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ORIGINAL RESEARCH

Clinically Significant Gains in Skillful Grasp Coordination by an Individual With Tetraplegia Using an Implanted Brain-Computer Interface With Forearm Transcutaneous Muscle Stimulation

Check for updates

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Abstract

Objective: To demonstrate naturalistic motor control speed, coordinated grasp, and carryover from trained to novel objects by an individual with tetraplegia using a brain-computer interface (BCI)-controlled neuroprosthetic.

Design: Phase I trial for an intracortical BCI integrated with forearm functional electrical stimulation (FES). Data reported span postimplant days 137 to 1478.

Setting: Tertiary care outpatient rehabilitation center.

Participant: A 27-year-old man with C5 class A (on the American Spinal Injury Association Impairment Scale) traumatic spinal cord injury

Interventions: After array implantation in his left (dominant) motor cortex, the participant trained with BCI-FES to control dynamic, coordinated forearm, wrist, and hand movements.

Main Outcome Measures: Performance on standardized tests of arm motor ability (Graded Redefined Assessment of Strength, Sensibility, and Prehension [GRASSP], Action Research Arm Test [ARAT], Grasp and Release Test [GRT], Box and Block Test), grip myometry, and functional activity measures (Capabilities of Upper Extremity Test [CUE-T], Quadriplegia Index of Function-Short Form [QIF-SF], Spinal Cord Independence Measure—Self-Report [SCIM-SR]) with and without the BCI-FES.

Results: With BCI-FES, scores improved from baseline on the following: Grip force (2.9 kg); ARAT cup, cylinders, ball, bar, and blocks; GRT can, fork, peg, weight, and tape; GRASSP strength and prehension (unscrewing lids, pouring from a bottle, transferring pegs); and CUE-T wrist and hand skills. QIF-SF and SCIM-SR eating, grooming, and toileting activities were expected to improve with home use of BCI-FES. Pincer grips and mobility were unaffected. BCI-FES grip skills enabled the participant to play an adapted "Battleship" game and manipulate household objects.

Conclusions: Using BCI-FES, the participant performed skillful and coordinated grasps and made clinically significant gains in tests of upper limb function. Practice generalized from training objects to household items and leisure activities. Motor ability improved for palmar, lateral, and

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tip-to-tip grips. The expects eventual home use to confer greater independence for activities of daily living, consistent with observed neurologic level gains from C5-6 to C7-T1. This marks a critical translational step toward clinical viability for BCI neuroprosthetics.
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Individuals with tetraplegia prioritize recovery of upper limb strength and dexterity to facilitate their independence.[1-5] Voluntary control of hand grasp has been restored to paralyzed limbs using noninvasive[6-11] and cortical microelectrode array (MEA)-based[12-16] brain-computer interfaces (BCIs) that translate brain activity to hand movements evoked through implanted[10-12] or transcutaneous[6-9,13-16] functional electrical stimulation (FES).[6-9,12,13] However, clinically significant gains on tests of upper limb function have not been demonstrated using BCI-FES. The critical translational path for BCI neuroprosthetics requires demonstration of clinically meaningful gains in speed, dexterity, and smooth integration of grip with other arm movements to perform complex tasks.

Our goal was to evaluate whether an individual with tetraplegia could make clinically significant gains in skillful grasp coordination[17,18] using an investigational MEA-BCI-FES. We formulated a framework[19] called Generalizability, Ability, Independence, Neurologic Level (GAIN) that reflects design goals for BCI neuroprosthetics to assist in this assessment. GAIN was inspired by end-user perspectives,[4,20,21] challenges to translation,[22,23] and clinical evaluations developed for surgical interventions for tetraplegia.[24] We anticipate it being useful for comparing performance across neuroprosthetic technologies and justifying (eg, to regulatory or payer sources) that a device measurably improves function on the International Classification of Functioning, Disability, and Health domains recognized by the World Health Organization.[25]

Devices meeting the GAIN standard include the following: (1) demonstrate generalizability, defined as *performing well without retraining for objects with similar grip features (e.g., lateral, tip-to-tip, palmar, pincer grasps)*; (2) confer clinically significant gains in motor ability on standardized, psychometrically validated, and expert-endorsed[24,26-33] tests of upper limb function; (3) affect daily life by facilitating functional independence for activities of daily living (ADLs) on psychometrically validated assessments[24,26-33]; and (4) improve the user's neurologic level of function on validated measures normed to the International Standards for the Neurological Classification of Spinal Cord Injury standards.[34]

List of abbreviations:

ARAT	**Action Research Arm Test**
BBT	**Box and Block Test**
BCI	**brain-computer interface**
CUE-T	**Capabilities of Upper Extremity Test**
FES	**functional electrical stimulation**
GAIN	**Generalizability, Ability, Independence, Neurologic Level**
GRASSP	**Graded Redefined Assessment of Strength, Sensibility, and Prehension**
GRT	**Grasp and Release Test**
MEA	**microelectrode array**
MMT	**manual muscle training**
QIF-SF	**Quadriplegia Index of Function-Short Form**
SCI	**spinal cord injury**
SCIM-SR	**Spinal Cord Independence Measure−Self-Report**
SRD	**smallest real difference**

Methods

This was a Phase I trial of a MEA-BCI interfaced with the Neurolife[a] transcutaneous, forearm FES. Like similar intracortical BCI studies,[12-18,35,36] this report was limited to 1 participant, the first to use the system, due to the invasive nature of the investigational brain implant and time required for training and assessment. Technical BCI-FES features[13,37] (fig 1), the Utah Array[b] MEA implantation procedures, and machine learning algorithms used to generate decoders were described previously. The participant provided written informed consent as approved by our local institutional review board.

Participant

The participant was a 27-year-old man with chronic, traumatic, C5 American Spinal Injury Association Impairment Scale A tetraplegia. He had 5 out of 5 strength for shoulder and elbow flexion; 1 out of 5 wrist extension; and flaccid paralysis with lack of sensation below C6.

Procedures

The participant began practicing BCI-FES-evoked movements of his right forearm and hand 1 month postimplant (3.5h/session, 2 to 3 sessions/wk) and started standardized testing 3 months later (fig 2). Only portions of standardized tests were given in any session due to time constraints, with the full battery of tests extending over months. Data reported here were collected between postimplant days 137 through 1478, with simpler standardized test items (eg, manual muscle training [MMT]) occurring earlier than more complex tasks (eg, pouring).

FES Calibration

Anode-cathode calibrations were developed for each object and grasp using knowledge of forearm anatomy. Initial calibrations took 30 to 60 minutes, while recalibration in subsequent sessions typically took 2 to 3 minutes to verify consistent electrode placement and adjust stimulation intensity. Figure 3 depicts representative stimulation patterns, target muscle groups, and FES-evoked movements.

Decoder training

For standardized testing, each decoder was trained with the number of grip classes needed to complete 1 subtest item (1 to 2 movements plus rest). We chose this for simplicity, minimizing

