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A kinematic-and-muscular modulation strategy for FES-assisted upper limb rehabilitation: a feasibility study

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Functional Electrical Stimulation (FES) is widely adopted for patient rehabilitation since it provides electrical pulses and, consequently, muscle contractions. The aim of the study is to develop a novel closed-loop multichannel contralaterally controlled FES technique for upper limb rehabilitation. In the proposed approach (Kinematic-and-Muscular-based Modulation Strategy, KMMS), the stimulation is off-line modulated by the difference of the myoelectric activity of the same muscle between limbs with the addition of on-line feedback due to kinematic patterns. The reference signals for stimulation were extracted from a dataset of myoelectric and kinematic patterns acquired from the dominant upper limb of ten healthy participants. KMMS represents an improvement of a literature technique (Muscular-based Modulation Strategy, MMS) where the stimulation is off-line modulated exclusively by electromyographic patterns. KMMS and MMS performance were compared by applying them to eight muscles of the non-dominant upper limb of ten healthy participants during ADL execution. KMMS demonstrated an improved completion rate during drinking (from 70% to 89%, *P* = 0.0200), pouring (from 75% to 89%, *P* = 0.0435), eating (from 72% to 86%) and handling objects (from 80% to 93%, *P* = 0.0414).

The presence of neurological disorders due to injuries of Central or Peripheral Nervous System[1,2] may cause severe upper limb sensorimotor disabilities compromising the execution of Activities of Daily Livings (ADLs)[3].

The Functional Electrical Stimulation (FES) is one of the most widely adopted techniques for the recovery of the affected neuromuscular functions. It provides low power electrical pulses to generate contraction of one or more muscles promoting joints movements and cortical excitability[4–6]. Typically, a multichannel FES is performed because it improves the patient's muscle coordination since humans recruit multiple muscles rather than a single one when performing movements[7]. In the last decades, FES was widely applied for the improvement of the muscles strength and spasticity during ADLs execution[8–10]. Recent studies showed that FES moderately improved upper limb activity in terms of Motor Assessment Scale, Action Research Arm Test and Box and Block Test scores compared with both no intervention and conventional training[11].

Most systems resorting to FES use open-loop stimulation modulation strategy where the stimulation patterns are defined a priori and manually triggered by the therapist or the patient[12]. Despite the promising results and ease of use[8–10], many studies demonstrated that closed-loop FES systems are more effective than open-loop ones for motor recovery[12] since they the patient's physical status monitoring enables aset real-time stimulation modulation[13]. Several FES modulation strategies based on Electromyographic (EMG) signals were proposed in literature[12]. In the simplest systems, FES is applied on a muscle when the relative EMG signal overcomes a patient-specific threshold determined before the task execution[13]. Other strategies are based on the use of the residual myoelectric signal to drive the stimulation[10]. The most complex systems adopt neural networks but they imply the learning of the inverse dynamic of the controlled system taking the output of a conventional feedback controller as a training signal[14]. A valid alternative is represented by the Iterative Learning Controller able to adjust FES intensity based on the tracking error of the previous movements but it requires a full FES-based human arm model to control the arm response[15]. Moreover, since EMG acquisition and FES are applied to the same muscle (i.e., ipsilateral stimulation), the EMG signals are characterized by artifacts that have to be removed to ensure an adequate FES modulation[16].

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Therefore, an emerging strategy is the Contralaterally Controlled Functional Electrical Stimulation (CCFES) since the intensity of the stimulation applied to the paretic muscle is controlled by the user's contralateral unimpaired muscle[17]. Recent literature studies have demonstrated that CCFES provided higher improvements in terms of Fugl-Meyer scores in post-stroke patients rehabilitation than ipsilateral one[18] since it produces peripheral neural activity temporally correlated with central one[17]. Nevertheless, most of the studies on CCFES focused exclusively on the restoration of upper limb distal joints capabilities (e.g., wrist, fingers and thumb)[19]. Furthermore, although the use of myoelectric information for controlling the stimulation is the most adopted approach, such technique is strongly influenced by several factors such as the electrodes position and tissue impedance which could alter the monitored signal and then the amplitude stimulation[19].

Given the aforementioned evidence, this study aims to propose and preliminary test a novel closed-loop multichannel CCFES technique for upper limb rehabilitation. In the proposed approach (Kinematic-and-Muscular based Modulation Strategy, KMMS), the stimulation to be applied to a muscle is off-line modulated by the difference of the myoelectric activity of the same muscle between the two limbs with the addition of an on-line feedback due to kinematic patterns. KMMS is an improvement of a literature technique, named in this paper Muscular based Modulation Strategy (MMS), where the stimulation is modulated only by EMG patterns[20,21]. The reference signals used for FES modulation were extracted from an *ad hoc* developed dataset of myoelectric and kinematic patterns of ten healthy participants' upper limbs. Since this work was conceived as a preliminary feasibility study, the performance of the proposed system was evaluated exclusively on healthy participants. Therefore, KMMS and MMS were applied to eight extrinsic muscles of the distal joints of ten healthy participants' non-dominant upper limb during ADLs execution and their performance were compared.

The paper is organized as follows: Sect. "Materials and methods" describes the two FES modulation strategies, the experimental setup and protocol for the generation of the dataset and KMMS and MMS performance comparison. Sects. "Results" and "Discussion" report and discuss the obtained results, while Sect. "Conclusions" is dedicated to conclusions and future works.

Materials and methods

The current study was divided in two main phases. The first one was dedicated to the development of a novel FES modulation strategy. The second phase aimed at the development of a dataset of myoelectric and kinematic patterns of ten healthy participants' upper limbs during ADLs execution. Subsequently, the novel FES modulation strategy was experimentally validated on the same healthy participants.

FES modulation strategies

In agreement with literature[5,6], the symmetric biphasic square wave shown in Fig. 1 was adopted since it induces charge transfer according to phase preventing galvanic process that can cause tissue damages[22–25]. The Pulse Width (PW) and the Pulse Frequency (PF) of the stimulation were always kept constant to 260 μs and 40 Hz, respectively[4–6]; whereas the Pulse Amplitude (PA) was modulated during task execution. The block diagrams of the two modulation strategies are reported in Fig.1 and they will be detailed in the following.

