

# From assistance towards restoration with an implanted brain-computer interface based on epidural electrocorticography: A single case study

Alireza Gharabaghi<sup>a,b,\*</sup>, Georgios Naros<sup>a,b</sup>, Armin Walter<sup>c</sup>, Florian Grimm<sup>a,b</sup>, Marc Schuermeyer<sup>a,b</sup>, Alexander Roth<sup>c</sup>, Martin Bogdan<sup>c,d</sup>, Wolfgang Rosenstiel<sup>c</sup> and Niels Birbaumer<sup>e</sup>

<sup>a</sup>*Division of Functional and Restorative Neurosurgery & Division of Translational Neurosurgery, Department of Neurosurgery, Eberhard Karls University Tuebingen, Tuebingen, Germany*

<sup>b</sup>*Neuroprosthetics Research Group, Werner Reichardt Centre for Integrative, Neuroscience, Eberhard Karls University Tuebingen, Tuebingen, Germany*

<sup>c</sup>*Department of Computer Engineering, Wilhelm-Schickard Institute for Computer, Science, Eberhard Karls University Tuebingen, Tuebingen, Germany*

<sup>d</sup>*Department of Computer Engineering, University of Leipzig, Leipzig, Germany*

<sup>e</sup>*Institute for Medical Psychology and Behavioural Neurobiology, Eberhard Karls, University Tuebingen, Tuebingen, Germany*

## Abstract.

**Purpose:** Today's implanted brain-computer interfaces make direct contact with the brain or even penetrate the tissue, bearing additional risks with regard to safety and stability. What is more, these approaches aim to control prosthetic devices as assistive tools and do not yet strive to become rehabilitative tools for restoring lost motor function.

**Methods:** We introduced a less invasive, implantable interface by applying epidural electrocorticography in a chronic stroke survivor with a persistent motor deficit. He was trained to modulate his natural motor-related oscillatory brain activity by receiving online feedback.

**Results:** Epidural recordings of field potentials in the beta-frequency band projecting onto the anatomical hand knob proved most successful in discriminating between the attempt to move the paralyzed hand and to rest. These spectral features allowed for fast and reliable control of the feedback device in an online closed-loop paradigm. Only seven training sessions were required to significantly improve maximum wrist extension.

**Conclusions:** For patients suffering from severe motor deficits, epidural implants may decode and train the brain activity generated during attempts to move with high spatial resolution, thus facilitating specific and high-intensity practice even in the absence of motor control. This would thus transform them from pure assistive devices to restorative tools in the context of reinforcement learning and neurorehabilitation.

**Keywords:** Electrocorticography, neuroprosthetics, epidural implant, brain-computer interface, brain-machine interface, neurorehabilitation, stroke

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\*Corresponding author: Dr. Alireza Gharabaghi, Division of Functional and Restorative Neurosurgery, & Division of Translational Neurosurgery, Department of Neurosurgery Eberhard Karls University Otfried-Mueller-Str. 45, 72076 Tuebingen, Germany. Tel.: +49 7071 29 83550; Fax: +49 7071 29 25104; E-mail: alireza.gharabaghi@uni-tuebingen.de.

## 1. Introduction

Despite intensive rehabilitation training following evidence-based guidelines (Kwakkel et al., 2003), functional restoration in patients with severe and persistent motor deficits, for example after suffering a stroke, is very limited (Buma et al., 2013). Investigational studies are therefore currently exploring novel therapeutic strategies based on brain stimulation (Fusco et al., 2014; Kwon et al., 2013) or neurofeedback (Buch et al., 2008; Buch et al., 2012). In this vein, electroencephalography (EEG)-based neurofeedback training with brain-computer interfaces (BCI) has already been shown to successfully prime behaviorally oriented physiotherapy for motor rehabilitation in chronic stroke patients (Ramos-Murguialday et al., 2013).

