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Bimanual function after cervical spinal cord injury: Development of the Berlin Bimanual Test for Tetraplegia (BeBiTT) and brain/neural hand exoskeleton assessment

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List of abbreviations

SCI	Spinal Cord Injury
cSCI	Cervical Spinal Cord Injury
ASIA	American Spinal Injury Association
BCI	Brain-computer interface
EMG	Electromyography
FES	Functional electric stimulation
MEA	Microelectrode arrays
EOG	Electrooculography
HOV	Horizontal oculoversions
EEG	Electroencephalography
SMR	Sensorimotor rhythm
ERD	Event-related desynchronization
ERS	Event-related synchronization
BeBiTT	Berlin Bimanual Test for Tetraplegia
TRI-HFT	Toronto Rehabilitation Institute – Hand Function Test
B/NHE	Brain/neural hand exoskeleton
CUE-T	Capabilities of Upper Extremity Test
FIM	Functional Independence Measure

SCIM	Spinal Cord Independence Measure
QIF	Quadriplegia Index of Function
ICF	International Classification of Functioning, Disability and Health
CVR	Content Validity Ratio
S_CVI	Scale Content Validity Index
I_CVI	Item Validity Index
QIF-SF	Quadriplegia Index of Function – Short Form
ICC	Intraclass correlation coefficient
FOI	Frequency of Interest
TH	Detection threshold

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1. General introduction

1.1 Cervical spinal cord injury

As part of the central nervous system, the spinal cord is responsible for transporting information between the brain and the peripheral nervous system, ensuring the proper functioning of the body's muscles, sensation, and autonomous regulation. The spinal cord can be divided into 31 segments, each forming a pair of spinal nerves that innervate a corresponding area of the body: Starting below the brain stem, the cervical spinal cord encompasses eight segments (C1-C8) that innervate the upper extremities, the diaphragm, and the neck. The following twelve thoracic segments (Th1-12) innervate the thorax and abdomen, and the sacral (S1-S5), lumbar (L1-L5) and coccygeal (Co1) segment(s) innervate the lower extremities and pelvic area.

Spinal cord injury (SCI) refers to damage of the spinal cord, affecting its proper function. In SCI, not only the segmental innervation on the lesion's location, but the entire innervation below the injury is impaired. Consequently, injuries to the cervical spinal cord do not only affect the sensory, motor, and autonomous function of the upper limb, but also of the thorax, abdomen, and lower extremities. Therefore, cervical spinal cord injury (cSCI) usually results in a total or partial paralysis of all four limbs, which is referred to as tetraplegia or quadriplegia.

1.1.1 Classification

Spinal cord injuries are classified by the neurological level of injury, defined as the last completely functioning segment of the spinal cord (Büttner, 2004). The level of injury is usually identified by testing the sensation and the strength of segment-indicating muscles, called myotomes. Further, modern imaging techniques such as magnetic resonance imaging (MRI) are applied to determine the lesion location (Ahuja et al., 2017). Beside the level of injury, SCI can be further characterized by defining the completeness/incompleteness of the injury. A ‘complete’ spinal cord injury refers to a total loss of all functions below the lesion location, whereas in an ‘incomplete’ SCI some connections to the lower segments are preserved, leading to partially remaining function. In the clinical context, the American Spinal Injury Association (ASIA) Impairment Scale is applied (Kirshblum & Waring, 2014; Roberts et al., 2017) (Table 1). Here, grade A is defined as a complete SCI with no motor or sensory function left in the sacral segments, while grades B to D account for incomplete lesions with function preserved below the lesion’s level (Kirshblum & Waring, 2014; Roberts et al., 2017) (Table 1).

Table 1: ASIA Impairment Scale

Grade	Complete/ Incomplete	Description
A	Complete	Motor or sensory function is not preserved below the lesion's level.
B	Incomplete	Sensory function is preserved but no motor function is preserved below the lesion's level.
C	Incomplete	Motor function is preserved below the lesion's level. More than 50% of key muscles below the lesion's level have a muscle grade less than 3.
D	Incomplete	Motor function is preserved below the lesion's level. More than 50% of key muscles below the lesion's level have a muscle grade of 3 or more.

From: Roberts et al. (2017)

Neurological classification and ASIA Impairment Scale have great impact on patient's life. Generally, the higher and more complete the level of injury, the more pronounced the impairment will be. For example, neurological level of injury at C4 normally results in severe impairment of the upper extremities including restricted arm, shoulder, and hand function. On contrast, injury at C6 only affects hand function, while arm and shoulder function are normally intact. Further, in incomplete injures (ASIA C-D) remaining muscle function possibly mitigates the extent of impairment.

1.1.2 Epidemiology

In 2016, the incidence of spinal cord injuries was around 13 per 100 000 on a global level and the worldwide prevalent cases were approximately 27 million, without having significantly changed since 1990 (James et al., 2019). Apart from conflict and terrorism - which were the most common cause in North Africa and the Middle East, the main cause for SCI were falls or traffic accidents (James et al., 2019). Global statistics, however, do not register demographic parameters such as neurological level and ASIA grade. Thus, one must refer to national databases to obtain a more detailed overview. The National Spinal Cord Injury Statistical Center (NSCISC) provides the worldwide largest database with almost 30,000 registered participants with SCI. According to the NSCISC (2019), 52.4% of all participants with SCI suffer from tetraplegia. Among them, 35.4% have complete cSCI (ASIA grade A), the rest showed incomplete injuries (ASIA grade B to D). The main causes for cSCI were vehicular accidents, sport accidents and falls (National Spinal Cord Injury Statistical Center, 2019). The results of the NSCISC database correspond well with a study that has assessed recent epidemiologic trends in traumatic cSCI. Likewise, etiology included falls (46.9%), traffic accidents (34.2%), and sports injuries (10.9%) and an increase in incomplete cSCI could be observed, whereas complete injuries decreased significantly (Aarabi et al., 2020). Among the 1420 participants, 78.3% were male with a mean age of 51.5 years (Aarabi et al., 2020).

1.1.3 Impairment in daily life

Persons with tetraplegia face multiple difficulties in their daily lives. The impairment of the lower extremity immensely hinders mobility, mainly caused by the inability to walk, but also by facing the impracticability of riding a common bicycle or driving a car. However, the impairments of the lower extremity can usually be compensated by the use of a wheelchair, restoring mobility to a considerable extent (Rushton et al., 2010). On the contrary, upper limb impairment leads to immense challenges in daily routine. Proper functioning of arm, shoulder and especially hand is required to execute many activities of daily living (ADLs). First introduced by Katz et al. (1963), ADLs refer to any person’s daily needs, such as dressing, bathing, eating, and preparing food. As a consequence of impaired hand function, persons with tetraplegia must often rely on daytime care or family support, helping them to dress, bathe, wash etc., which enormously restricts the opportunity to live an independent life (Edemekong et al., 2017). Considering that, it is clear why regaining arm and hand function is seen as highest priority in rehabilitation by persons with tetraplegia (Anderson, 2004; Lo et al., 2016; Snoek et al., 2004).

1.1.4 Restoration of hand function

To date, there is no universal strategy available for restoring hand function in individuals with tetraplegia. However, several approaches have been developed to address this issue. A common method in this field is surgical intervention. In a procedure called tendon transfer, tendons of properly innervated muscles are surgically transferred from their initial point of insertion to a new insertion in order to replace function (Bednar & Woodside, 2018). Although the outcome of such intervention is usually satisfying for patients, not all persons with tetraplegia have suitable muscles and tendons that can be transferred (Bunketorp-Käll et al., 2017; Dunn et al., 2016). Another drawback lies in the risk of surgery, including infection, anesthesia complications and damage to tissue.

Non-surgical rehabilitation mainly focuses on learning compensatory techniques (Bryden et al., 2005). Here, the so-called ‘tenodesis grasp’ represents a common approach to improve hand function in persons with tetraplegia. By actively extending the wrist, hand flexor muscles are passively put under tension, resulting in a passive insufficiency of hand flexors that allows to grasp objects (Johanson & Murray, 2002). Although the tenodesis grasp represents a useful strategy to regain some degree of hand function, it often cannot replay function to such degree that complex ADLs like eating with cutlery or close the zipper of a jacket can be performed (Smaby et al., 2004). Furthermore, use of orthosis can support persons with tetraplegia to maintain proper positioning of the hand. However, orthoses have not been shown to improve hand function in persons with tetraplegia, but only to prevent deterioration by stabilizing the architecture of the hand. (DiPasquale-Lehnerz, 1994; Krajnik & Bridle, 1992).

1.2 Neurotechnology

Since common methods for restoring hand function in persons with tetraplegia have several limitations, it is worth considering alternative rehabilitation approaches. Here, latest developments in neurotechnology and robotics represent offer promising possibilities such as the application of hand exoskeletons and robotic end-effectors (Mekki et al., 2018). Hand exoskeletons are wearable robotic devices that are attached to the user’s hand.

Powered by electric motors or pneumatics, they are able to initiate, support or completely imitate hand movements. Conversely, robotic end-effectors are not attached to the user's body but connected to a detached robotic arm. Robotic end-effectors can perform reaching and grasping movement independent of the user's body and, in contrast to hand exoskeletons, are not bound to physiological characteristics such as limited degrees of freedom.

Assistive devices like hand exoskeletons and robotic end-effectors can be controlled in several ways, the most ordinary being to simply enter commands into a control unit. A more intuitive but also more complex way to command such devices can be established by recording bio signals that are related to the desired movement and translating them into control signals. For example, it has been shown that residual arm and hand muscle activity recorded via electromyography (EMG) can be translated into commands to operate a hand exoskeleton (Lu et al., 2017). Such technology is mainly suitable for persons with incomplete cSCI, as residual muscle activity in forearm and hand is required. Alternatively, control of external devices can be established via brain-computer interfaces (BCIs) (Wolpaw et al., 2002). By recording and analyzing brain signals, BCIs can detect a user's intention and convert it into volitional control commands of external devices like hand exoskeletons or robotic end-effectors (Wolpaw, 2007).

1.2.1 Brain-computer interfaces

There are several examples where BCI based devices have been used for the restoration of arm and hand function following cSCI. In 2006, a BCI system allowed an individual with tetraplegia to control a robotic end-effector by decoding brain data using an implanted 96-microelectrode array (MEA) (Hochberg et al., 2006). Further developments in BCI systems lead to a more precise control of robotic end-effectors, allowing persons with tetraplegia to perform three-dimensional movements and grasp objects of daily living (Collinger et al., 2013; Hochberg et al., 2012). Also, it has been shown by Benabid et al. (2019) that individuals with tetraplegia are able to control BCI-based exoskeletons via epidural electrocorticography (ECoG).