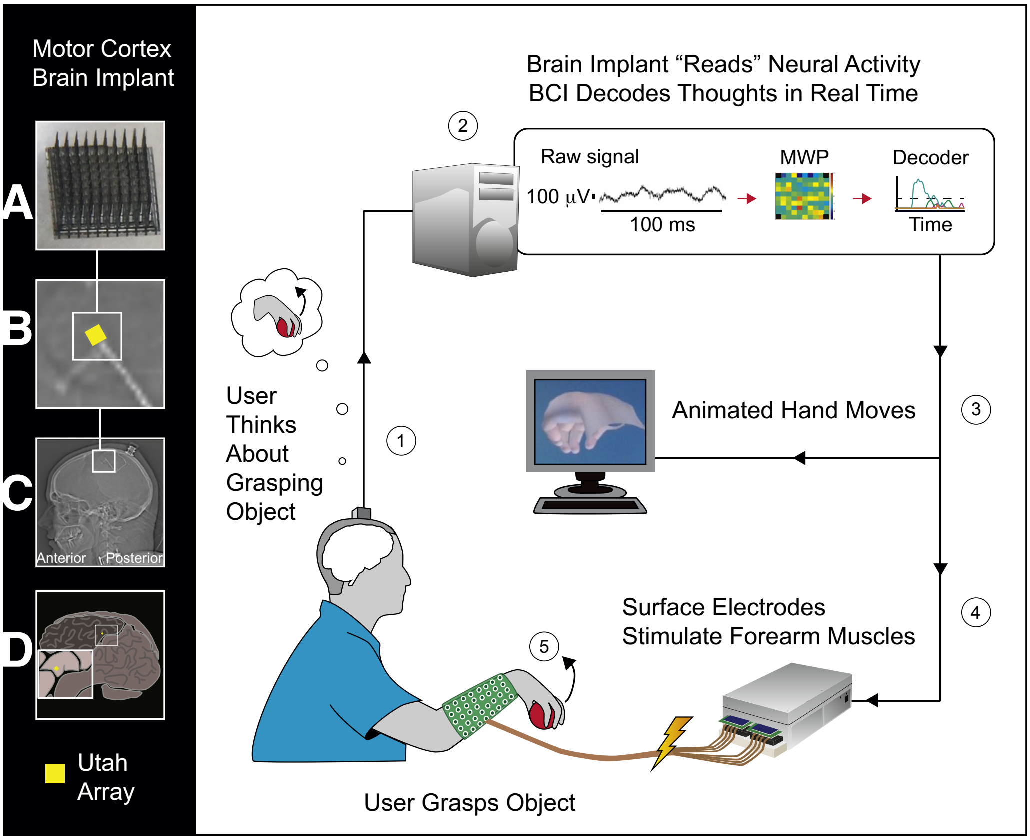

Fig 1 Cortical implant and NeuroLife BCI-FES system. (At left) A. 96-channel Utah MEA. B. Close-up view of array orientation (yellow) on the left motor cortex. C. Head computerized tomography image showing the implant location. D. Rendering of the location of the array (yellow) on the precentral gyrus. (At right) BCI-FES Operation: (1) Neurons fire when the user thinks about grasping. (2) Neural data is sampled at 30,000Hz with a Neuroport system[b], converted into 100-ms blocks of MWP, and analyzed with nonlinear, SVM-movement decoders trained in MATLAB. Each decoder is trained iteratively over 5 blocks (3 to 4 trials/block) using MWP in multiunit activity frequency bands as described previously.[13,37] (3) Continuous decoder outputs, updated every 100 ms, animate a computer-generated hand and (4) Stimulate transcutaneous, forearm, cathode and anode electrode sites calibrated to finger and wrist flexors and extensors. (5) FES-evoked movements allow the user to manipulate objects. NOTE. Figures and photographs by M. Bockbrader and N. Austin. Abbreviations: MWP, mean wavelength power; SVM, support vector machine.

training time, and facilitating subtest comparison across days. In some cases, 1 grasp type or decoder was used to test several similarly shaped objects (eg, day 833: Grasp and Release Test (GRT) fork decoder was used to "eat" polystyrene foam "food" with a metal dinner fork and to transfer Action Research Arm Test [ARAT] cylinders). Multiple, sequentially-trained decoders were often built on the same day to allow testing for multiple items per session. To demonstrate that performance obtained during standardized testing was reproducible with multiclass decoders, we compared single-class GRT performance to previously published results[41] for a decoder with classes for all GRT objects or grips.

Decoder training took 10 to 15 minutes, with 3 to 4 repetitions of each movement across 4 to 6 blocks. Decoders appeared to be sensitive to grasp context[42]; thus, they were trained with objects and any voluntary shoulder or elbow movements required for performing the task. Figures 3 and 4 describe representative examples of decoder activation (line graphs) and evoked movements (pictures) for items from each outcome measure.

Standardized testing

Measures of motor ability (see fig 2), functional independence, and neurologic level of function[24,26-33] were obtained with and without BCI-FES. Functional independence without BCI-FES was rated as the participant's home level of function. Functional independence with BCI-FES was his expected level of function if he was able to use BCI-FES at home. Generalization of upper limb motor ability was evaluated by training decoders with standardized test objects and testing with household objects.

Instruments

Graded and Redefined Assessment of Sensibility, Strength, and Prehension (GRASSP[34,43-45])

Dorsal and palmar sensation on digits I, III, and V were scored from 0 (unable) to 4 (0.4 kg) using Semmes-Weinstein

Fig 2 Standardized tests. A. Upper limb motor ability measures. I. GRASSP[34] objects II. Black mechanical pinch gauge (0 kg to 13.6 kg) III. Electronic handgrip digital dynamometer (0 kg to 90 kg) IV. ARAT[38] objects V. GRT[39] objects VI. BBT[40] box with blocks B. Examples of grip types in each upper limb motor ability measure. The GRASSP and ARAT assess the ability to form palmar and precision grips independently from other upper limb movements. The GRASSP, ARAT, GRT, and BBT assess integration of palmar or precision grasps with upper limb movements required to transfer objects (shoulder internal and external rotation) or transfer and lift objects (shoulder internal and external rotation and flexion and extension). The GRASSP and ARAT also assess integration of palmar or precision grasps with forearm pronation and supination (as in pouring or turning a doorknob) or radial and ulnar deviation (as in twisting a lid). NOTE. Figures and photographs by M. Bockbrader and N. Austin.

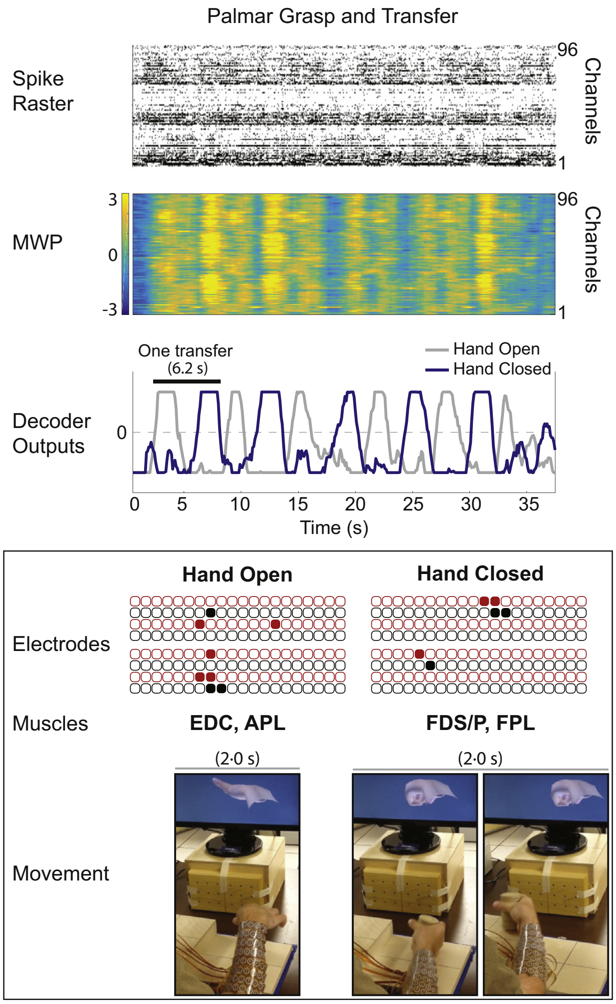

Fig 3 BCI-FES activation for GRT can grasp sequences. A representative example of neural modulation, decoder outputs, electrode calibration, target muscles, and evoked movements is shown for one 30-second trial of GRT can manipulation. The spike raster plots threshold-crossing events (per 100 ms) across channels. The heatmap depicts normalized MWP ("db4" wavelet scales 3 to 6; 234 Hz to 3750 Hz) across channels. Decoder outputs for "hand open" (blue) and "hand closed" (gray) palmar grips were modulated with activity changes in the spike raster and the MWP heatmap. "Rest" states occurred when all decoder outputs were less than zero. Five paired "hand open"—"hand closed" decoder peaks are shown in 30 seconds, corresponding to 5 successful transfers. The inset depicts electrode stimulation patterns, target muscle groups, and FES-evoked movements during "hand open" (left) and "hand closed" (right) states. Cathodes are shown in black and anodes are shown in red. NOTE. See supplemental videos for a demonstration of object manipulation with BCI-FES. Figures by M. Bockbrader and N. Austin, photographs by M. Bockbrader and S. Colachis. Abbreviations: APL, abductor pollicis longus; EDC, extensor digitorum communis; FDS/P, flexor digitorum superficialis/profundus; FPL, flexor pollicis longus; MWP, mean wavelength power.

Monofilament[c] testing. Strength was graded from 0 (flaccid) to 5 (full) using MMT. Prehension ability was scored for lateral, palmar, and tip-to-tip grips from 0 to 4 (unable; moves wrist; moves wrist and fingers, no force; moves wrist and fingers, some force; moves wrist and fingers, full force). Prehension performance included: pouring, unscrewing lids, turning keys, 9-Hole Peg, inserting coins into slots, and fastening nuts onto bolts. Scores were rated (0 to 5) reflecting best performance within 75 seconds (unable; object grasped, <50% complete; object grasped, >50% complete; task completed, incorrect grip; task completed slowly, correct grip; task completed normally).

