A Virtual Reality-Based Protocol to Determine the Preferred Control Strategy for Hand Neuroprostheses in People With Paralysis

Elena Losanno, Matteo Ceradini, Filippo Agnesi, Gabriele Righi, Giulio Del Popolo, Solaiman Shokur, *Senior Member, IEEE*, and Silvestro Micera, *Fellow, IEEE*

***Abstract*— Hand neuroprostheses restore voluntary movement in people with paralysis through neuromodulation protocols. There are a variety of strategies to control hand neuroprostheses, which can be based on residual body movements or brain activity. There is no universally superior solution, rather the best approach may vary from patient to patient. Here, we propose a protocol based on an immersive virtual reality (VR) environment that simulates the use of a hand neuroprosthesis to allow patients to experience and familiarize themselves with various control schemes in clinically relevant tasks and choose the preferred one. We used our VR environment to compare two alternative control strategies over 5 days of training in four patients with C6 spinal cord injury: (a) control via the ipsilateral wrist, (b) control via the contralateral shoulder. We did not find a one-fits-all solution but rather a subject-specific preference that could not be predicted based only on a general clinical assessment. The main results were that the VR simulation allowed participants to experience the pros and cons of the proposed strategies and make an educated choice, and that there was a longitudinal improvement. This shows that our VR-based protocol is a useful tool for personalization and training of the control strategy of hand neuroprostheses, which could help to promote user comfort and thus acceptance.**

***Index Terms*— Hand neuroprostheses, control strategy, immersive virtual reality, personalization, spinal cord injury.**

I. INTRODUCTION

NEUROPROSTHESES represent a radical solution for restoring hand function in people with severe paralysis due to neurological diseases such as stroke, spinal cord injury (SCI), or amyotrophic lateral sclerosis [1]. Hand neuroprostheses bypass the neurological lesion and artificially restore movement through neuromodulation techniques. The most traditional approaches are transcutaneous stimulation over the forearm and hand [2], [3] and implanted muscle stimulation [4], [5]. More recently, implanted devices targeting more proximal areas of the nervous system such as the peripheral nerves [6], [7] or the spinal cord [8] have been developed.

Enabling voluntary control of hand functions generated by neuroprostheses necessitates the integration of stimulation with effective control strategies. Traditionally, residual body movements have served as control inputs for hand neuroprostheses [2], [3], [4], [5]. Various body control strategies have been investigated, both homologous and non-homologous, that is, aligning with or deviating from the natural hand control pathway [1], with the goal of catering to individuals with diverse impairment levels and severities. These strategies encompass non-homologous proximal functions like head orientation [9], [10], contractions of neck muscles [9], [10], contractions of facial muscles [11], [12], or tongue movements [13], [14]; these movements may be the sole residual options, for example in cases of high complete tetraplegia. For patients with low complete tetraplegia or those recovering from a stroke, distal non-homologous sources can also be leveraged, such as arm or shoulder movements on the ipsilateral [2], [5] or contralateral [4] sides. In instances where forearm muscles exhibit detectable electromyographic (EMG) activity, as seen, for example, after incomplete or discomplete

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This work involved human subjects in its research. Approval of all ethical and experimental procedures and protocols was granted by the Ethical Committee of Careggi University Hospital (Florence, Italy), and performed in line with the Declaration of Helsinki and Good Clinical Practice Norms.

Elena Losanno, Matteo Ceradini, and Filippo Agnesi are with the BioRobotics Institute and the Department of Excellence in Robotics and AI, Scuola Superiore Sant'Anna, 56127 Pisa, Italy (e-mail: elena.losanno@santannapisa.it).

Gabriele Righi and Giulio Del Popolo are with the Careggi University Hospital, 50134 Florence, Italy.

Solaiman Shokur is with the Bertarelli Foundation Chair in Translational Neuroengineering, Center for Neuroprosthetics, and the Institute of Bioengineering, École Polytechnique Fédérale de Lausanne (EPFL), 1015 Geneva, Switzerland.

Silvestro Micera is with the BioRobotics Institute and the Department of Excellence in Robotics and AI, Scuola Superiore Sant'Anna, 56127 Pisa, Italy, and also with the Bertarelli Foundation Chair in Translational Neuroengineering, Center for Neuroprosthetics, and the Institute of Bioengineering, École Polytechnique Fédérale de Lausanne (EPFL), 1015 Geneva, Switzerland.

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spinal cord injury (SCI) [15], homologous control based on myoelectric pattern recognition is also a viable option [16], [17], [18].

An alternative is to decode the motor intention from brain activity [19], [20], [21], [22]. This in an intrinsically homologous approach that can be implemented with increasingly invasive interfaces, which in turn leads to higher decoding accuracy and control dimensionality [1].

From this short summary, it is evident that the control of hand neuroprostheses can be reached using different approaches, and there is no universally superior strategy. Rather, the best solution should be tailored to each patient's clinical condition and personal preferences. In this view, patients should have the opportunity to choose between different control options based on a meaningful experience of neuroprosthesis use.

Here, we propose a protocol for patients with paralysis to engage in and practice different control schemes for hand neuroprostheses, allowing them to express an educated preference. To simulate a realistic neuroprosthetic experience, we exploited virtual reality (VR), which is increasingly used in clinical settings [23]. Specifically, we developed a fully immersive VR environment that emulates the functionality of a hand neuroprosthesis capable of restoring various grasp types with graded force. Tailored for individuals with impaired hand movements but intact arm movements, the user assumes control over the upper limb of a human avatar. The actual reaching movements of the user are tracked and virtually replicated, while virtual grasping is governed by a discrete and a continuous command. The software is designed to easily and modularly integrate various control signals, providing flexibility in adapting to different user needs.