Within BCI technology, there are various methods of detecting brain signals such as the mentioned methods of ECoG and MEA. These methods, however, are cost-intensive and invasive and thus carry the risk of brain surgery and infection of the implanted device. On the contrary, electroencephalography (EEG), magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI) and near-infrared spectroscopy (fNIRS) represent common non-invasive methods to collect brain data. Among them, EEG is generally regarded as the most popular method for BCI applications, since it is an economical and practicable method with high temporal resolution (Al-Quraishi et al., 2018).

1.2.2 Sensorimotor rhythm-based control

A common approach for EEG-based BCI control of external devices uses modulation of the sensorimotor rhythm (SMR) (Birbaumer & Cohen, 2007). SMR is a synchronized electric brain activity that typically oscillates in a range of 8–12 Hz (Pfurtscheller & Lopes da Silva, 1999). The amplitude of SMR increases during idle state, i.e., in the state of immobility, and decreases during motor execution and motor imagery (MI), the mental visualization of a certain movement (Pfurtscheller & Neuper, 1997). The phenomena of a decrease in SMR amplitude related to motor behavior or MI is known as event-related desynchronization (ERD) of the SMR (Pfurtscheller & Aranibar, 1979). The desynchronization of the SMR (SMR-ERD) can be explained by the fact that resting-state neurons tend to fire synchronously, while in motor behavior and MI neurons start firing in a complex and individualized pattern, disturbing the synchronized rhythm, and thus lowering the SMR amplitude. By detecting SMR-ERD, BCIs can identify a subject's motive to move and translate it into control commands of an external device. For example, a user's intention to grasp can be translated into an actual hand-closing motion driven by a hand exoskeleton. This way, the spinal cord can be bypassed and the lost link between brain and hand re-established, representing a very intuitive way to restore hand function in persons with cSCI (Collinger et al., 2013).

1.2.3 Hybrid brain/neural control

There have been several successful attempts to implement EEG-based exoskeletons in healthy subjects and stroke survivors (Broetz et al., 2010; Ramos-Murguialday et al., 2013; Tang et al., 2016). However, low signal-to-noise ratios and susceptibility to environmental artifacts limit the application of non-invasive BCI systems despite their advantage of being safe and economic. As response to this, a hybrid BCI paradigm has been introduced that combines EEG with electrooculography (EOG) signals to establish feasible hand exoskeleton control (Witkowski et al., 2014). Here, EOG recorded maximal horizontal eye movements, so called horizontal oculoversions (HOVs), to open the exoskeleton and to interrupt unintended closing (veto command), while closing of the exoskeleton were still controlled by brain signals. Soekadar et al. (2016) showed that such hybrid brain/neural hand exoskeleton (B/NHE) improves the performance of unilateral tasks in everyday situation in patients with cSCI. For example, the B/NHE allowed individuals with tetraplegia to eat in a restaurant without help of supervisors. Through the robust hybrid control paradigm, a non-invasive BCI system could, for the first time, be controlled by persons with tetraplegia outside the laboratory, representing a big step towards a soon-to-be application in patients' daily lives (Soekadar et al., 2016).

1.3 Assessment of hand function

When considering assistive devices like BCI-based hand exoskeletons as a new opportunity to restore hand function in persons with tetraplegia, it is of high importance to reliably evaluate their actual impact on hand function. To ensure this, good assessment tests need to be available which evaluate hand function comprehensively and, at the same time, are suitable to assess modern tools in neurotechnology. Without appropriate measurement tools, the benefit of assistive devices cannot be properly validated and their establishment as useful strategy for restoring hand function in individuals with tetraplegia remains contestable.

So far, the use of hand exoskeletons in persons with tetraplegia has been assessed by the Toronto Rehabilitation Institute - hand functioning test (TRI-HFT) (Cappello et al., 2018; Osuagwu et al., 2020; Soekadar et al., 2016; Yoo et al., 2019). The TRI-HFT is a hand function test that has been originally designed to assess functional electrical stimulation (FES) in persons with tetraplegia. The TRI-HFT is divided into two parts: The first part consists of several tasks that assess the subjects' ability to manipulate objects of daily living. In the second part, the strength of the subjects' lateral pinch and palmar grasp is being measured (Kapadia et al., 2012).

Reviewing the test´s method to evaluate hand function, it is noticeable that the TRI-HFT exclusively consist of tasks that must be performed unilaterally, i.e., with a single hand. However, many activities of daily life require not only the use of one hand, but the interaction of both hands. By engaging both hands in a concerted spatial and temporal interaction skillful tasks can be performed that would not be possible with unilateral hand control, representing the main characteristic of bimanual function (Franz, 2003).

With the TRI-HFT, hand exoskeletons have so far only been investigated on their capability to restore unilateral hand function. However, bimanual function also plays a major role following SCI considering the relevance of bimanual tasks in everyday situation (Herrmann et al., 2011; Spooren et al., 2009) and the fact that persons with tetraplegia experience exacerbated deficits in bimanual tasks compared to single-handed ones (Britten et al., 2017; Calabro & Perez, 2016). Therefore, the use of BCI-based hand exoskeletons has yet to prove a positive impact on bimanual function in individuals with tetraplegia.

1.3.1 Hand function tests

Since the TRI-HFT is not designed to assess bimanual functions, a suitable alternative must be found to evaluate BCI-based exoskeletons with respect to this important aspect. The Jebsen Test of hand function, the Grasp and Release Test (GRT) and the Graded Redefined Assessment of Strength, Sensibility and Prehension (GRASSP) are commonly applied hand function tests for persons with tetraplegia. However, they do not consist of any bimanual item (Jebsen, 1969; Kalsi-Ryan et al., 2009; Wuolle et al., 1994). The Capabilities of Upper Extremity Test (CUE-T) consists of just one bimanual item, compared to 31 single-handed ones (Marino et al., 2012). The Sollerman hand function test (Sollerman & Ejeskär, 1995) explicitly states to represent common ADLs. However, three bimanual tasks seem underrepresented compared to 17 unilateral ones. The Van Lieshout test includes tasks that require bimanual function (e.g., transferring from wheelchair to bed). These tasks, however, also account for stability of the trunk and mobility of the lower extremity. Poor performance in these traits negatively affect the score even though bimanual function might be well preserved.

1.3.2 ADL scores

Commonly used hand function tests seem not suitable to properly assess bimanual function in persons with tetraplegia. Thus, it is worth considering ADL scores for such purpose as bimanual tasks play an essential part in many daily life activities. Common ADL tests applied in individuals with tetraplegia are the Functional Independence Measure (FIM), the Spinal Cord Independence measure (SCIM) and the Quadriplegia Index of Function (QIF) (Catz et al., 1997; Gresham et al., 1980; Van Tuijl et al., 2002). Among them, the QIF and SCIM include several bimanual items (e.g., cutting food, open carton, put on socks, and propel a wheelchair) and are able to track minimal change in functionality (Catz et al., 1997; Gresham et al., 1986). A major drawback, however, lies in their scoring system: Both the QIF and the SCIM rate a subject according to the extent of assistance the individual requires to perform a task. Since using an exoskeleton always means relying on assistance, performing tasks with its support could never lead to full score, even though all tasks might be successfully accomplished. Hence, these scores cannot reliably reflect functional improvement induced by application of BCI-based devices. Further, many items within the QIF and SCIM do not only account for hand function but also for characteristics such as trunk stability and lower extremity function. Strong impairment in these traits lower the score significantly, even though bimanual function might be well preserved.

When reviewing the literature on clinical measurement tools for assessing bimanual function in persons with tetraplegia and their suitability to evaluate assistive devices such as BCI-based hand exoskeletons, one encounters two major problems: (I) functional tests do not account for bimanual function sufficiently and (II) ADL tests are not equipped with a scoring system that is suitable to assess external devices. Hence, there is so far no possibility to assess hand exoskeletons on their capability to restore bimanual function in persons with tetraplegia, demanding for a new clinical measurement tool to be developed.

1.4 Research purpose

Hand exoskeletons have, to date, only been assessed on their capability to improve unilateral hand function, neglecting the relevant aspects of bimanual function. As shown, there is no clinical test available that is appropriate for evaluating bimanual function in individuals with tetraplegia. In response to this, the first step of this work is to develop a new hand function test suitable to assess bimanual function in persons with cSCI and compatible with state-of-art tools in neurotechnology. This will fill a notable gap identified in existing hand function tests and provide a comprehensive method for evaluating modern devices like hand exoskeletons for their effects on bimanual function.

In a second step of this work, the developed test is used to detect change in bimanual function induced by hybrid brain/neural hand exoskeleton (B/NHE) application among persons with tetraplegia. Such evaluation is of high interest, since it provides further information on the role of modern neurotechnology in the restoration of hand function following cSCI. Moreover, the newly developed test is validated according to common psychometric evaluations to promote its role as a valid clinical test.

2. Development of the Berlin Bimanual Test for Tetraplegia

There is a considerable need to develop a new measurement tool to assess bimanual function in persons with tetraplegia. The development of such test is outlined in the present chapter. Since a significant part of the present work has been done at the clinical neurotechnology lab of the Charité (Berlin), the newly developed test is called **Berlin Bimanual Test for Tetraplegia (BeBiTT).**

Up to date, a sound methodology for test development are mainly found within the educational and psychological research field, contributing to a large number of well-standardized achievement, intelligence and personality tests (Hathcoat et al., 2016). In health science, however, there has not been a consensus on standardization guidelines yet, resulting in a variety of different approaches for developing a clinical measurement tool. For developing the BeBiTT, the methods proposed by Lynn (1986) and Streiner et al. (2015) were regarded most suitable. They provide a clear structure that guides through the important stages of test development and give useful instructions on how to transfer methodical concepts into practical steps. Considering the methodology of Lynn (1986) and Streiner et al. (2015), the present chapter covers the following steps of test development:

- Identification of the test´s theoretical framework and definition of the test´s construct (Chapter 2.1)
- Generation and selection of suitable test items (Chapter 2.2)
- Content validity assessment of items (Chapter 2.3)
- Evaluation of items´ feasibility (Chapter 2.4)
- Development of a scoring system (Chapter 2.5)

2.1 Theoretical framework

In an initial step of test development, the theoretical framework must be defined. The theoretical framework represents a leading structure throughout the whole process of test development, outlining the components, guidelines, and limitations of the test. Within the theoretical framework the test´s underlying construct and its related concepts are a core element, and their detailed definition is essential.

The BeBiTT intends to measure the construct of bimanual function in persons with tetraplegia. When reviewing the literature on bimanual function, one comes across a suitable definition proposed by the developers of the Chedoke Arm and Hand Activity Inventory (CAHAI) - a tool that assesses upper limp function in stroke survivors with a strong focus on bimanual tasks

(Barreca et al., 2004). Based on their approach and adjusted to cSCI, bimanual function is defined as the following:

> Bimanual function is the ability to move both arms/ hands in a **coordinated** way so as to **grasp, lift** and **manipulate** different objects of various weight and size in order to perform **activities of daily living**.

