Hybrid neuroprostheses for upper limb rehabilitation after stroke: From overview to application

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Background: After a stroke, 38 % of patients admitted to a rehabilitation hospital show severe motor impairments in their upper limbs, 26 % experience mild to moderate, and 13 % minimal impairments [11]. Throughout the rehabilitation process patients typically achieve improvements in upper limb structures and functions [6, 10]. However, after the termination of standard care, a persisting paresis is present in the majority of patients, affecting 55-75% of cases [7, 10]. Only 11 % of patients achieve full recovery of upper limb function six months post-stroke [6].

Functional Electrical Stimulation (FES) and robotic therapy have appeared as established methods for upper limb rehabilitation post-stroke [4]. Nonetheless, FES can lead to muscle fatigue due to nonphysiological muscle recruitment [2, 8], potentially limiting its effectiveness as a neuroprosthesis. On the other hand, robotic devices can be cumbersome and restrict the portability of the system. Combining both therapeutic approaches in a so-called hybrid neuroprostheses **(Figure 1)** aims to address the limitations of each technology alone. Hybrid neuroprostheses are anticipated to alleviate muscle fatigue by incorporating external force generation [3], thereby allowing for a reduction in stimulation intensity, frequency, or duration [13]. Simultaneous stimulation also decreases the torque required from the robotic actuators [1], enhancing the portability of the device.

Figure 1. Upper limb rehabilitation after stroke delivered by a hybrid neuroprosthesis with proximal support by FES plus robotics and distal support by FES alone. This hybrid device has been developed within the ReHyb project and is currently tested for feasibility. Informed consent was collected to publish the picture

Hybrid neuroprostheses have been under development over the past decade, but still, there is no consistent definition for this technology. Some definitions specify hybrid control of actuation at the same joint as a requirement [9], while others extend the definition to devices applying both robotic and FES assistance, not necessarily at the same joint but within the same limb [13].

A systematic review was published [5] giving an overview of existing hybrid devices combining FES and robotics for upper limb rehabilitation and pooling results on their efficacy in upper limb recovery after stroke. In the analysis presented here, the focus is set on the characteristics of the devices and how frequently they are incorporated in existing hybrid neuroprostheses.

Methods: Systematic literature search was performed in databases from clinical and engineering disciplines. The search string was generated including the following PICO(S) criteria: Population - patients after stroke; Intervention – robot and FES use at the upper limb; Control – no simultaneous use of robot and FES at the upper limb; Outcome – upper limb function; Study design – randomized controlled trial (RCT; only defined for meta-analysis).

Two independent reviewers (CH and CK) screened all identified titles, abstracts and full-texts according to defined eligibility criteria. Consensus had to be reached in case of discrepancies in the reviewers' ratings. Data was extracted following the same procedure.

Outcomes of interest regarding the devices' characteristics included 1) the study design in which they were evaluated, 2) the robotic architecture (i.e., exoskeleton, end-effector or glove), 2) the type of support (i.e., active or passive), 3) the supported joints (wrist and hand were defined as distal, elbow and shoulder as proximal)