To let patients assess the effectiveness of different control strategies, their performance is quantitatively measured during carefully designed unimanual and bimanual tasks inspired by validated clinical tests and relevant for the evaluation of control strategies for neuroprostheses. Additionally, feedback on usability and comfort is gathered through a questionnaire, offering valuable insights into the user experience with a certain control scheme. This comprehensive approach aims to enhance the development and personalization of neuroprosthetic technologies for individuals with specific motor impairments.

We tested our VR-based protocol in four patients with C6 tetraplegia who longitudinally compared two popular control strategies based on residual movements of the ipsilateral and contralateral limbs. We show that our VR-based protocol is useful to personalize control as it allows patients to experience the advantages and disadvantages of each strategy and provide informed feedback.

II. MATERIALS AND METHODS

A. Implementation of the VR Environment

We implemented the VR environment using Unity3D Game Engine software. We developed the environment for use with an HTC Vive system (Taiwan), but it can be easily adapted to other VR systems. The user is immersed in the VR environment by wearing a VR headset (in our case the HTC Vive Pro Eye) and controls the upper limbs of a human avatar with a first-person perspective (Fig. 1A). The position in space of the subject's arms is tracked by 2 HTC Vive Trackers 3.0 worn on the wrists with straps and replicated in the avatar. Avatar's inverse kinematics is provided by the Final IK Unity plugin. The avatar's dominant hand is controlled by the subject using two commands, (i) a binary command to sequentially switch between grasp types and release an object once grabbed, (ii) a proportional command to modulate fingers flexion (Fig. 1B). This scenario mimics the operation of a neuroprosthesis restoring multiple grasps and allowing graded grasp control, such as those based on electrodes implanted in the nerves [6], [7] or muscles [4], [5]. The two commands are driven by two data streams input via Lab Streaming Layer (LSL) [24]. In this way, various control signals can be easily and modularly integrated. The binary command is active when the corresponding signal is positive. The proportional signal linearly modulates the flexion angle θ of each finger joint, as follows:

$$\begin{aligned} \theta &= gain \cdot prop \\ gain &= (\theta_{max} - \theta_{min}) \big/ \left(prop_{sat} - prop_{thr}\right) \\ if\ \ prop > prop_{sat} &\rightarrow prop = prop_{sat} \end{aligned}$$

where θ_{min} and θ_{max} are preset angle values for preshaped hand and fully closed hand, respectively, for a certain grasp type. A non-immersive VR scene was developed to calibrate the control parameters $prop_{thr}$ and $prop_{sat}$, as well as to let the user familiarize with the control strategy. The user tests the binary command in switching between grasp types and the proportional command in modulating fingers flexion; we consequently adjust $prop_{thr}$ and $prop_{sat}$ to minimize required effort and undesired commands while spanning a large range of modulation.

We implemented four virtual tasks, half unimanual and half bimanual, three to evaluate the efficacy of a proportional control source alone and one to evaluate a combination of proportional and binary control sources. Except the grasp-and-release (GR) task (see below), these tasks are novel compared to previous tests used for the evaluation of hand neuroprostheses control [25]. These tasks were inspired by validated clinical tests of upper-limb function such as the ARAT [26] and the GRASSP [27] and designed to test various aspects of control strategies for a neuroprosthesis – also under stressed conditions – to help patients consciously determine the preferred solution. The two bimanual tasks were designed as feasible tasks for the tetraplegic population, considering the manipulation of a primary object with the dominant hand restored by the neuroprosthesis and the non-dominant hand used only to hold a secondary object, for example with the aid of a hand splint [28].

The precision (PR) task (Fig. 1C) assesses how precisely the proportional control source can be graduated; this replicates precise control of the grasp closure elicited by a neuroprosthesis in a real scenario, which would be important for grasping objects of different sizes, as assessed in the ARAT. The user is asked to reach five ranges of activation of the proportional command (equally spaced between $prop_{thr}$ and $prop_{sat}$)