Within this definition, there are related concepts that need to be explained in more detail. These concepts will be outlined in the following abstract.

2.1.1 Related concepts

In bimanual function, there are three main components, i.e., grasp, lift and manipulate. **Grasping** is a crucial part of hand function, representing a prerequisite for many subsequent hand actions in daily life**.** According to Light et al. (2002) grasp patterns can be classified into six categories: tripod pinch, tip pinch, lateral pinch, power grip, spherical grip, and extension grip. **Lifting** represent a key element of bimanual function in daily life activities, mainly when transferring objects. Lifting requires proper function in the entire upper extremity, including bilateral arm and shoulder function. Besides grasping and lifting, **manipulating** is an essential feature of bimanual function. In most bimanual actions, one hand stabilizes an object while the other performs fine manipulation movements. For manipulating, both strength and dexterity as well as a highly coordinated movements are required, making it the most complex component of bimanual function.

Bimanual coordination is the interaction of both arms/hands in which each hand contributes to a component of action while closely interacting with the other. Regarding bimanual coordination, Kantak et al. (2017) developed a classification framework for bimanual actions. The taxonomy of Kantak et al. (2017) classifies arm/hand movements on whether they are carried out asymmetrically or symmetrically. Symmetric bimanual movements engage homologous muscles, while asymmetric movements engage non-homologous ones, requiring different neurological recruitments. Furthermore, bimanual actions are classified on whether the goal tasks are perceived as independent or as a common goal, which has proven to be essential in how bimanual movements are programmed (Shea et al., 2016). In common goal tasks, movements can be either performed in a sequential manner (referred to as parallel) or necessitate cooperative spatio-temporal interaction.

Activities of daily living (ADLs) refer to any person's daily needs and can be grouped in basic ADLs and instrumental ADLs (IADLs). Basic ADLs encompass physical skills, such as dressing, bathing or eating (Katz, 1983). IADLs are regarded as non-essential for fundamental functioning, but important to live an autonomous and independent life (Bookman et al., 2007). Examples for IADLs are shopping, doing house chores and using the telephone. Among persons with tetraplegia, it is highly individual which ADLs are seen as most relevant, and level of difficulty varies between individuals due to the wide range in impairment characteristics.

2.1.2 Guidelines and limitations

Next to defining the underlying construct and outlining its related concepts, it is recommended to consider common guidelines within test development (Streiner et al., 2015). The World Health Organization (WHO) proposed a guideline for measuring a person's level of functioning in society: The International Classification of Functioning, Disability and Health (ICF). According to the ICF, functioning can be assessed by regarding the following three domains: (I) body function, which refers to the physiological functions of body systems, (II) activity, which is the performance of a task or action by an individual and (III) participation – that is the involvement in a life situation.

Also, limitations must be considered within the theoretical framework. As mentioned, the BeBiTT should be suitable to assess the capability of hand exoskeletons to restore bimanual function and thus ought to be conformant with the characteristics of such devices. Further, the test should be practical and easy-to use, paving the way for wide clinical acceptance. Considering that time is a rare asset in clinical environment, administration of the BeBiTT should be short and easy. Additionally, the test's equipment needs to be affordable and available everywhere in the world, reducing acquisition efforts to a minimum.

Summarizing, the BeBiTT's theoretical framework is illustrated in Figure 1.

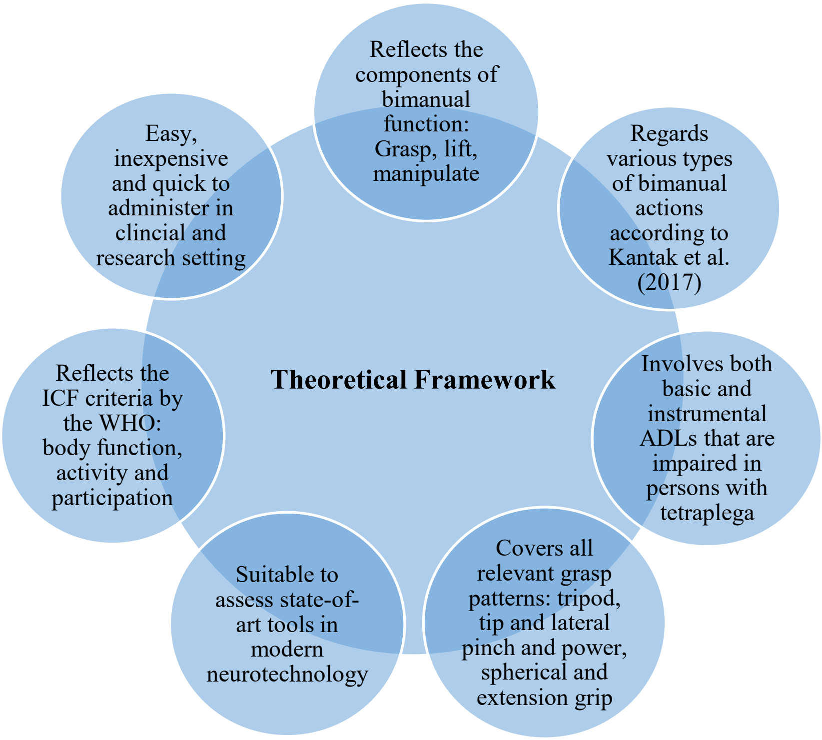

Figure 1: Theoretical Framework of the BeBiTT

From: Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17

2.2 Item generation and selection

After having developed a theoretical framework, the next step in test development involves the generation of items. Here, “patients and potential research subjects are an excellent source for generating items” (Streiner et al., 2015, p. 21). Interviews or surveys can be used to get a better understanding of subjective components of the underlying construct. Apart from patients, experts in the field can be questioned. Combined with their experience from clinical observation, experts can be a very fruitful source for items (Streiner et al., 2015).

2.2.1 Methods

An online survey with individuals with tetraplegia was conducted to identify bimanual task that are impaired following cSCI and which could be transferred into possible test items. Further, semi-structured interviews were held with persons with tetraplegia and therapists to collect detailed qualitative data.

Seven persons (5 male, 2 female, mean age 41.6 ± 11.9) with complete (n = 3; ASIA grade A) and incomplete (n = 4; ASIA grades B, C) cSCI (C4 to C6) in chronic stage (i.e., suffering from tetraplegia for at least 1 year) participated in the online survey. Additionally, three male persons (mean age 46.6 ± 13.5) with complete (n = 2) and incomplete (n = 1) cSCI (C4 to C5) in chronic stage were interviewed. Participants were recruited in Tübingen, Germany. Further, a physiotherapist from the BG Unfallklinik Murnau and an occupational therapist from the BG Unfallklinik Tübingen were interviewed. Both had longtime working experience (more than 5 years) with both acute and chronic tetraplegic patients.

The interview guide had a semi-structured design, providing a framework in which at any time the interviewee could elaborate on certain points. Likewise, the online survey comprised of open questions without any word limit. The interview guide for persons with tetraplegia and the online survey followed the same template (Appendix A). In both, the rationale for developing a bimanual function test was explained, followed by a short introduction to the relevant aspects of the theoretical framework. Then, the interviewee/survey respondents were asked to name/write down bimanual activities of daily living in which they experience impairment; how exactly they are impaired; which bimanual activities can still be performed; and what type of compensatory strategies are applied. Within the interview, further information was gathered by specifically querying each ADL category for impaired bimanual tasks.

An adjusted version of the interview guide was used to interview the therapists. Similarly, the expert interviews intended to tape in the same direction: which and to what extent bimanual tasks of daily life are impaired in persons with tetraplegia; how exactly are tetraplegics impaired when performing these tasks; which bimanual tasks of daily life can generally be performed and what kind of compensatory strategies are applied.

Due to the Covid pandemic, interviews were conducted via telephone. A declaration of consent was sent to the interviewee that had to be signed electronically before the interview. The interviews lasted approximately 20 minutes and were held in German. The interviews were audiotaped, using the Audacity software (Version 2.4.2), the audio scripts were anonymized and saved on a lab computer. The online survey was conducted in German via Google Forms. A declaration of consent was obtained. All data was anonymized.

The audio records were screened, and all bimanual tasks mentioned by the respondents were collected. Similarly, the answers of the online surveys were analyzed. Identified bimanual tasks were pooled (in case they appeared twice or more), transformed in a list of possible test items and grouped according to the corresponding ADL categories. In a next step, the possible items were reviewed on their conformity to the theoretical framework: Items were selected that (a) involve components of bimanual function (grasping, lifting, manipulating); (b) represent bimanual actions following the taxonomy of Kantak et al. (2017); (c) include common grasp types (tripod, tip and lateral pinch and power, spherical and extension grip); (d) can be easily assessed in a clinical and research environment and (e) are conformant with the use of state-of-the-art tools in neurotechnology.

2.2.2 Results

All bimanual tasks that were identified in the interviews and online survey were listed and grouped according to their corresponding ADL category. The results are illustrated in the tables below (Table 2 and Table 3). In total, 35 bimanual tasks of daily living were identified.

Table 2: Generated Items (Basic ADLs)

Eating and Drinking	Dressing	Personal hygiene	Continence
Eating with cutlery (knife and fork)	Button up trousers	Washing hair	Self-catheterization
Cutting piece of meat	Close zipper of jacket	Apply toothpaste on toothbrush	Toileting
Open water bottle (screw top)	Put on trousers	Open toothpaste	
Open bottle with crown cap	Put on socks	Shaving	
Pour glass of water		Hair Styling	
		Perform manicure and pedicure	
		Wring out wash cloth	

From: Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17

Table 3: Generated Items (Instrumental ADLs)

Communication	**Transportation**	**Managing finance**	**Preparing food**	**Housekeeping**
Charge a smart phone	Propel a wheelchair	Take coins out of wallet	Open food packages	Rinsing dishes
Type on keyboard	Transfer from bed to wheelchair	Take note out of wallet	Open coffee bin	Lift up objects from the ground
Sign a contract	Drive a car		Light a cigarette	Lift up pan
Play games			Cut a slice of bread	
			Chop vegetables (e.g. cucumber)	

From: Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17

All listed bimanual tasks were reviewed on their alignment with the proposed theoretical framework. Since they did not meet the theoretical framework's criteria, the following items were discarded: *Light a cigarette*, *Drive a car*, *Shaving, Washing hair*, *Self-catheterization, Toileting*, *Type on keyboard, Play games* and *perform manicure and pedicure.* Further, *Propel wheelchair, Transfer from bed to wheelchair* and *Lift objects from the ground* were discarded as they do not only assess bimanual function, but also account for trunk strength and stability.