Myometry[46-48]

Pinch force (tip-to-tip, lateral) and palmar grip were measured with a Black Mechanical Pinch Gauge[d] (range: 0 to 13.6 kg, accuracy: ±0.05 kg) and the Camry Electronic Digital Dynamometer[e] (range: 0 to 90 kg, accuracy: ±0.1 kg).

Action Research Arm Test[38,48-51]

Objects included blocks (2.5 cm^3, 5 cm^3, 7.5 cm^3, 10 cm^3), balls (6-mm, 16-mm, 7.1-cm diameter), bar (10 cm × 2.5 cm × 1 cm), cup (7-cm diameter), cylinders (1-cm, 2.5-cm diameter), and 3.5-cm ring. Scoring ranged from 0 to 3 based ability to grasp and transfer objects (unable in 60 s, partially performed in 60 s, performed >5 s, performed <5 s).

Grasp and Release Test[39,52]

Objects included peg (0.6 cm × 7.6 cm), weight (5 cm × 1.4 cm), block (2.5 cm^3), can (5.4 cm × 9.1 cm), video tape (20.4 cm × 12 cm × 3 cm), and fork (1.2 cm × 14.5 cm). Most objects were grasped, transferred lateral-to-medially, and released. The fork was grasped, depressed 2 cm against a 4.4-N spring, and released. Item scores were median successes across 3, 30-second trials.

Box and Block Test (BBT)[40,48]

Scoring reflected the number of successful (2.5 cm^3) block transfers in a 2-compartment box over 3, 60-second trials.

Capabilities of Upper Extremity Test (CUE-T)[53,54]

Thirty-two activities in 4 domains (reaching and lifting, pushing and pulling, wrist actions, hand and finger actions) were scored from 0 to 4 (unable, severe difficulty, moderate difficulty, mild difficulty, no difficulty) based on participant self-report and physiatrist observation.

Quadriplegic Index of Function-Short Form (QIF-SF)[55]

Scores (0 to 4) reflected participant self-ratings (dependent, physical assistance, supervision, independent with device, independent without device) on 6 self-care tasks.

Spinal Cord Injury Independence Measure-Self-Report (SCIM-SR)[56]

Scores reflected participant self-ratings on 17 activities in 3 domains (self-care, respiration and sphincter management, mobility).

Analyses

Best performance with and without BCI-FES were reported. Nonparametric statistics were used due to small sample size and nonnormal distributions. Smallest real difference (SRD) and minimum clinically important difference were used to interpret scores (fig 5). Calculations were performed using MATLAB[f] software.

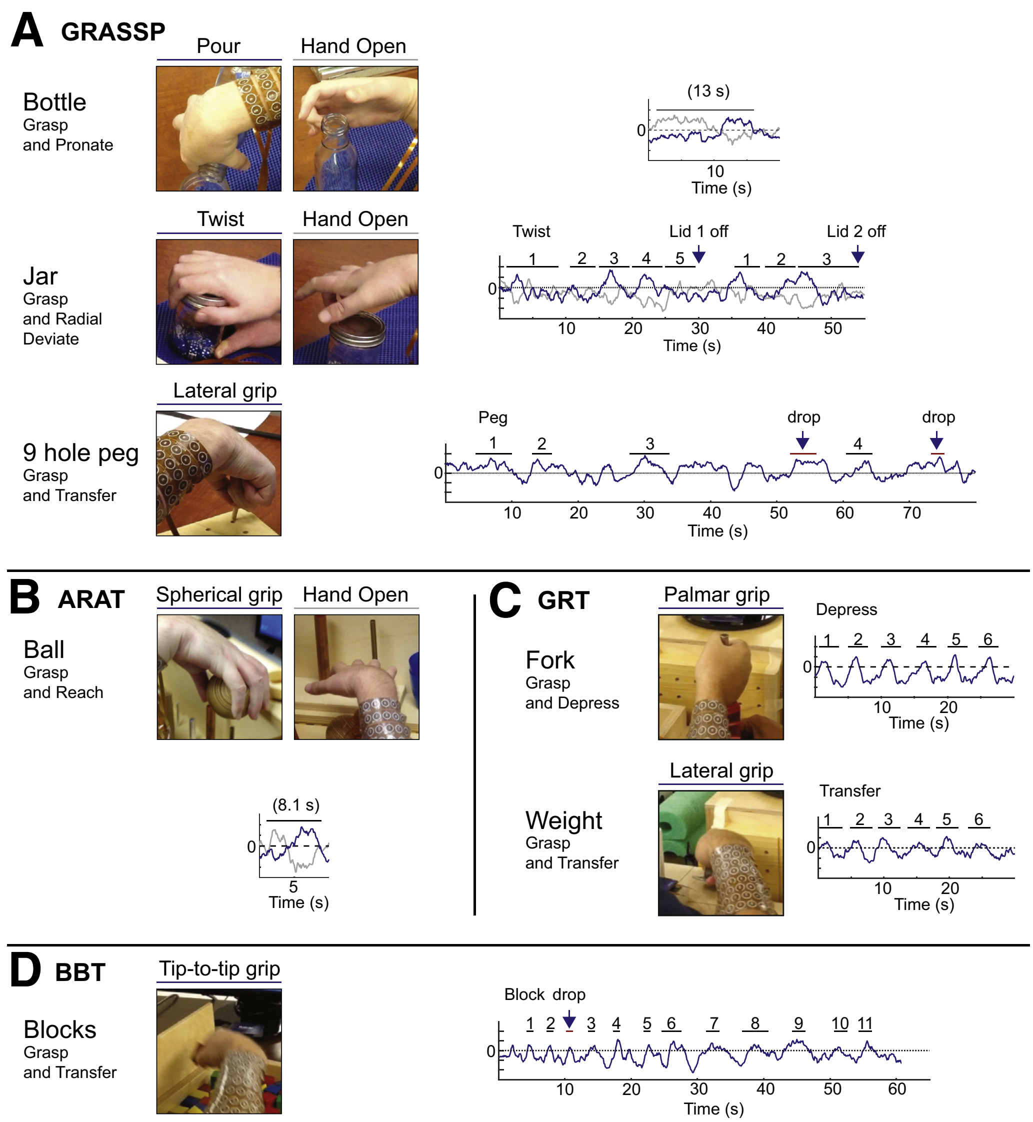

Fig 4 BCI-FES evoked grips in upper limb motor tasks. Representative examples of decoder activation (line graphs) and evoked movements (pictures) are shown for single trials from each outcome measure. GRASSP Pour (A), GRASSP Jar (A), and ARAT Ball (B) required sustained decoder activation to maintain grip during reaching, pronating, or twisting, respectively. Timed tests like the GRASSP 9-Hole Peg (A), GRT (C), and BBT (D) required rapid initiation and termination of decoder activity to optimize performance. Tasks that required a series of movements are labeled with stages of task completion (or failed attempts) along the decoder timeline to correlate decoder activity with behavioral performance. For example, the GRASSP Jar (A) task consisted of a series of integrated hand, wrist, forearm, and shoulder movements to twist lids off of 2 jars. The first jar's lid was removed after 5 sequential pairs of hand-open and shoulder flexion (gray peaks) and hand-close and shoulder extension with radial deviation (blue peaks). In the BBT (D) trial, the participant dropped a block coincident with a short duration peak in decoder activity (at approximately 11 s). Drops could be explained as user control failures (ie, inability to sustain decoder activation above threshold as [D]) or due to FES calibration difficulty (sustained, correct, suprathreshold decoders in GRASSP 9-hole peg [A]) associated with muscle fatigue or surface electrode displacement. NOTE. See also supplemental videos for performance on these tasks. Figures by M. Bockbrader and N. Austin, photographs by M. Bockbrader, S. Colachis, and M. Zhang.

