

Perspective

Invasive brain–machine interfaces: a survey of paralyzed patients’ attitudes, knowledge and methods of information retrieval

Jacob Lahr^{1,2,3,4,9}, Christina Schwartz^{6,9}, Bernhard Heimbach³,
Ad Aertsen^{5,7,8}, Jörn Rickert^{6,9} and Tonio Ball^{4,5,9}

¹Freiburg Brain Imaging, University Medical Center, Freiburg, Germany

²Department of Psychiatry and Psychotherapy, University Medical Center, Freiburg, Germany

³Department of Neurology, University Medical Center, Freiburg, Germany

⁴Intracranial EEG and Brain Imaging Group, University Medical Center, Freiburg, Germany

⁵BrainLinks-BrainTools, University Freiburg, Germany

⁶CorTec GmbH, Freiburg, Germany

⁷Bernstein Center Freiburg, University of Freiburg, Germany

⁸Faculty of Biology, University of Freiburg, Germany

E-mail: jacob.lahr@uniklinik-freiburg.de

Abstract

Objective. Brain–machine interfaces (BMI) are an emerging therapeutic option that can allow paralyzed patients to gain control over assistive technology devices (ATDs). BMI approaches can be broadly classified into invasive (based on intracranially implanted electrodes) and noninvasive (based on skin electrodes or extracorporeal sensors). Invasive BMIs have a favorable signal-to-noise ratio, and thus allow for the extraction of more information than noninvasive BMIs, but they are also associated with the risks related to neurosurgical device implantation. Current noninvasive BMI approaches are typically concerned, among other issues, with long setup times and/or intensive training. Recent studies have investigated the attitudes of paralyzed patients eligible for BMIs, particularly patients affected by amyotrophic lateral sclerosis (ALS). These studies indicate that paralyzed patients are indeed interested in BMIs. Little is known, however, about the degree of knowledge among paralyzed patients concerning BMI approaches or about how patients retrieve information on ATDs. Furthermore, it is not yet clear if paralyzed patients would accept intracranial implantation of BMI electrodes with the premise of decoding improvements, and what the attitudes of a broader range of patients with diseases such as stroke or spinal cord injury are towards this new kind of treatment. *Approach.* Using a questionnaire, we surveyed 131 paralyzed patients for their opinions on invasive BMIs and their attitude toward invasive BMI treatment options. *Main results.* The majority of the patients knew about and had a positive attitude toward invasive BMI approaches. The group of ALS patients was especially open to the concept of BMIs. The acceptance of invasive BMI technology depended on the improvements expected from the technology. Furthermore, the survey revealed that for paralyzed patients, the Internet is an important source of information on ATDs. *Significance.* Websites tailored to prospective BMI users should be further developed to provide reliable information to patients, and also to help to link prospective BMI users with researchers involved in the development of BMI technology.

Keywords: brain–machine interface (BMI), brain–computer interface (BCI), electrocorticography (ECoG), intracranial EEG (iEEG), survey, electroencephalography (EEG)

⁹ Contributed equally to this work.

(Some figures may appear in colour only in the online journal)

1. Introduction

Brain–machine interfaces (BMIs) are new therapeutic options that are currently being developed for paralyzed patients. There are, basically, two approaches for BMIs. The first approach uses noninvasive techniques that are predominantly based on scalp electroencephalography (EEG); the second uses invasive recordings that are based on intracranial EEG (iEEG, such as the ECoG, for electrocorticography, as seen in figure 1), intracortical local field potentials, or neuronal spiking activity. Invasive approaches have the advantage of a higher bandwidth and a higher signal-to-noise ratio compared to BMIs based on scalp EEG (Ball *et al* 2009) and are therefore promising for therapeutic BMI applications. Pilot studies with paralyzed patients enabled the decoding of on/off decisions (Kennedy and Bakay 1998, Levine *et al* 2000), cursor control (Milekovic *et al* 2012), and control over a robotic arm (Collinger *et al* 2013, Hochberg *et al* 2012, 2006) using BMIs based on signals from intracranially implanted electrodes.

The prospective clinical applications of BMIs on a larger scale raises questions about which group of patients is eligible for therapeutic BMI implantations and whether these patients find intracranial electrode implantation acceptable for a BMI. Previous studies highlighted that generally, a broad group of patients with severe motor disabilities may benefit from a BMI, including patients affected by stroke, spinal cord injury (SCI), and neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS) (Collinger *et al* 2013, Hochberg *et al* 2006, Kennedy and Bakay 1998, Simeral *et al* 2011).