Such non-invasive BCI approaches are characterized by low spatial resolution, with each EEG contact sampling of the order of  $10^5$ – $10^8$  neurons, a low signal-to-noise-ratio due to signal attenuation caused by the skull, possible contaminations by muscle artifacts and external electrical activity, and a relatively long training time to reach real-time control of devices (Leuthardt et al., 2009). By contrast, electrocorticographic (ECoG) BCI approaches may overcome these limitations thanks to their proximity to the neural signal source. Nonetheless, up until recently, ECoG devices in stroke patients have been implemented as assistive devices for prosthetic control (Yanagisawa et al., 2011) rather than for functional restoration in the context of neurorehabilitation. Moreover, current implantable BCIs in patients with motor deficits remain in direct contact with the brain via subdural grids (Yanagisawa et al., 2012; Wang et al., 2013) or even penetrate the tissue with intracortical microelectrodes (Hochberg et al., 2012; Collinger et al., 2013) bearing additional risks with regard to safety and stability in long-term application.

Implantable but less invasive approaches might therefore enable us to devise novel rehabilitation tools for patients with severe motor deficits. Such tools would have to utilize spared neural networks to address the neurobiology of motor learning, e.g. by volitional control of cortical signals and facilitating practice with feedback and reward (Birbaumer and Cohen, 2007; Dobkin, 2007).

We therefore implemented a neurofeedback rehabilitation set-up on the basis of an epidural implant that provides real-time feedback of motor-related

electrocorticographic brain activity to operate a virtual grasping movement according to the principles of motor learning (Hebb, 1949).

## 2. Methods

### 2.1. Patient

The 68-year-old, male patient had suffered a hemorrhagic stroke of the left thalamus associated with pyramidal tract damage at the level of the posterior limb of the internal capsule (see Fig. 1) 34 months before implantation. This had led to intractable pain on the right side of his body, including arm, hand and face area, and a persistent right-sided severe hemiparesis associated with an increased muscle tone of the affected body side. In particular, he had also lost the functional use of his upper extremity (Medical Research Council motor scale <2).

As a candidate for long-term cortical stimulation to reduce his chronic pain, the patient underwent implantation of an electrode array covering the left motor cortex to determine treatment response and optimal

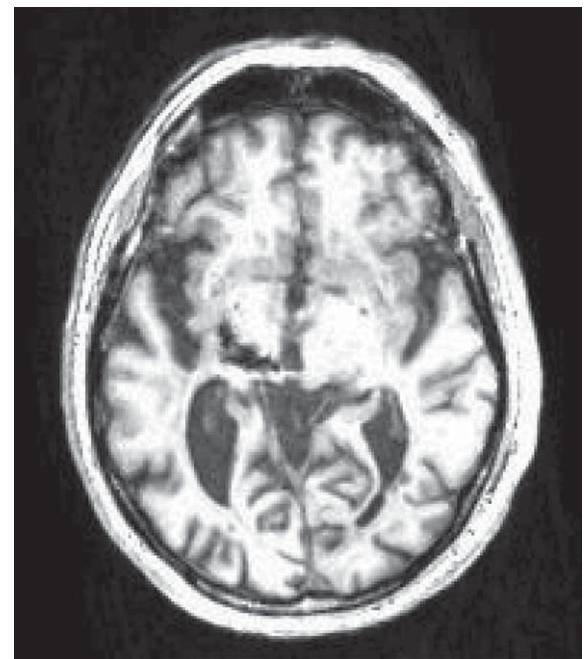


Fig. 1. T1-weighted axial MR image at the level of the lesion, indicating that the hemorrhagic stroke of the left thalamus also affected the posterior limb of the internal capsule.

stimulation sites for maximum pain reduction. Indication for implantation, array location and duration of implantation were determined solely by clinical criteria. The patient also gave informed consent to a study exploring a neurofeedback approach for motor restoration, which was conducted in accordance with the Declaration of Helsinki and the guidelines of the local ethics committee. Preoperative evaluation with electroencephalographic recordings and neurofeedback ensured that the patient was capable of controlling his oscillatory brain activity and that he was familiar with the experimental set-up. After implantation of the electrode array, the patient underwent seven training sessions with BCI neurofeedback on days 1, 2, 3, 4, 7, 8 and 9 after surgery. He performed 100–170 feedback trials per training session, resulting in a total of ~900 feedback trials.