Muscular based modulation strategy (MMS)

In the FES Muscular based Modulation Strategy (MMS), the current delivered to a muscle is calculated as follows

$$PA = \frac{RMS_D - RMS_{ND}}{RMS_D} \cdot PA_{MAX} \tag{1}$$

where PA_{MAX} is the maximum current value producing a painless muscular contraction and a movement of the joint of interest such as to cover its entire range of motion. RMS_D and RMS_{ND} indicate the median Root Mean Square (RMS) values of activation of a dominant and non-dominant upper limb muscle in each subtask of each task among all the participants, respectively. Both values were extracted from the dataset. This FES modulation strategy was proposed in[20,21] and applied to five extrinsic muscles of the hand of six healthy participants during grasping task execution.

Kinematic-and-Muscular based modulation strategy (KMMS)

In the proposed FES Kinematic-and-Muscular based Modulation Strategy (KMMS), the stimulation applied to a muscle is modulated by the difference of the myoelectric activity of the same muscle between the dominant and non-dominant limb (blue box in Fig.1.B) with the addition of an on-line feedback due to kinematic patterns (red box in Fig.1.B). The current delivered to a muscle is calculated as follows

$$PA = \begin{cases} \frac{RMS_D - RMS_{ND}}{RMS_D} \cdot PA_{MAX} & \text{when } 0 < t \le t^* \\ \left[\frac{RMS_D - RMS_{ND}}{RMS_D} + \frac{\theta_D(t^*) - \theta_{ND}(t^*)}{\theta_D(t^*)} \right] \cdot PA_{MAX} & \text{when } t > t^* \end{cases} \tag{2}$$

where θ_D and θ_{ND} indicate the angle of the joint of interest of the dominant and non-dominant upper limb, respectively.

KMMS and MMS exhibit identical behavior from the beginning of the task until a time t* equal to 75% of a task execution time: therefore, the stimulation applied to a muscle is off-line modulated by the difference of the myoelectric activity of the same muscle between the two limbs. Afterwards, the two modulation strategies differ from each other. As for KMMS, whether the difference between $\theta_D(t^*)$ and $\theta_{ND}(t^*)$ is higher than an empirically determined threshold (i.e., 0.17 rad), the stimulation current provided to a muscle is linearly increased with respect to the error. Conversely, as for MMS, the addition of an on-line feedback due to kinematic

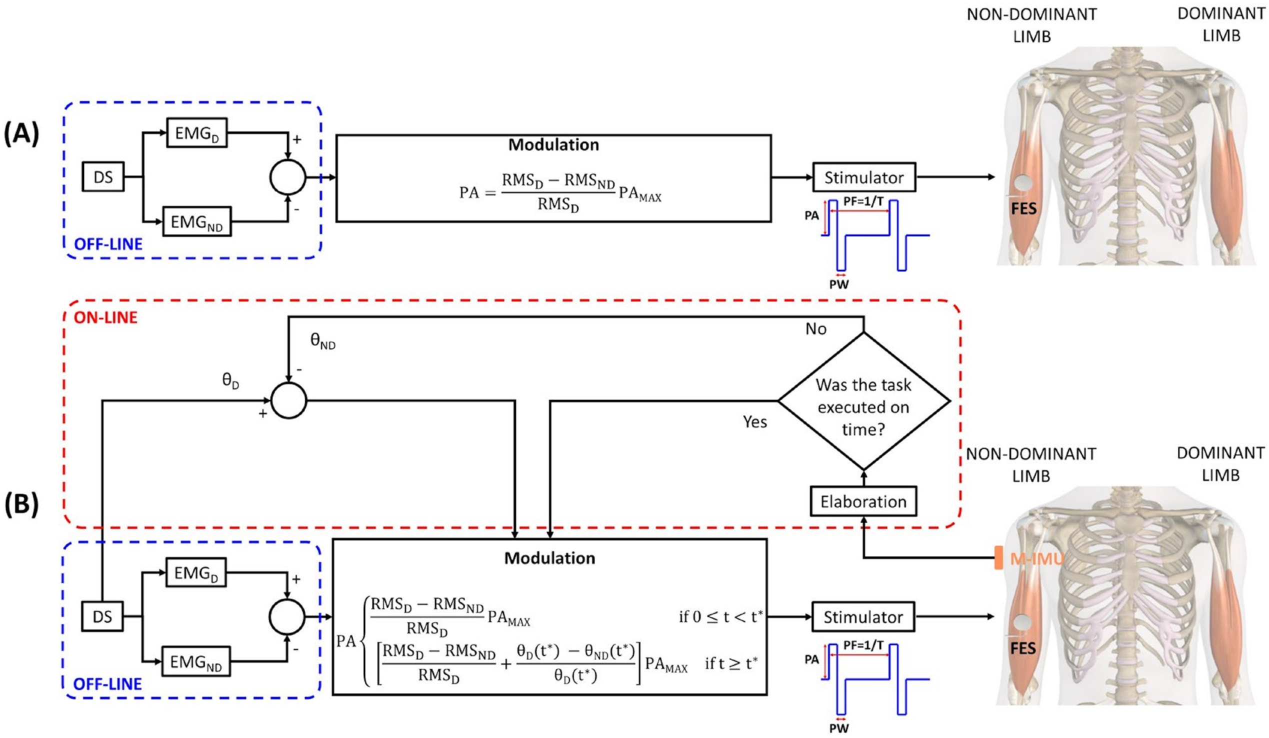

Fig. 1. (**A**) FES Muscular based Modulation Strategy (MMS): off-line modulation stimulation based on EMG patterns extracted from a dataset (DS)[20,21]; (**B**) FES Kinematic-and-Muscular based Modulation Strategy (KMMS): off-line modulation based on EMG patterns extracted from a dataset with an on-line feedback due to kinematic pattern.

patterns is absent. Such threshold value was the same for all the muscles of each participant and it was selected in accordance with human biomechanics and preliminary test. Specifically, the threshold was so-defined since its value corresponds to approximately 7–11% of the physiological range of motion of elbow, wrist and fingers range of motion (i.e., 2.44 rad, 2.22 rad and 1.74 rad, respectively)[26]. The myoelectric and kinematic patterns and the task execution time to be used as reference signals during the stimulation modulation were extracted from the dataset.

