 ± 0.16; all r^2 values plotted in [10]). However, count task r^2 values reported here are in the same range as count task r^2 values reported for three able-bodied epilepsy patients in [15] (r^2 = 0.79, 0.53, and 0.65). The lower r^2 in the count task could be explained by the fact that a motor attempt strategy is more consistent than the use of variable starting numbers and step sizes, some of which may be easier than others. Varying degrees of difficulty may be associated with varying degrees of HFB power increase in some trials, and thus, on average, lower r^2 values. It has been shown before that HFB response in left-dlPFC varies between different mental calculation trials [15]. Moreover, the claim that difficulty may affect HFB power modulation is supported by the marked difference in difficulty and r^2 values between UNP4's first (week 6) and following (week 8 and thereafter) sessions. In the first session, UNP4 used a fixed step size (2) which – she reported - was quite easy. In the next session, she switched to a larger step size, which resulted in an increase of the r^2 values in the following sessions.

The dlPFC may provide a useful complement to a sensorimotor-based BCI system. We envision users of such a system could switch to dlPFC control when sensorimotor control does not work optimally, for instance due to interference caused by care or passive movement of limbs. However, it is currently unclear to what extent everyday cognitive tasks would interfere with a dlPFC-based BCI. Similar to sensorimotor areas, dlPFC-based BCI may work well in some situations, but not in others. This topic deserves further investigation. Moreover, HFB modulation during mental arithmetic (as expressed here by r^2 values) fluctuates. To what extent the relative unruly HFB modulation can be used to control a BCI application reliably is unknown.

The next steps in this avenue of BCI research are ongoing in our group, and include using HFB power from dlPFC for cursor control and for generating brain-clicks to control scanning software for communication purposes. It is preferable if the mental tasks used for BCI control can be performed without cues. Therefore, future research should in part focus on training the user to activate the left dlPFC without cues, testing which tasks work best (e.g. random number generation, mental arithmetic, or a combination) and elucidate how this training could be optimized.

CONCLUSION

These results indicate that the dlPFC may be a viable alternative for BCI users, when sensorimotor-based BCI is not an option. Future research should confirm the feasibility of home use of a dlPFC-based BCI by a user with LIS.

FUNDING

This study was funded by grants from the Dutch Technology Foundation STW and European Research Council.

ACKNOWLEDGEMENTS

We thank our participants for their courage, motivation, input, and hospitality.

REFERENCES

1. Smith, E., & Delargy, M (2005). Clinical Review: Locked-in syndrome. BMJ 2005;330:406, https://doi.org/10.1136/bmj.330.7488.406
2. Glennen, L. G., & DeCoste, D. C. (1997). The Handbook of Augmentative and Alternative Communication. Singular Publishing Group, Inc. San Diego, London.
3. Wolpaw, J. R., & McFarland, D. J. (2004). Control of a two-dimensional movement signal by a noninvasive brain-computer interface in humans. Proceedings of the national academy of sciences, 101(51), 17849-17854.
4. Hochberg, L. R., Serruya, M. D., Friehs, G. M., Mukand, J. A., Saleh, M., Caplan, A. H., ... & Donoghue, J. P. (2006). Neuronal ensemble control of prosthetic devices by a human with tetraplegia. Nature, 442(7099), 164.
5. Kim, S. P., Simeral, J. D., Hochberg, L. R., Donoghue, J. P., & Black, M. J. (2008). Neural control of computer cursor velocity by decoding motor cortical spiking activity in humans with tetraplegia. Journal of neural engineering, 5(4), 455.
6. Jarosiewicz, B., Sarma, A. A., Bacher, D., Masse, N. Y., Simeral, J. D., Sorice, B., ... & Cash, S. S. (2015). Virtual typing by people with tetraplegia using a self-calibrating intracortical brain-computer interface. Science translational medicine, 7(313), 313ra179-313ra179.
7. Bacher, D., Jarosiewicz, B., Masse, N. Y., Stavisky, S. D., Simeral, J. D., Newell, K., ... & Hochberg, L. R. (2015). Neural point-and-click communication by a person with incomplete locked-in syndrome. Neurorehabilitation and neural repair, 29(5), 462-471.
8. Nuyujukian, P., Sanabria, J. A., Saab, J., Pandarinath, C., Jarosiewicz, B., Blabe, C. H., ... & Hochberg, L. R. (2018). Cortical control of a tablet computer by people with paralysis. PloS one, 13(11), e0204566.
9. Pandarinath, C., Nuyujukian, P., Blabe, C. H., Sorice, B. L., Saab, J., Willett, F. R., … &