The remaining bimanual tasks were considered to be in alignment with the proposed theoretical framework, as they (a) include the main components of bimanual function (grasping, lifting, and manipulating); (b) include common grasp pattern (tripod pinch, tip pinch, lateral pinch, power grip, spherical grip, and extension grip) and (c) represent bimanual actions according to the taxonomy of Kantak et al. (2017) (Table 4). Further, all remaining tasks were regarded as conformant to modern robotic devices and easy to assess in a clinical or research environment.

Table 4: Items in alignment with theoretical framework

Bimanual Task	**Required Components of bimanual function**	**Grasp pattern**	**Bimanual action (according to Kantak)**
Cut piece of meat	Grasping: knife and fork; Manipulating: knife cuts, while fork stabilizes	Lateral pinch (both hands)	Asymmetric, common goal, cooperative bimanual action
Open water bottle (screw top)	Grasping: bottle and lid; Lifting: bottle; Manipulating: one hand opens lid, while the other stabilizes bottle	Power grip (bottle) Tip pinch (lid)	Asymmetric, common goal, bimanual action

Bimanual Task	Required Components of bimanual function	Grasp pattern	Bimanual action (according to Kantak)
Pour glass of water	Grasping: water bottle and glass; Lifting: water bottle and glass; Manipulating: one hand pours in water, while the other stabilizes glass	Power grip (bottle) Power grip (glass)	Symmetric, common goal, bimanual action
Open beer bottle (crown cap)	Grasping: bottle and bottle opener; Manipulating: one hand opens crown cap with opener, while the other stabilizes bottle	Power grip (bottle) Power grip (opener)	Asymmetric, independent goal, bimanual action
Button up trousers	Grasping: trousers and button; Manipulating: one hand Insert button into button eyelet, while other stabilizes trousers	Lateral pinch (trousers) Tip pinch (button)	Asymmetric, common goal, bimanual action
Close zipper of jacket	Grasping: zipper and jacket; Manipulating: one hand closes the zipper, while other stabilizes jacket	Tip pinch (both hands)	Asymmetric, independent goal, bimanual action
Put on trousers	Grasping: trousers; Lifting: trousers	Power grip (both hands)	Symmetric, common goal, bimanual action
Put on socks	Grasping: socks; Lifting: socks	Lateral pinch (both hands)	Symmetric, common goal, bimanual action

Bimanual Task	Required Components of bimanual function	Grasp pattern	Bimanual action (according to Kantak)
Open toothpaste	Grasping: toothpaste and lid; Lifting: toothpaste; Manipulating: one hand opens lid, while the other stabilizes toothpaste	Lateral pinch (toothpaste) Tip pinch (lid)	Asymmetric, common goal, bimanual action
Apply toothpaste and toothbrush	Grasping: toothpaste and toothbrush; Lifting: toothpaste and toothbrush; Manipulating: one hand puts on toothpaste, while the other holds toothbrush	Lateral pinch (both hands)	Asymmetric, common goal, bimanual action
Wring out wash cloth	Grasping: wash cloth; Lifting: wash cloth; Manipulating: both hands perform wringing motion	Power grip (both hands)	Asymmetric, common goal, bimanual action
Charge smart phone	Grasping: smart phone and charging cable; Lifting: smart phone and charging cable; Manipulating: one hand inserts charging cable, while other stabilizes smart phone	Extension grip (smart phone) Tip pinch (charging cable)	Symmetric, independent goal, bimanual action
Sign a contract	Grasping: pen; Manipulating: one hands signs, while	Tripod pinch (pen)	Asymmetric, common goal, bimanual action

Bimanual Task	**Required Components of bimanual function**	**Grasp pattern**	**Bimanual action (according to Kantak)**
	the other stabilizes the contract		
Take coins out of wallet	Grasping: wallet and coins; Lifting: wallet; Manipulating: one hand takes out note, while the other holds wallet	Tip pinch (coins) Extension grip (wallet)	Asymmetric, common goal, bimanual action
Take note out of wallet	Grasping: wallet and bank note; Lifting: wallet; Manipulating: one hand takes out note, while the other holds wallet	Lateral pinch (bank note) Extension grip (wallet)	Asymmetric, common goal, bimanual action
Open coffee tin	Grasping: coffee tin and lid; Lifting: coffee tin; Manipulating: one hands opens lid, while the other stabilizes coffee tin	Spherical grip (lid) Power grip (coffee tin)	Asymmetric, common goal, bimanual action
Open crisps package	Grasping: crisps package; Lifting: crisps package; Manipulating: both hands tear the package open	Tip pinch (both hands)	Symmetric, common goal, bimanual action
Chop vegetables (e.g., cucumber)	Grasping: knife and vegetable; Manipulating: one hands cuts with knife, while other stabilizes vegetable	Lateral pinch (knife) Spherical grip (vegetable)	Asymmetric, common goal, bimanual action

Bimanual Task	Required Components of bimanual function	Grasp pattern	Bimanual action (according to Kantak)
Cut slice of bread	Grasping: knife and bread loaf; Manipulating: one hands cuts with knife, while other holds bread loaf	Lateral pinch (knife) Spherical grip (bread loaf)	Asymmetric, common goal, bimanual action
Rinse a plate	Grasping: plate and sponge: Lifting: plate and sponge; Manipulating: one hand performs rinsing motions with sponge, while other stabilizes plate	Extension grip (plate) Spherical grip (sponge)	Asymmetric, common goal, bimanual action
Lift up pan	Grasping: saucepan handle; Lifting: pan	Lateral pinch (handles)	Symmetric, common goal, bimanual action

Summary

Within the process of item generation, 35 bimanual tasks were identified that are impaired in daily life of tetraplegic individuals. 21 of these tasks met the required criteria outlined by the theoretical framework (Table 4) and were included in the pool of possible test items for the BeBiTT.

2.3 Content validity assessment

After having selected a pool of items, their content validity should be assessed (Lynn, 1986). Content validity is defined as the degree to which items of a test are representative and relevant to the test's underlying construct (Yusoff, 2019). Content validity needs to be assessed by a group of recognized subject matter experts, called expert panel (Streiner et al., 2015). For content validity assessment, it is recommend to include at least 6 experts within the expert panel (Lynn, 1986; Polit et al., 2007). A common approach to quantitatively assess content validity can be achieved by calculating the Content Validity Ratio (CVR) (Lawshe, 1975). While being often overlooked as a measure of validity, content validity is an important aspect and minimum requirement to assess the feasibility and practicability of a test (DeVon et al., 2007; Haynes et al., 1995).

2.3.1 Methods

Seven physiotherapists and two occupational therapists with working experience in cSCI participated in the content validation of the items (n = 9). Only respondents that have been working for at least 5 years in rehabilitation of persons with tetraplegia were regarded for the expert panel. Respondents were recruited from the BG Unfallklinik Tübingen. Respondents did not participate in the interviews of chapter 2.2 (Item generation and selection).

To assess the content validity of the generated items, a questionnaire (Appendix B) was developed and distributed among the expert panel. In the questionnaire, the BeBiTT's underlying construct and theoretical framework were outlined. Subsequently, experts should - in regard to their expertise - evaluate each item according to the following aspects:

- Does the item represent a relevant everyday activity that is impaired in tetraplegics?
- Is the item of relevance in motor rehabilitation?
- Does the item seem relevant to you to assess bimanual function in tetraplegics?

Experts were asked to rate each item on a 1 to 4 Likert-type scale (1 = Not relevant, 2 = Little relevant, 3 = Fairly relevant; 4 = Highly relevant). Further, the respondents were asked to rate the overall content validity, i.e., whether the test, as a whole, seems relevant to assess bimanual function in persons with tetraplegia. Moreover, respondents were asked to suggest further items and to comment on the test if desired. The questionnaire took approximately 6 minutes to complete. The questionnaire was given to experts in paper form or via a shareable link, provided by LimeSurvey.

For evaluating the responses, the ratings of each expert were converted into a dichotomous rating: Scores of 3 and 4 on the Likert-Scale were converted into 1, representing a “relevant” rating of the item, and items scored 1 or 2 were converted into 0, representing a “not relevant” rating of the item (Polit et al., 2007; Yusoff, 2019). Then, the Content Validity Ratio (CVR) was calculated. The CVR ranges between -1 and 1, in which 0 means that half of the expert panel considers the item relevant, and that the agreement may be due to chance. According to Lynn (1986), CVR must exceed 0.78 for an item to be regarded content valid in case six or more raters are involved. All items that showed content relevance according to the CVR were retained, while those that did not meet the criterion were discarded. To illustrate the effect of item selection on the overall test’s content validity, the Scale Content Validity Index (S_CVI) - a common way to indicate the content validity of a measurement tool as a whole (Yusoff, 2019) - was calculated before and after item selection.

2.3.2 Results

The Content Validity Ratio (CVR) for items was calculated and ranged from 0.111 to 1 (Table 5). *Button up trousers* (CVR = .56), *Put on socks* (CVR = .56), *Wring out wash cloth* (CVR = .56), *Open coffee tin* (CVR = .33), *Open packet of crisp* (CVR = .11), *Cut slice of bread* (CVR= .11) did not meet the required threshold (CVR >= .78) and were not regarded as content valid (Table 5). By discarding these items, Scale Content Validity Index (S_CVI) improved from 0.85 to 0.92 (Table 5). Regarding the overall content validity of the BeBiTT, all experts considered the test to be relevant for its stated purpose.

Table 5: Content validity assessment

Task	No. of raters that endorse item as "relevant"	No. of raters that endorse item as "non-relevant"	CVR	I_CVI
Cut piece of meat	9	0	1.00	1.00
Open water bottle (screw top)	8	1	0.78	0.89
Pour glass of water	8	1	0.78	0.89
Open beer bottle (crown cap)	8	1	0.78	0.89
Button up trousers	7	2	0.56	0.78
Close zipper of jacket	8	1	0.78	0.89
Put on trousers	8	1	0.78	0.89
Put on socks	7	2	0.56	0.78
Open toothpaste	8	1	0.78	0.89
Apply toothpaste and toothbrush	9	0	1.00	1.00
Wring out wash cloth	7	2	0.56	0.78
Charge smart phone	8	1	0.78	0.89
Sign a contract	8	1	0.78	0.89
Take note out of wallet	9	0	1.00	1.00
Take coins out of wallet	9	0	1.00	1.00
Open coffee tin	6	3	0.33	0.67
Open packet of crisp	5	4	0.11	0.56
Chop vegetables	8	1	0.78	0.89
Cut slice of bread	5	4	0.11	0.56
Rinse a plate	8	1	0.78	0.89
Lift up saucepan	8	1	0.78	0.89
S_CVI (before selection)				0.85
S_CVI (after selection)				0.92

CVR = Content Validity Ratio; I_CVI = Item Content Validity Index; S_CVI = Scale Content Validity Index

Summary

Within content validity assessment, the following 15 items were regarded content valid as evidenced by a CVR >= 0.78 (Table 5) and kept within the pool of test item: *Cut piece of meat, Open water bottle (screw top), Pour glass of water, Open beer bottle (crown cap), Close zipper of jacket, Put on trousers, Open toothpaste, Apply toothpaste and toothbrush, Charge smart phone, Sign a contract, Take note out of wallet, Take coins out of wallet, Chop vegetables (e.g. cucumber), Rinse a plate, Lift up saucepan.*

2.4 Feasibility assessment

As a next step of test development, the feasibility of items needs to be assessed. For this purpose, common aspects of feasibility such as cost, time, comprehensibility, practicality, and safety must be considered (Streiner et al., 2015). Time is an important aspect as in case a test requires too much of it, the respondent will lack motivation and concentration. Costs should be held to a minimum, ensuring that the test is generally accessible. High costs can occur in tests that are licensed or requires specific equipment. Administering the test should be practical in the intended environment. Test's instruction should be easy to follow to reduce misunderstanding and frustration among subjects.