Experimental setup

Ten right-handed healthy participants (6 males and 4 females, 26.6±1.6 years) were enrolled for the study. Their hand dominance was assessed using the Edinburgh Handedness Inventory (EHI)[27]. The study was approved by by the Comitato Etico Territoriale Lazio Area 2 Policlinico Tor Vergata (18.24EM. CETcbm) in accordance with the Helsinki Declaration and following amendments; the main aspects of the study were explained to the participants in a comprehensive language and they signed an informed consent.

The experimental setup used for the dataset generation included the following components: (i) four Magneto-Inertial Measurement Units M-IMUs (Xsens Technologies BV, Enschede, NL)[28] placed on the lateral side of the arm, the forearm, on the back of the hand and of the fingers of the participants' upper limb for measuring the elbow, wrist and fingers kinematics. The shoulder's movements were not monitored because FES was not applied to the shoulder's muscle since it has never been accomplished in an useful manner[29]. Sensors' readouts were acquired through their proprietary software MT Manager with a sampling frequency of 75 Hz; (ii) eight EMG Trigno Wireless sensors (Delsys Inc., Natick, MA, USA) for monitoring the electrical activity of the following upper limb muscles: Biceps Brachii (BB, elbow flexion), Triceps Brachii (TB, elbow extension), Flexor Carpi Radialis (FCR, wrist flexion), Extensor Carpi Ulnaris (ECU, wrist extension), Flexor Digitorum Superficialis (FDS, fingers flexion), Extensor Digitorum Communis (EDC, fingers extension), Abductor Pollicis Brevis (APB, thumb abduction) and Extensor Pollicis Longus (EPL, thumb extension). These muscles were selected as the superficial ones most involved during upper limb ADLs execution[30]. The sensors placement was in accordance with Surface EMG for Non-Invasive Assessment of Muscles guidelines[31] and therefore they were placed in the center of the muscle bellies away from tendons and the edge of the muscle. Sensors' readouts were acquired through their proprietary software EMGWorks with a sampling frequency of 1.1 kHz. The M-IMUs' reference frames, the GRF and both sensors locations on a representative participant's dominant upper limb are shown in Fig. 2A, B.

The experimental setup adopted for delivering FES to the muscles of the participants' non-dominant upper limb included the following components: (i) the multichannel electric stimulator STG4008 (Multichannel System MCS GmbH, Reutlingen, DE) for delivering stimuli through the application of two circular (25 mm

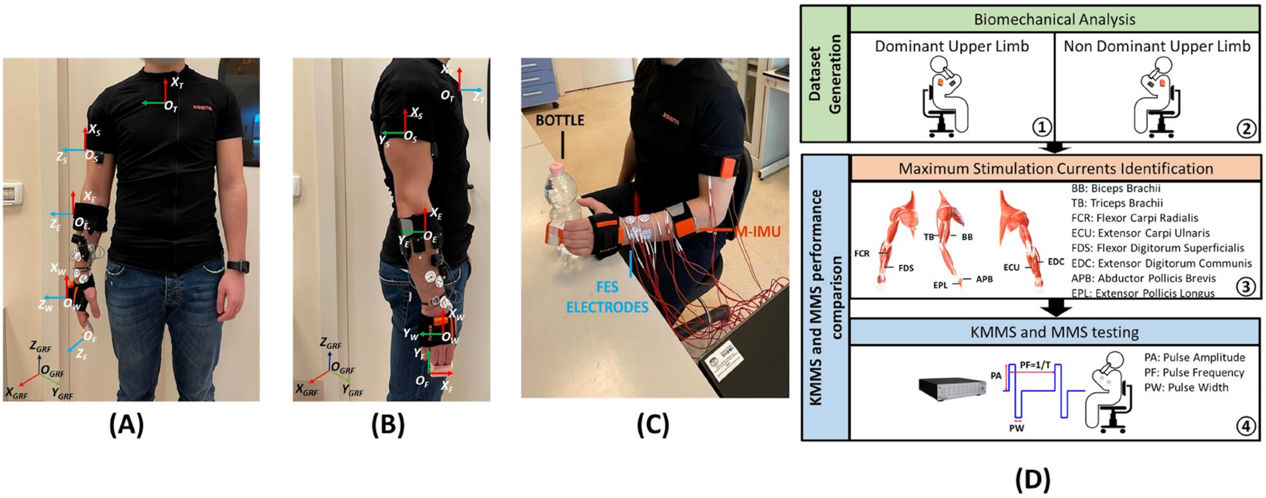

Fig. 2. (**A**, **B**) Frontal and lateral view of a representative participant with M-IMU and EMG sensors placed on the dominant upper limb, respectively. The axes x, y and z of the sensors' reference frames and of the Global Reference Frame (GRF) are reported in red, green and blue, respectively. (**C**) Representative participant during the execution of drinking task with FES applied on the non-dominant upper limb's muscles. (**D**) Diagram of the different phases of the experimental protocol.

diameter), commercial, auto-adhesive and superficial electrodes (TensCare Ltd, Epsom, UK) located over each muscle of interest; (ii) four M-IMUs placed on the lateral side of the arm, the forearm, on the back of the hand and of the fingers for monitoring the non-dominant upper limb kinematics during task execution via FES; (iii) a custom-made Graphic User Interface developed in C# using Visual Studio 2019 (Microsoft, Redmond, WA, USA) for synchronizing all the components, acquiring the M-IMUs signals, managing the electrical stimulation and storing data. The electrodes and sensors' location on a representative participant's non-dominant upper limb are shown in Fig. 2C.

Experimental protocol

The experimental protocol was divided into four phases and its diagram is reported in Fig. 2D.

The first and second phases were dedicated to the development of the dataset through the acquisition of myoelectric and kinematic patterns of the dominant and non upper limbs of the ten healthy participants during the execution of ADLs, respectively. From literature analysis[8,9] and focus group results on seven patients with brachial plexus injury and five post-stroke ones investigating their functional needs[32], the following ADLs were defined: drinking, pouring, eating and handling object. The first three activities were divided into the following six subtasks: (i) S1: object reaching from home position (i.e., limb parallel to the trunk); (ii) S2: object grasping (power grasp for drinking and pouring; lateral and pinch grasp for eating and handling object, respectively); (iii) S3: task execution (i.e., bringing a 500 g bottle of water to the mouth; pouring water from a 500 g bottle into a glass on the left placed 300 mm away; bringing a 45 g spoon to the mouth); (iv) S4: object re-positioning; (v) S5: hand opening; (vi) S6: back to home position. The last ADL (i.e., handling object) did not include the fourth subtask since the object (18 g, 15 × 25 × 70 mm wooden block) was only moved to the left at a distance of 300 mm and not bring back to initial position. Each participant sat in a chair in a comfortable position and he was asked to perform in a natural way three repetitions for each ADL with both upper limbs: 24 repetitions in total with a 60 s rest from each other for each participant. The order of phases and ADLs execution was random.

