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A brain-computer interface for chronic pain patients using epidural ECoG and visual feedback

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***Abstract*—Electrocorticography (ECoG) offers the possibility of decoding movement intention even in the absence of motor control, making it a powerful signal source for brain-computer interfaces (BCI). We designed a BCI that translates attempts to move the hand into movements of a video of an opening hand to investigate its use for pain therapy and stroke rehabilitation. One patient with phantom limb pain after amputation of the arm and one patient suffering from chronic pain and paralysis after a stroke trained with this BCI for several sessions. Signals were acquired with epidural ECoG grids placed over the motor cortex contralateral to the affected or missing hand. The analysis of data obtained in screening sessions with cued attempted movements showed highly significant ($p < 0.01$, permutation test) r^2 values for the discrimination between movement and rest conditions for most frequencies up to 200 Hz. Both patients acquired control of the BCI system which was verified by the evaluation of three measures of the ability to start and stop the video application. In particular, both patients learned to reliably start the video application in all trials. This demonstrates that it is feasible for patients with phantom limb pain and chronic pain as well as paralysis after stroke to operate a BCI that targets their missing or impaired limb, making it a potentially useful tool for new approaches in pain therapy and stroke rehabilitation.**

***Index Terms*—Brain-computer interfaces, chronic pain, phantom limb, stroke, electrocorticography**

I. Introduction

Electrocorticography (ECoG) has been employed as a signal source for brain-computer interfaces (BCI) in recent years for several studies, mostly with subdural placement of the electrodes (e.g. [1], [2]), although a few BCI studies with epidural placement exist [3], [4]. Even though there is a decrease of power in lower frequencies in epidurally recorded signals compared to subdural recordings, the signal quality is suitable for driving a BCI [5]. ECoG offers the possibility of acquiring signals with a higher spatial resolution than EEG [6], thus providing the clinician with the ability to target very specific brain regions for feedback training in patients with cortical maladaptation. In addition, implanted electrodes can be used to deliver electrical stimuli for direct interaction with the brain. This could be a promising tool for the induction of cortical plasticity to provide a beneficial effect in conditions such as chronic pain or stroke. So far, the use of implanted electrodes for brain-computer interfaces has been largerly restricted to epilepsy patients (e.g. [1], [2], [7], [8] and in some cases to patients with severe motor impairments because of for example spinal-cord injury [9] or late-stage amyotrophic lateral sclerosis (ALS) [10].

We demonstrate in this work the feasibility of applying ECoG-BCIs to other patient groups and report the results of BCI training with one phantom limb pain patient and one patient suffering from chronic pain after a stroke. By evaluating three performance measures for BCI control, we show that both patients gained control of a BCI that translated attempted movements of the amputated or impaired hand into movements of a virtual hand by using epidural ECoG signals from the affected brain hemisphere. These experiments were part of a study on the use of a bidirectional cortical interface that employed cortical stimulation and BCIs for movement restoration in stroke and the establishment of a communication channel with ALS patients [11].

II. Materials and Methods

A. Patients

Two patients with chronic pain participated in this study. Patient S was a 63 year old man whose right arm was amputated after a motorcycle accident, leading to chronic phantom limb pain. Imaging studies suggest [12], that phantom limb pain might be related to reorganisation of the somatosensory cortex following the amputation [13]. He regularly experienced pain attacks in his phantom arm and was able to perform movements with his phantom arm. He had received several pain treatments, including mirror therapy [14] that provided no beneficial effect for him.

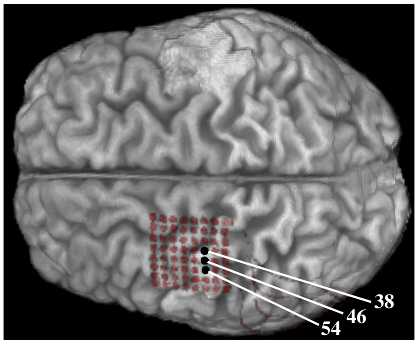
Patient P0 was a 68 year old man who suffered from chronic pain following a subcortical stroke which also lead to paralysis of his left hand. Patient P0 was accustomed to the BCI setup, because he had trained with the system for five sessions before the implantation using EEG.