Above all, the most important criterion in feasibility assessment is safety. During the entire procedure of assessment, the subject's mental and physical well-being must not be at risk at any time (Streiner et al., 2015).

2.4.1 Methods

To assess the feasibility of selected items, five male tetraplegics (mean age = 53.2 ± 13.8) with complete (n = 2; ASIA grade A) and incomplete (n = 3; ASIA grades B and C) cSCI (C4 to C6) were invited. Recruitment took place in Tübingen, Germany. "Participants were selected based on the following inclusion criteria: Age: 18 – 85; interval after spinal cord injury at least 6 months; lesion height C4 – C6, ASIA grade A – C. Exclusion criteria were the following: Consumption of alcohol (more than 2 alcoholic beverages per day), illegal drug consumption, severe neurological disease other than SCI (e.g., multiple sclerosis, stroke and cerebral palsy), severe medical conditions (e.g., renal failure, liver insufficiency, heart failure; malignant tumor disease), serious cognitive impairment (minimum status below 23 points) and severe spasticity (Ashworth grade ≥ 4)" (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17). Items of the feasibility study are based on the outcomes of content validity assessment (Chapter 2.3). Items' material is displayed in Table 6.

Table 6: Material list for feasibility study

Item	Material
Sign a contract	Piece of paper (210 x 297 mm) Normal ball pin
Charge a smart phone	Common smart phone (e.g. iPhone 6, Samsung Galaxy S20) Corresponding charging cable
Open a water bottle	1 liter plastic bottle of water (filled), screwed on by hand
Pour glass of water	1 liter plastic bottle of water (filled) Water glass (200ml, empty)
Open a beer bottle	0,5 littler glass bottle with crown cork closure, Bottle opener
Rinse a plate	Dinner plate (approx. 25 cm in diameter) Kitchen sponge
Cut meat-like putty	Medium resistance putty resembling the consistency of a piece of meat Knife and fork
Cut vegetable-like putty	Soft resistance putty resembling the consistency of vegetable Paring knife
Lift up pan	Saucepan of around 28x40cm with flat handles (empty)
Open toothpaste	Normal 75ml toothpaste with screwed lid, >50% full
Apply toothpaste on toothbrush	Normal 75ml toothpaste with screw lid, >50% full Toothbrush
Take note out of wallet	Common leather wallet 10 Euro note
Take coins out of wallet	Common leather wallet 1 Euro and 2 Euro coins
Close zipper of a jacket	Metal zipper in a jacket

The feasibility study took place in specified rooms of the Applied Neurotechnology Lab at the Clinic of Psychiatry and Psychotherapy of the University Hospital in Tübingen. At the beginning, signed informed consent was obtained from all, including consent to be videotaped during the tasks. Participants were comfortably placed with the wheelchair in front of a desk. The instructor explained and demonstrated the items to the participants. Participants were asked to perform the task using both hands. Participants were reminded that if at any point they felt pain, discomfort or wanted to rest or interrupt, they should immediately say so. The entire test's administration was videotaped, and the time needed to complete the item was recorded. After the test, the participants were handed a questionnaire in which they were asked to rank each item on the task difficulty (very difficult, difficult, medium, easy, very easy), to indicate the extent to which they felt physically and mentally exhausted after having participated in the test and whether they had any security concerns during the test. Approval from the Ethical Committee of the Medical Faculty of the University of Tübingen, with Reference Number 201/2018BO1, was obtained in accordance with ethical guidelines. All data were anonymized prior to paper entry.

All videotaped items were evaluated regarding the following aspects:

- Is the item practical to be assessed in clinical and research environment?
- Is the item's equipment affordable and easy to acquire?
- Does the participant face any physical or mental risk while performing the item?
- Does the participant experience some degree of difficulties while performing the item?
- Does the item lead to fatigue that affects the performance on following items?
- Does any form of misunderstanding occur?
- Does the administration of the test take longer than 20 minutes?
- Are there any further limitations that occur?

The questionnaires were analyzed on the items' level of difficulty and whether they represent a good mix of easy, medium, and difficult items. Further, questionnaire responses were scanned on whether any security concerns were expressed by participants and if items' description and demonstration was comprehensively perceived by the participants.

2.4.2 Results

Practicability

All items appeared to be practical to assess in clinical and research settings except from the item *Put on trousers*. All participants reported that they usually put on trousers while sitting on the bed with legs outstretched. This requires transfer from wheelchair to bed takes considerable amount of time, making it impracticable to assess in clinical and research settings.

Expenses

Equipment such as a piece of paper and a 1-liter plastic bottle is assumed to be available in a clinical or research environment. Common smart phones are nowadays always at hand and either the smart phone of the instructor or of the participant can be used for item performance. Further equipment can be easily acquired in local shops or online. Overall expenses to acquire all equipment were approx. 110 Euro. All items were reusable, apart from the item *Open bottle (crown cap).* When applied in bigger scales, this could increase costs, which is why the item *Open bottle (crown cap)* was discarded.

<u>Level of difficulty</u>

Regarding the task difficulty of items, responses to the questionnaire are illustrated in Figure 2.

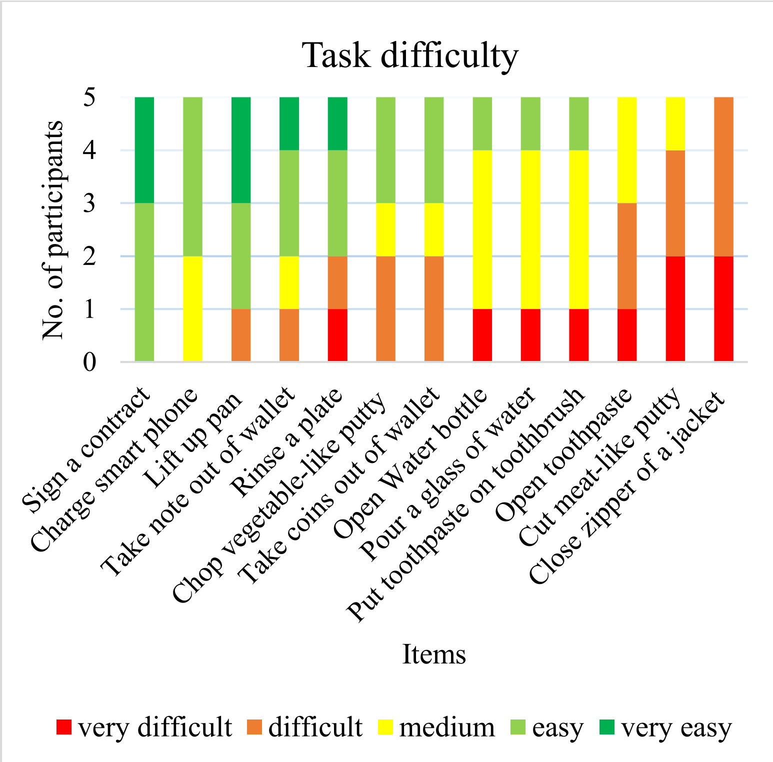

Figure 2: Experienced difficulty in items

Based on the responses, items were grouped in three categories:

- easy items = majority of participants perceived these items as easy or very easy
- medium items = majority of participants perceived these items as medium or as easy and difficult in equal parts
- difficult items = majority of participants perceived these items as difficult or very difficult.

Accordingly, *Sign a contract, Charge smart phone, Lift up pan, Take note out of wallet* and *Rinse a plate* were classified as easy items; *Chop vegetable-like putty, Take coins out of wallet, Open water bottle, Pour glass of water, Rinse a plate* and *Apply toothpaste on toothbrush* were classified as medium items; *Open toothpaste, Cut meat-like putty* and *Close zipper of a jacket* were classified as difficult items.

Due to an overrepresentation of easy and medium items, the following items were discarded: *Chop vegetable-like putty, Take coins out of wallet, Lift up pan* and *Sign a contract.* These items were selected, because there are overlaps to other items (like *Cut meat-like putty* and *Take note out of wallet)* or because they did not present an observable challenge to majority of participants (*Sign a contract)*.

Security – Comprehensibility – Fatigue - Time

In the videotaped items, no physical or mental risk to the participant could be detected at any time. This was in line with participants' responses to the questionnaire: All participants answered that they had absolutely no safety concerns. During the whole assessment, it appeared that all instructions and demonstration could be easily followed. Likewise, all participants responded in the questionnaire that they had no problems at any time to follow instructions and demonstration. Further, it could not be observed that participants faced fatigue or tiredness at any point during the assessment. Within the questionnaire, all participants indicated that the test was neither mentally nor physically exhausting to them. Total assessment time in each participant was below 20 minutes.

Summary

After having selected items on criteria of feasibility, nine items remained. As they passed through all steps of test development, the following nine items were chosen for the final version of the BeBiTT:

1. Charge a smart phone (easy item)
2. Open a water bottle (medium item)

3. Pour glass of water (medium item)
4. Rinse a plate (easy item)
5. Cut meat-like putty (difficult item)
6. Open toothpaste (difficult item)
7. Put toothpaste on toothbrush (medium item)
8. Take note out of wallet (easy item)
9. Close zipper of a jacket (difficult item)

2.5 Development of scoring system

To complete test development, a scoring system capable of systematically obtaining responses to items must be developed (Streiner et al., 2015). In this context, the properties of the score, which can be either nominal, ordinal, interval, or ratio scaled, must be chosen. Established hand function tests for persons with tetraplegia used mostly interval scaled scores: For each item, subjects are given points in case predefined features are performed and points are then added up to an overall score (Kalsi-Ryan et al., 2009; Kapadia et al., 2012; Sollerman & Ejeskär, 1995).

2.5.1 Methods

Criteria must be defined that reflect the underlying construct and to which a precise score can be assigned. Following the definition of the BeBiTT's underlying construct, bimanual function in activities of daily life can be broken down into three main components: grasping, lifting, and manipulating. Instead of just checking whether an object is grasped, lifted, and manipulated, the BeBiTT aims to evaluate performance of action components in a more detailed way.