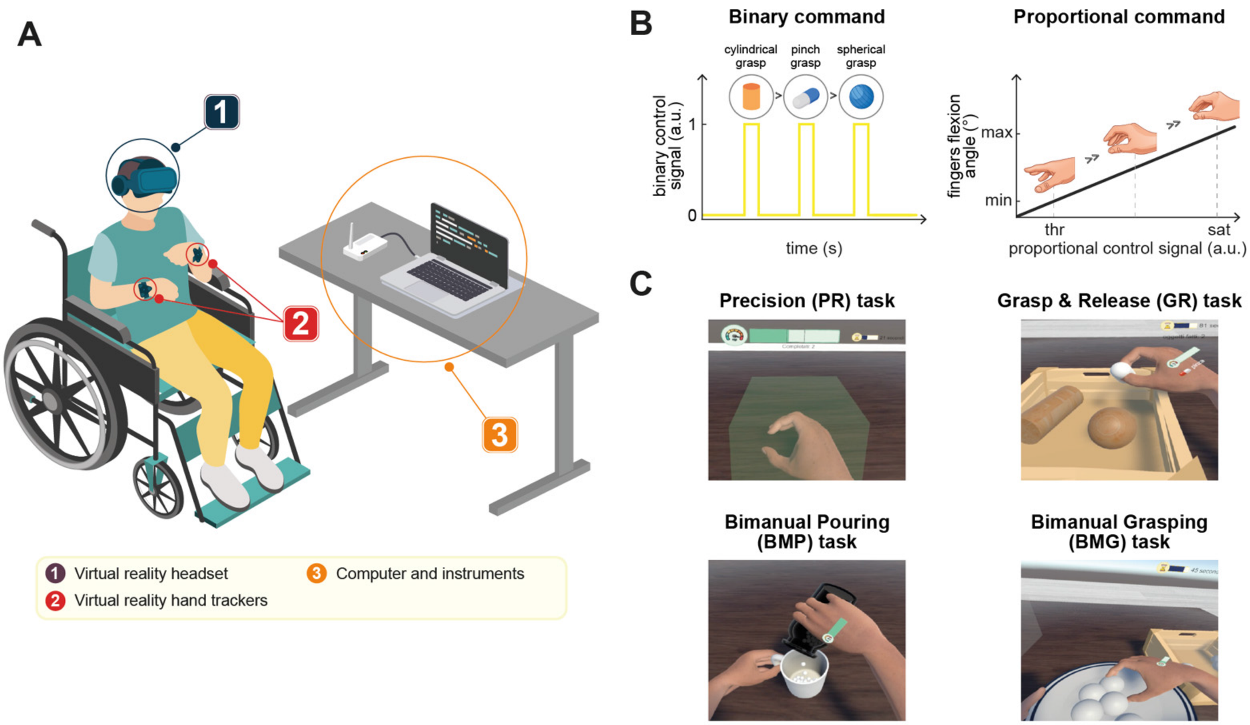

Fig. 1. VR system. (A) The VR setup includes a VR headset and two VR trackers on the wrists, which are used to track the position of the user's head and arms and replicate it in the virtual avatar, and the control computer running the software. (B) Virtual grasping is controlled using two commands, (i) a binary command to sequentially switch between grasp types, (ii) a proportional command to modulate fingers flexion. (C) The VR system includes four virtual tasks: (i) precision (PR) task, in which the user is asked to precisely modulate the proportional command to close the virtual hand of a target quantity; (ii) grasp-and-release (GR) task, in which the user must grab three different objects, namely a ball, a cylinder, and a capsule with the corresponding grasp type and release the objects into a crate; (iii) bimanual pouring (BMP) task, in which the user must pour the balls contained in a bottle into a cup (the balls do not come out of the bottle by gravity alone, but the subject must squeeze the bottle by closing the hand with the proportional command); (iv) bimanual grasping (BMG) task, in which the user must grasp sliding balls on a plate held with the non-dominant hand and release them into a crate. Abbreviations: arbitrary units (a.u.), threshold (thr), saturation (sat).

presented in a pseudorandom order. To succeed the user is required to maintain the activation within the target range for 0.5 s. Visual feedback on the value of the proportional command is provided by the level of hand closure as well as a progress bar. A square on the bar indicates the target range. After a success, the subject must lower the proportional signal below the threshold $prop_{thr}$ for a new target to appear. For reproducibility between trials, the hand must be maintained in a marked area in space for the subject to be able to perform the task. Proportional control is temporarily paused when the subject's hand exits this designated area. Performance is evaluated by measuring the number of successes in a specific time interval.

The GR task (Fig. 1C) reproduces the grasp-and-release test used to measure the benefit provided by hand neuroprostheses in previous studies [29] and evaluates the combination of proportional and binary control sources in a unimanual activity that requires picking up different objects. The user is asked to grab three different objects, namely a ball, a cylinder, and a capsule, which are presented in a pseudorandom order. These objects must be grasped using the corresponding grasp type, namely spherical, cylindrical, and pinch grasps. These different grasp types are assessed both in the ARAT and GRASSP. After grasping the subject must release the objects into a crate. The subject uses the binary command to select the grasp type and the hand is preshaped accordingly. The proportional command is then used to modulate the level of hand closure into the selected grasp, which the user needs to adjust depending on the object size. An object is indeed grabbed if predefined finger phalanges collide with it. Once grabbed, the object remains attached to the hand, until the subject uses the binary command to release it. A graphical user interface (GUI) on the dominant hand provides visual feedback on the current grasp type and value of the proportional command. Performance is evaluated by measuring the number of objects the subject successfully releases in the crate in a specific time interval.

The bimanual pouring (BMP) task (Fig. 1C) evaluates the efficacy of the proportional control source alone in a pouring activity, included both in the ARAT and GRASSP. The user holds a bottle filled with small balls in the dominant hand and is asked to pour the balls into a cup held by the non-dominant hand. The balls do not come out of the bottle by gravity alone, but the subject must squeeze the bottle by closing the dominant hand with the proportional command. The higher the proportional command, the faster the balls come out of the bottle. Squeezing was added to investigate whether the task was affected by movements of the non-dominant arm and was inspired by activities of daily living such as squeezing toothpaste on a toothbrush. Once the bottle is emptied, the subject must lower the proportional signal below the threshold $prop_{thr}$ and return the dominant hand to a marked point in space for the bottle to be refilled. A GUI on the dominant hand provides visual feedback on the current value of the

TABLE I
SUBJECTS INVOLVED IN THE STUDY

ID	Sex	Age	SCI classification	Time since injury (y)	Use of tenodesis grasp
S1	m	52	C6 AIS A	2.3	Y
S2	m	33	C6 AIS A	8.5	Y
S3	m	26	C6 AIS A	6.2	Y
S4	m	58	C6 AIS A (ZPP in DH)	6.5	N

Abbreviations: zone of partial preservation (ZPP), dominant hand (DH)

proportional command. Performance is evaluated by measuring the number of balls the subject successfully pours into the cup in a specific time interval. To encourage precision, each ball that falls out of the cup is scored −1 point.

The bimanual grasping (BMG) task (Fig. 1C) evaluates the efficacy of the proportional control source alone still in a prehension activity but based on picking up objects from a container held with the non-dominant hand. This task was specifically designed to require stability of the non-dominant arm. The user holds a plate of sliding balls in the non-dominant hand and is asked to grab each ball with the dominant hand and release it into a crate. The proportional command modulates the level of hand closure, and a ball is grabbed when the distal phalanges of the thumb, index, and middle fingers collide with it. Once the ball is grabbed, it remains attached to the hand until it enters the crate area. Once the plate is emptied, the subject must bring the proportional signal below the threshold $prop_{thr}$ and return the non-dominant hand to a marked area in space to refill the plate. A GUI on the dominant hand provides visual feedback on the current value of the proportional command. Performance is evaluated by measuring the number of balls the subject successfully releases into the crate in a specific time interval. To encourage precision, each ball that falls out of the plate is scored −1 point.