Both patients were implanted with an epidural ECoG grid for a period of two weeks to select target areas as well as stimulation parameters to be used later in a chronically implanted stimulator applying motor cortex stimulation for pain reduction [15].

B. Electrophysiological recording

Patient S was implanted epidurally with an 8x8 ECoG grid of platinum contacts (Ad-Tech, Rancine, WI) with 2.3 mm diameter of the exposed electrode surface and 5 mm center-to-center distance. The grid was centered on the anatomical

(a)



(b)

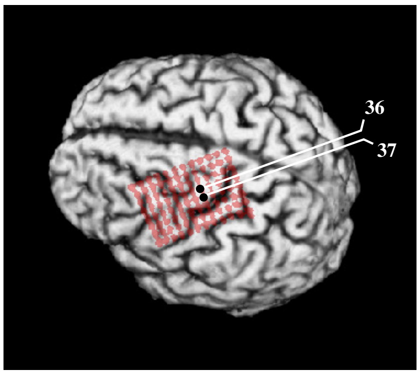


Fig. 1. Position of the ECoG electrodes, determined by fusion of pre-surgical MRI and a CT obtained after implantation. The electrodes used for the feedback experiments are marked as black dots. (a) Patient S, channels 38, 46 and 54 marked. (b) Patient P0, channels 36 and 37 marked.

hand knob of left primary motor cortex contralateral to the amputated arm. It covered a large part of left primary motor cortex along the diagonal of the grid as well as premotor and sensory areas (Fig.1 (a)).

Patient P0 was implanted with an 8x12 ECoG grid with the same electrode properties as patient S. The grid was also centered on the anatomical hand knob of left M1 but extended further towards the premotor cortex (Fig.1 (b)).

Signals were acquired with a BrainAmp (Brain Products, Munich, Germany) with a high pass filter at 0.15 Hz and sampling rate $f_s = 1000$ Hz. We also recorded EMG activity from the left arm of patient S using bipolar electrodes to check for movements of the healthy side.

C. *Channel and feature selection*

Each patient performed two screening sessions prior to BCI training to identify channels and features for classification. The patients performed 24-30 trials per session of cued attempted movements of the phantom hand or the paralyzed hand. Each trial consisted of a movement cue in form of a picture of a hand with extended fingers shown for 4 seconds, 2 seconds of movement, 2 seconds of hold and 4 seconds of relaxation. The patient was instructed to attempt to open his left hand during the movement period. During the hold phase, the patient had to stop the movement and to attempt to hold the hand in the current position. We expected to find features that discriminate between the movement phase and the resting phase in the spectral domain due to event-related desynchronization (ERD) of sensory motor rhythms (SMR) and synchronization (ERS) in the γ and high-γ frequency bands [16]. We estimated the spectral power between 1 and 200 Hz for all channels and computed r^2 scores for the discrimination between movement and rest (Fig.2). Significance of the r^2 values was assessed with a permutation test, using 10^5 random permutations of the class labels (*movement* and *rest*). We computed the r^2 values for each permutation, extracted the maximum of the values for all channels and frequencies, sorted them and used the $0.99 \cdot 10^5$-th value as the significance threshold. To make sure that the patient was relaxed, we used only data from seconds 1 to 3 of the relaxation phase instead of the full 4 seconds for the analysis.

An additional source of information for patient S was data generated by cortical mapping with electrical stimulation. Channels for feedback training of S were chosen from the subset of channels eliciting phantom hand sensations during cortical mapping. We found highly significant r^2 values ($p < 0.01$) on channels 38, 46 and 54 for frequencies in the range 10-40, 55-145 and 170-190 Hz. We decided to use the frequency band of 130-145 Hz as part of the high γ band for feedback training because the highest r^2 values for this band were found for channels that also elicited hand sensations during stimulation. Also, high frequency information seems to be beneficial for decoding of movements and is associated with activity of a small cortical area, thus it is very well suited for our application which relies on the feedback of very specific cortical activations.

In the case of patient P0, cortical stimulation did not lead to additional insight. We selected channels 36 and 37 for the feedback training because these channels displayed the highest r^2 values for the discrimination between hand movement and rest for all channels located close to the region in sensorimotor cortex associated with hand function in healthy subjects. In contrast to patient S, r^2 values for frequencies greater than 50 Hz were clearly smaller than the ones for low frequencies, leading us to use the frequency band between 13 and 19 Hz for feedback.