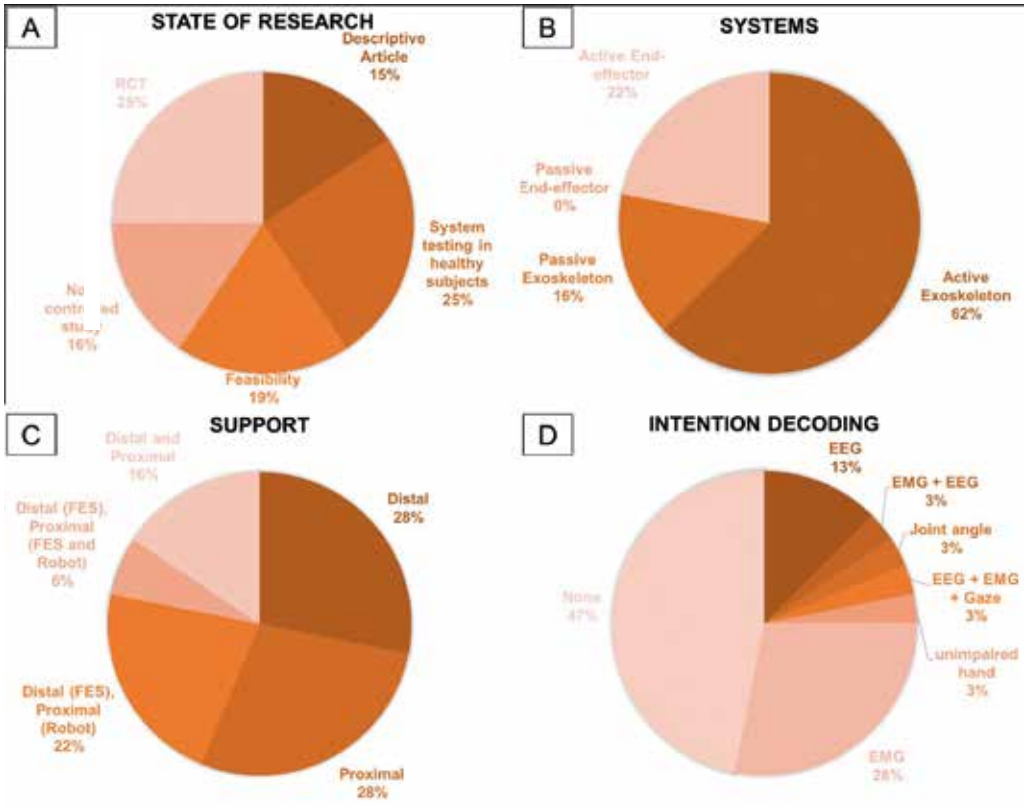

Figure 2. Proportion of A) levels of evidence, B) types of systems, C) locations of support, and D) intention decoding mechanisms of existing hybrid devices

and 4) the implemented sensors for intention detection (e.g., electromyography (EMG), electroencephalography (EEG), joint angle). Outcome of interest for the meta-analysis was the difference in the upper extremity Fugl-Meyer (FM) between intervention and control group after the intervention and at three months follow-up.

The devices' characteristics were analysed descriptively calculating the frequency of occurrence. Inferential analysis was performed with respect to the overall efficacy of hybrid devices by means of a random-effect model. Subgroup analyses were performed according to the severity level of the paresis (based on the baseline FM [14]). The alpha level was set to .05 and inferential analysis was performed using the Review Manager software (version 5.4).

Results: The systematic literature search revealed 542 items of which 133 were duplicates. During title and abstract screening, 297 records were excluded and five full texts were not retrieved, leaving 107 studies for full text screening. In the end, 73 studies were eligible for the review, including 32 different hybrid systems (see full list of references listed in [5].

Existing hybrid devices have been solely described without any data acquisition in 15% of identified studies. Data was collected in the remaining 85% of references, either in healthy subjects (25%), or in patients after stroke to assess feasibility (19%) or therapeutic effects (16% not-controlled and 25% controlled [**Figure 2**]).

Regarding the devices' characteristics, active exoskeletons made the biggest proportion of existing systems (62%). End-effectors are located at the distal part of the arm and were actively actuated in 22% of devices, while none of the end-effectors were applied passively. Passive actuation means that the patient needs to at least initiate the movement and is then supported. This mechanism was implemented in 16% of the devices, all of which are exoskeletons **(Figure 2)**.

In more than half of the devices the assistance focusses on supporting one part of the arm, either distally (28%) or proximally (28%). The whole arm is assisted by FES and the robotic component in 16% of studies. Furthermore, the whole arm receives support in 22% of studies, but here the FES and robotic module is split (i.e., FES support distally and robotic support proximally in 22%, FES support distally and FES and robotic support proximally in 6%, **Figure 2**). Considering the two different definitions of hybrid devices, 18% of existing systems are called hybrid as they apply a FES and robotic component at the same limb, while 72% incorporated true hybrid control of both components at the same joint.

The patients' intention to move is neglected in 47% of devices. In the other half of existing systems, the intention is most frequently decoded using EMG (26%) or EEG (13%) data **(Figure 2)**.

Regarding the pooled therapeutic effect of seven identified RCTs, hybrid neuroprostheses were effective in

upper limb recovery. After the intervention, the hybrid group showed a significantly higher FM value than the control group (*Mdiff* = 7.8 points, p < .001). This effect remained at three month follow-up (*Mdiff* = 8.4 points, p < .001). The difference between intervention and control group was larger in the group of severely impaired patients (*Mdiff* = 11.1 points, p < .003) compared to moderately impaired patients (*Mdiff* = 6.2 points, p = .005). Still, the therapeutic effect was significant for both groups of different impairment levels.

Conclusion: The overview of current hybrid devices showed that most of them feature active actuation. In most cases, these devices support the same joint simultaneously using both components, with an even split between focusing on the proximal and distal aspects. However, only half of these devices include mechanisms for detecting the patient's intentions, typically utilizing EMG or EEG data.

Applying hybrid neuroprostheses for upper limb rehabilitation after stroke showed a positive effect on upper limb recovery that persisted at least three months following the intervention. The effect was present independent of the impairment severity, but severely impaired patients showed a larger difference in the FM score after the intervention than moderately impaired patients.

In addition to further technical development such as incorporation of intention decoding, further RCTs are needed to make assumptions about the determinants (e.g., intervention and patient characteristics) of successful therapy.

Acknowledgements:
This project has received funding from the European Union Horizon 2020 research and innovation program ReHyb under grant agreement n° 871767.

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