## 2.2. Measurement of movement extension

During the training period, changes in the maximum amplitude of movement extension of the upper extremity were quantified by measuring the status with an ultrasonic motion detection system (Zebris Medical GmbH, Isny, Germany). The maximum movement extension was measured for each trial, and mean amplitude (+SD) for each session was calculated in five measurement sessions: one session 5 days before implantation (session 1), and four sessions on days 3 (sessions 2 and 3), 12 (session 4) and 24 (sessions 5) after implantation. On day 3 after implantation, one measurement session was performed before (session 2) and one measurement session (session 3) after the training session, respectively. The measurement sessions 1, 2, 3, 4, and 5 consisted of 14, 25, 15, 30, and 30 trials, respectively, and were independent of the BCI neurofeedback sessions. The motion detection system was based on ultrasound triangulation. Markers small enough to be attached to the hand enabled us to measure finger and wrist trajectories. During each measurement session, the patient was seated in a standardized fashion with a 45° angle between the upper arm and torso and a 90° angle in the elbow joint. For measurements of the wrist and fingers, the hand was positioned on a custom-built armrest. During measurements of the patient's hand function, 20 markers were attached to the knuckles and fingertips of his hand as well as to his wrist and forearm. The patient was visually and acoustically cued to maximally extend and relax his hand in each run. On the basis of the position of the

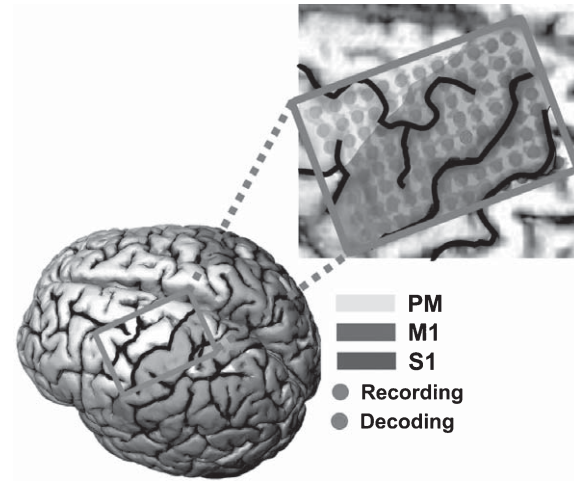


Fig. 2. Zoom out showing the implanted ECoG grid in relation to the reconstructed cortical anatomy of the patient. The grid covers the primary motor (M1) somatosensory (S1) and premotor cortex (PM). In addition, the orientation of the grid is projected onto a standard 3D brain reconstruction. The two contacts (green) used for the feedback training are projected onto the anatomical hand knob.

markers, the amplitudes of different movement angles were calculated to indicate the range of motion during each task.

## 2.3. Implanted neural interface

The epidurally implanted 8 × 12 electrode array consisted of platinum contacts with 4 mm contact diameter (2.3 mm exposed), and 5 mm center-to-center distance (Ad-Tech Medical Instrument Corp., Racine, Wisconsin, USA), covering a broad area of the left motor cortex (arm, hand and face area) as well as parts of the premotor and somatosensory cortex (see Fig. 2).

Following a two-week evaluation period, the array was removed and replaced by four permanent electrode leads for chronic application (Resume II, Medtronic, Minneapolis, USA) with four platinum iridium electrode contacts each (4 mm diameter, 10 mm center-to-center distance) at the sites where stimulation provided optimal pain control. This pain treatment is not part of the present report.

## 2.4. Neurofeedback set-up and training

The integrated system (see Fig. 3) consisted of an internal component, the implanted neural interface for electrocorticographic (ECoG) recordings, externalized with percutaneous extensions connecting to the exter-

174 nal components. These external components consisted  
175 of a recording and processing unit and of a feedback  
176 unit.

177 Recording of ECoG signals was performed with a  
178 monopolar amplifier (Brain Products, Munich, Ger-  
179 many) with a high-pass filter at 0.15 Hz and a sampling  
180 rate of 1000 Hz. Online processing of brain signals  
181 was performed with a BCI 2000 framework (Schalk  
182 et al., 2004) extended with custom-built features to  
183 control a video player via UDP. The patient received  
184 a visual movement cue with an open hand for 4 sec-  
185 onds followed by a 4 second relaxation period and was  
186 instructed to parallel this cycle by imagining finger and  
187 wrist extension. Feedback was provided contingent on  
188 movement intention related oscillatory brain activity  
189 by a video player displaying a virtual grasp movement  
190 from the perspective of the patient when observing  
191 his hand (Minimal Video Player, Phonon API). There  
192 was a short break after every ten trials (i.e. after each  
193 run). The patient performed 100–170 feedback trials  
194 per training session. On days 1, 2, 3, 4, 7, 8 and 9  
195 after implantation, one training session was performed,  
196 resulting in a total of seven training sessions with BCI  
197 neurofeedback and some 900 feedback trials in all.