Results

The participant improved qualitatively over time in his ability to use BCI-FES to evoke movements of his dominant arm and hand. We observed hypertrophy of right forearm and hand muscles over the first 2 months, resulting in a relative reversal of his SCI-related atrophy, but no change in his International Standards for the Neurological Classification of Spinal Cord Injury exam or electromyogram and nerve conduction study findings.[13]

Initially, the participant reported concentrating intensely "like taking a calculus test" when imagining gross motor movements. He experienced mental fatigue and found fine motor control and individual finger movements onerous. After 8 to 12 months, however, he began to require fewer training blocks and less intense focus to master new movements. Figure 5A shows the progression of testing, beginning with GRASSP and ARAT (supplemental video S1), progressing to BBT and GRT

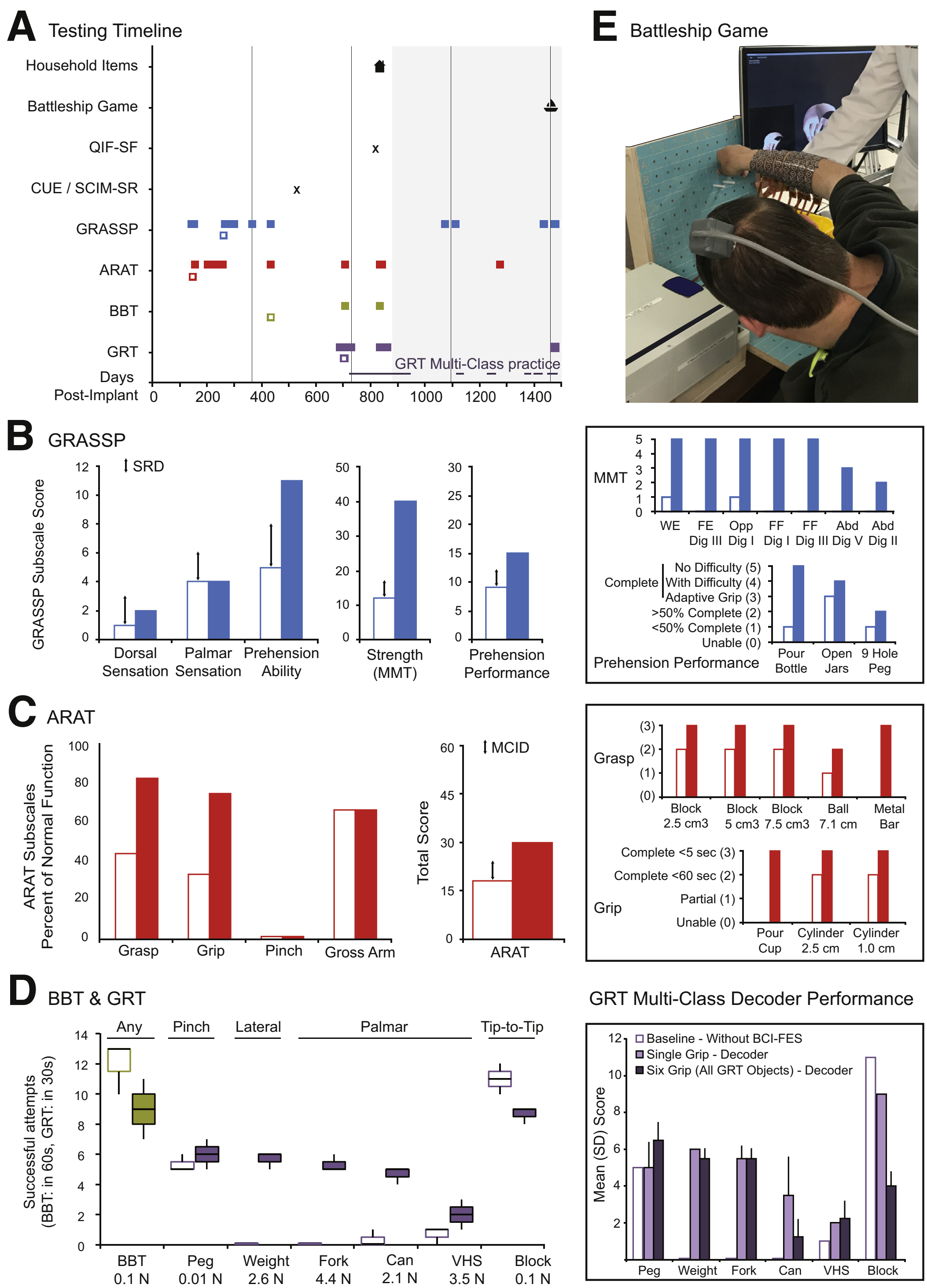

Fig 5 Motor function with and without BCI-FES. All open squares and white bars represent performance without BCI-FES; all filled squares and colored bars represent performance with BCI-FES. A. Timeline for standardized testing, ADL measures, and generalization tasks (household objects, adapted "Battleship" game). The shaded region to the right of day 875 indicates when training sessions focused on multiclass decoders that allowed for switching between grips. B. Scores on GRASSP subscales improved beyond the test's SRD for strength, prehension ability and prehension performance. The inset shows items that improved with BCI-FES on MMT (top) and prehension performance (bottom). C. Overall ARAT score improved by 12 points, which exceeds the minimum clinically important difference for the test subscales showing improvement were Grasp and Grip. The inset shows items that improved on the Grasp (top) and Grip (bottom) subscales. D. BBT and GRT scores only improved for objects the user could not manipulate at baseline Figure at left displays BBT (days 137, 835) and GRT (days 703, 833 to 835) boxplots for median number of successes across 3 trials. The inset (right) contrasts transfer performance at baseline (day 137, without BCI-FES), using the single grip decoders trained for standardized test items (days 833 to 835 and 1473 to 1476), and a multiclass decoder trained to switch between all grips needed for GRT objects (days 855, 857, 869, 897). When the participant used the multiclass decoder to perform the GRT, he appropriately switched between

(supplemental video S2), then addressing ADLs and ability to transfer skills to household objects (toothbrush, fork, book, beverage can; supplemental video S3, available online only at http://www.archives-pmr.org/) and leisure activities (adapted "Battleship" supplemental video S4) (see fig 5E).

Graded Redefined Assessment of Strength, Sensibility, and Prehension

GRASSP strength improved from 12 to 40 (24% to 80% normal), achieving normal strength for 5 forearm muscle groups (see fig 5B, table 1). Force increased on myometry for all grips (table 2). However, maximal palmar, lateral, and tip-to-tip grip force could not be accurately quantified. High compressive force altered the participant's ability to apply force directly to the pinch gauge and dynamometer transducers. Prehension ability scores were therefore based on ability to grip objects against resistance. BCI-FES improved prehension ability scores from 5 to 11 (42% to 92% normal), with submaximal tip-to-tip grip noted from inadequate thenar muscle stimulation. Prehension performance improved with BCI-FES from 9 to 15 (30% to 50% normal), due to better ability to pour a bottle (supplemental video S5), unscrew lids, and perform 9-Hole Peg. No gains were noted for key, coins, or fastener items (no FES-evoked pinch grips could be calibrated for these objects). Dorsal and palmar sensation did not change.

Action Research Arm Test

BCI-FES improved manual dexterity on total ARAT, grasp, and grip scores (see fig 5C, table 3), increasing from 18 to 30 (32% to 53% normal), 8 to 15 (44% to 83% normal), and 4 to 9 (33% to 75% normal), respectively. Performance improved with BCI-FES for the 7.1-cm ball, bar, both cylinders, cup (pouring) and 2.5-cm^3, 5-cm^3, and 7.5-cm^3 blocks. No change was observed for gross movement, pincer items, the 10-cm^3 block, and ring.

Grasp and Release Test

BCI-FES improved median success rates for peg, weight, fork, can, and tape, but not block (see fig 5D, table 4). This pattern of results was also found when the GRT was performed using a multiclass decoder that included grips for all GRT objects[16] (see fig 5D).

Box and Block Test

Transfer rates did not improve with BCI-FES (9 blocks/min) compared to baseline (12 blocks/min) (table 5, fig 5D, fig 6A, supplemental video S4).

Capabilities of Upper Extremity Test

BCI-FES improved unilateral arm and hand function on the CUE-T (table 6, fig 7C). Total score increased from 27 to 49 (45% to 82% normal) due to gains for wrist actions (from 4 to 8 points; 50% to 100% normal) and hand actions (4 to 22 points; 17% to 92% normal). BCI-FES did not change reaching and lifting or pushing and pulling scores.

Quadriplegia Index of Function-Short Form

BCI-FES raised the participant's expected level of independence for ADLs (see table 6, fig 7C) beyond his home function ($QIF\text{-}SF_{actual}=4$, $QIF\text{-}SF_{expected}=13$). At baseline, the participant was "dependent" for bed mobility, lower body dressing, opening jars, and transferring from bed to chair; required (minimum to moderate); "physical assistance" for grooming; and was "independent with assistive device" to lock his powerchair. Using BCI-FES, he expected to gain "independence with assistive device" for grooming, feeding, and patient-lift transfers.