D. *Setup of the BCI experiments*

We employed the BCI2000 software package (http://www.bci2000.org) [17] for feedback training. The signal processing stage consisted of the estimation of spectral power values for the selected channels and frequencies which were used as input features for an adaptive linear classifier. For the computation of the spectral features, we estimated the coefficients an autoregressive model with order 16 with the Burg algorithm [18] which was fitted to a data buffer containing the signal acquired during the last 500 msec. The linear classifier produced a weighted sum of the power values which was normalized relative to the distribution of classifier outputs of the last three movement phases. All classifier weights were set to 1 for patient S and to -1 for patient P0. This differentiation was necessary due to the different frequency bands used for feedback: During a movement

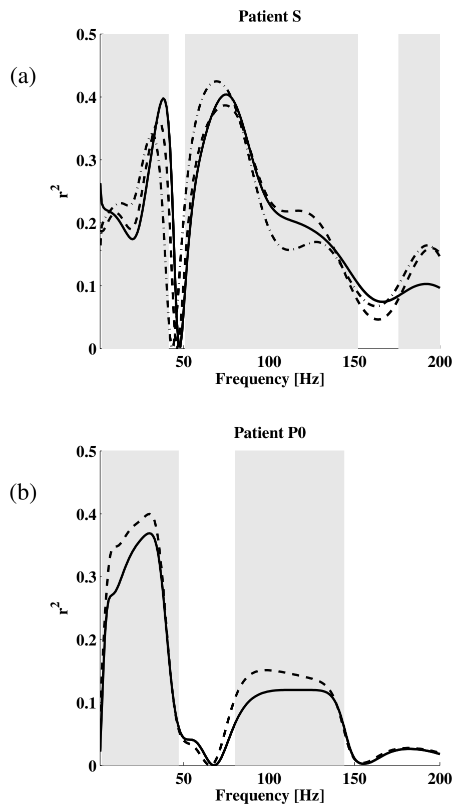


Fig. 2. r^2 values of screening data for the ECoG channels used in the feedback experiments. The grey shaded areas contain the frequencies with significant ($p < 0.01$) r^2 values for all channels. (a) r^2 values for channels 38 (dashed-and-dotted), 46 (solid) and 54 (dashed) of patient S. (b) r^2 values for channels 36 (solid) and 37 (dashed) of patient P0.

(active, attempted or imagined) one can find an increase in power for high frequency bands such as the band used for patient S and a decrease in low frequency bands [16]. The inverted sign of the classifier weights therefore ensures that a positive output of the normalization stage was associated with movement, while a negative value represented rest.

Data packets were received and processed by the application every 40 ms, resulting in 25 outputs of the classifier per second. In order to smoothen the display and to make it harder to change the state of the feedback, 5 consecutive outputs of the normalization stage with the same sign were necessary to switch the feedback on (in case of a positive sign and stopped feedback) and off (negative sign, running feedback). We chose as feedback device a video of an opening hand which was shown on a screen placed in front of the patient. This was implemented as a minimal video player using the Phonon API which received the control signal from BCI2000 via UDP. The video was shot from the perspective of the patient looking at his opening hand, thus providing more realistic feedback. Each session was subdivided into several runs separated by short breaks, each run consisting of 10 trials. Patient S trained for 5 sessions (53-190 trials per session) with this BCI, resulting in 682 trials. Patient P0 completed 7 sessions (100-170 trials per session) for a total of 908 trials.

In each trial, the patient received an auditory cue (”Go!”), prompting him to attempt to open his paralyzed or phantom hand. He had to maintain this attempted movement for several seconds. For our first patient S, this period had a length of 5 seconds. After finishing the BCI experiments, he stated that he was not always able to sustain the opening of his phantom hand as one continuous movement over the whole 5 seconds which may have affected his concentration at the end of the trial. We therefore reduced the duration of the movement period to 4 seconds for the next patient P0. After the movement period, the patient received another auditory cue (”Relax!”), followed by 5 seconds of relaxation before the next trial started. If the BCI system detected an intention to move the hand during the movement phase, the video was either started or resumed to play, if not, then the video was paused.