## 198 2.5. Brain-computer-interface

199 Prior to the neurofeedback sessions, we performed  
200 two screening sessions with approximately 60 trials  
201 to select channels and features for the BCI training,  
202 estimating the spectral power for all electrode channels  
203 up to 200 Hz, computing  $r^2$  scores and assessing their  
204 significance with a permutation test. The two channels  
205 with the highest  $r^2$  scores for discrimination between  
206 movement and rest for all channels located close to the  
207 sensorimotor hand representation were selected for the  
208 feedback sessions and were kept constant throughout  
209 the training period.

210 During the training sessions, the spectral power of  
211 the two channels between 13 and 19 Hz was com-  
212 puted every 40 ms from a data buffer of length 500 ms.  
213 This entailed using an autoregressive model (Burg  
214 algorithm) with a model of the order of 16 (McFar-  
215 land and Wolpaw, 2008). These power values were  
216 taken as input for an adaptive linear classifier, result-  
217 ing in 25 classifier outputs per second. Five consecutive  
218 classifier outputs (200 ms) of the same feature were  
219 necessary to switch from one feedback condition to  
the other (e.g. to initiate virtual grasp movement).

## 220 2.6. Performance evaluation

221 To assess the patient's ability to modulate his brain  
222 activity contingent on the feedback task, i.e. his per-  
223 formance in gaining control of the BCI neurofeedback  
224 system, we calculated the average video movement  
225 time divided by the total feedback duration phase. We  
226 also measured a baseline condition to monitor natural  
227 perturbations of brain activity. Although not related  
228 to the task, these could have distorted the online BCI  
229 performance during the feedback task. This baseline  
230 condition consisted of several ECoG recordings while  
231 the patient was at rest with his eyes open throughout  
232 the 2-week study period. All in all, ~30 minutes of this  
233 spontaneous baseline ECoG activity were recorded for  
234 offline analysis, segmented into trials of the same struc-  
235 ture and processed in the same manner as the feedback  
236 sessions. For statistical analysis, the distribution of per-  
237 formance values per run in each feedback session was  
238 compared with the distribution of performance values  
239 for the baseline data (Wilcoxon rank-sum test).

## 240 3. Results

241 The epidural implant reliably detected electro-  
242 corticographic brain activity for providing real-time  
243 feedback of movement intention-related oscillations to  
244 control a virtual grasping movement. The brain sig-  
245 nals, detected by the same two adjacent contacts with  
246 a center-to-center distance of only 5 mm projecting  
247 onto the anatomical hand knob of the affected hemi-  
248 sphere, were sufficient for consistent neurofeedback  
249 throughout the whole training period (see Fig. 2).

250 Epidural recordings of field potentials revealed  
251 the beta-frequency band superior to alpha- and  
252 gamma-frequency bands for discrimination between  
253 movement intention and rest condition in this patient  
254 (see Fig. 4). The frequency band between 13–19 Hz  
255 was therefore applied in all training sessions for feed-  
256 back.

257 In each of the seven training sessions, the patient  
258 was able to modulate his brain activity contingent on  
259 the feedback task throughout the whole session. He  
260 thus acquired significant control of the BCI neurofeed-  
261 back system. In fact, he controlled the virtual hand  
262 movement for approximately 60% of the duration of  
263 feedback in each session. His performance in con-  
264 trolling the feed-back device in an online closed-loop  
265 paradigm was therefore constant and was significantly