The third phase of the experimental protocol aimed to the identification of the electrodes' optimal position for each of the eight muscles of the participant's non-dominant upper limb and the relative maximum stimulation currents. Each participant was asked to sit in a chair in a comfortable position with the non-dominant upper limb placed on a table to find the optimal electrodes location for inducing the contraction of each muscle. Based on biological landmarks, the skin surface above the muscles was located and cleaned using alcohol pad. The PW, PF, stimulus duration and rest between two consecutive stimuli were kept constant to 260 μs, 40 Hz, 1 and 5 s, respectively[4-6]. The PA was incremented from 2.0 mA with a step of 0.1 mA until a current value producing a painless muscular contraction and a movement of the joint of interest such as to cover its entire range of motion was reached (PA_{MAX}).

The fourth phase of the experimental protocol was dedicated to the application of the FES to the eight selected muscles of the participants' non-dominant upper limb for ADLs execution. The participants were asked to perform each ADL three times with both FES modulation strategies in a random order: 24 repetitions in total with a 60 s rest from each other for each participant. In order to ensure that the ADLs execution via FES was not influenced by the participants' unconscious myoelectric activity, the participants were deeply instructed to not perform any voluntary movements during FES delivery and be completely passive. Whether during task execution, the participants were not able to carry out a subtask in a proper way (i.e., grasping not performed or performed incorrectly, object fallen or re-positioned in an incorrect way), the subtask was considered failed and the experimenter assisted the participant in assuming the correct kinematic configuration for continuing the ADL execution.

Evaluation metrics

All data were exported and processed offline in MATLAB (R2020a, MathWorks, Natick, MA, USA).

Concerning the dataset, exclusively the parameters needed for the FES modulation strategies were computed. The tasks and subtasks execution times provided a quantitative evaluation of the time needed to accomplish a specific ADL. The data of the dominant upper limb were adopted for timing the electric currents in both FES modulation strategies: therefore, the participants were induced to execute the ADLs via FES with the same dataset timing. The upper limb joint kinematics was extracted in order to quantify the kinematic configuration assumed by the participants during ADLs execution. The upper limb was modeled as a sequence of rigid links so that the exact positioning of the sensors along the greater dimension of the body districts did not influence the measured angle. Each sensor provided its orientation information with respect to a Global Reference Frame (GRF) defined as follows: the X-axis pointed at the magnetic North, the Z-axis was aligned with the gravitational axis pointing upwards and the Y-axis was defined as the cross vector between Z and X axes. Given the rotation matrices $R_i^{GRF}(t)$ and $R_j^{GRF}(t)$ provided by the M-IMUs indicating the rotations of the joint i_{th} and j_{th} with respect to the GRF at the time t, the i_{th} joint rotation with respect to j_{th} one is expressed by $R_i^j(t)$ calculated as follows

$$R_i^j(t) = \left(R_j^{GRF}(t)\right)^{-1} \cdot R_i^{GRF}(t) = \begin{pmatrix} r_{11}(t) & r_{12}(t) & r_{13}(t) \\ r_{21}(t) & r_{22}(t) & r_{23}(t) \\ r_{31}(t) & r_{32}(t) & r_{33}(t) \end{pmatrix} \tag{3}$$

where $r_{nm}(t)$ indicates the matrix element in the row n_{th} and column m_{th} at time t. The Roll-Pitch-Yaw angles have been extracted from this matrix to obtain the intra/extrarotation (sIE), flexion/extension (sFE) and adduction/abduction (sAA) of the shoulder, the elbow flexion/extension (eFE), the pronation/supination (wPS), flexion/extension (wFE) and adduction/abduction (wAA) of the wrist, and the fingers flexion/extension (fFE). The muscular activity was analyzed in order to allow FES modulation in both MMS and KMMS (see Eq. 1 and Eq. 2, respectively). The acquired EMG signals were pre-processed by using a fourth-order Butterworth bandpass filter with cut-off frequencies (30,450) Hz and a second-order Butterworth notch filter (50 Hz) to remove noise from power lines[3]. Finally, the filtered EMG signals of each muscle were normalized respect the minimum and maximum value of activity reached by that specific muscle during all the repetitions. The RMS values of each muscle were extracted for both upper limbs since they were used in both FES modulation strategies.

Concerning the FES modulation strategies comparison, the maximum stimulation currents, the Success Rate and Completion Rate were computed. During test execution, for each repetition, a score of 1 or 0 was assigned to each subtask depending on whether the participants were able to carry out them successfully or not, respectively. The Success Rate (SR) was introduced as the percentage of successfully completed subtasks compared to the total (N=30, defined as the product between the number of enrolled healthy participants and the number of repetitions of each subtask for each participant). The Completion Rate (CR) was introduced as the percentage of successfully completed subtasks compared to the total number of subtasks of that specific task (N=5 for handling object and 6 for the others ADLs).

Statistical analysis

A statistical analysis was carried out on the aforementioned performance indicators.

Since these indicators were obtained from the same group of participants under two different conditions (i.e., dominant vs. non-dominant upper limb; KMMS vs. MMS performance comparison), the data were paired. The Shapiro–Wilk test was used to assess the normality of the data distribution. Accordingly, differences between the same indicators across the two conditions were evaluated using the Wilcoxon signed-rank test when the data were not normally distributed, or the paired t-test otherwise. Unless differently reported in figures' caption and text, significance level P was 0.05 and Bonferroni correction was executed in case of multiple comparisons among groups of data.

Results

This section is dedicated to the presentation of the results obtained from the dataset and the evaluation of the performance of the proposed FES modulation strategy. The obtained results were characterized by a non-gaussian distribution and thus the eventual presence of statistically significant differences was evaluated through the Wilcoxon signed-rank test.

Dataset of myoelectric and kinematic patterns

Execution time

The participants performed the proposed ADLs with no time constraints and, consequently, they accomplished the required tasks in different durations. The Fig. 3A–D show the execution times of all subtasks of all tasks of all the participants for both upper limbs.