In the present study, a survey was conducted among these various groups of patients. The survey covered the participants' motor impairments, dependency on care, their requirements for medical devices, and their attitude toward invasive BMIs.

Major novel aspects arising from the present study were that ALS patients significantly differed from the other groups of patients, in that they had the highest level of acceptance toward invasive BMI technology. Further, information sources about ATDs and knowledge about BMIs were evaluated. The Internet turned out to be one of the most important information sources on ATDs. Websites tailored to paralyzed patients are thus important in providing reliable information, and they also may help to link prospective BMI users with researchers involved in the development of BMI technology, thus facilitating the participation of motivated patients in upcoming BMI studies.

2. Methods

Characteristics of patient groups that are eligible for therapeutic BMI application were explored by a survey of paralyzed patients. Participants were approached via self-help organizations, medical offices, specialized outpatient

departments, and by an advertisement in a journal for disabled persons (*HANDICAP*, Wilhelmshafen, Germany). A total of 169 questionnaires was returned. Among those, 38 had to be discarded because more than 25% of the questions were not answered. Therefore, 131 questionnaires entered the final analysis, with 82 completed questionnaires returned in paper form, and 49 questionnaires returned by online submission. The study was approved by the Ethics Review Board of the University Medical Center, Freiburg, Germany.

Patient's attitudes were assessed using a standardized questionnaire with 28 items (see the Supplementary Material). The items consisted of multiple-choice questions, free-text questions, and rating scales. The questionnaire was structured as follows: (i) an introductory information part that described the aim of the questionnaire (one page), (ii) the informed consent section (one page), (iii) demographic information about the participant, and (iv) specific questions about their impairments and (v) assistive technology devices (ATDs) (see box 1 and the Supplementary Material).

2.1. Data analysis

Descriptive statistics were applied to the survey data (median for continuous variables, frequencies for categorical variables). Motor impairment was calculated as the mean of impairments in the domains 'muscle power,' 'mobility,' 'gait and posture,' and 'grasp and grip.' Differences of openness between diagnoses were assessed using a Kruskal-Wallis test and rank-sum tests for post-hoc analyses. The correlation between motor impairments and the openness to BMIs was calculated using Spearman's rank correlation. Correlation between age and use of the Internet as a source of information, as well as between age and knowledge about invasive BMIs, was calculated using point-biserial correlation (Howell 2013). To enable the detection of relationships between the different variables, a correlation matrix was calculated using Spearman's rank correlation. ATDs indicated by the participants were assigned to four categories: mobility, communication, care/hygiene, and other. Given the explorative characteristic of the study, we did not apply correction for multiple testing. Free-text answers were categorized (e.g., positive/negative/neutral attitude toward BMI) and representative examples were cited.

3. Results

3.1. Demographic data

Of the 131 surveyed patients, 76 were male and the mean (\pm SD) age was 56.3 ± 13.0 years (range: 13–81 years). Regarding their socioeconomic background, 88.5% ($n = 116$) of the patients in the study were unemployed, 76.3% ($n = 100$) were married or in a relationship, 72.5% ($n = 95$) lived with a partner or family, 16% ($n = 21$) lived alone, and 0.8% ($n = 1$)