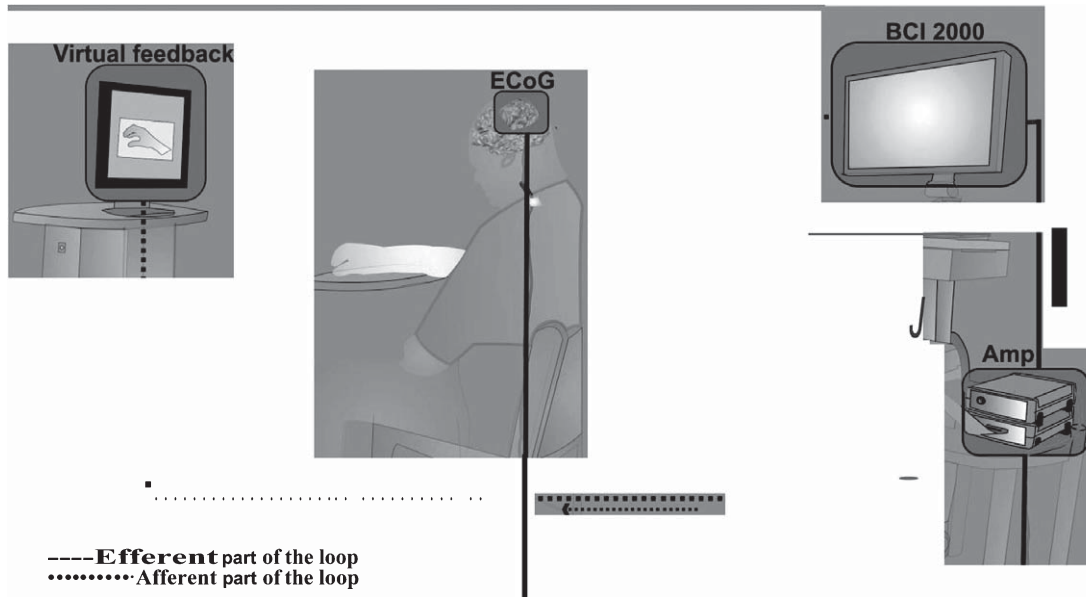


Fig. 3. Experimental set-up for reinforcement training with an implanted brain-computer interface including electrocorticography (ECoG) recording, signal amplification (Amp), software for online analysis and triggering (BCI2000) of visual feedback within a closed-loop framework.

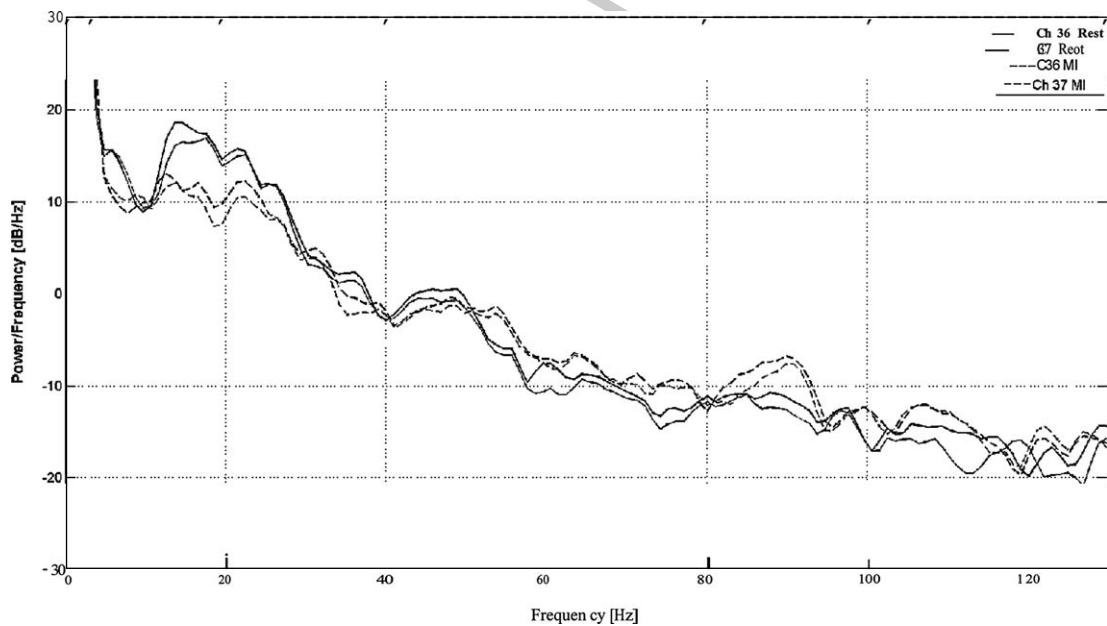


Fig. 4. Power/frequency plot for attempted hand movement (dotted lines) vs. rest (solid lines) for the two ECoG channels (black and gray) used in the feedback experiments (see also Fig. 2). We observed the anticipated desynchronization in the beta-band and the synchronization in the gamma-band.