Spinal Cord Independence Measure—Self-Report

BCI-FES raised the participant's expected level of independence for self-care and toileting but not mobility (see table 6, fig 7C). At baseline (SCIM-SR = 15), he had normal function for respiration; moderate impairments (25% to 70% normal) for upper body dressing, bowel management, grooming, and feeding; and severe impairments (0% to 10% normal) for mobility and transfers, toileting, bladder management, and lower body dressing. Using BCI-FES (SCIM-SR = 24), he anticipated becoming independent from others (100% normal) for feeding and grooming; increasing his independence for bladder management, bowel management, toileting, and bed mobility (30% to 60% normal).

Discussion

Our objective was to evaluate, using GAIN criteria, whether an individual with tetraplegia could make clinically significant gains in grasp coordination with an investigational MEA-BCI-FES (fig 7). GAIN is a framework for evaluating clinical utility of a device, based on measured recovery of motor function, improved neurologic level, and independence for ADLs. Use of this metric can facilitate reproducibility across studies; identify design and performance strengths and challenges for research and development; enable objective comparison of features and limitations across devices; and aid decision making—for both clinicians and end-users—to balance expected costs and benefits.

Generalizability

Generalizability, the ability to transfer skills from trained objects or grips to untrained but similar objects or grips, is an important practical step toward clinical translation. We suspected it could be achieved with MEA-BCI-FES given overlap in neural representations for GRT objects handled with similar grips[16] and other evidence that motor cortex encodes grip shape.[42,57] We demonstrated generalizability by performing ADL-like activities with

grip types to use the optimal grip for the object he was manipulating. The decoder had 7 classes: hand open, peg (index-thumb pinch), fork (tight palmar grip), block (tripod grip), can (cylindrical palmar grip), weight (lateral grip), and video tape (palmar power grip with extended fingers). Data represent mean GRT scores (each of which was calculated per test instructions as the median of 3 trials for each test day). Scores that were obtained on more than 1 day have SD depicted as error bars. E. Generalization of grips from GRT peg and 9-Hole Peg to video game pieces transfer of horizontal and vertical peg grip skills enabled the participant to play "Battleship" (day 1466). NOTE. See supplemental videos for BBT task performance with and without the BCI-FES. Figures by M. Bockbrader and N. Austin.

Table 1 GRASSP performance across subscales for the right upper limb with and without the BCI-FES

	Baseline Adaptive Grip (Day 260)		BCI-FES Controlled Grip			
Item	Score	Description	Test Days	Best Score	Description	n
Dorsal Sensation: Semmes-Weinstein Monofilament Testing						
Hand, Digit I (C6)	1	300-kg force was detected on 2/3 trials	260, 1357, 1476*	2	4-kg force was detected	3
Hand, Digit III (C7)	0	No force was detected	260, 1357, 1476	0	No force was detected	3
Hand, Digit V (C8)	0	No force was detected	260, 1357, 1476	0	No force was detected	3
TOTAL (Max 12)	1 (8% of normal)*; C6*			2 (17% of normal)*; C6*		
Palmar Sensation: Semmes-Weinstein Monofilament Testing						
Hand, Digit I (C6)	4	0.4-kg force was detected	260, 1357, 1476	4	0.4 kg-force was detected	3
Hand, Digit III (C7)	0	No force was detected	260, 1357, 1476	0	No force was detected	3
Hand, Digit V (C8)	0	No force was detected	260, 1357, 1476	0	No force was detected	3
TOTAL (Max 12)	4 (33% of normal)*; C6*			4 (33% of normal)*; C6*		
Strength: MMT						
MMT: Shoulder flexion (C5)	5	Full ROM against gravity, maximum resistance	260, 1476	5†	-	-
MMT: Elbow flexion (C5)	5	Full ROM against gravity, maximum resistance	260, 1476	5†	-	-
MMT: Elbow extension (C7)	0	No visible or palpable contraction	260, 1476	0†	-	-
MMT: Wrist extension (C6)	1	Visible or palpable contraction	265*, 1476*	5	Full ROM against gravity, maximum resistance	2
MMT: Hand, Digit III extension (C7)	0	No visible or palpable contraction	265*, 1476*	5	Full ROM against gravity, maximum resistance	2
MMT: Hand, Digit I opposition (T1)	1	Visible or palpable contraction (likely fasciculations)	265, 1476	5	Full ROM against gravity, maximum resistance	2
MMT: Hand, Digit I flexion (C8)	0	No visible or palpable contraction	265*, 1476*	5	Full ROM against gravity, maximum resistance	2
MMT: Hand, Digit III flexion (C8)	0	No visible or palpable contraction	272*, 1476*	5	Full ROM against gravity, maximum resistance	2
MMT: Hand, Digit V abduction (T1)	0	No visible or palpable contraction	272*, 1476*	3	Full ROM against gravity	2
MMT: Hand, Digit II abduction (T1)	0	No visible or palpable contraction	275, 1476*	2	Full ROM gravity eliminated	2
TOTAL (Max 50)	12 (24% of normal)*; C6*			40‡ (80% of normal)*; C8*		
Prehension Ability						
Cylindrical grasp	2	Moves fingers into the prehension pattern; fails to generate force	143*, 153*,275*, 1476*	4	Able to keep the wrist in neutral & generate the grasp with full thumb & finger movement	2
Lateral key pinch	1	Moves wrist actively and fingers passively into the prehension pattern	275*, 1476*	4	Able to keep the wrist in neutral & generate the grasp with full thumb & finger movement	2
Tip-to-tip pinch	2	Moves fingers into the prehension pattern; fails to generate force	278*, 1476*	3	Positions fingers and thumb into the prehension pattern with some force	2
TOTAL (Max 12)	5 (42% of normal)*; C5-6*			11‡ (92% of normal)*; C7-T1*		
Prehension Performance						
Pour bottle (cylindrical grasp; 242 g)	1	<50% complete >75 s (0 drops)	286, 1476*	5	Completed in 8 s without difficulty 0 drops	4
Unscrew lids (spherical grasp; small 13.6 g, large 19.0 g)	3	Completed in 47 s Alternate grasp (0 drops)	300*	4	Completed in 51 s with difficulty 0 drops	4
9-hole peg (tip-to-tip pinch; 0.7 g each)	1	<50% complete >75 s (2 drops)	288*, 1073, 1434, 1438, 1476, 1478*	2	>50% complete >75 s 0 drops (5 of 9 pegs)	11

(*continued on next page*)

Table 1 (*continued*)

Item	Baseline Adaptive Grip (Day 260)		BCI-FES Controlled Grip			
	Score	Description	Test Days	Best Score	Description	n
Turn key in lock (lateral grip; 6.9 g)	2	>50% complete >75 s (Multiple drops)	290	2†	-	-
Transfer coins (tip-to-tip pinch; largest to smallest: 6.3 g, 4.5 g, 3.9 g, 1.8 g)	1	<50% complete >75 s (Multiple drops)	290, 297	1†	-	-
Screw nuts (tip-to-tip pinch; largest to smallest: 10.3 g, 4.6 g, 1.0 g, 0.7 g)	1	<50% complete >75 s (1 drop)	302	1†	-	-
TOTAL (Max 30)	9 (30% of normal)*; C5-7*			15† (50% of normal)*; C5-7*		
Total GRASSP (Max 115)	31 (27% of normal)*			72 (63% of normal)*		

NOTE. International Standards for the Neurological Classification of Spinal Cord Injury sensory and motor level interpretations for subset scores are listed with item totals. Completion times and number of drops are given for prehension performance tasks.
Abbreviations: ROM, range of motion.
* Dates (postimplant day) for best performance beyond baseline scores.
† Items could not be performed with FES.
‡ Change exceeds smallest real difference.[30]

household objects using palmar, lateral, and tip-to-tip grip decoders trained on GRT objects (fig 7A, supplemental video S3): the participant mimicked brushing with a toothbrush using peg decoder-calibrations. Similarly, the fork grip carried over to successful use of a dinner fork to "eat" polystyrene foam "food," the video tape grip enabled manipulation of a book, and the can grip enabled simulated drinking. The participant also played a 20-minute adapted "Battleship" game using decoder-calibrations built on GRASSP, 9-Hole-Peg, and GRT peg, dividing his focus to strategize and win while also switching between grips for the vertical and horizontal game boards.