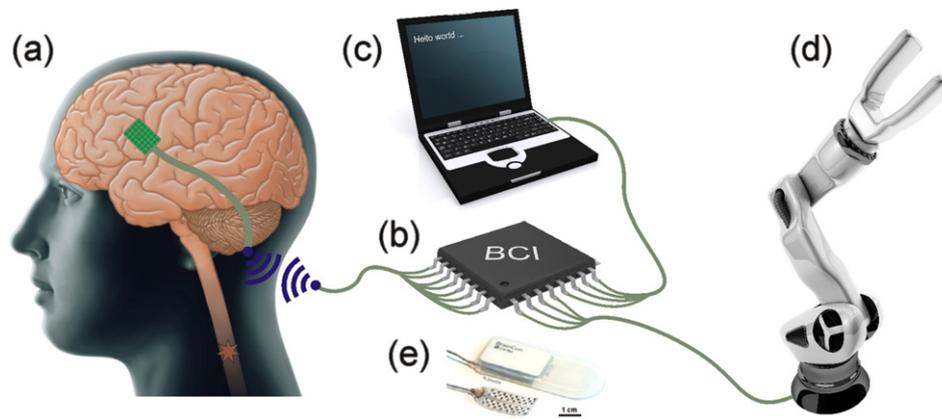


Figure 1. Schematic BMI setup in a person with a spinal-cord injury. Independent of peripheral nerves, brain activity is recorded from (a) a subdurally placed electrode array and transmitted wirelessly to (b) an external signal processing unit. Then, the decoded signals may be used to control (c) a spelling device or a cursor, (d) a robotic arm, or other actuators. In (e), a photograph of a prototype electrode and implant developed at the BMI Initiative Freiburg in cooperation with CorTec, Freiburg is shown © 2012 IEEE. Reprinted, with permission from Schuetzler *et al* (2012) other images from Fotolia.com: C Contet; Lom123; Typomaniac.

Box 1. Questionnaire summary. FT: free-text answer; MC: multiple-choice answer; RS: rating-scale answer.

- (1) Demographic data (gender, age, profession, socioeconomic status) (FT + MC)
- (2) Diagnosis
 - a. What are the main symptoms? (MC + FT)
 - b. When did the symptoms start? (FT)
 - c. How is the subjective mental and physical quality of life? (RS)
 - d. Who provides care to the patient? (MC)
- (3) Impairments
 - a. Is the patient suffering from pain? (RS)
 - b. Which activities are impaired? (RS + FT)
 - c. Which impairment is most burdensome? (FT)
- (4) Assistive technology devices (ATDs)
 - a. Which ATDs are already in use by the patient? (FT)
 - b. How satisfied is the patient with these ATDs? (RS)
 - c. Which new ATDs does the patient plan to acquire? (FT)
 - d. Who is paying for the ATDs? (MC)
 - e. Who consults with the patient about new ATDs? (MC)
 - f. Where does the patient get information about ATDs? (MC)
 - g. Which self-help or interest groups is the patient affiliated with? (FT)
 - h. What are the most important criteria for ATDs? (RS)
 - i. What is the ideal future ATD? (FT)
 - j. Is the patient aware of implantable ATDs? (MC)
 - k. Is the implantation of an ATD an option, if it would significantly improve mobility and communication skills? (RS)
 - l. Does the patient know about invasive BMIs? (MC)
 - m. What are the patient's thoughts about the surgical implantation of subdural electrodes for control of an ATD? (FT)

lived in a care facility. The remaining 8.4% ($n = 11$) gave no answer.

3.2. Impairments

The diagnoses in the study sample were stroke ($n = 66$), ALS ($n = 37$), SCI ($n = 10$), and other ($n = 18$, e.g., muscular dystrophies, neuropathies). The characteristics of the study sample and the results of the questions on individual impairments are summarized in figure 2.

3.3. Care and assistive technology

Of the patients surveyed, 94.7% ($n = 124$) regularly received support from caregivers. Therapists and physicians were indicated as the most common caregivers, at 68.7% ($n = 90$), followed by partners (59.5%; $n = 78$), family (51.1%; $n = 67$), friends (35.9%; $n = 47$), and professional caregivers (32.1%; $n = 42$). According to survey results, 91.6% ($n = 120$) of the patients were already using ATDs. Across all patients, the use of 443 ATDs was reported (multiple responses were possible, with a mean of 3.38 devices per patient). Of the ATDs cited