B. Participants and Experimental Procedures

We performed experiments with SCI patients to test our VR system. Inclusion criteria were patients with C6 SCI classified as motor complete (AIS A or B) and with detectable EMG activity of the extensor carpi radialis (ECR) muscle. We recruited four male participants (age from 26 to 58 years, Table I) with chronic SCI and no major age-related physical problems. All participants were able to move the dominant arm and had some degree of wrist extension in the dominant hand. The participants gave written informed consent to participate in the study.

In the four patients we longitudinally compared two proportional control sources: (i) extension of the ipsilateral wrist, measured via the EMG activity of the ECR muscle, (ii) elevation of the contralateral shoulder, measured as rotation of the sternoclavicular joint (Fig. 2). These two strategies were selected because they are used in commercial neuroprostheses [2], [3], [5] and allow comparison between control based on the ipsilateral and contralateral limbs. Note that strategy (i) exploits the mechanism of the tenodesis grasp, a passive grasp induced by the extension of the wrist that people with tetraplegia learn to use as a compensatory movement. Here, all subjects were accustomed to using the tenodesis grasp, except S4 who was able to actively grasp light and small objects due to a zone of partial preservation in the dominant hand (Table I).

The four subjects participated in five experimental sessions distributed over five consecutive days, in which they performed the four virtual tasks using these two proportional sources (see Supplementary Video 1 for example trials). In the GR task, both proportional sources were coupled to the same binary source, namely a switch button whose position could be chosen by each subject. S1 and S2 chose to place the button on the chest, whereas S3 and S4 opted to have it on the contralateral thigh, intending to press it with the non-dominant hand (S1, S3, S4) or chin (S2). In each session, subjects performed 3 repetitions of each task (2-minute-long repetitions of the GR task, 1-minute-long repetitions of the other three tasks) for each control strategy. Tasks and control strategies were evaluated in a pseudorandom order. All subjects had stability and sitting balance problems, which were accentuated during bimanual tasks. Therefore, during the experiments, they were secured to the wheelchair with a harness to improve their stability. Due to time constraints, S1 performed the BMG task for three sessions only, and S4 did not perform any task using the ipsilateral wrist extension on the fifth session.

C. Questionnaire on Usability and Comfort

To assess the participants' mental and physical effort, comfort, and perceived performance in the virtual tasks with the two control strategies, in the first and last experimental sessions they were administered with a custom questionnaire. The questionnaire consisted of eight questions scored on a 0-10 scale, which were asked for both control strategies to assess them on the following aspects: intuitiveness (Q1), physical ease (Q2), perceived performance in the PR task (Q3), perceived performance in the GR task (Q4), perceived performance in BMP task (Q5), perceived performance in BMG task (Q6), satisfaction and relax (Q7), social acceptance (Q8). Moreover, participants were asked an additional question (Q9), "*Which of the two strategies do you prefer?*", to ascertain their preferred strategy and validate whether the cumulative scores derived from questions Q1-8 was consistent with their preference.

D. Data Acquisition

A custom MATLAB (MathWorks, Natick MA) routine recorded and processed the control signals in real-time to compute the binary and proportional commands and streamed them to Unity via LSL. The EMG activity of the ECR muscle was acquired at 1 kHz using the Sessantaquattro system (Ot Bioelettronica, Italy) with bipolar electrodes. EMG signals were digitally filtered (notch at 50 Hz, band-pass between 20 and 500 Hz, 3rd order Butterworth filters), rectified, smoothed with a moving window root mean square (window length of 720 ms updated every 80 ms), and normalized to the maximum voluntary contraction (MVC) determined during calibration. EMG processing parameters were set based on pilot tests in healthy subjects during software development to find a good trade-off between response time and stability of the signal. The rotation of the contralateral sternoclavicular joint