Generalizability can also refer to the number of grip types that a user can switch between using the same decoder. A limitation of training minimal-class decoders for individual test items is that additional setup time is needed to switch grips, resulting in standardized testing that stretches across days. This can confound effects specific to objects (eg, weight, shape) with time effects (eg, learning) and limit opportunities for reassessing performance over time. It also fails to address user priorities of spontaneity, decreased setup times, and number of functions available per decoder. For this reason, multiclass GRT decoders were implemented[16] that allowed assessment of all objects without retraining. Performance with the multiclass decoder (see fig 5D) was similar to the single-class decoder for some objects (peg, weight, fork, video tape) but not others (can, block). For block and can, the participant required more time to select the appropriate grip decoder-calibration, reducing transfer rate in multiclass conditions compared to simpler 1 to 2 class decoders. The additional selection time for block was likely related to observed overlap in cortical representation with other GRT object or grips, and subsequent decreased separability of decoders.[16] For can, incremental multiclass decoder delays were likely compounded when performing 2 hand states (hand open, palmar grip) in sequence.

Motor ability

BCI-FES yielded clinically significant improvements in our participant's ability to manipulate objects with speed, dexterity, and coordination (see fig 5 and 7B). This was evidenced by ARAT change (score = 12), exceeding the test's SRD[48] (score = 5.5) and theoretically-derived[49] or experimentally-estimated[47] minimum clinically important difference (scores of 5.7 or 12, respectively). BCI-FES improved palmar, lateral, and tip-to-tip grip force and dexterity for objects across sizes and weights (GRASSP, ARAT). No improvement was observed for pincer grips or fine grips with forearm pronation and supination, due to absence of thenar electrodes. BCI-FES facilitated dynamic grips (eg, palmar, lateral, tip-to-tip grasps with transfer or reaching, and complex movements; and palmar grip with pronation or radial deviation [GRASSP jar, GRASSP pour, ARAT pour]); dynamic grips are essential for ADLs and desired by end-users,[20] but difficult to perform with rigid exoskeletons, tendon transfers,[24] or BCI-controlled robotic arms.[17,18]

Motor strength on grip myometry could not be accurately measured with the pinch gauge and hand dynamometer, necessitating an alternate measurement method in the future. Values obtained were consistent with individuals with tetraplegia using implanted FES[58,59] and below age and gender norms[46] (see table 2), which was expected as SCI alters muscle fibers, causing early fatigability and decreased maximal contractile force.[60]

Table 2 Maximum grip measured by hand-held myometry

Grip	Baseline Adaptive Grip	BCI-FES Controlled Grip	Healthy Norms	Implanted FES
Lateral pinch	0 kg (day 279)	1.15 kg (day 279)	11.8 kg	0.82-2.8 kg[26-28]
Tip-to-tip pinch	0 kg (day 276)	1.35 kg* (day 276)	8.2 kg	
Palmar grasp	0 kg (day 153)	2.9 kg* (day 153)	54 kg	0.21-2.8 kg[26-28]

* Change exceeds smallest real difference,[35] but not minimum clinically important difference.[34]

Table 3 ARAT performance for the right upper limb with and without the BCI-FES

	Baseline Adaptive Grip (Day 148)		BCI-FES Controlled Grip					
					Time (s)			
Item	Score	Time	Test Days	Best Score	Minimum	Average Mean ± SD	Maximum	n
Grasp Subscale								
Transfer Block 2.5 cm^3* (9.1 g)	2	5.6	707[†]	3	4.5	6.9±2.7	12.9	22
Transfer Block 5 cm^3* (91.2 g)	2	9.4	223, 227, 1274[†]	3	2.7	10.7±3.9	>60	10
Transfer Block 7.5 cm^3* (287.6 g)	2	17.6	209, 227, 241, 258, 1274[†]	3	3.6	9.6±3.6	>60	10
Transfer Block 10 cm^3* (>500 g)	1	>60	-	1	-	-	-	-
Transfer Ball 7.1 cm* (142.8 g)	1	>60	209[†], 234[†], 237, 1274[†]	2	4.6	12.7±16.5	>60	12
Transfer Bar 10 × 2.5 × 1 cm* (151.8 g)	0	>60	155, 202[†]	3	2.9	4.6±2.6	8.5	4
TOTAL (Max 18)	8[†]			15[†,‡]				
Grip Subscale								
Pour 7-cm cup* (146.2 g)	0	>60	840 842[†]	3	6.4	11.4±4.5	19.9	19
Transfer Cylinder 2.5 cm* (32.4 g)	2	37.3	833[†]	3	4.1			1
Transfer Cylinder 1.0 cm* (6.5 g)	2	15.2	833[†]	3	4.0			1
Transfer Ring 3.5 cm (9.2 g)	0	>60	-	0	-	-	-	-
TOTAL (Max 12)	4[†]			9[†,‡]				
Gross Arm Movement Subscale								
Hand to back of head	2	5.0	-	2	-	-	-	-
Hand to mouth	2	1.9	-	2	-	-	-	-
Hand on top of head	2	2.6	-	2	-	-	-	-
TOTAL (Max 9)	6[†]			6[†]				
Pinch Subscale								
6-mm ball, Dig I-IV (0.9 g)	0	>60	-	0	-	-	-	-
16-mm ball, Dig I-II (13.6 g)	0	>60	-	0	-	-	-	-
16-mm ball, Dig I-III (13.6 g)	0	>60	-	0	-	-	-	-
16-mm ball, Dig I-IV (13.6 g)	0	>60	-	0	-	-	-	-
6-mm ball, Dig I-II (0.9 g)	0	>60	-	0	-	-	-	-
6-mm ball, Dig I-III (0.9 g)	0	>60	-	0	-	-	-	-
TOTAL (Max 18)	0[†]			0[†]				
Total ARAT (Max 57)	18[†]			30[†,‡]				
Modified ARAT Total* (Max 27)	12[†]			24[†]				

NOTE. All baseline scores were obtained on postimplant day 148. Minimum, maximum and average (SD) time to task completion and number of trials are listed for items that could be completed with FES grips. All other items are marked with dashes (-).
Abbreviations: n, number of trials.
* Included in modified ARAT.[11,12]
† Dates with best item performance beyond baseline scores.
‡ Change exceeds smallest real difference and minimum clinically important difference for ARAT.

BCI-FES evoked greater wrist extension strength (5 out of 5) than has been found for individuals with C5 SCI[58] (0 out of 5 to 3 out of 5), potentially due to the participant's partially preserved (1 out of 5) wrist extension strength. Consequently, evoked FES stabilized his wrist against gravity without splinting, facilitating naturalistic forearm range of motion. However, wrist stabilization through FES risks prosthetic failure from muscle fatigue. This can be mitigated by optimizing FES parameters[61-64] and employing spatially distributed sequential stimulation.[62] We encountered fatigue-induced weakness only when stimulating for long periods without breaks.

BCI-enabled manual dexterity and skilled object manipulation have been reported for robotic limbs using 7 to 10 degrees of freedom to control translation, orientation, and hand shape.[17,18] BCI-robot performance on a modified BBT (<1 block/min) was significantly slower than BCI-FES BBT performance (8.7 blocks/min) (see fig 6). Similarly, BCI-robot transfer speed for a cylindrical object by 2 participants (mean transfers per

Table 4 GRT median number and interquartile range (IQR) of successful transfers and drops with and without BCI-FES

Item (Weight or Force)	Baseline Adaptive Grip: Success Median (IQR)	Maximum	Drop	Postimplant Day	BCI-FES Controlled Grip: Success Median (IQR)	Maximum	Drops Median (IQR)	Postimplant Day
Peg (1.6 g)	5.0 (0.5)	6	1.0 (0.5)	703	6.0 (1.0)	7	1.0 (0.5)	833
					4.0 (1.5)	6	0.0 (0.0)	1473
Toothbrush: 10.5 g								
Weight (264 g)	0.0 (0)	0	7.0 (1.5)	702	6.0 (0.5)	6	0.0 (0.5)	833
Fork (4 N)	0.0 (0)	0	1.0 (0.0)	702	5.0 (0.5)	6	0.0 (0.5)	833
					6.0 (1.0)	7	0.0 (0.0)	1473
Dinner fork: 70 g								
Can (214 g)	0.0 (0.5)	1	1.0 (1.0)	702	5.0 (0.5)	5	0.0 (0.0)	835
					2.0 (1.5)	3	0.0 (0.5)	1476
Espresso can: 169 g								
Video tape (356 g)	1.0 (0.5)	1	1.0 (1.5)	702	2.0 (1.0)	3	0.0 (1.0)	835
Hardbound book: 500 g								
Block (10.6 g)	11.0 (0.25)	12	0.0 (0.0)	702	9.0 (0.5)	9	0.0 (0.0)	835

NOTE. One run for each GRT object consisted of 3 trials of 30 seconds. In each trial, the participant was asked to transfer the object as many times as possible within the time limit. The score for that object was the median across the 3 trials.[49] To quantify variability in performance across the 3 trials in each run, we calculated the interquartile range for the run. To describe the upper limit of function observed on any one trial within the run, we report the within-run maximum. Novel items manipulated with GRT decoders are listed below GRT items with their weights.

min ± SD: 1.09±1.09 and 5.28±1.21) was slower than GRT can rate (7 transfers/min) with BCI-FES. In addition, BCI-FES enabled comparatively higher modified ARAT scores (score = 24) than the BCI-robotic limb[17,18] (score = 17). Higher scores were due to significantly faster grip and transfer speed, which met general population norms for many ARAT objects (see fig 6B: metal bar, cylinders, and blocks). Speed was achieved by leveraging our participant's preserved shoulder strength and simplifying neural decoding into FES-calibrated grip states.