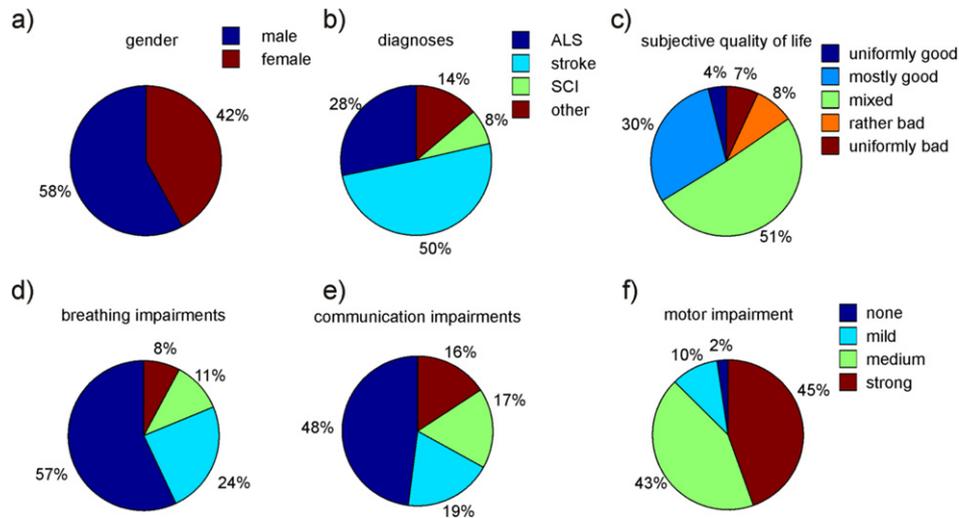


Figure 2. Characteristics of the study population.

by patients, 42.7% (n = 189) were in the ‘mobility’ category (e.g., wheelchairs, walking canes), 23.3% (n = 103) were in the ‘autonomy/food intake’ category (e.g., carrying aids, reaching aids), 8.1% (n = 36) were in the ‘care and hygiene’ category (e.g., hospital beds, urinary catheters, aspirators), 6.3% (n = 28) were in the ‘communication’ category (e.g., head-controlled computers, special communication software), and 19.6% (n = 87) were in the ‘other’ category. The satisfaction with the ATDs was rated using a five-point scale, with 29.8% of the ratings at ‘very satisfactory,’ 45.8% at ‘satisfactory,’ 10.8% at ‘neutral,’ 8.6% at ‘less satisfactory,’ and 1.35% at ‘not satisfied;’ 3.8% did not supply an answer.

Asked about the importance of some criteria of ATDs (mobility, gait and posture, general muscle strength, grasp and grip, communication, pain reduction, autonomous breathing, natural physiognomy), support for mobility was indicated to be most important (87.0%, n = 114), followed by improvements in grasp and grip (77.1%, n = 101), gait and posture (71.0%, n = 93), support for general muscular strength (58.8%, n = 77), and communication improvements (47.3%, n = 62).

Furthermore, the patients were asked who they consulted with regarding new ATDs and about their sources of information on ATDs (figure 3(a)). Of the patients surveyed, 63.4% (n = 83) were advised on ATD use by their physician or therapists, 47.3% (n = 64) acquired information on ATDs by themselves, 29.8% (n = 39) got advice from their partner, and 22.1% (n = 29) got advice from their family. The Internet turned out to be the most important information source on ATDs. Websites of ATDs suppliers were used by 38.9% (n = 51) of the respondents, directly followed by Web forums (36.6%; n = 48). There was a significant negative correlation between age and the use of the Internet as information source ($r_{pb} = -0.222$, $p = 0.014$). Other information channels were self-help groups and patient associations (36.6%; n = 48), catalogs (33.6%; n = 44), specialized journals (31.3%; n = 41), and trade fairs (20.6%; n = 27).

The patients were also asked if they had heard about BMI technology for paralyzed patients prior to the survey

(figure 3(b)), and 61.1% (n = 80) of the patients responded that they had. Survey results indicated that 54.2% (n = 71) of the patients knew about implantable ATDs, and the correlation between knowledge on implantable ATDs and age was significant ($r_{pb} = -0.252$, $p = 0.005$). When asked about their attitudes concerning the implantation of a medical device such as electrodes for BMIs, 48% (n = 60) of the respondents answered that they could imagine the implantation of a medical device if it would crucially improve their mobility and ability to communicate, whereas only 7% (n = 9) indicated that they could not imagine this kind of treatment at all (see figure 4 for further details). ALS patients showed a significantly higher degree of openness toward invasive BMIs (Kruskal-Wallis test: $p < 0.005$, post-hoc rank-sum test of ALS against other diagnoses: $p = 0.01$). The correlation between motor impairments and openness to invasive BMIs was not significant ($\rho = 0.053$, $p = 0.559$).

Using open questions, the participants were asked about their associations with BMIs in general and the implantation of intracranial electrodes for a BMI in particular. Here we list a selection of typical answers given by the participants.

The answers about BMIs in general (n = 61) underlined a positive attitude toward research on BMIs (e.g., ‘I find this fantastic and would like to take part in an experiment.’ ‘It is good that research is done.’ ‘The development is laudable in every aspect and should be further followed.’). Only a small number of participants expressed doubts about the technology (n = 18; e.g., ‘will not work in everyone ...,’ ‘sounds very complex’).