It is noteworthy noticing that the task execution with the non-dominant upper limb took longer than that with the dominant one. This is evident both in subtasks primarily involving eFE and in those ones where a greater contribution was required from the wrist and fingers. In the first and third subtask, the participants were asked to reach the desired object from a sitting position and, once grasped, bring it to the mouth. Therefore, they mainly exerted shoulder flexion/extension in the first subtask followed by eFE in the third one. The use of the non-dominant limb led to a increase of the execution times in both subtasks of each ADL: drinking (from 3.55

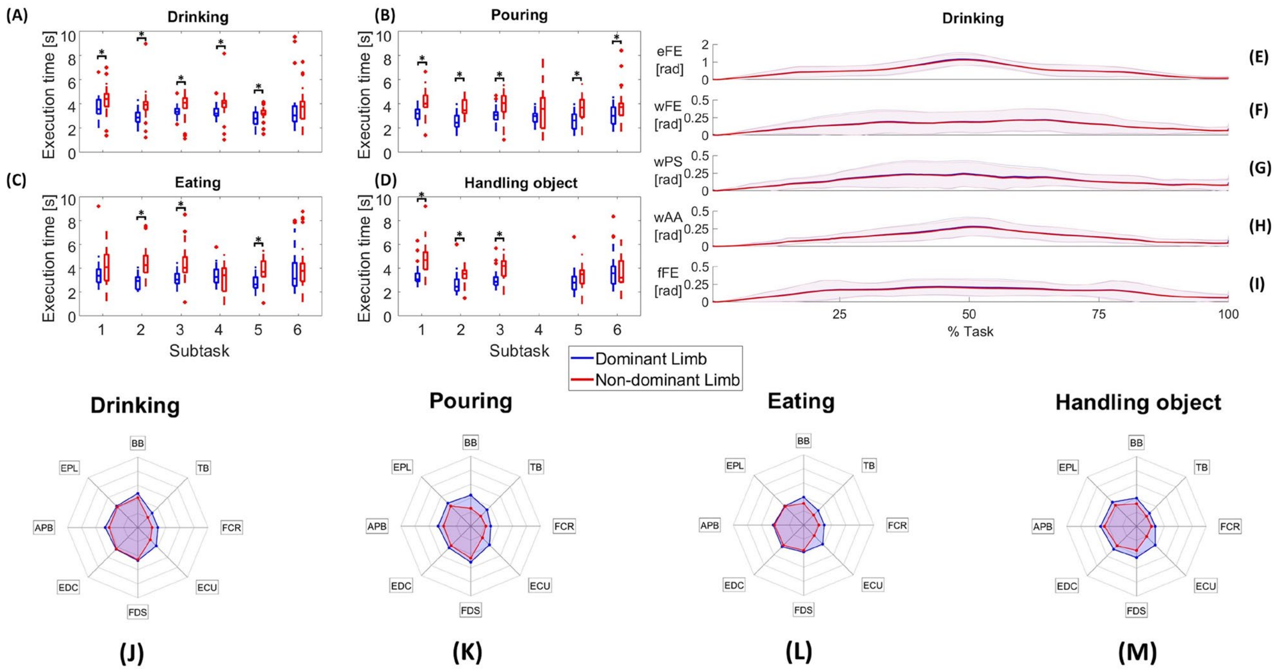

Fig. 3. (**A**–**D**) Execution times of subtasks of the participants during drinking, pouring, eating and handling object (subtask 4 was absent), respectively. The red + sign indicates the outlier. * indicates a statistically significant difference (Wilcoxon signed-rank test, $P < 0.05$). (**E**–**I**) Mean values (continuous lines) and standard deviations (shaded areas) of the participants' eFE, wFE, wPS, wAA and fFE represented respect to the percentage of task completion. (**J**–**M**) Median RMS values of the eight selected muscle's activities of the participants' upper limbs during drinking, pouring, eating and handling object, respectively.

s to 4.39 s, $P = 0.0316$; from 3.34 s to 4.09 s, $P = 0.0285$), pouring (from 3.20 s to 4.01 s, $P < 0.001$; from 3.07 s to 4.06 s, $P < 0.001$), eating (from 3.38 s to 4.10 s and from 3.05 s to 4.04 s, $P < 0.001$) and handling object (from 3.10 s to 4.69 s, $P < 0.001$; from 2.87 s to 4.19 s, $P = 0.0030$). Similarly, the use of the non-dominant upper limb led to an increase of the execution times in the second and fifth subtask where the participants mainly exerted fFE for grasping the object and, once the task was completed, release it opening the hand. This is evident in all the ADLs: drinking (from 2.87 s to 3.93 s, $P < 0.001$, from 2.80 s to 3.22 s, $P = 0.0125$), pouring (from 2.44 s to 3.46 s, $P < 0.001$, from 2.63 s to 3.70 s, $P < 0.001$), eating (from 2.94 s to 4.28 s, $P < 0.001$, and from 2.65 s to 3.70 s, $P < 0.001$) and handling object (from 2.45 s to 3.53 s, $P = 0.0073$, from 2.80 s to 3.50 s).

The values of the subtasks execution times were used for timing the electric currents provided to the muscles during both FES modulation strategies.

Joint kinematics

The participants executed the proposed ADLs with their personal style and therefore with different upper limb joint kinematic patterns. The Fig. 3E–I show the mean upper limb joint kinematics during a representative task (i.e., drinking) for both limbs.

Although the use of the dominant or non upper limb significantly affected task execution time, no differences were encountered on the upper limb joint kinematics. In the first two subtasks, the participants reached the desired object and grasped it: therefore, an increase of all degrees of freedom of the joints of interest was evident. Subsequently, the participants brought the object to the mouth and then re-positioned it on the table: these subtasks mainly involved eFE and therefore the other joints' degrees of freedom kept a plateau value. Finally, in the last two subtasks, the participants released the grasp and went back to the home position leading to a decrease of all the degrees of freedom to their resting values.

Upper limb joint kinematics was used as reference for FES KMMS (see Eq. 2).

Muscular activity

The Fig. 3J–M show the median RMS values of the eight selected muscle's activities of the participants' both upper limbs during all the ADLs execution.