The critical advance reported here for BCI-FES is intuitive control[12] of high-performance grasp[17] at naturalistic speed. BCI-FES had previously only demonstrated rudimentary grasping[6,10-13] or slow performance[11] (GRT weight rate = 1.7 transfers/min). However, observation of BBT performance with BCI-FES on a task the participant could do at baseline (supplemental video S4) reveals an opportunity to further improve system speed: though grasp strength and time to transfer each block improved with BCI-FES, total transfers within 60 seconds remained below baseline rates due to delays for decoder processing and neuromuscular stimulation. These were visible as delayed initiation and release of block grasps when using BCI-FES.

Independence

Our participant expected home use of BCI-FES to increase independence for self-care, toileting, and food preparation (QIF-SF, SCIM-SR) (see fig 7C). The magnitude of his expected functional gain was greater than those reported for myoelectrically-controlled, implanted FES[65] (CUE-T: 2.75 to 17.25) and FES-mediated exercise in chronic SCI[66] (bilateral CUE-T hand: 31.6 to 38.0; QIF-SF: 1.4 to 9.2) but similar to SCIM-SR self-care change seen after FES-therapy in incomplete tetraplegia[67] (1.9 to 12.1).

Neurologic level

Over time, the participant gained skill and coordination on GRASSP tasks with BCI-FES. This change likely correlated with

Table 5 BBT median (interquartile range; IQR) values of successful transfers with and without BCI-FES were equivalent*

	Baseline Adaptive Grip Postimplant Day 137		BCI-FES Controlled Grip Postimplant Day 835	
	Median (IQR)	Maximum	Median (IQR)	Maximum
2.5-cm^3 blocks (10 g) any grip	13.0 (1.5)	13	9.0* (2.5)	11
Transfer times:	5.3-9.9 s/block		3.0-7.5 s/block†	

NOTE. One run of the BBT consisted of 3 trials of 60 s. In each trial, the participant was asked to transfer as many blocks as possible within the time limit. The score for that day was the median across the 3 trials.[49] To quantify variability in performance across the 3 trials in each run, we calculated the interquartile range for the run. To describe the upper limit of function observed on any one trial within the run, we report the within-run maximum.

* Change does not exceed smallest real difference (5.5).[35]

† Transfer time measurement started at grasp initiation, included the transfer period, and stopped when the object was released.

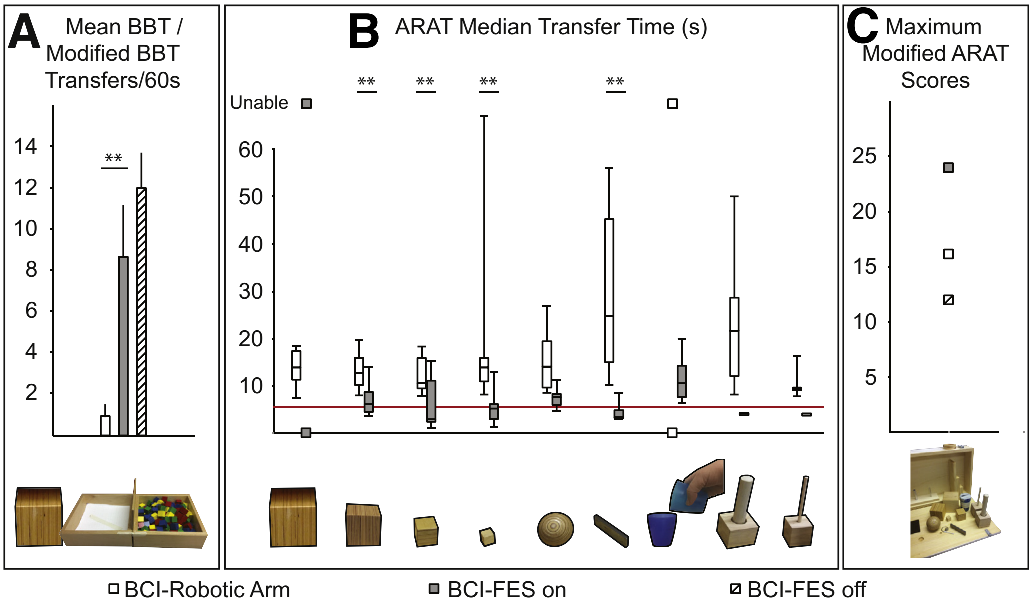

Fig 6 Comparison of BCI-FES performance with BCI control of robotic limbs. A. Mean BBT speed for BCI-FES was significantly faster than BCI control of a robotic limb on a modified BBT task using a 7.5-cm^3 block,[18] $t_5=6.06$, $P<.01^*$. However, our participant's performance with and without BCI-FES was equivalent, with difference between scores within the SRD (5.5) for the test. B. Median transfer speeds of BCI-FES on ARAT items fell within general population norms (red line) for many objects[38] and were significantly faster than speeds reported for BCI control of a robotic limb[18] for the bar and 2.5-cm^3, 5-cm^3, and 7.5-cm^3 blocks, all $P<.01^*$ by Mann-Whitney U tests. (Median transfer speed for the ball did not differ significantly between BCI-FES and the robotic limb, $P>.05$. Statistical tests were not conducted for the 10-cm^3 block, cup, and cylinders due to inadequate sample sizes.) C. Faster transfer speed resulted in a higher maximum modified ARAT score for BCI-FES than reported for BCI control of a robotic limb.[17,18] Performance differences between BCI-FES and our participant's baseline as well as differences between BCI-FES and the BCI-robotic limb were real and clinically significant; they were greater than the SRD and minimum clinically important difference for the ARAT.[49] NOTE. Figures and photographs by M. Bockbrader and N. Austin.

use-dependent cortical plasticity under the implant, retuning neurons to the distal limb movements he wished to evoke. By 4 years postimplant, GRASSP strength, prehension ability, and prehension performance improvements exceeded subscale SRDs[43] (see fig 5B), consistent with International Standards for the Neurological Classification of Spinal Cord levels of C8, C7-T1, and C5-7, respectively. Thus, BCI-FES improved the user's neurologic level from C5-6 to C7-T1 (see fig 7D), a clinically important change conferring potential to live independently.

Study limitations

Findings are limited to 1 participant with a C5 American Spinal Injury Association Impairment Scale class A SCI, and may not generalize across tetraplegia: maximal benefit for grasp requires some residual ability to reach and not all end-users are successful with BCI or transcutaneous FES components.[7] Clinical implications of standardized test performance should be interpreted cautiously, because most are not normed for SCI. In addition, clinical gains were demonstrated with test item-specific decoders which lack multifunctionality and translational practicality, though results appear replicable with multiclass decoders for the GRT[16] (see fig 5D). Furthermore, implications for independence were extrapolated, rather than observed.

Multiple design challenges were revealed by functional testing, including: suboptimal thenar stimulation; need for sensors to self-calibrate FES based on pronation state; barriers to portability and independent setup by end users; and requirements for daily decoder retraining. Future work should also optimize multiclass decoders to facilitate demonstrations of GAIN that can be evaluated in a single day.

Conclusions

Implanted BCI is a viable FES control mechanism for chronic tetraplegia, performing well >4 years after MEA implantation. With home use, BCI-FES-evoked grips are expected to confer greater independence for self-care. Next steps will address translational barriers: (1) developing accurate, faster, performance sustaining decoders and (2) developing wireless, portable, and wearable components.

Suppliers

a. NeuroLife brain-computer interface functional electrical stimulation; Battelle.
b. Utah Array; Blackrock Microsystems.
c. Semmes-Weinstein monofilaments; Fabrication Enterprises.
d. Black Mechanical Pinch Gauge; B&L Engineering.
e. Electronic Handgrip Digital Dynamometer; Camry Scale Store.
f. MATLAB; The MathWorks, Inc.