When asked specifically about the subdural implantation of electrodes for a BMI, answers were more differentiated. Some participants emphasized the risks of the implantation and explicitly declined a surgical intervention (n = 17; e.g., ‘The thought of it is highly unpleasant to me. I don’t want another head surgery.’ ‘I don’t want an intervention.’). Some expressed doubts about the functionality of current approaches (n = 22; ‘not yet enough elaborated to be ready for everyday use’). The majority of the responses (n = 69)

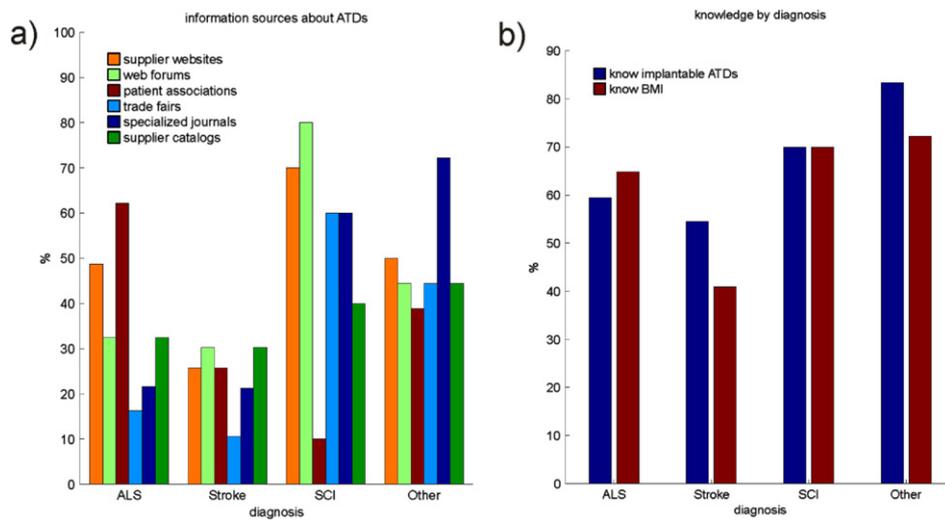


Figure 3. (a) Information sources on ATDs, and (b) knowledge about implantable ATDs and BMIs in paralyzed patients.

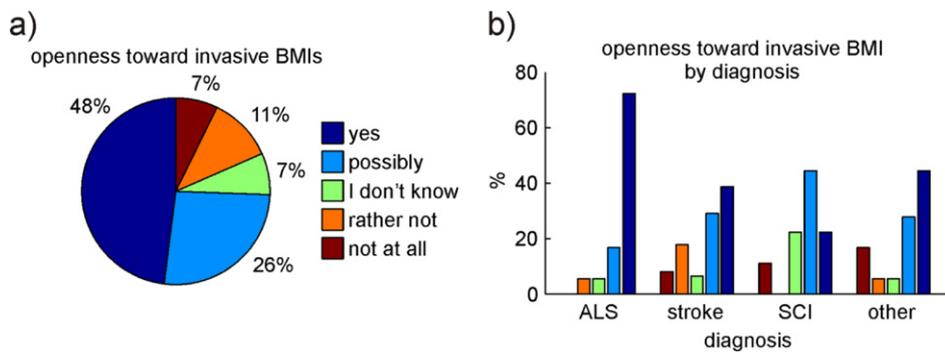


Figure 4. Attitudes of patients toward implantable BMIs. (a) Almost half of the respondents (48%) could imagine a surgical implantation of medical devices if it would crucially improve mobility and the ability to communicate. (b) Breaking down the answers by diagnoses reveals that mainly ALS patients are open to invasive BMI devices.

revealed positive or ambivalent feelings and highlighted that the level of improvement is crucial for the decision about the implantation of electrodes (‘a queasy feeling, but for more mobility and the perspective to use my hand again—even if only in a limited fashion—I would give a lot.’ ‘On the one hand scary, on the other hand certainly better than previously known ATDs ...’ ‘I don’t feel at ease thinking about the head surgery, but given a probable success, I would be ready for it.’ ‘If I would know that it helps, I would try it.’ ‘If there would be the possibility to control my muscles again, I would immediately be ready for it.’ ‘I am afraid of further operations, but the hope for improvements triggers ambivalent feelings.’ ‘I would accept every ATD that improves the quality of life.’ ‘I would do it immediately if it would help.’).