266 higher than the baseline condition ( $29.3 \pm 11\%$ )  
 267 throughout the training period (see Fig. 5).

268 It took only seven training sessions, each last-  
 269 ing between 30 and 45 minutes, to significantly

improve maximum wrist extension (which was  
 quantified in separate measurement sessions) from  
 $7.25^\circ \pm 2.09^\circ$  (measurement session 1) before train-  
 ing,  $6.0^\circ \pm 2.70^\circ$  (measurement session 2) and

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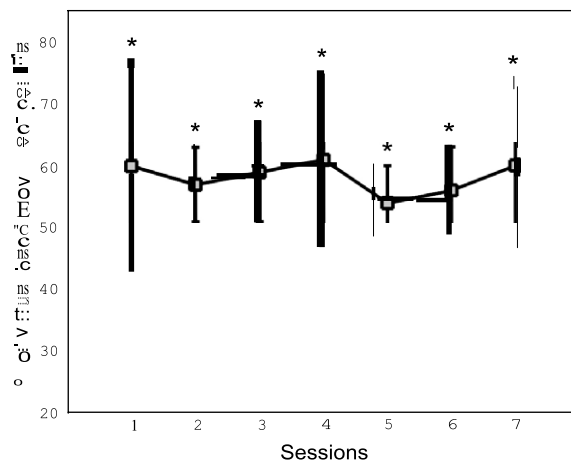


Fig. 5. Percentage of average movement time of the virtual hand divided by the total feedback duration phase. The mean  $\pm$  standard deviation of the performance measure per session is indicated by solid lines. The mean of the baseline data is indicated by a dotted line. An asterisk (\*) marks sessions where the median of the performance measure differs significantly ( $p < 0.05$ ) from the median of the baseline value (modified from Walter et al., 2012, presented at the 12th International Conference on BioInformatics and BioEngineering, Larnaca, Cyprus).

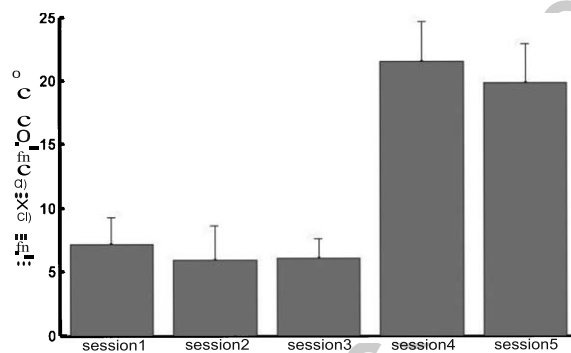


Fig. 6. Comparison of measurements of maximum wrist extension taken by an ultrasonic motion detection system before (session 1), during (sessions 2 and 3) and after (sessions 4 and 5) the training sessions, respectively.

274  $6.19^\circ \pm 1.45^\circ$  (measurement session 3) during training  
 275 to  $21.58^\circ \pm 3.13^\circ$  (measurement session 4) and  
 276  $19.91^\circ \pm 3.1^\circ$  (measurement session 5) after training  
 277 ( $t$ -test between sessions 1,2,3 and 4,5:  $p < 0.0001$ , see  
 278 Fig. 6). In summary, measurement session 3 was performed  
 279 after three training sessions, and measurement  
 280 4 was performed after seven training sessions. This  
 281 might well explain the performance change between  
 282 measurements sessions 3 and 4.

283 This improvement was specific for the trained mus-  
 284 cle and was not observed in other paretic muscles  
 285 which remained unchanged throughout the observation  
 286 period, producing either fasciculations or no move-  
 287 ments whatsoever. Feedback sessions and sessions for  
 288 movement evaluation were performed independently  
 289 of each other. The results therefore reveal a transfer and  
 290 a real improvement of voluntary control. Since the last  
 291 feedback training took place 9 days after implantation  
 292 and the last two sessions for movement evaluation were  
 293 performed 12 and 24 days after implantation, i.e. 3 and  
 294 15 days after the last feedback training, the movement  
 295 gains reveal lasting motor learning.