The obtained results demonstrated how the non-dominant upper limb muscles exhibit less activity than their counterparts of the dominant one. This is evident during each ADL and in all the muscles, especially for those ones concerning the movement of the elbow and wrist. Indeed, the BB, TB, FCR and ECU presented the following statistically significant reductions: from 0.48 to 0.42 ($P = 0.0132$), from 0.20 to 0.14 ($P < 0.001$), from 0.29 to 0.20 ($P = 0.0093$) and from 0.26 to 0.18 ($P < 0.001$) respectively during drinking; from 0.44 to 0.26 ($P = 0.0125$), from 0.23 to 0.15 ($P < 0.001$), from 0.29 to 0.22 ($P = 0.0132$) and from 0.27 to 0.22 ($P = 0.0011$) respectively during pouring; from 0.40 to 0.31 ($P = 0.0111$), from 0.21 to 0.14 ($P < 0.001$), from 0.29 to 0.22 (P

< 0.001) and from 0.27 to 0.15 ($P < 0.001$) respectively during eating; from 0.40 to 0.32 ($P = 0.0207$), from 0.19 to 0.14 ($P < 0.001$), from 0.27 to 0.21 ($P < 0.001$) and from 0.27 to 0.15 ($P < 0.001$) respectively during handling.

The RMS values were used as reference for both FES modulation strategies (see Eqs. 1 and 2).

Functional electrical stimulation

Maximum stimulation currents

The maximum stimulation currents delivered to the muscles were specific for each participant and they are represented in Fig. 4A. The Fig. 4B shows the maximum currents needed to generate eFE (BB and TB), wFE (FCR and ECU), fFe (FDS and EDC), thumb abduction (APB) and extension (EPL) in all the participants.

Two different statistical analyses were carried out in order to investigate differences in the maximum stimulation currents provided to the muscles and to the joints (Wilcoxon signed-rank test with Bonferroni correction, $P < 0.0018$ and $P < 0.0083$, respectively). The former pointed out the BB current (10.0 mA) was significantly ($P < 0.001$) higher than those ones of FCR (8.5 mA) and APB (6.0 mA). The latter pointed out the current provided to the thumb muscles (7.0 mA) were significantly ($P < 0.001$) less than those ones of the elbow flexor/extensor muscles (10.0 mA) and fingers (9.0 mA).

FES modulation strategies

Once the maximum stimulation currents were defined for each muscle, the participants were asked to perform each ADL three times using both FES modulation strategies in a random order.

The pulse amplitude of the stimulus delivered to a representative muscle (i.e., FDS) of a representative participant along the drinking task performed via MMS and KMMS is represented as percentage of PA_{MAX} in Fig. 4C and D, respectively.

As can be inferred by the obtained results, regardless FES modulation strategies, FDS was not stimulated in some subtasks. In the first and last subtask, the pulse amplitude was null since the required movement did not mainly involve fFE: indeed, the participants were asked to reach the object and go back to the home position, respectively. Similarly, no stimulation was delivered in the fifth subtask, too. Indeed, the participants were asked to open hand to release the object and therefore the mainly activity was performed by the EDC as fingers extensor muscle. The difference between MMS and KMMS come across in the central subtasks where the required FDS activation was greater than in the previous ones. As for MMS, in the second subtask, the participants grasped the object and then FDS activation was induced with a stimulation current of 50%. Subsequently, the participants carried out a firm and stable grasp during task execution and object re-positioning on the table. Therefore, fFE was induced via FDS stimulation with stimulus intensities of 65 and 75%, respectively.

KMMS and MMS exhibit identical behavior from the beginning of the subtask until a time t* equal to 75% of a task execution time. Hence, the stimulation applied to a muscle was off-line modulated by the difference of the myoelectric activity of the same muscle between the value extracted from the dataset and that one specific for each participant (see Eq.1). Afterwards, to allow the participants to assume the desired upper limb kinematic configuration and then be successful in task execution, the stimulation current provided to a muscle is linearly increased with respect to the error (see Eq.2). Therefore, the current delivered to the FDS was increased at 75% of the subtask execution time. In details, the current was increased from 50% to 70%, from 65% to 80% and from 75% to 90% in the second, third and fourth subtask, respectively.

Success rate

The SR values of each subtask of each task using the two different FES modulation strategies are represented in Fig.5A–D.

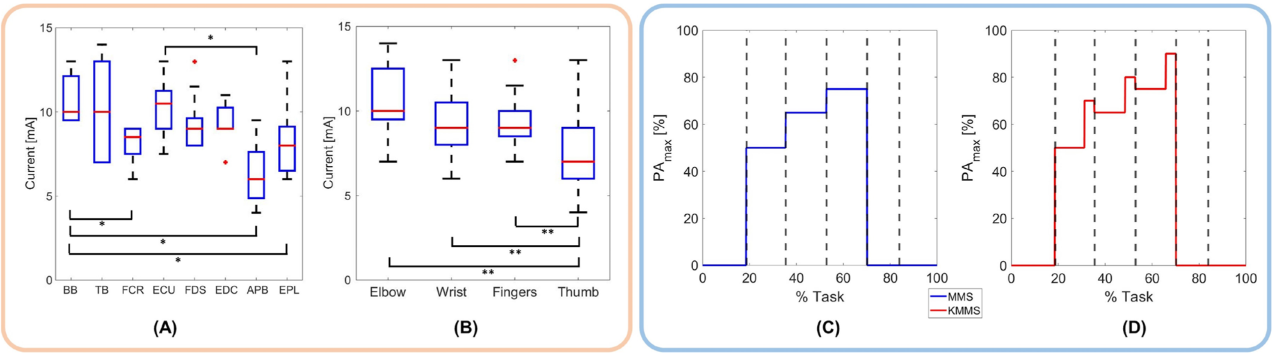

Fig. 4. (**A**, **B**) Maximum stimulation currents delivered to each participant's muscle and joint (elbow: BB and TB, wrist: FCR and ECU, fingers: FDS and EDC, thumb: APB and EPL) respectively. The red + sign indicates the outlier. * and ** indicate a statistically significant difference (Wilcoxon signed-rank test with Bonferroni correction, $P < 0.0018$ and $P < 0.0083$, respectively). (**C**, **D**) Pulse amplitude of the stimulus delivered to the FDS of a representative participant during the drinking task performed via MMS and KMMS represented respect to the percentage of task completion. The grey vertical dashed lines indicate the mean values of each subtask duration. The current intensity is expressed as a percentage of the relative PA_{MAX}.