3.4. Correlation matrix

The correlation analysis (figure 5) showed expected positive correlations among the motor impairment ratings and between painlessness and subjective quality of life. Further, it revealed a negative correlation between patients’ age and the use of Web forums as an information source, as well as with the

knowledge about implantable ATDs. Patients that used the Websites of ATD suppliers as an information source were more likely to know about BMIs and implantable ATDs.

4. Discussion

Knowing the individual needs of patients affected by paralysis is important to successfully developing a BMI that will find high user acceptance. The present study analyzed the impairments of chronically paralyzed patients, and especially their subjective needs that may be addressed by an invasive BMI-based therapy.

The present study is the first survey on BMIs conducted with a larger body of paralyzed patients. While previous surveys targeted ALS patients (Blain-Moraes *et al* 2012, Huggins *et al* 2011), this study covered patients with ALS and several other diagnoses who would presumably be eligible for the implantation of an invasive BMI, particularly stroke and SCI patients. Furthermore, this study also assessed the patients’ knowledge about BMIs, and approached the question of which sources patients used to inform themselves

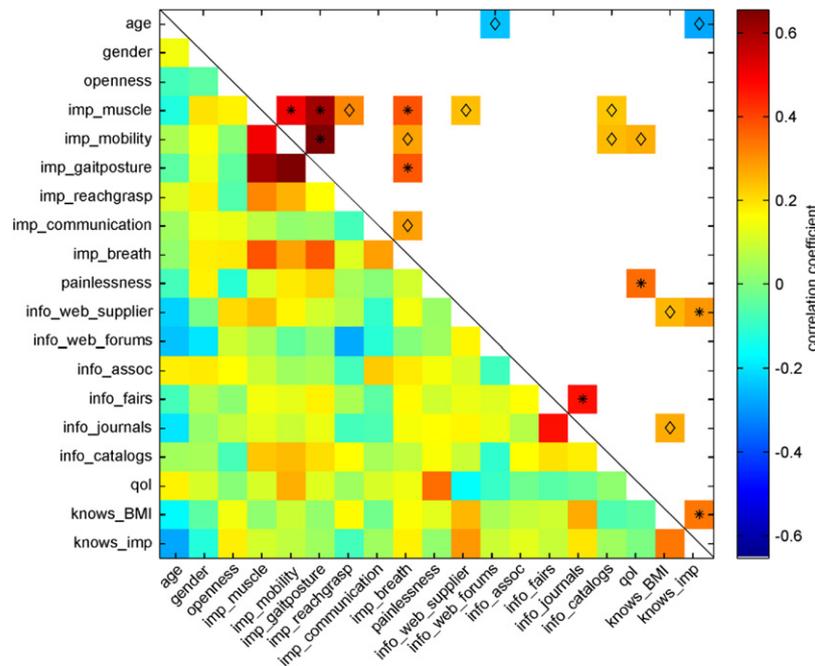


Figure 5. Correlation matrix of the key items in the study population. Below the diagonal (black line), all correlation coefficients are shown, while above the diagonal, only significant correlations are plotted (\diamond : $p < 0.01$; *: $p < 0.001$). Abbreviations: imp_muscle: impairments in muscle power; imp_mobility: impairments in mobility; imp_gaitposture: impairments in gait and posture; imp_reachgrasp: impairments in reach and grasp; imp_communication: impairments in communication; imp_breath: impairments in breathing; info_web_supplier: ATD supplier websites as information source; info_web_forums: web forums as information source; info_assoc: patient associations as information source; info_fairs: specialized trade fairs as information source; info_journals: specialized journals as information source; info_catalogs: catalogs by ATD suppliers as information source; qol: quality of life; knows_BMI: knowledge about BMIs; knows_imp: knowledge about the possibility to implant ATDs.

about ATDs and how satisfied they were with the ATDs they already have.

The majority of the patients knew about and had a positive attitude toward invasive BMIs on the premise of benefits concerning their individual impairments. The group of ALS patients showed the highest level of openness toward invasive BMIs. The openness of the participants was confirmed by the free-text answers: For the most part, the participants highly support the development of BMI technology. However, not surprisingly, the results of our questionnaire indicate that the final acceptance of implantable BMI technology will strongly depend on the ratio of the risks of the implantation to the possible advantages offered to the users.