Table 6 Observational ratings on the CUE-T and subjective ratings on the QIF-SF and SCIM-SR

	Baseline Adaptive Grip	BCI-FES Controlled Grip
CUE-T (Day 532): Unilateral Items		
Reach out	3	3
Reach overhead	0	0
Reach down	0	0
Reaching and Lifting (Maximum 12)	3 (25% of normal)	3 (25% of normal)
Pull light object	4	4
Pull heavy object	4	4
Push light object	4	4
Push heavy object	4	4
Pushing and Pulling (Maximum 16)	16 (100% of normal)	16 (100% of normal)
Wrist up	0	4
Palm down	4	4
Wrist Actions (Maximum 8)	4 (50% of normal)	8 (100% of normal)
Grasp hammer	0	4
Small pinch	1	4
Key pinch	0	4
Wide grasp	0	4
Manipulate coin	0	2
Push with finger	3	4
Hand and Finger Actions (Maximum 24)	4 (17% of normal)	22 (92% of normal)
CUE-T unilateral Total score (Maximum 60)	27 (45% of normal)	49* (82% of normal)
QIF-SF (Day 821)		
Wash/dry hair	1	3
Supine to side	0	1
Lower body dressing	0	0
Open carton/jar	0	3
Bed to chair	0	3
Lock wheelchair	3	3
QIF-SF Total score (Maximum 24; Maximum using any device 18)	4 (13% of normal; 22% of independent with device)	13* (54% of normal; 72% of independent with device)
SCIM-SR (Day 532)		
Feeding	2	3
Bathing		
Upper body	1	1
Lower body	0	0
Dressing		
Upper body	1	1
Lower body	0	0
Grooming	2	3
Self-care (Maximum 20)	6 (30% of normal)	8 (40% of normal)
Respiration	5	5
Bladder	0	3
Bowel	1	2
Toileting	0	2
Respiration and Sphincter Management (Maximum 17)	6 (30% of normal)	12 (71% of normal)
Bed mobility	0	1
Bed transfer	0	0
Bath transfer	0	0
Indoor mobility	1	1
Mobility 10-100 m	1	1
Outdoor mobility	1	1
Stairs	0	0
Car transfer	0	0
Ground transfer	0	0
Mobility (Maximum 37)	3 (8% of normal)	4 (11% of normal)
SCIM-SR Total score (Maximum 74)	15 (20% of normal)	24* (32% of normal)

NOTE. CUE-T ratings were jointly made by the participant and the research physiatrist based on observed performance in the lab of arm actions without using the BCI-FES (baseline) and with the BCI-FES. The participant provided QIF-SF and SCIM-SR ratings for his actual baseline level of function at home and his expected ability if he could use the BCI-FES at home. Higher scores indicate greater level of independence.

* Change exceeds minimum clinically important difference calculated as 10% of test range.

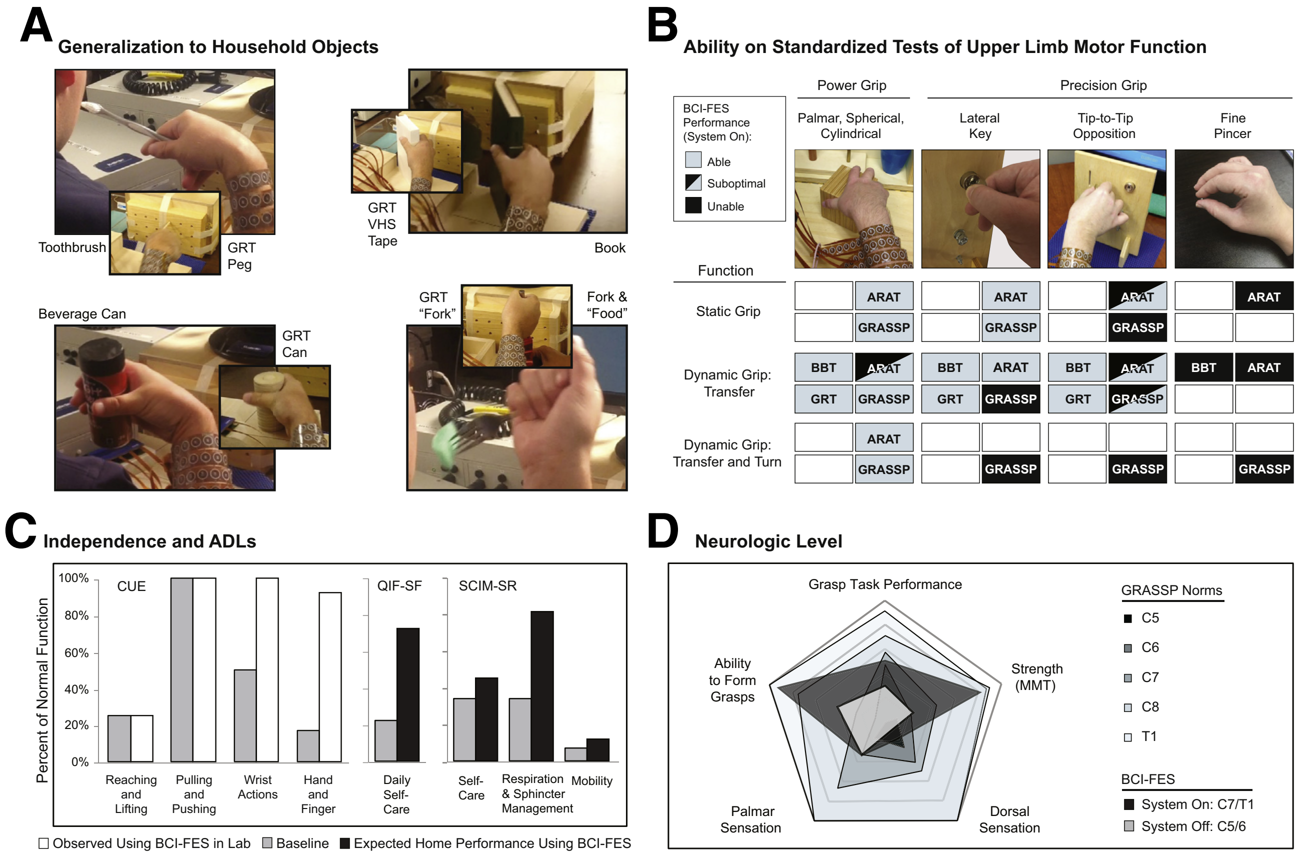

Fig 7 The GAIN model: implications for neuroprosthetic use in daily life. A. Generalization to everyday objects. Our participant practiced with BCI decoders and FES grips for standardized GRT objects (peg, video tape, can, "fork") and successfully transferred these skills to grasp and manipulate a toothbrush, hardcover book, metal dinner fork (stabbing a piece of polystyrene foam "food"), and full beverage container B. Ability on activity measures. BCI-FES enabled our participant to form palmar, lateral, and tip-to-tip grips, but not fine pincer grips due to lack of thenar muscle stimulation. Use of the device enabled successful object manipulation activities, like pouring and twisting, which required integration of palmar grip with shoulder and forearm movements. Tip-to-tip grip integrated with shoulder movements was also successful, but not always faster than the participant's baseline performance with adaptive grips. Some tip-to-tip grips with forearm and wrist pronation and all dynamic pincer grips were a challenge, due to lack of thenar muscle stimulation. C. Independence on functional participation measures. Our participant reported that he expected to make gains in SCIM-SR and QIF-SF self-care, toileting, and upper limb-related mobility tasks if he could use the BCI-FES at home. He did not expect BCI-FES to affect lower limb-related mobility tasks. Expectations for increased independence for self-care were attributed to observed normalization of CUE-T Hand and Wrist domain abilities with BCI-FES. Overall, he reported BCI-FES in the home would allow him to require fewer hours of home care assistance for his ADLs. D. Neurologic level of performance. Based on GRASSP norms for the International Standards for Neurological Classification of Spinal Cord Injury neurologic levels, our participant started at C5-6 and improved to C7-T1 with BCI-FES. This is a clinically significant improvement of upper limb motor control that confers increased independence for activities of daily living. NOTE. See supplemental videos S1-S3. Figures by M. Bockbrader, photographs by M. Bockbrader and N. Austin, N. Annetta, and M. Zhang.

Keywords

Activities of daily living; Brain-computer interfaces; Hand strength; Quadriplegia; Rehabilitation; Transcutaneous electric nerve stimulation

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