#### 4. Discussion

296 Some essential questions with regard to the clinical  
 297 viability of implantable BCI approaches remain unan-  
 298 swered. For instance, is a severely impaired patient  
 299 with a central nerve system lesion able to gain online-  
 300 control of a BCI even in the absence of volitional  
 301 control of hand and arm movements? Are less invasive  
 302 approaches for BCI control, such as epidural implants  
 303 and few decoding channels, feasible in this group of  
 304 patients? Could such devices be used as training tools  
 305 for rehabilitation in the absence of physiotherapists  
 306 and applied for repetitive exercises without having to  
 307 periodically update the neural decoding?

308 In the present study, we used an ECoG-based BCI  
 309 set-up to address these questions. This implanted inter-  
 310 face was a safe and feasible tool for neurofeedback-  
 311 based motor rehabilitation training of a chronic stroke  
 312 patient with severe and persistent hemiparesis. This  
 313 patient, who was otherwise unable to actively partici-  
 314 pate in conventional physiotherapy training of his  
 315 affected upper extremity, could gain volitional control  
 316 of the feedback device and thus engage himself in  
 317 repetitive, high- intensity exercises of intending finger  
 318 and wrist extension. He was able to participate in  
 319 the exercises without the assistance of a physiotherapist,  
 320 while monitoring online his own ability for volitional  
 321 modulation of brain activity and receiving immediate  
 322 reward for successful performance in this task by video  
 323 feedback of the intended movement.

324 Like earlier reports on able-bodied individuals  
 325 (Leuthardt et al., 2006), we too succeeded in  
 326 showing that epidurally recorded signals were appro-  
 327 priate for reliable BCI control in a motor-impaired  
 328 patient, thereby further increasing the safety of such  
 329

330 applications with intracranial recordings. Moreover,  
331 the same two adjacent electrode contacts were suf-  
332 ficient for BCI feedback throughout the training,  
333 indicating that smaller electrode grids with fewer  
334 contacts might suffice for future applications of this  
335 technique. These results tally with recent observations  
336 in epilepsy patients who had been subjected to a BCI  
337 visual speller with a single subdural contact (Zhang  
338 et al., 2013). Our findings therefore demonstrate the  
339 feasibility of less invasive and more straightforward  
340 approaches with only a small number electrode con-  
341 tacts in the epidural space for therapeutic applications  
342 of ECoG BCI.

343 Furthermore, it was not necessary to adjust the  
344 parameterization between the recorded brain signals  
345 and the BCI control algorithms during the two-week  
346 training period. These findings tally well with a report  
347 on multiple-day ECoG BCI control with fixed param-  
348 eters in an able-bodied patient with an implanted grid  
349 for seizure localization (Blakely et al., 2009). Simi-  
350 larly, we performed an initial screening and feature  
351 selection followed by a robust and stable-state control  
352 of the interface on the following training days. This is  
353 an important requirement for future real-life applica-  
354 tion of such tools for rehabilitation training, regardless  
355 of the necessity of periodical software adaptations by  
356 specialists at respective institutions.

357 Despite the massive hemiparetic motor impairment  
358 of this patient due to stroke, channels projecting onto  
359 the anatomical hand knob of the affected hemisphere  
360 provided sufficient information about his movement  
361 intention to permit robust and stable BCI feedback  
362 training of the brain activity generated during the  
363 attempt to move. This indicates that the somatotopic  
364 organization of the affected hemisphere has been at  
365 least partially preserved. It also demonstrates that  
366 even patients suffering from severe central nerve sys-  
367 tem lesions are suitable recipients of implantable BCI  
368 devices that address restoration of the compromised  
369 brain hemisphere.

370 ECoG studies in patients without motor deficits  
371 have shown movement-related spectral changes, i.e.  
372 decreases in the low-frequency band (8–32 Hz) with a  
373 larger cortical distribution and increases in the high-  
374 frequency band (76–100 Hz) with a more focused  
375 projection onto the sensorimotor cortex (Miller et al.,  
376 2007). The BCI ECoG cases in tetraplegia (Wang  
377 et al., 2013) and in moderate hemiparesis (Yanagisawa  
378 et al., 2011) have identified the gamma frequency band  
379 as the most informative band for decoding movement