E. Performance analysis

We removed all trials showing artefacts (e.g. from cable movements) on the channels used for classification. In the case of patient S, we also excluded all trials showing EMG activity of the healthy arm. Trial rejection was performed using a semi-automated method based on the variance of the signal and visual inspection to detect outlier. This was done in order to ensure that the BCI was only driven by movements of the phantom arm. In total, we had to remove 396 trials (43 %) for patient S and 203 trials (22 %) for patient P0. To assess whether our patients were able to control the BCI, we defined three measures of performance and computed these for all sessions. Measure (1) (percentage of trials with video, TWV) is defined as: Number of trials in which a ”Go”-signal was sent to the video divided by the total number of trials. This captures how often the patient was able to overcome the initial hurdle of starting the video. Measure (2) (video movement per trial, VPT) is the average time per trial in which the video moved divided by the total duration of the feedback phase per trial. The third measure (consecutive video movement, CVM) is computed as the average consecutive runtime of the video per trial. Measures 2 and 3 represent the ability of the patient to modulate his brain activity for a certain amount of time, but measure 3 targets specifically the issue, whether the patient is able to keep the feedback device in the desired state (i.e. the video running). These measures are appropriate for our BCI with continuous visual feedback, because they reflect the experiences the users make with the system: Did the video start to run? How far did the video hand open? Was it running smoothly or stuttering?

Due to the adaptive stage of the classifier it is possible that even non task-related activity can start the video. In order to state whether the patient gained control of the system, i.e. whether he learned to perform better than chance, we recorded in total 24 minutes of ECoG data for patient S and 29 minutes for patient P0 over the course of the two weeks of training while he was instructed to relax with open eyes. This data was offline segmented into trials of the same structure as the trials of the feedback experiments and processed with the same signal processing algorithms and parameters as in the online experiments. The output of a simulated version of the video feedback device was used to compute the performance measures described above on the resting data.

F. Statistical analysis

We performed a statistical analysis on the results of the performance analysis in section II-E. To assess, whether the performance measure of a single training session was different from the baseline, we computed the performance measures for each run of the session and compared this distribution with the distribution of performance values for the resting state ECoG data. To do this, we treated each resting state recording as a single run, thus generating a distribution of baseline performance values. We performed a Wilcoxon rank-sum test for each training session and performance measure, comparing it to the baseline distribution of the measure to determine whether the medians of baseline and training values were significantly different.

The significance of the trend over time in the performance data was estimated with the following procedure: We first computed the slope of the linear trend by least-squares fit of a line to the mean of the performance measures for each session. We drew n values from a gaussian distribution with the same mean and variance as the set of session means, where n is the number of sessions (S: $n = 5$, P0: $n = 8$) and computed the slope of the trend for these n random values. We repeated this 10^5 times and denoted p as the fraction of random trends having a steeper slope with the same sign as the trend estimated on the training data.

III. Results

Patient S reached a level of 100 % in measure TWV (Fig.3 (a)), starting from 71.7% in the first session. From the second session on, the TWV measure was significantly higher ($p < 0.05$) compared to the baseline value of $63.2 \pm 13.3\%$ for unrelated data. A strong significant ($p = 0.02$) positive trend ($r^2 = 0.96$) is apparent in the performance data. One can also find a non-significant ($p = 0.06$) positive trend (Fig.3 (b)) for measure 2 ($r^2 = 0.59$) with the last three sessions of BCI training resulting in significantly higher VPT values than baseline ($84.8 \pm 12.1\%$, $77.0 \pm 19.1\%$ and $67.9 \pm 17.5\%$ compared to $49.1 \pm 10.6\%,\ p < 0.05$). Measure 3 (Fig.3 (c)) showed significantly decreased values for CVM in the last session (3.0 ± 1.1 sec compared to 3.8 ± 0.4 sec) and exhibits no clear trend over time ($r^2 = 0.06, p = 0.32$).

Patient P0 already had experience with the BCI using EEG prior to the surgery. In the ECoG sessions, he achieved perfect scores of 100% in all sessions for measure TWV, all significantly ($p < 0.05$) different from the baseline level at $50.34 \pm 20.14\%$ (Fig.4 (a)). VPT values in all sessions varied around 60%, all being significantly higher than baseline values of $29.3 \pm 11\%$ (all $p < 0.01$) (Fig.4 (b)). CVM scores for all sessions were lower than the baseline of 2.37 ± 0.81 sec but did not differ significantly from baseline (all $p > 0.15$) (Fig.4 (c)). There was no significant trend for any measure for patient P0.