Henderson, J. M. (2017). High performance communication by people with paralysis using an intracortical brain-computer interface. Elife, 6, e18554 Pandarinath, C., Jarosiewicz, B., Blabe, C. H., ... & Hochberg, L. R. (2018). Cortical control of a tablet computer by people with paralysis. PloS one, 13(11), e0204566..

10. Vansteensel, M. J., Pels, E. G., Bleichner, M. G., Branco, M. P., Denison, T., Freudenburg, Z. V., ... & Van Rijen, P. C. (2016). Fully implanted brain–computer interface in a locked-in patient with ALS. New England Journal of Medicine, 375(21), 2060-2066.
11. Mutsaarts, M., Steenbergen, B., & Bekkering, H. (2007). Impaired motor imagery in right hemiparetic cerebral palsy. Neuropsychologia, 45(4), 853-859.
12. Mohammadi, B., Kollewe, K., Samii, A., Dengler, R., & Münte, T. F. (2011). Functional neuroimaging at different disease stages reveals distinct phases of neuroplastic changes in amyotrophic lateral sclerosis. Human brain mapping, 32(5), 750-758.
13. Ramsey, N. F., van de Heuvel, M. P., Kho, K. H., & Leijten, F. S. (2006). Towards human BCI applications based on cognitive brain systems: an investigation of neural signals recorded from the dorsolateral prefrontal cortex. IEEE Transactions on Neural Systems and Rehabilitation Engineering, 14(2), 214-217.
14. Vansteensel, M. J., Bleichner, M. G., Freudenburg, Z. V., Hermes, D., Aarnoutse, E. J., Leijten, F. S., ... & Ramsey, N. F. (2014). Spatiotemporal characteristics of electrocortical brain activity during mental calculation. Human brain mapping, 35(12), 5903-5920.
15. Vansteensel, M. J., Hermes, D., Aarnoutse, E. J., Bleichner, M. G., Schalk, G., van Rijen, P. C., ... & Ramsey, N. F. (2010). Brain–computer interfacing based on cognitive control. Annals of neurology, 67(6), 809-816.
16. Daniels, C., Witt, K., Wolff, S., Jansen, O., & Deuschl, G. (2003). Rate dependency of the human cortical network subserving executive functions during generation of random number series–a functional magnetic resonance imaging study. Neuroscience Letters, 345(1), 25-28.
17. Knoch, D., Brugger, P., & Regard, M. (2004). Suppressing versus releasing a habit: frequency-dependent effects of prefrontal transcranial magnetic stimulation. Cerebral Cortex, 15(7), 885-887.
18. Jahanshahi, M., Saleem, T., Ho, A. K., Dirnberger, G., & Fuller, R. (2006). Random number generation as an index of controlled processing. Neuropsychology, 20(4), 391.
19. Koike, S., Takizawa, R., Nishimura, Y., Marumo, K., Kinou, M., Kawakubo, Y., ... & Kasai, K. (2011). Association between severe dorsolateral prefrontal dysfunction during random number generation and earlier onset in schizophrenia. Clinical neurophysiology, 122(8), 1533-1540.
20. Crone, N. E., Miglioretti, D. L., Gordon, B., & Lesser, R. P. (1998). Functional mapping of human sensorimotor cortex with electrocorticographic spectral analysis. II. Event-related synchronization in the gamma band. Brain: a journal of neurology, 121(12), 2301-2315.
21. Levy, R., & Goldman-Rakic, P. S. (2000). Segregation of working memory functions within the dorsolateral prefrontal cortex. In Executive control and the frontal lobe: Current issues (pp. 23-32). Springer, Berlin, Heidelberg.
22. Wilson, F. A., Scalaidhe, S. P., & Goldman-Rakic, P. S. (1993). Dissociation of object and spatial processing domains in primate prefrontal cortex. Science, 260(5116), 1955-1958.