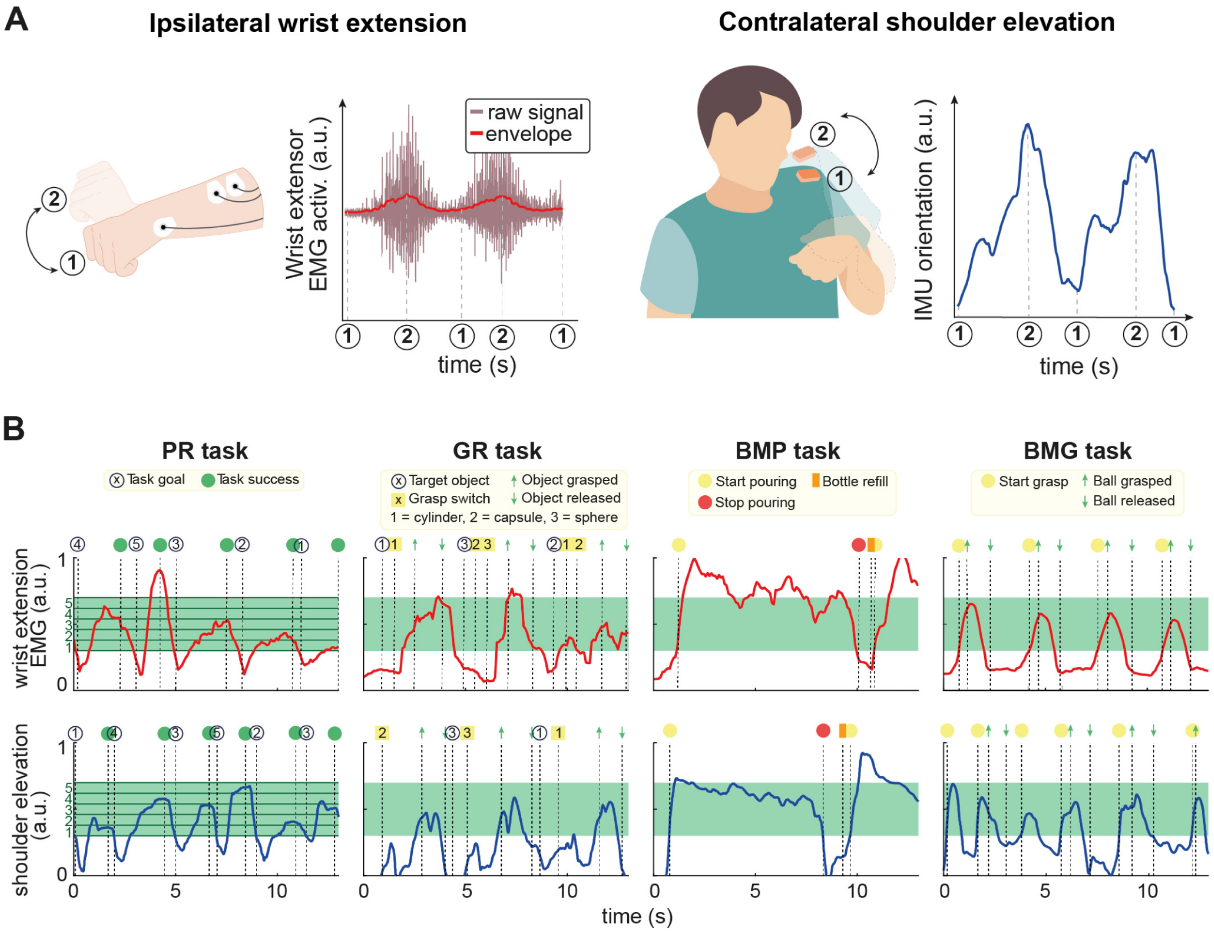

Fig. 2. Control strategies tested with the VR system. (A) Sensor position and example signals for the two tested proportional control sources, (i) extension of the ipsilateral wrist, measured via the EMG activity of the extensor carpi radialis (ECR) muscle, (ii) elevation of the contralateral shoulder, measured as rotation of the sternoclavicular joint with an IMU sensor. (B) Example traces of the two signals during the four virtual tasks. Abbreviations: arbitrary units (a.u).

was recorded at 100 Hz using an IMU sensor (MTw Awinda, Xsens, Netherlands) positioned on the subject's shoulder with a strap. The orientation signal provided by the IMU sensor was min-max normalized based on the range determined during calibration.

A soft button (Pillow, Albamatic Srl, Italy) was used to implement the binary command. The sensor was secured to a harness (for S1 and S2) or a thigh strap (for S3 and S4) using a safety pin. Button presses were detected by an Arduino board and sent via serial communication to the control computer.

The timing of relevant events in the tasks, such as the start and end of a trial, success, etc., were saved by the Unity routine.

E. Parameters Calibration

At the beginning of each session, we computed the normalization parameters for the two control sources, i.e., EMG MVC and min-max shoulder elevation. Control parameters ($prop_{thr}$, $prop_{sat}$) were then calibrated using the VR calibration scene described in section II-A.

F. Data Analysis

The scores of each participant in each virtual task were normalized to the minimum and maximum obtained throughout all training days. To assess the learning curve of each control strategy, linear regression models were fitted to the longitudinal performance data; statistical significance of the model was evaluated using the F-test. To statistically compare the two control strategies, for each session we considered the average score across the repetitions of each task of each participant and pairwise compared the performance of all participants using the t-test. Normality was assessed using the Kolmorov-Smirnov test.

III. RESULTS

Fig. 3 shows the performance of the four subjects in the four virtual tasks using the two proportional control strategies. Over time, patients significantly improved their scores in all tasks using both control sources (Fig. 3A; slope of regression lines > 0, p-value at least < 0.05, F-test), with a few exceptions including S1 in the BMG task using shoulder elevation, S3 in the PR task, and S4 in the PR, BMP, and BMG tasks using wrist extension. As for the comparison between the two strategies, as shown in Fig. 3B, in the PR task, shoulder elevation greatly outperformed wrist extension and resulted in a higher score in all sessions, with the difference in sessions 3 to 5 being statistically significant (p-value at least < 0.05, paired-sample t-test). Conversely, wrist extension was much more effective in the BMG task and patients kept performing significantly better with this strategy (p-value at least < 0.05, paired-sample t-test). In the BMP task, the two control strategies were almost equivalent for S2-S4; only S1 had much higher scores in all sessions using wrist extension (mean score at session 1: 0.25 vs 0.43 a.u.; mean score at session 3: 0.55 vs 0.93 a.u.; shoulder vs wrist). Finally, the GR task provided the most subject-specific results. For S1, wrist extension kept being better than shoulder elevation across all sessions, even with a slightly higher learning rate (slope of regression line: 0.08 vs 0.1 score/sessions, shoulder vs wrist). Conversely, S2 showed better performance and slightly higher improvement using the shoulder (slope of regression line: 0.1 vs 0.07 score/sessions, shoulder vs wrist). S3 and S4 showed similar results, as they both started with higher scores using wrist extension in session 1, but they had a much greater learning rate using shoulder elevation (slope of regression line: 0.17 vs 0.06 score/sessions for S4, 0.12 vs 0.05 score/sessions for S5, shoulder vs wrist), so that it exceeded wrist extension in sessions 4 and 5.