The results of our survey clearly demonstrate that there is a demand for therapeutic BMIs in paralyzed patients. This conclusion is in line with previous research on patients' expectations for BMIs. In a survey with 61 ALS patients, Huggins *et al* (2011), showed that more than 90% of the patients were interested in participating in BMI research. Interestingly, the positive attitude toward invasive BMIs in our study population did not depend on the individual patient's level of motor impairment.

Improvements in mobility, grasp/grip, gait/posture, and communication skills were rated as most important in the present study. This is in agreement with the results of a previous survey among 347 quadriplegic SCI patients, where regaining hand and arm function, followed by sexual function

(not assessed in the present study), trunk stability, bladder/bowel function (not assessed in the present study), and mobility improvements were the most important features in improving quality of life (Anderson 2004).

The approach of invasive BMIs circumvents some disadvantages of EEG-based noninvasive BMIs. Most of the patients surveyed in the present study, and in particular ALS patients, were open to the possible implantation of a medical device on the premise of improvements in mobility and communication abilities. This is in line with the responses to questions regarding implantable electrodes in previous BMI studies: In a recent study with 8 BMI-experienced ALS patients (Blain-Moraes *et al* 2012), current noninvasive BMI approaches were classified as not ready for day-to-day use in a real-world environment. The drawbacks cited included a long setup time, eye strain, fatigue, and daily maintenance. Furthermore, patients were attracted to the concept of implantable intracutaneous electrodes that might facilitate the use of the BMI appliances. Similarly, in the study by Huggins *et al* (2011), 72% of the patients would accept surgical implantation of electrodes for a BMI if they were implanted during outpatient surgery, and 41% would accept them if their implantation necessitated a short hospital stay.

For the most part, the patients in the present study were satisfied with their existing ATDs (>75% of the ratings for ATDs were 'satisfied' or 'very satisfied'), confirming a high satisfaction level with ATDs in an earlier study with 63 ALS

patients (Gruis *et al* 2011) and extending these results to a broader group of diagnoses. The openness toward invasive brain-computer interfaces revealed in the present study was not contingent on unsatisfactory ATDs currently in use by the patients, which suggests a high interest in new treatment opportunities, possibly with improved performance.

The correlation matrix of responses (figure 5) served as a means to ensure the internal validity of our survey: The items that were expected to be linked were indeed correlated (e.g., significant correlation between breathing impairments and communication impairments, between different items of motor impairments, or between painlessness and quality of life). Further validation of our questionnaire by assessing the test-retest reliability would be desirable, though this is complicated by the progressive character of the involved diseases. The aim of the present study was to assess a wide range of topics and functional domains in patients with different diseases. Subsequently, we had to agree with a reasonable trade-off between comprehensive information and a feasible duration for the completion of the questionnaire. While established rating instruments for distinct diagnoses—such as the *revised amyotrophic lateral sclerosis functional rating scale* (ALSFRS-R) for ALS patients—would capture impairments more precisely, time constraints and a heterogeneous study population covering several diagnoses hindered their use in the context of a pilot study. Given the broad range of patients participating in the present study, some of the rating scales were affected by ceiling effects (e.g., motor impairment). While the overall study population is relatively large, only a small number of patients was surveyed in some diagnostic subgroups (e.g., SCI: $n = 10$), bringing the generalizability of our results into question.

Finally, we have created the broadest body of knowledge currently available about the needs and opinions of prospective invasive BMI users on ATDs. A new insight found by the present study is that young patients are better informed about invasive BMIs than older patients. Furthermore, our results indicate that young patients are more likely to use the Internet as a source for information on ATDs. As a consequence, it is important to optimize the information supplied on the Internet, but also to develop adequate alternative information channels for older patients.

5. Conclusion

First, most paralyzed patients have a positive attitude toward invasive BMIs, and in particular, ALS patients are open to the implantation of invasive BMIs. This may be influenced by the progressive nature of ALS, which makes it hard to adapt to the deteriorating situation that the patients are faced with. In contrast, SCI patients have a more stable state of health and may, therefore, be better able to adapt to their situation over a longer period of time. Second, the final decision about the implantation of an invasive BMI depends on the risk/reward ratio concerning the individual impairments of the patients. Third, the Internet is an important source of information on BMIs for potential invasive BMI users. Consequently,

Websites tailored to prospective BMI users may bring together prospective BMI users and researchers involved in the development of BMI technology, thereby facilitating the participation of motivated patients in upcoming studies, and evoking a differentiated opinion on invasive BMIs.