Regarding grasping, it is reasonable to assess whether an object is grasped passively (with help of passive tension in fingers as it is applied in the widely used tenodesis grasp) or whether an object is grasped with active finger force. An active grip contributes more control and security over an object and should be regarded with a higher score. Regarding manipulating, a participant that manipulates an object without any difficulties should naturally score higher than a participant that struggles to manipulate the object successfully. Further, compensation strategies that are applied while manipulating must be considered. Compensatory strategies involve utilizing body parts typically uninvolved in a specific action to make up for impaired function (e.g., using both hands for a task that typically requires one hand, pressing an object against the torso to manipulate it, or stabilizing an object by pinching it between the legs). Moreover, evaluating the capacity to lift objects serves as an effective means of assessing bilateral arm and shoulder function. However, lifting is often not primarily required to perform tasks: For example, a water bottle does not necessarily need to be lifted in order be opened. Hence, lifting should have less weight in the scoring system compared to grasping and manipulating.

2.5.2 Results

To systematically obtain scores, a standardized scoring sheet has been developed (Figure 3 and Figure 4). The scoring sheet gives a brief explanation of terms and instruction on how to score the BeBiTT. Per item, a score of 2 points is given in case an active/firm grip is performed and 1 point if a passive/loose grip is performed (evaluated for each hand). Within the manipulating component, a score of 4 points indicates no difficulty, while a score of 3 points suggests slight difficulty. In cases of great difficulty, a score of 2 points is given, and when compensatory strategies are applied, a score of 1 point is assigned. Further, a score of 2 points is given if the object is completely lifted and has no contact to any surface while manipulating. This way, 10 points can be reached for each item: 4 points in grasping (two point for each hand), 4 points in manipulating and 2 points in lifting. Since the items *Cut meat-like putty* and *Close zipper of jacket* do not have a meaningful lifting component, a maximum of 6 points were assigned to the manipulating component to level the maximum scores between all items.

The points achieved within each item are added up to an overall score. With 9 items in total and a maximum score of 10 points per item, the total score is a maximum of 90 points. Further, subscores for each component are provided, accounting for points achieved throughout all items in the components of grasping, lifting, and manipulating, respectively.

Scoring Sheet BeBiTT

Patient´s name/ ID: ___________________________

Examiner Name: ___________________________

Date: ___________________________

Comment: ___________________________

Overview

Item	Points
1. Charge a smartphone	/10
2. Open a water bottle	/10
3. Pour a glass of water	/10
4. Rinse a plate	/10
5. Cut meat-like putty	/10
6. Open toothpaste	/10
7. Put toothpaste on toothbrush	/10
8. Take note out of wallet	/10
9. Close zipper of a jacket	/10
IN TOTAL	/90

Components of hand function	Points
Grasping	/36
Manipulating	/40
Lifting	/14
IN TOTAL	/90

Grasping

Active/firm grip = Object is firmly grasped with active finger force

Passive/*loose grip* = Object is loosely grasped with the help of passive tension in fingers (e.g. tenodesis grasp)

Manipulating

Slight difficulty = Patient has minor problems to manipulate object successfully.

Great difficulty = Patient has major struggles to manipulate object successfully

Compensation = Patient needs compensation strategy to manipulate object successfully. Compensatory strategies include actions in which both hands are used for a one-handed activity, in which the object is pressed against torso for manipulation or in which the object is pinched between legs for manipulation.

Lifting

In lifted position = Object are supposed to have no contact to any surface (including trunk) while manipulating. To score, elbows can rest on the table as long as object is in midair.

Observe the patient during the tasks and check the box if mentioned activity is observable. In case mentioned activity is not observable, the associated box is not to be checked and no point are given. Add point for each task and each component and transfer score to overview table.

1. Charge a smartphone

Grasping

Smartphone is grasped with active/firm grip ☐ = 2
- with passive/loose grip ☐ = 1

Charging cable is grasped with active/firm grip ☐ = 2
- with passive/loose grip ☐ = 1

Manipulating

Smartphone is plugged without difficulty ☐ = 4
- with slight difficulty ☐ = 3
- with great difficulty ☐ = 2
- with compensation ☐ = 1

Lifting

Smart phone is plugged in lifted position ☐ = 2

Total: ___/10

2. Open a water bottle

Grasping

Water bottle is grasped with active/firm grip ☐ = 2
- with passive/loose grip ☐ = 1

Lid is grasped with active/firm grip ☐ = 2
- with passive/loose grip ☐ = 1

Manipulating

Water bottle is opened without difficulty ☐ = 4
- with slight difficulty ☐ = 3
- with great difficulty ☐ = 2
- with compensation ☐ = 1

Lifting

Water bottle is opened in lifted position ☐ = 2

Total = ___/10

3. Pour a glass of water

Grasping

Water bottle is grasped with active/firm grip ☐ = 2
- with passive/loose grip ☐ = 1

Glass is grasped with active/firm grip ☐ = 2
- with passive/loose grip ☐ = 1

Manipulating

Glass is poured without difficulty ☐ = 4
- with slight difficulty ☐ = 3
- with great difficulty ☐ = 2
- with compensation ☐ = 1

Lifting

Glass is poured in lifted position ☐ = 2

Total= ___/10

Figure 3: Scoring sheet BeBiTT (part 1)

From: Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17

Scoring Sheet BeBiTT

Patient´s name/ ID: ______________________________

Examiner Name: ______________________________

Date: ______________________________

Comment: ______________________________

4. Rinse a plate

Grasping	
Plate is grasped with active/firm grip	☐ = 2
– with passive/loose grip	☐ = 1
Sponge is grasped with active/firm grip	☐ = 2
– with passive/loose grip	☐ = 1
Manipulating	
Plate is rinsed without difficulty	☐ = 4
– with slight difficulty	☐ = 3
– with great difficulty	☐ = 2
– with compensation	☐ = 1
Lifting	
Plate is rinsed in lifted position	☐ = 2

Total = ___/10

5. Cut meat-like putty

Grasping	
Fork is grasped with active/firm grip	☐ = 2
– with passive/loose grip	☐ = 1
Knife is grasped with active/firm grip	☐ = 2
– with passive/loose grip	☐ = 1
Manipulating	
Putty is cut without difficulty	☐ = 6
– with slight difficulty	☐ = 4
– with great difficulty	☐ = 3
– with compensation	☐ = 2

Total = ___/10

6. Open toothpaste

Grasping	
Toothpaste is grasped with active/firm grip	☐ = 2
– with passive/loose grip	☐ = 1
Lid is grasped with active/firm grip	☐ = 2
– with passive/loose grip	☐ = 1
Manipulating	
Toothpaste is opened without difficulty	☐ = 4
– with slight difficulty	☐ = 3
– with great difficulty	☐ = 2
– with compensation	☐ = 1
Lifting	
Toothpaste is opened in lifted position	☐ = 2

Total = ___/10

7. Put toothpaste on toothbrush

Grasping	
Toothpaste is grasped with active/firm grip	☐ = 2
– with passive/loose grip	☐ = 1
Toothbrush is grasped with active/firm grip	☐ = 2
– with passive/loose grip	☐ = 1
Manipulating	
Toothpaste is put on brush without difficulties	☐ = 4
– with slight difficulty	☐ = 3
– with great difficulty	☐ = 2
– with compensation	☐ = 1
Lifting	
Toothpaste is put on brush in lifted position	☐ = 2

Total = ___/10

8. Take note out of wallet

Grasping	
Wallet is grasped with active/firm grip	☐ = 2
– with passive/loose grip	☐ = 1
Note is grasped with active/firm grip	☐ = 2
– with passive/loose grip	☐ = 1
Manipulating	
Note is taken out of wallet without difficulty	☐ = 4
– with slight difficulty	☐ = 3
– with great difficulty	☐ = 2
– with compensation	☐ = 1
Lifting	
Note is taken out of wallet in lifted position	☐ = 2

Total = ___/10

9. Close zipper of a jacket

Grasping	
Jacket is grasped with active/firm grip	☐ = 2
– with passive/loose grip	☐ = 1
Zipper is grasped with active/firm grip	☐ = 2
– with passive/loose grip	☐ = 1
Manipulating	
Zipper is closed without difficulties	☐ = 6
– with slight difficulty	☐ = 4
– with great difficulty	☐ = 3
– with compensation	☐ = 2

Total = ___/10

Figure 4: Scoring sheet of BeBiTT (part 2)

From: Angerhöfer et al., 2023, J NeuroEngineering *Rehabil 20, 17*

2.6 Discussion

The present chapter demonstrated the development of a new measurement tool and introduced the BeBiTT. This way, the lack of existing tests to assess bimanual function in individuals with tetraplegia has been addressed. Beginning with the generation of items from patients and experts, through item selection according to a predefined theoretical framework, up to feasibility testing, the development of the BeBiTT followed a clear and coherent structure. Selected items were shown to comprise of common grasp pattern applied in daily life, include various bimanual actions according to Kantak et al. (2017) and reflect main components of bimanual function (grasping, lifting, manipulating). Further, selected items align with the International Classification of Functioning of Health and Disability, reflecting body function, activity, and participation. An expert panel confirmed robust agreement with the construct of bimanual function, with 15 items demonstrating high content validity as evidenced by a Content Validity Ratio (CVR) > 0.78 (Lawshe, 1975). Following the results of the feasibility study, the final version of the BeBiTT consists of 9 items that are practicable and quick to assess, balanced in task difficulty and composed of reusable and affordable equipment. Items did not cause measurable fatigue or physical exhaustion and did not expose the participants to any physical or mental risk. The BeBiTT's scoring system uses an interval scaled score and systematically assesses item performance in relation to components of bimanual function (grasping, lifting, manipulating). To detect minimal improvement, components are evaluated in a detailed manner. For each item within the BeBiTT, 10 points can be achieved, resulting in an overall score of 90 points that reflects level of bimanual function in individuals with tetraplegia.

Although the BeBiTT´s theoretical framework provides a clear and coherent guide for item development, it also has drawbacks. Relevant bimanual tasks such as 'light a cigarette' and 'drive a car' were not regarded as possible items since they cannot not be easily assessed in research and clinical setting. Further, to keep hygiene standards and compatibility with state-of-the-art tools in neurotechnology, bimanual tasks such as self-catheterization and body care could not be included within the BeBiTT. However, these tasks represent very important ADLs in the lives of persons with tetraplegia. Additionally, by restricting administration time and reducing items to a minimum for the cause of practicability, items were discarded that might assessed bimanual function more comprehensively. In response, it makes sense to consider introducing a long version of the BeBiTT that includes more items. In terms of safety, comprehensibility, and fatigue, larger sample sizes may have been needed to further support the feasibility of the BeBiTT. Moreover, the lack of standardized protocols in test development, especially in performance-based assessment, might have influenced the quality of the BeBiTT, even though the methodologies proposed by Lynn (1986) and Streiner et al. (2015) were followed.