380 types accordingly. Interestingly enough, in our case,  
381 the beta-frequency band was superior to the gamma-  
382 frequency band for decoding. This might be related  
383 to the fact that, in the reported cases of spinal cord  
384 injury (Wang et al., 2013) and moderate brain lesion  
385 (Yanagisawa et al., 2011), the cortical physiology was  
386 less affected than in our case. Moreover, while these  
387 two approaches applied more complex decoding algo-  
388 rithms based on additional features such as a broader  
389 frequency band to control 3D cursor control (Wang  
390 et al., 2013) or different movement types (Yanagisawa  
391 et al., 2011), our less sophisticated approach, which  
392 was confined to a narrow frequency band (13–19 Hz),  
393 was sufficient for a robust discrimination between  
394 movement intention and rest condition for high-density  
395 training.

396 This fact illustrates the major difference between the  
397 present approach and previous applications of ECoG  
398 BCI in motor impaired patients. Other approaches  
399 aimed at controlling external devices such as cursors  
400 or prosthetic arms as assistive tools, and did not yet  
401 strive to become neurorehabilitative tools for training  
402 and restoring lost motor function.

403 Such restorative tools would have to address princi-  
404 ples of motor learning such as facilitating practice  
405 with feedback and reward (Dobkin, 2007) while mak-  
406 ing use of the specific advantages of ECoG-based BCI  
407 technology. ECoG recordings allow for both tempo-  
408 rally and spatially precise and robust online detection  
409 of movement imagery/intention in the absence of real  
410 movement (Miller et al., 2010). This paves the way  
411 for neurofeedback-based rehabilitation training for  
412 patients who lack volitional control of their limbs.  
413 The effectiveness of such approaches based on rein-  
414 forcement learning would depend on factors such as  
415 need, effort, immediacy, contingency and desirable  
416 cost-benefit ratio and effort.

417 The present set-up met the need of a severely  
418 impaired stroke survivor to actively engage in reha-  
419 bilitation exercises in the absence of volitional motor  
420 control of his hand. The *effort* was deemed appropriate  
421 and motivating since the device enabled him to per-  
422 form autonomous training without the assistance of a  
423 physiotherapist.

424 *Immediacy* and *contingency* posed the greatest chal-  
425 lenges to this tool. The BCI set-up enabled us to  
426 make an update of the control signal as often as  
427 every 40 ms. However, our algorithm did not pro-  
428 vide visual feedback until 5 consecutive 40 ms epochs  
429 had been classified consistently, thus avoiding a noisy

control signal or false positive feedback. This trade-off between immediacy and contingency was sufficient both for robust BCI control and for the patient to comprehend that there is a direct link between his attempt to move and the virtual grasp movement. This is in agreement with earlier psychophysical studies in which participants who were repeatedly exposed to an artificially introduced 250 ms delay between voluntary actions and sensory consequences perceptually combined their voluntary actions with the sensory consequences and perceived that the delay was shortened by approximately 100 ms (Haggard et al., 2002).

The most intriguing observation was that, after only a small number of training sessions of this reinforcement learning paradigm, an improvement in the function of the targeted muscle could be established. We propose that this is due to repetitive engagement of a visuomotor loop relevant to the specific movement. The contingent activation of the respective neural correlates strengthened the connection between brain activity generated during the attempt to move and movement execution up to a level resulting in voluntary movement. This connection might be further reinforced by applying brain stimulation during the BCI training (Gharabaghi et al., 2014).

Due to the lack of cortical implants allowing for wireless BCI control, we devised an interface by connecting the intracranial implant to an external online processing framework for recording and BCI control. To this end, extension leads had to be externalized through the skin, thus limiting the possible duration of this set-up. Future clinical applications of this novel approach will require wireless devices capable of fast and reliable information transfer (Borton et al., 2013). This would enable us to perform long-term training periods of this paradigm in home-based environments, and thus provide the potential for more major motor recovery to improve the patients' quality of life.

In conclusion, epidural implants are a feasible tool for volitional control of cortical signals with high spatial resolution and, as such, facilitate specific and high-intensity practice with feedback and reward matching principles of motor learning. For patients with severe motor deficits, for example as a result of a stroke, such implanted brain-computer-interfaces may decode and train the brain activity generated during the attempt to move, even in the absence of motor control. This could transform them from pure assistive devices into restorative tools in the context of reinforcement learning and neurorehabilitation.

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