Concerning usability and comfort, both control schemes became more intuitive and effortless for all participants over time; however, their preferred strategies remained consistent (see Fig. 4). The response scores to questions Q1-8, representing the rating of the two control strategies, varied between the subjects (Fig. 4A). Participant S1 conveyed that wrist extension felt more instinctive and less fatiguing than shoulder elevation, establishing it as his preferred strategy. In contrast, subject S2, despite initially expressing that shoulder elevation was mentally and physically more demanding, consistently favored this strategy underlying its superior precision. From the outset, S3 indicated that both strategies required minimal mental effort, but the physical exertion was higher with the shoulder. Therefore, he reported that wrist extension was his preferred strategy. Finally, S4 preferred shoulder elevation because he found it much more intuitive. The cumulative scores of questions Q1-8 reflected the participants' preferences as expressed in the responses to question Q9 (Fig. 4B). The only case of a tie between wrist and shoulder control using Q1-8 occurred with subject S4 on day 1, making Q9 crucial to determine his preference.

IV. DISCUSSION

In this study, we designed a protocol based on an immersive VR environment that simulates daily use of a hand neuroprosthesis for personalization of the control paradigm. With our system, patients can familiarize themselves with different control schemes and select the preferred strategy based on a realistic and meaningful simulation of neuroprosthesis use. Compared to previous evaluations of control strategies for hand neuroprostheses [25], we developed novel tasks allowing for a more comprehensive and revealing comparison. These tasks could be used in future studies both with actual neuroprostheses and VR, not only for personalization purposes but also on larger samples to gain population-level findings; this could be useful for example to determine the most effective set of solutions on average to be implemented in commercial devices.

We conducted experiments involving four patients with C6 SCI to assess the effectiveness of our protocol. Across five experimental sessions, we compared the use of ipsilateral wrist extension and contralateral shoulder elevation as proportional control sources. These two strategies were executed based on distinct signals: wrist extension was measured through muscle activity, while shoulder elevation was gauged through kinematics. This approach enabled a comprehensive comparison of both ipsilateral and contralateral control, as well as an evaluation of the two types of biosignals.

Performance in the virtual tasks was quite homogeneous across subjects. In general, shoulder elevation resulted in higher precision, leading to a higher score in the PR task for all subjects in all sessions. This result can be attributed to the fact that kinematics is generally easier to control than muscle activity, as shown in previous studies [30]. However, half of the subjects also improved with EMG-based wrist control, those that preferred the wrist overall and therefore likely made a higher learning effort. With longer training, we expect further improvements in patients with high motivation, up to top performance such as with shoulder kinematics. Moreover, while we set the EMG processing parameters based on software validation tests in healthy subjects, tailoring the parameters to each specific patient, as was done for the Freehand system [25], could further improve performance. As regards the GR task, it highlighted inter-subject differences more than the other tasks, as in previous studies [25]. However, if we look at the results from a broader perspective, we can see that while wrist control started above for three subjects, in the last session it remained superior only for S1. A possible reason for this result, besides the higher precision of kinematics-based shoulder control, is that in unimanual tasks the contralateral limb has not an effect on the task, whereas the extension of the ipsilateral wrist may have it. This observation held true for participant S2; because his wrist extension was radially deviated and coupled with forearm supination, he encountered significant challenges in grasping small objects like the capsule when extending the wrist due to the hand moving away from the object. Conversely, but for a similar underlying reason, wrist extension proved more effective in the BMG task, where the elevation of the contralateral shoulder had a pronounced impact on the task compared to the ipsilateral wrist for all subjects, leading to increased inaccuracy. In contrast, during the BMP task, a bimanual activity that was less affected by movements of the non-dominant arm by design, the two strategies exhibited a comparable level of effectiveness.

In terms of ease of use, comfort, and final choice, despite the fairly homogeneous clinical and demographic characteristics of the participants, we did not find a one-fits-all solution. Indeed, subjects S1 and S3 chose wrist control, while S2 and S4 preferred shoulder control, as consistently indicated by their responses to question Q9 and cumulative scores of questions Q1-8. We describe here the possible rationale for each participant's choice based on their questionnaire responses and verbal feedback. The preference of subject S1 for the wrist was due to his proficiency in using the tenodesis grasp. Participant S2 was also accustomed to using the tenodesis grasp, but experienced difficulties in grasping small objects with wrist