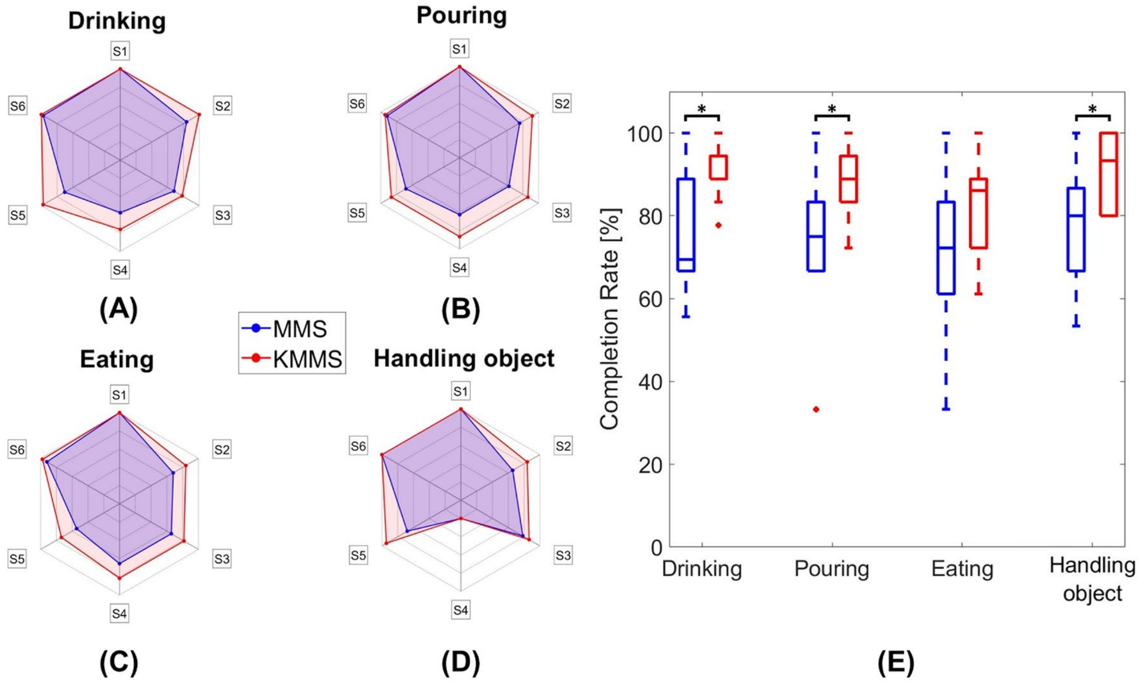

Fig. 5. (**A**–**D**) Success Rate (SR) values of the participants in each subtask (S_i) of drinking, pouring, eating and handling object, respectively. The handling object task did not include S4. (**E**) Completion Rate (CR) values of the enrolled participants during the ADLs execution. The red + sign indicates the outlier. * indicates a statistically significant difference (Wilcoxon signed-rank test, $P < 0.05$).

The first subtask (i.e., object reaching) was always successfully executed adopting both MMS and KMMS. In the final subtask (i.e., back to home position), KMMS obtained good SR values (i.e., 100% for drinking, 93% for pouring, 97% for eating and 90% for handling). Conversely, MMS obtained the following lower SR values: 97%, 90%, 90% and 100% for drinking, pouring, eating and handling objects. No statistically significant differences were found between the SR values of the same subtask using the two FES modulation strategies. In the second subtask of each ADL, the participants were asked to grab three objects with as many different grips: a power grasp for a bottle of water during drinking and pouring; a lateral one for a spoon during eating; a pinch one for a wooden block during handling object. The three grasps execution via stimulation presented different SR values according to FES modulation strategies. Using MMS, the power grasp obtained a SR value of 80% and 70% during drinking and pouring, respectively: these values were significantly increased to 100% and 90% during drinking and pouring with KMMS ($P = 0.0495$). A similar trend was also reported for the other two hand grips where KMMS has always obtained at least the same SR value of MMS. The lateral grasp during eating obtained a SR value of 60% and 80% with MMS and KMMS, respectively. The pinch grasp during handling object obtained a SR values of 60% and 80% with MMS and KMMS, respectively Regardless FES modulation strategies, the third and fourth subtask (i.e., task execution and object re-positioning) of drinking and pouring have obtained lower SR values than the other ones: this may be due to the load to move.

Finally, the contribution of the on-line feedback due to kinematic patterns was evident in the fifth subtask where the participants were required to release the object opening the hand. All the SR values obtained through the adoption of MMS were strongly improved during KMMS: from 63% to 96%, from 60% to 85%, from 43% to 67% and from 60% to 93% for drinking, pouring, eating and handling object, respectively. The low values of SR obtained in the subtask of interest during eating can be due to the type of grasping required: indeed, in this task the participants performed a lateral grasp which required more synchronization of muscular activation of wrist, fingers and thumb muscles rather than in others ADLs.

Completion rate
The CR values of each task using the two different FES modulation strategies are represented in Fig. 5E.

As can be inferred by the obtained results, the CR values obtained by KMMS were always greater than those ones of MMS. The statistical analysis pointed out a significant improvement of the CR values in the following ADL: drinking (from 70% to 89%, $P = 0.0200$), pouring (from 75% to 89%, $P = 0.0435$) and handling object (from 80% to 93%, $P = 0.0414$). Although not statistically significant, also an increase of CR values was evident in eating (from 72% to 86%).

Discussion
The results from dataset demonstrated how the use of the non-dominant upper limb rather than the dominant one influenced more the task execution time and muscular activity than the joint kinematics.

Indeed, as can be seen in Fig. 3, the two limb kinematic patterns are overlapping and thus the participants assumed the same kinematic configuration with both dominant and non upper limb. This can be due to the fact the motor strategy is unique and it is exploited by the participants for performing the proposed ADLs regardless the adopted limb (i.e., dominant or non). Conversely, it is possible noticing how the use of non-dominant limb rather than the dominant one significantly increased the execution times in each ADL. In details, the following statistically significant time increases were observed: from 19.41 s to 22.89 s ($P = 0.0218$), from 17.37 s to 22.63 s ($P < 0.001$), from 19.35 s to 22.90 s ($P < 0.001$) and from 15.22 to 19.54 s ($P = 0.0053$) for drinking, pouring, eating and handling object, respectively. Consequently, the use of the non-dominant limb required more attention and control than the dominant one, which tends to move in a more automated manner. Similarly, the influence of the adopted limb was evident in the muscular patterns. Indeed, the median RMS values demonstrated a reduction of myoelectric activity of each muscle during each ADL. Hence, although the use of the non-dominant upper limb rather than the dominant one did not affect the joint kinematics, the participants accomplished the task by taking more time and with a less muscular effort.