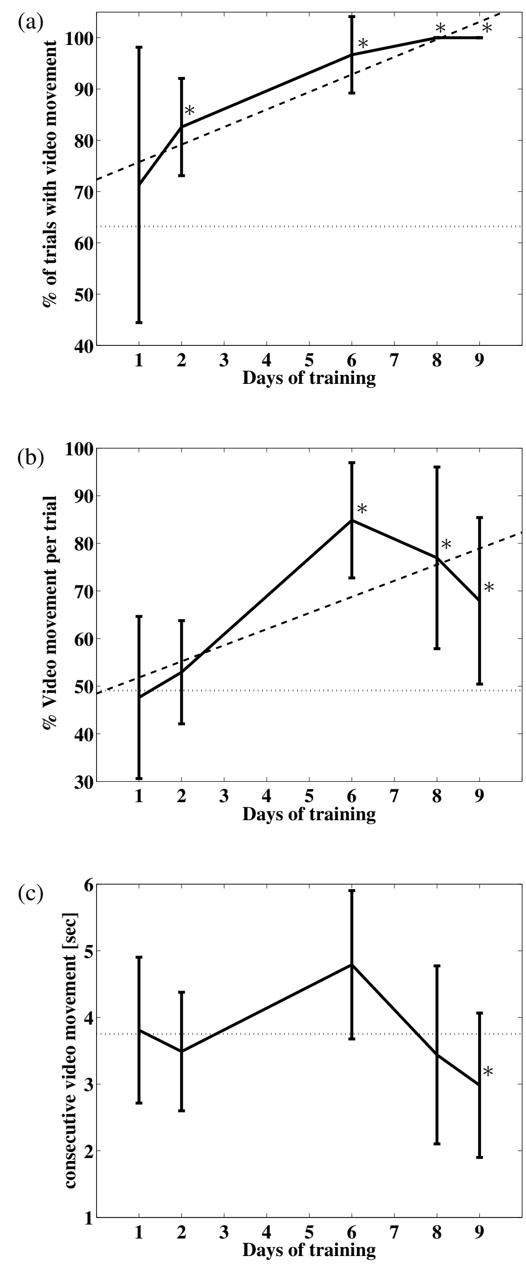


Fig. 3. Performance curves of patient S for the three measures TWV (a), PVT (b) and CVM (c). Solid lines indicate the mean $\pm$ standard deviation of the performance measure per BCI feedback session. Dashed lines in (a) and (b) show the trend line determined by linear least squares regression. Dotted lines denote the mean of the performance measure for resting state ECoG data (baseline). An asterisk ($*$) marks sessions where the median of the performance measure differs significantly ($p < 0.05$) from the median of the baseline values.

IV. Discussion

The lack of a significant trend in measures VPT and CVM indicates that our patients were able to learn to reliably produce the necessary activity in order to start the feedback