After having designed a new measurement tool, it must be evaluated according to common psychometric features (Streiner et al., 2015). For a clinical test to be acknowledged, it is to be demonstrated that measuring individuals under different circumstances produce the same or similar results (reliability), and that the test is really measuring what it is supposed to measure (validity). Therefore, the next chapter illustrates the validation of the BeBiTT in a larger sample of 14 tetraplegic individuals. Beyond that, the next chapter examines the effects of a hybrid brain/neural hand exoskeleton (B/NHE) on bimanual function in person with tetraplegia using the BeBiTT. This way the BeBiTT´s suitability to evaluate modern assistive devices such as BCI-based hand exoskeletons is demonstrated.

3. Assessment of brain/neural hand exoskeleton

Brain-controlled hand exoskeletons have not been studied yet for their effects on bimanual function in persons with tetraplegia. Therefore, in a second step of the present work, the change in bimanual function induced by the application of a hybrid brain/neural hand exoskeleton (B/NHE) is investigated with the newly developed BeBiTT. Given the relevance of bimanual tasks in daily life, such evaluation provides further information on the capability of modern assistive devices to restore hand function following cSCI. Further, the BeBiTT's psychometric properties are assessed in this section to support its reliability and validity as a clinical assessment.

3.1 Methods

To detect change in bimanual function induced by B/NHE application, a non-randomized interventional study design was chosen. Here, the BeBiTT was performed without intervention (baseline condition) and then while participants were wearing a B/NHE system on one hand (intervention). The baseline test was used to evaluate the psychometric characteristics of the BeBiTT, namely internal consistency, interrater-reliability, and construct validity.

3.1.1 Participants

“14 persons with tetraplegia were recruited (13 male, 1 female, mean age 48.6 ± 18.5) with complete (n = 6; ASIA grade A) and incomplete (n = 8; ASIA grades B - D) cervical SCI (C4 to C6). Recruitment took place at the University Hospital of Tübingen, Charité - University Medicine Berlin and Neurological Rehabilitation Clinic Beelitz-Heilstätten. Participants were selected based on the following inclusion criteria: Age between 18 and 85 years; interval after SCI at least 6 months; lesion height C4 – C6, ASIA grade A – C. Exclusion criteria were the following: Consumption of alcohol (more than 2 alcoholic beverages per day), illegal drug consumption, severe neurological disease other than SCI (e.g., multiple sclerosis, stroke and cerebral palsy), severe medical conditions (e.g., renal failure, liver insufficiency, heart failure, malignant tumor disease), serious cognitive impairment (minimum status below 23 points) and severe spasticity (Ashworth grade ≥ 4). All 14 participants took part in the baseline test. 10 out of 14 participants (10 male, mean age 44.7 ±14.6) with complete (n=5; ASIA grade A) and incomplete (n=5; ASIA grades B to D) cSCI (C5 to C6) participated in the intervention and completed the BeBiTT again while wearing a B/NHE. The reasons why four participants refrained to participate in the intervention condition were due to inability to wear the hand exoskeleton, arthritic pain, upcoming hand surgery and skepticism towards modern neurotechnology" (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17).

3.1.2 Study procedure

All tests took part in specified rooms of the Applied Neurotechnology lab at the University Hospital of Tübingen, of the Clinical Neurotechnology lab at the Charité – University Medicine Berlin, Campus Mitte (CCM), or at the Neurological Rehabilitation Clinic Beelitz. At the beginning, all participants provided their informed consent, which included consent to be video-taped. For the baseline test of the BeBiTT, the participant was comfortably placed with the wheelchair in front of a desk. The items of the BeBiTT were explained, and its proper execution was demonstrated to the participant by the instructor. "The participant was encouraged to perform the tasks as close to the instructor's demonstration as possible. The participant was reminded of the importance to use both hands and to avoid compensatory strategies if possible" (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17). The participant could try each item various times until either success or decision to give up. The entire baseline administration was videotaped.

Participants who were willing to repeat the BeBiTT while wearing the B/NHE (intervention) were given a short break to relax. Then, the exoskeleton was mounted on the participant´s weaker hand. The participant was prepared with an EEG cap and EOG electrodes (see chapter 3.1.3). After successful BCI calibration (see chapter 3.1.4), participants were given a few minutes to get used to the control paradigm of the B/NHE. Subsequently, the BeBiTT assessment was conducted once again, following the same procedure as in the baseline condition, but this time with use of the B/NHE system. Participants were reminded that if at any point they felt pain, discomfort or wanted to rest, they should immediately say so. The performance of all items within the intervention condition was videotaped. After completion, all participants (also including those who only took part in the baseline testing) were interviewed on the self-care category of SCIM and QIF-SF. Those who participated in the intervention were asked to answer further questions regarding the safety and feasibility of the B/NHE.

3.1.3 Experimental setup and signal processing

The applied B/NHE system uses brain signals (event-related desynchronization of the sensorimotor rhythm (SMR-ERD)) recorded via EEG to identify intended motor behavior and transfer it into closing motions of a hand exoskeleton. Horizontal oculoversions (HOV) in electrooculogram (EOG) were used to stop closing motions and to control the exoskeleton’s opening. The hand exoskeleton in question was the Handy Rehab hand exoskeleton from Zunosaki Ltd., Hong Kong (Figure 5). The Handy Rehab is a wireless and lightweight robotic hand exoskeleton, originally design for stroke rehabilitation. It consists of 9 autonomous motor units that allow precise hand closing.

Figure 5: The Handy Rehab hand exoskeleton

From: Zunosaki Ltd., Hong Kong

Brain signals were recorded through a 9-channel EEG system from conventional recording sites (F3, T3, C3, P3, Cz, P4, C4, T4, F4) according to the international 10/20 system (Figure 6). Reference electrode was placed at FCz and ground electrode was placed at AFz. The side contralateral to the hand that wears the exoskeleton was selected for further signal procession (i.e., C3 for right hand exoskeleton control and C4 for left hand exoskeleton control with the respective four surrounding electrodes). For signal acquisition and processing, the Smarting amplifier and software (mBrainTrain, Serbia) and a semi-dry saline-based cap by Wuhan Greentek Pty. Ltd (Wuhan, China) were used. Signals were recorded at a sampling frequency of 500Hz and filtered between 0.1Hz and 70Hz using a Butterworth filter. To minimize the signal-to-noise ratio of the targeted electrodes C3 or C4, a surface Laplacian filter was employed, subtracting the activity measured in the surrounding electrodes from the target electrodes.

To identify horizontal eye movements (HOV), two electrodes were positioned on the outer canthus of both the right and left eyes. By subtracting the left outer canthus electrode signal from the right outer canthus electrode signal, the EOG signal was transformed into a bipolar signal. This conversion effectively reduced noise resulting from vertical eye movements and eyeblinks. The EOG signal was low-pass filtered at 1.5Hz, removing high-frequency noise.

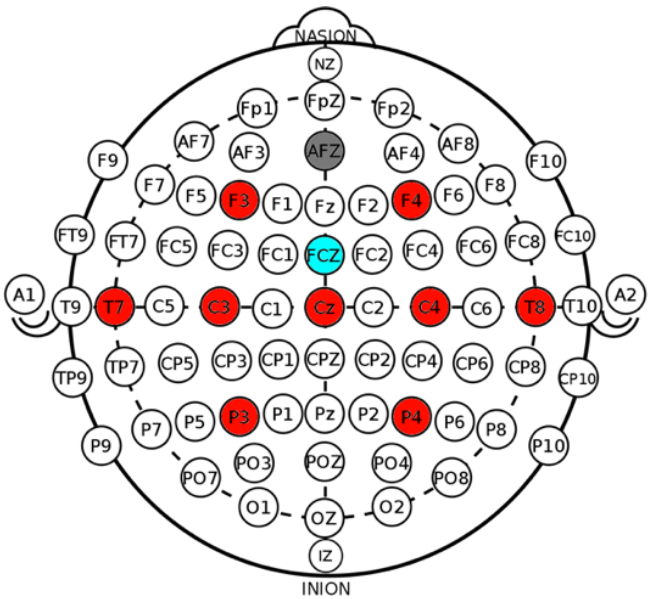

Figure 6: EEG recording sites according to the international 10/20 system.

Recording electrodes are marked in red, reference electrode in light blue and ground electrode in grey.

For the online brain/neural control of the hand exoskeleton, the signals were streamed to a real-time signal processing unit translating EEG and EOG signals into control signals of the hand exoskeleton, using a modified version of the BCI2000 software platform (available at www.bci2000.org). Detection of SMR-ERD (voluntarily generated by motor imagery and/or intended motor behavior) resulted in sending a closing command to the exoskeleton. As a veto command, detection of HOV stopped the closing motion of the hand exoskeleton immediately. Once stopped or fully closed, the exoskeleton could be opened through a HOV, and by detection of another HOV, the exoskeleton became again responsive for SMR-ERD control.

3.1.4 Brain-computer interface calibration

For the EOG calibration, a screen was placed in front of participants on which an arrow appeared, cueing them to perform a maximal horizontal ocular movement (HOV) for 10 times. The detection threshold for HOV was set to 2/3 of the median maxima of all EOG-single trial outputs.

For calibration of the EEG-based hand exoskeleton control, participants were instructed to attempt to close the hand that was chosen for exoskeleton application for the whole duration that a corresponding cue (‘Close hand’) appeared on a screen. This was alternated with a cue ‘relax’ asking participants to rest. The Frequency of Interest (FOI) was individually adjusted to the optimal SMR frequency for each participant. Detection thresholds (TH) for individual SMR event-related desynchronization (SMR- ERD) were determined based on the average ERD observed during all 'close' phases (Figure 7).

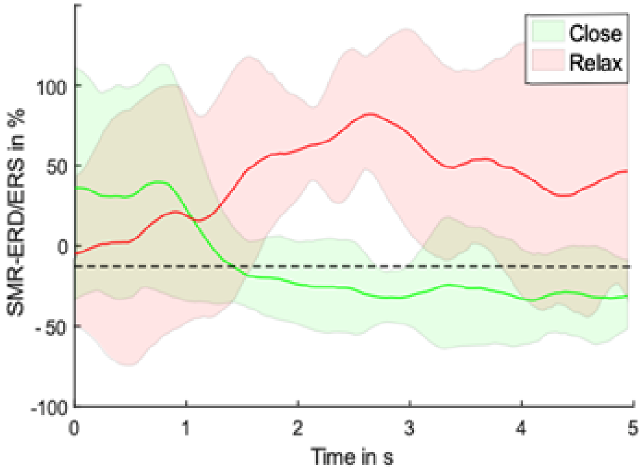

Figure 7: Example data of the sensorimotor rhythm

The red line shows the power spectrum of the Frequency of Interest (FOI) at the relax conditions. The green line shows the power spectrum of the FOI during attempted hand closing, representing the event-related desynchronization of the sensorimotor rhythm (SMR-ERD). The SMR-ERD detection threshold (TH) is indicated with the black dotted line. Shaded areas represent the 95% Confidence Interval for average close and relax conditions, respectively.