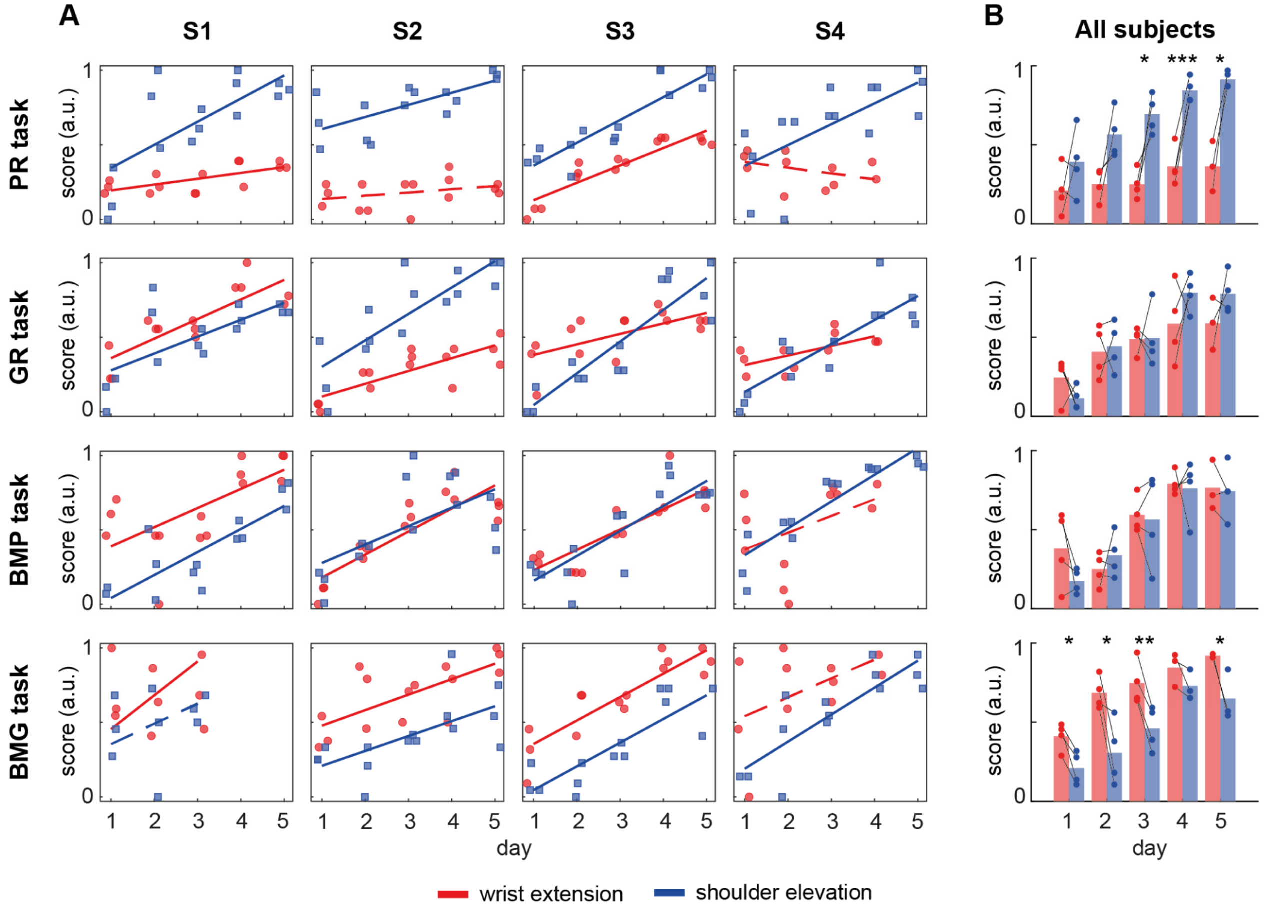

Fig. 3. Participants' performance in the virtual tasks using the two control strategies. (A) Participants' learning curves in the virtual tasks using the two control strategies. Each point represents a repetition of the task; apart from few exceptions, participants performed three repetitions of each task for each control strategy on each day. Linear regression models were fitted to the longitudinal performance data corresponding to the same control strategy (full line when significant, i.e., $p<0.05$, F-test, dashed line otherwise). The hypothesis of normality could not be rejected for none of the distributions of the residuals ($p>0.05$, Kolmorov-Smirnov test). (B) Comparison between the two control strategies in the four virtual tasks; each point represents a participant (his average score across the repetitions of the task), bars indicate the average across participants. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, paired-sample t-test. The hypothesis of normality could not be rejected for none of the distributions ($p>0.05$, Kolmorov-Smirnov test). In both panels, scores are normalized to the minimum and maximum obtained by each patient in each task throughout all training days. Abbreviations: arbitrary units (a.u).

extension because this movement was partially impaired. As a result, he preferred the shoulder control strategy. Participant S3 highlighted greater physical demand utilizing the shoulder, which was attributed to pronounced balance issues that were especially evident during bimanual tasks. The increased effort required to maintain stability and the resulting discomfort led him to favor the wrist control strategy. Finally, subject S4, who had a zone of partial motor preservation in the dominant hand (Table I) that allowed him to grasp objects and therefore not reliance on the tenodesis function, underlined much lower intuitiveness using the wrist. Indeed, when he was supposed to close the virtual hand by extending the wrist, he often mistakenly flexed the fingers. Therefore, he preferred the shoulder. From this description of the rationale for the participants' feedback, it is evident that the extensive control experience within the VR environment allowed them to detect the pros and cons of each strategy and to determine the most comfortable one overall. Moreover, we can note that personal ratings were based on subtle inter-subject differences in motor deficits and habits; therefore, the participants' choices could be hardly predicted based only on a general clinical assessment. This shows that our VR-based protocol is effective in determining the preferred control paradigm for a hand neuroprosthesis, as it allows patients to become aware of the differences between paradigms and make an educated choice.

As regards the longitudinal trend, participants' performance in the virtual tasks improved over sessions for both control strategies and the physical and mental effort required decreased, highlighting that our VR environment could be used not only for detecting the preferred control strategy, but also as a training tool. Moreover, we note that while in the current protocol the participants' choices did not change between day 1 and day 5 of the training, we cannot yet conclude – given the small sample size – that one day of testing would be sufficient, in general, to identify the preferred solution.

But how could the VR-based protocol presented in this study be used in a general clinical case for a person with paralysis? As discussed earlier, we propose to use our VR system to identify a good control strategy for each person. We describe here the envisioned process to find it (see Fig. 5). Once it is ascertained that a patient is a candidate for neuroprosthesis use based on an initial clinical assessment, the