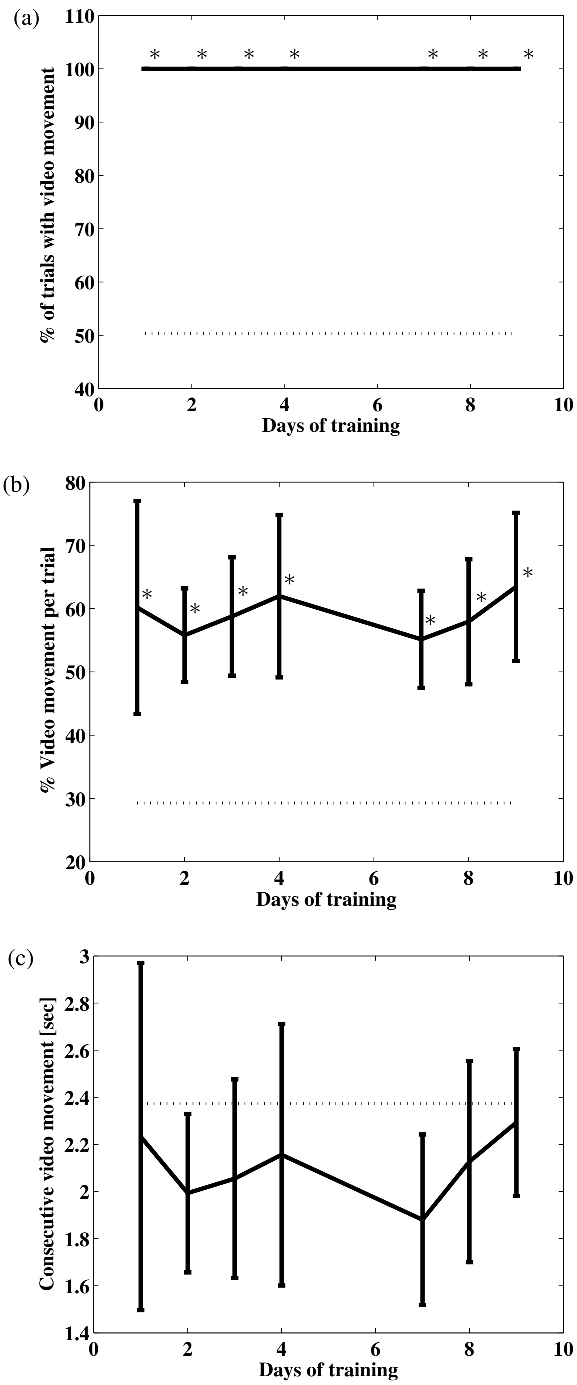


Fig. 4. Performance curves of patient P0 for the three measures TWV (a), PVT (b) and CVM (c). Solid lines indicate the mean $\pm$ standard deviation of the performance measure per BCI feedback session. Dotted lines denote the mean of the performance measure for resting state ECoG data (baseline). An asterisk ($*$) marks sessions where the median of the performance measure differs significantly ($p < 0.05$) from the median of the baseline values.

(measure TWV), but that they did not learn to lengthen the amount of time in which they are consecutively producing the right activity. The significantly increased VPT in the last three sessions shows that patient S learned to increase the video coverage of a trial. The significantly decreased CVM in the last session indicates that this is probably due to the patient being able to restart the video if it stopped during the trial, thus resulting in an (on average) reduced consecutive video movement time. One reason for this could be, that the patient was not able to learn to perform the opening of the phantom hand for more than a constant amount of time. Patient S himself stated that he was not always able to extend his phantom hand during the whole feedback period of 5 seconds. Instead, he reached the maximum extension point of his phantom fingers earlier and thus might not have produced suitable ECoG activations after stopping the movement. This implies that either a reduction of the length of the feedback period or a video of a continuously opening and closing hand might be helpful for future studies. The latter suggestion would then have to be accompanied by either the patient anticipating the video movement when deciding on the direction of the phantom hand movement or by using more sophisticated signal processing methods to discriminate between an opening and closing phantom movement from the recorded ECoG signal and then driving the video application according to the decoded movement direction. Otherwise, the visual feedback would not be contingent to the phantom movements and maybe even counterproductive by confusing the patient.

Patient P0 on the other hand was able to start the video in all trials and all sessions, indicating that he was able to translate the control he had acquired with the EEG-based training to the ECoG-based training. Taken together, he only displayed during his first EEG session a TWV score that was not significantly better than chance and improved in all other sessions to an almost perfect TWV score. Although he also obtained a VPT score higher than chance, no significant trend was visible and measure CVT was always near chance.

Although the approach described here for feature selection and classification has the advantage of requiring only a small amount of screening data before the first BCI session for manual parameter selection, more sophisticated classification algorithms such as support vector machines combined with automatic feature selection methods might provide a better decoding of movement intentions than the adaptive linear classifier employed here. However, manual (pre-)selection of features might be more appropriate for "restorative" BCIs such as the system reported here, because it allows the researcher/clinician to specifically target brain areas and rhythms as input for training for which improved control might result in functional improvements for the patient.

V. Conclusion

In conclusion we found that two chronic pain patients that had lost control over their hand, either by amputation or because of a paralysis induced by a stroke, were able to quickly gain control over a brain-computer interface using spectral modulations of epidural ECoG signals induced by attempted movements of the impaired or phantom hand and sustain this control over several sessions. This demonstrates the feasibility of therapeutic approaches in which intended movements of strongly impaired patients are translated into movements of virtual or robotic limbs. Target groups for such approaches are patients suffering from paralysis or chronic pain.

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