As for FES modulation strategies comparison, the obtained results demonstrated a moderate correlation (Spearman coefficient ρ_s=0.58, P=0.1341) between the PA_{max} values and the muscular volumes[33]. Indeed, the BB and the APB represent on average the 14.5 and 0.5% of the whole upper limb volume and they needed 10.0 mA and 6.0 mA, respectively. This result was confirmed by the presence of a moderate correlation (ρ_s=0.75, P=0.0403) between the stimulation currents and the joints' ranges of motion,[34,35]. Indeed, the eFE range of motion is 2.53 rad and the elbow flexor/extensor needed 10.0 mA, whereas, the ranges of motion of thumb abduction and extension are 1.22 rad and 1.05 rad and they needed current of 6.0 mA and 8.0 mA, respectively. The use of indicators such as the SR and CR enabled the quantification of both FES modulation strategies performance. KMMS and MMS obtained similar good results (SR always greater than 90%) in simple movement mainly involving eFE such as the first (i.e., object reaching) and last (i.e., back to home position) subtask. Regardless the adopted FES modulation strategy, the subtasks involving the interaction with an object obtained lower SR values than the others. In details, the power grasp obtained SR values ranging from 70% to 100% that are higher than those ones of the lateral and pinch grasp (both ranging from to 60% and 80%). Indeed, the lateral and pinch grasp are precision grips and thus the proposed non-invasive electrical stimulation system was not performed as well as in drinking and pouring where fine manipulation is not required. Nevertheless, the use of KMMS increased the SR values improving the overall quality of the proposed system.

Conclusions

The aim of the current work was to propose and preliminary test a novel closed-loop multichannel CCFES technique for upper limb rehabilitation. The proposed approach (KMMS) was applied to eight extrinsic muscles of the distal joints of ten healthy participants' non-dominant upper limb during ADLs execution and its performance was compared with a literature one (MMS). As for KMMS, the stimulation to be applied to a muscle is off-line and modulated by the difference of the myoelectric activity of the same muscle between the two limbs with the addition of an on-line feedback due to kinematic patterns. As for MMS, such feedback was absent. The reference signals used for FES modulation were extracted from an *ad hoc* developed dataset of myoelectric and kinematic patterns of ten healthy participants' upper limbs.

The dataset analysis demonstrated how the use of the non-dominant upper limb rather than the dominant one influenced more the task execution time and muscular activity than the joint kinematics. Indeed, the differences between the kinematic patterns of both limbs are negligible. Conversely, a statistically significant increase of the task execution time and reduction of muscular activity were reported for each ADL.

The two FES modulation strategies obtained similar performance in simple movement mainly involving eFE, while KMMS obtained better results than MMS in subtasks involving the interaction with an object. This led to an increase of CR values for drinking (from 70% to 89%, $P = 0.0200$), pouring (from 75% to 89%, $P = 0.0435$), eating (from 72% to 86%) and handling object (from 80% to 93%, $P = 0.0414$).

Although the obtained results were promising, the current study presented different limitations. The main limitation is the lack of experimental validation on target population: therefore, further steps will be devoted to an extensive validation of the proposed system for rehabilitation of post-stroke patients. Indeed, such patients often experience muscle weakness and impaired voluntary control. As reported in literature[8–11], FES can be effective to restore or assist functional movements by directly activating the affected muscles in a coordinated manner. The proposed control strategy could be advantageous, as it may allow muscular contraction and thus ADLs execution.

Moreover, in the current solution, the stimulation was off-line modulated according to the myoelectric activity of the selected muscles. In the future, it could be useful developing a closed-loop FES system able to on-line adapt the stimulation intensity according to the residual motor activity of the patients. Therefore, the system should be integrated with a FES artifacts removal algorithm. In this context, several software solutions have been proposed in literature to extract the volitive EMG signal during stimulation: (i) decomposition methods[36]; (ii) suppression methods[37]; (iii) comb filters[38]. Thanks to this integration, the proposed system will be able to remove FES artifacts, on-line monitor myoelectric activity and then modulate the stimulation delivered to the muscles. This improvement would make the proposed approach more suitable for clinical application in hemiplegic patients where motor impairments differ substantially from the physiological observed inter-limb asymmetries.

In addition, although the adopted stimulator STG4008 was effective in FES delivering, its large form factor (310 × 325 × 85 mm, 2.8 kg) and dependence on mains power strongly limit its use in real-world application. Therefore, further studies will be dedicated to the development of a more portable solution. The novel stimulator should be able to provide electrical stimulation in more than one channel with stimulation parameters high enough to induce a muscular contraction. In this field, a critical parameter will be represented by the stimulator voltage compliance since it should be able to ensure adequate stimulation parameters (i.e., PA more than 10 mA, PW of 260 μs and PF of 40 Hz in all the channels) overcoming the tissue impedance. To guarantee the stimulator's usage in everyday life, the device should be wearable (e.g., 60 × 30 × 30 mm, 0.1 kg), battery-powered (e.g., ±5 V), attachable to the arm through velcro straps and manageable through a wireless connection. The use of such wearable solution rather than a benchtop one should be the execution via FES of upper limb ADLs more complex than the selected one (i.e., drinking, pouring, eating and handling objects) such as bimanual task. Moreover, this should allow the testing of the system robustness and clinical relevance. As conclusion, this system could be integrated with a robot for the development of a hybrid robotic system for upper limb rehabilitation.

Data availability
All data needed to evaluate the conclusions are present in the manuscript. Additional data may be requested from the corresponding author upon reasonable request.

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Author contributions
A.D. designed the study, contributed to the development of the overall system, analyzed the data, wrote and review the paper. F.C. designed the study and review the paper. F.S.D.L. contributed to the development of the overall system and review the paper. V.I. performed the literature analysis and the experiments. L.Z. supervised the experiments and reviewed the paper. All the authors discussed the results, commented on the manuscript and declared no competing interests.

Declarations

Competing interests
The authors declare no competing interests.

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