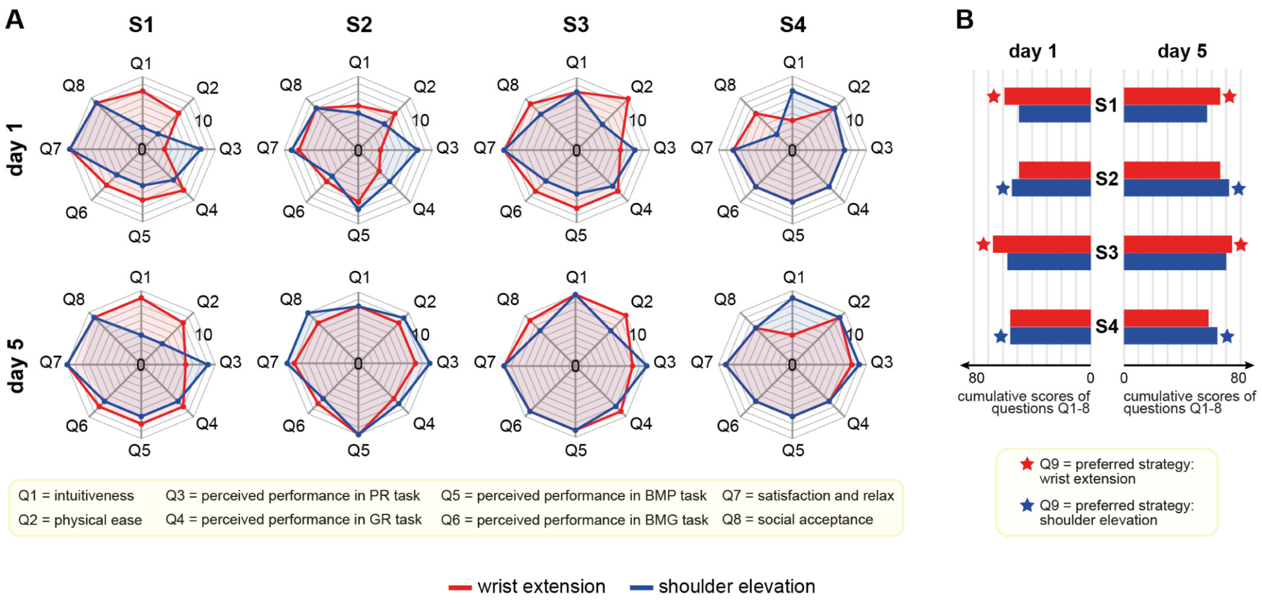

Fig. 4. Participants responses to the questionnaire on usability and comfort completed in the first and last days. (A) Response scores to questions Q1-8 on a 0-10 scale. (B) Cumulative response scores to questions Q1-8 compared with response to question Q9, that is “Which strategy do you prefer?”, indicated by the star color.

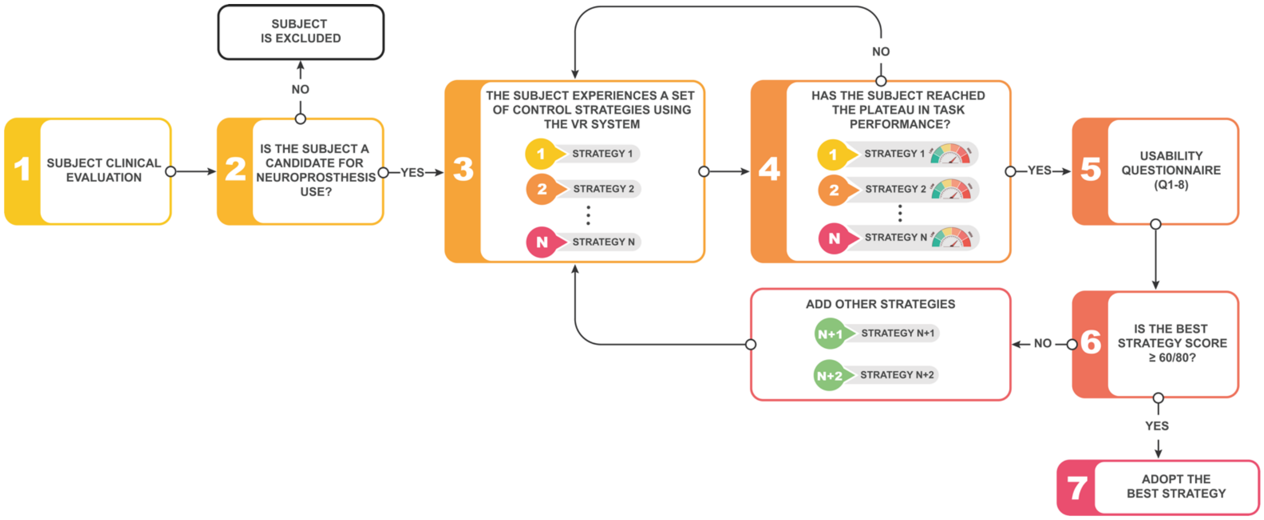

Fig. 5. Decision tree diagram illustrating the application of our VR-based protocol to determine a good control strategy for a specific patient in a real scenario.

patient is proposed a range of control options and experiences them in the presented tasks using VR. The tests are repeated over multiple sessions until all proposed strategies reach a plateau in task performance within a certain period of time (we suggest 5-10 days). The preferred strategy is then determined by administering the proposed questionnaire to the patient and becomes the final solution if the patient is satisfied, that is if the cumulative score of questions Q1-8 is at least 60/80 points; otherwise, new strategies must be designed to meet the patient’s expectations and additionally tested. If there is uncertainty about the preference between the strategies, that is, if the difference in their summed Q1-8 scores is equal to or less than 5 points, we recommend to explicitly ask the patient about the preference. Once the final solution is determined, it is integrated into the neuroprosthesis. The binary and proportional commands computed from the chosen control sources are no longer converted into virtual hand kinematics but into stimulation parameters: the binary command allows the user to switch between a set of stimulation protocols optimized to evoke different grasp types, while the proportional command regulates the level of grasp closure by modulating the charge injected or the frequency of the stimuli. Similar control paradigms have been used in widely adopted neuroprostheses such as the Freehand system [5]. Functional recovery induced by the assistance of the neuroprosthesis and eventual neurological recovery induced by its prolonged use could be assessed by evaluating changes in muscle strength using clinical measures such as the MRC scale and changes in grasp functionality and independence using measures such as the ARAT [26], the GRASSP [27], and the SCIM [31].

V. CONCLUSION

To conclude, the outcomes indicate that our protocol is effective in pinpointing a tailored control strategy for hand neuroprostheses that suits a particular patient and promotes habituation to it. Through the personalization of the control strategy, there is a potential to enhance user comfort and, consequently, foster acceptance of hand neuroprostheses. The adaptability and customization features of VR enable seamless expansion to additional simulated scenarios.

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