Acknowledgments

The authors wish to thank Doris Broetz and Niels Birbaumer (Institute of Medical Psychology and Behavioral Neurobiology, Tübingen, Germany) for patient recruitment; Darcey Terris (Mannheim Institute of Public Health, Mannheim, Germany), Gabriele Lucius, and Harald Seelig (Institute of Psychology, Freiburg, Germany) for their assistance in the conception of the questionnaire; Ulrike Förster (Faculty of Biology, Freiburg, Germany) for transcription of the questionnaire; and Ulla König-Cardanobile (Bernstein Center, Freiburg, Germany) for preliminary data analysis.

Funding

This study was supported by the German Federal Ministry of Education and Research (BMBF Grants 01GQ0830 to BFNT, and BMBF-GoBio) and the BrainLinks-BrainTools Cluster of Excellence funded by the German Research Foundation (DFG, grant no. EXC 1086).

Conflict of interest

JL, BH and AA declare no conflict of interest. JR is CEO, CS is an employee and TB is scientific counselor of CorTec GmbH, a supplier of implantable iEEG electrodes.

References

- Anderson K D 2004 Targeting recovery: priorities of the spinal cord-injured population *J. Neurotrauma* **21** 1371–83
- Ball T, Kern M, Mutschler I, Aertsen A and Schulze-Bonhage A 2009 Signal quality of simultaneously recorded invasive and non-invasive EEG *NeuroImage* **46** 515–6
- Blain-Moraes S, Schaff R, Gruis K L, Huggins J E and Wren P A 2012 Barriers to and mediators of brain-computer interface user acceptance: focus group findings *Ergonomics* **55** 515–6
- Collinger J L, Wodlinger B, Downey J E, Wang W, Tyler-Kabara E C, Weber D J, McMorland A J, Velliste M, Boninger M L and Schwartz A B 2013 High-performance neuroprosthetic control by an individual with tetraplegia *The Lancet* **381** 557–64
- Gruis K L, Wren P A and Huggins J E 2011 Amyotrophic lateral sclerosis patients' self-reported satisfaction with assistive technology *Muscle Nerve* **43** 643–7
- Hochberg L R *et al* 2012 Reach and grasp by people with tetraplegia using a neurally controlled robotic arm *Nature* **485** 372–5
- Hochberg L R, Serruya M D, Friehs G M, Mukand J A, Saleh M, Caplan A H, Branner A, Chen D, Penn R D and Donoghue J P

- 2006 Neuronal ensemble control of prosthetic devices by a human with tetraplegia *Nature* **442** 164–71
- Howell D C 2013 *Statistical methods for psychology* 8th ed (Belmont, CA: Wadsworth Cengage Learning)
- Huggins J E, Wren P A and Gruis K L 2011 What would brain-computer interface users want? Opinions and priorities of potential users with amyotrophic lateral sclerosis *Amyotroph. Lateral Scler.* **12** 318–24
- Kennedy P R and Bakay R A E 1998 Restoration of neural output from a paralyzed patient by a direct brain connection *NeuroReport* **9** 1707–11
- Levine S P, Huggins J E, BeMent S L, Kushwaha R K, Schuh L A, Rohde M M, Pasaro E A, Ross D A, Elisevich K V and Smith B J 2000 A direct brain interface based on event-related potentials *IEEE Trans. Rehabil. Eng.* **8** 180–5
- Milekovic T, Fischer J, Pistohl T, Ruescher J, Schulze-Bonhage A, Aertsen A, Rickert J, Ball T and Mehring C 2012 An online brain-machine interface using decoding of movement direction from the human electrocorticogram *J. Neural Eng.* **9** 046003
- Schuettler M, Kohler F, Ordonez J S and Stieglitz T 2012 Hermetic electronic packaging of an implantable brain-machine-interface with transcutaneous optical data communication *Proc. Ann. Int. Conf. of the IEEE Engineering in Medicine and Biology Society (EMBC)* pp 3886–9
- Simeral J D, Kim S-P, Black M J, Donoghue J P and Hochberg L R 2011 Neural control of cursor trajectory and click by a human with tetraplegia 1000 days after implant of an intracortical microelectrode array *J. Neural Eng.* **8** 025027