In a second calibration run, participants were provided with visual feedback on their SMR-ERD performance. In case the power spectrum of the FOI falls below the TH, a cue, represented by a

Pacman on a screen closing its mouth, visualized successful performance of the SMR-ERD. This allowed the participant in real time to adjust the strategy to generate an SMR-ERD. Finally, individual SMR-ERD detection threshold was adjusted to the average ERD elicited within all ‘close’ phases of both calibration trials.

3.1.5 Material list

To assess bimanual function in both the intervention and baseline condition, the final version of the BeBiTT was applied. For material list of items, see Table 7. As cutlery appeared to be too slippery to be grasped with the hand exoskeleton, rubber handles were used in both the baseline and intervention condition for the item *Cut meat-like putty*.

Table 7: Material List BeBiTT

Item	Material
Charge a smart phone	Common smart phone (e.g. iPhone 6, Samsung Galaxy S20) Corresponding charging cable
Open a water bottle	1 liter plastic bottle of water (filled), screwed on by hand
Pour glass of water	1 liter plastic bottle of water (filled) Water glass (200ml, empty)
Rinse a plate	Dinner plate (approx. 25 cm in diameter) Kitchen sponge
Cut meat-like putty	Medium resistance putty resembling the consistency of a piece of meat Knife and fork Rubber handles
Open toothpaste	Normal 75ml toothpaste with screwed lid, >50% full
Apply toothpaste on toothbrush	Normal 75ml toothpaste with screw lid, >50% full Toothbrush
Take note out of wallet	Common leather wallet 10 Euro note
Close zipper of a jacket	Metal zipper in a jacket

From: Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17

3.1.6 Data management and analysis

The study protocol complied with the Declaration of Helsinki. Approval from the Ethical Committee of the Medical Faculty of the University of Tübingen, with Reference Number 201/2018BO1, was obtained in accordance with ethical guidelines. All data was anonymized prior to paper entry. Test scoring was obtained by evaluating video recordings of the participants (baseline and intervention) with the BeBiTT scoring system (chapter 2.6).

After having scored the participants, internal consistency of the BeBiTT was assessed by calculating Cronbach's alpha using SPSS version 27 (SPSS, Inc., Chicago, IL). Internal consistency evaluates whether items designed to measure the same underlying construct produce similar outcomes (Streiner et al., 2015). Alpha values above 0.7 are considered as acceptable, above 0.8 as good and above 0.9 as excellent. To further assess internal consistency, the corrected item-total correlations for all items were calculated by Pearson's correlation of a particular item with the total score omitting that item. Corrected item-total correlation is supposed to be above 0.30, otherwise the item should be discarded (Kline, 2015).

Three independent raters' scores were obtained to assess the interrater reliability of the BeBiTT. A physiotherapist with 20 years of working experience and two members of the lab who were not involved in the test development were asked to rate the video recordings of the participants (both baseline and intervention). "The raters were blinded to the participants' diagnosis and AISA classification. Raters were given the scoring sheet [Chapter 2.6] along with a short explanation of the scoring system. Raters were asked to fill out the scoring sheets for each participant individually and not to discuss the video clips or the assigned scores with each other" (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17). The constellation of the raters was chosen to account for a clinical (physiotherapist) as well as research setting (lab members). Interrater reliability measures to which extent the scores assigned by different raters produce similar and consistent outcomes (Streiner et al., 2015). "Agreement in scores between raters (interrater reliability) was tested by calculating the intraclass correlation coefficient (ICC) using SPSS version 27. The ICC was calculated based on an absolute-agreement, 2-way mixed-effects model" (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17). The ICC reflects the proportion of variance between different raters. The ICC can range from 0 (no agreement) to 1 (perfect agreement). According to Koo and Li (2016), ICC below 0.5 is poor, between 0.5 and 0.75 is moderate, between 0.75 and 0.90 is good and above 0.90 is excellent.

Construct validity is evaluated by examining the correlation between the test and variables that are known or suggested to be associated with the test´s construct (Streiner et al., 2015). For evaluation of the BeBiTT´s construct validity, two commonly used

ADL tests were employed: the self-care category of the Spinal Cord Independence Measure III (SCIM III) and the Quadriplegia Index of Function-Short Form (QIF-SF) (Catz et al., 1997; Marino & Goin, 1999) (Appendix C). While both the SCIM III and QIF-SF assess a broader range of functions beyond hand function alone, they include many bimanual activities and thus related to the BeBiTT´s test construct. Especially with the SCIM self-care category, it has been shown that it contains useful items that are related to upper extremity function (Rudhe & van Hedel, 2009). To reduce participation time, assessment of the SCIM III and QIF-SF was obtained by interview. “The construct validity of the BeBiTT was assessed by computing Pearson’s correlation coefficient [represented by r] between BeBiTT baseline scores and the SCIM III self-care category as well as the QIF-SF” (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17). An r value of 0.1 to 0.3 was considered as weak correlation, 0.3 to 0.5 as moderate correlation, and anything above 0.5 as strong correlation.

To test for differences in the BeBiTT scores before (baseline) and during the application of the B/NHE (intervention), “a non-parametric bootstrapped paired t-test with 1000 permutations was applied using SPSS version 27” (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17). As sample size was small (n=10) and normality distribution could not be assumed (skewness = -1.40; kurtosis = 2.12), the bootstrap method for paired matches appeared most suitable. It has been shown that bootstrap schemes are valid procedures for matched pairs (Konietschke & Pauly, 2014). Further, descriptive analysis was carried out to show detailed difference between baseline and intervention.

3.2 Results

3.2.1 Reliability and validity

An internal consistency analysis was carried out comprising all nine items of the BeBiTT baseline. Cronbach's alpha showed to reach α = 0.91. Most items appeared to result in a decrease in the alpha if deleted. The two exceptions were the items *Pour glass of water* and *Put toothpaste on toothbrush*, which would marginally enhance the alpha to α = 0.92 if discarded (Table 8). For an exploratory analysis of internal consistency, the corrected item-total correlations were calculated. "All tasks of the BeBiTT positively correlated with the overall score and exceed the threshold of $r > 0.30$" (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17) (Table 8).

Table 8: Internal consistency analysis

Items	Corrected Item - Total Correlation	Cronbach's Alpha if Item Deleted
Charge a smart phone	0.862	0.891
Open a water bottle	0.840	0.886
Pour glass of water	0.411	0.919
Rinse a plate	0.663	0.900
Cut meat-like putty	0.859	0.886
Open toothpaste	0.937	0.877
Apply toothpaste on toothbrush	0.435	0.920
Take note out of wallet	0.810	0.895
Close zipper of a jacket	0.633	0.903

From: Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17

To test for agreement among raters (n = 4) in baseline condition, ICC was calculated. For agreement of raters in single values, "ICC was 0.959 with a 95% confidence interval (CI) from 0.811 to 0.985, F(13,39) = 101.5" (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17), p < 0.001. For agreement of raters in means, ICC was "0.989 with a 95% CI [0.976; 0.996], F(13,39) = 101.5" (Angerhöfer et al., 2023, J NeuroEngineering

Rehabil 20, 17), $p < 0.001$. For detailed overview of each raters' scoring, see Table 9.

Table 9: Baseline BeBiTT scores of all raters

Participant	Rater 1	Rater 2	Rater 3	Rater 4	Mean	SD
ID_1SCI	69	70	63	64	66.5	2.72
ID_2SCI	45	45	42	47	44.8	1.60
ID_3SCI	42	43	45	41	42.8	1.32
ID_4SCI	38	46	37	38	39.8	3.25
ID_5SCI	28	25	35	24	28.0	3.85
ID_6SCI	65	68	71	70	68.5	2.05
ID_7SCI	67	70	69	75	70.3	2.64
ID_8SCI	56	57	59	69	60.3	4.62
ID_9SCI	39	40	45	48	43.0	3.29
ID_10SCI	75	73	71	88	76.8	5.95
ID_11SCI	0	0	0	0	0.0	0.00
ID_12SCI	58	72	62	79	67.8	7.39
ID_13SCI	35	34	33	36	34.5	1.00
ID_14SCI	23	22	21	17	20.8	2.04
Mean	45.7	47.5	46.6	49.7	47.4	
SD	20.1	21.5	20.0	24.7	21.3	

"To assess construct validity of the BeBiTT, Pearson's correlation was calculated between the BeBiTT baseline scores ($M = 45.7$, $SD = 20.8$) and scores in SCIM III self-care category ($M = 11.6$, $SD = 6.00$) as well as QIF-SF scores ($M = 16.0$, SD =

6.62) [of all participants (n = 14)]. There was a strong correlation between BeBiTT baseline scores and SCIM self-care category scores, r(14) = 0.77, p < 0.001 [Figure 8]. Also, BeBiTT baseline scores and QIF-SF scores were positively correlated, r(14) = 0.66 , p = 0.011 [Figure 9]” (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17).

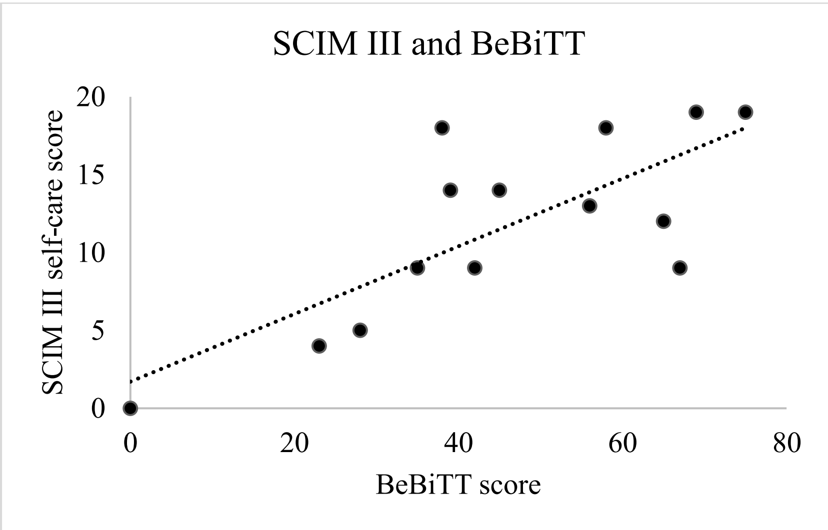

Figure 8: Correlation between BeBiTT scores and SCIM III scores

Correlation of the Berlin Bimanual Test for Tetraplegia (BeBiTT) scores compared to scores of the Spinal Cord Independence Measure III (SCIM III) self-care category (r = 0.77).

From: Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17

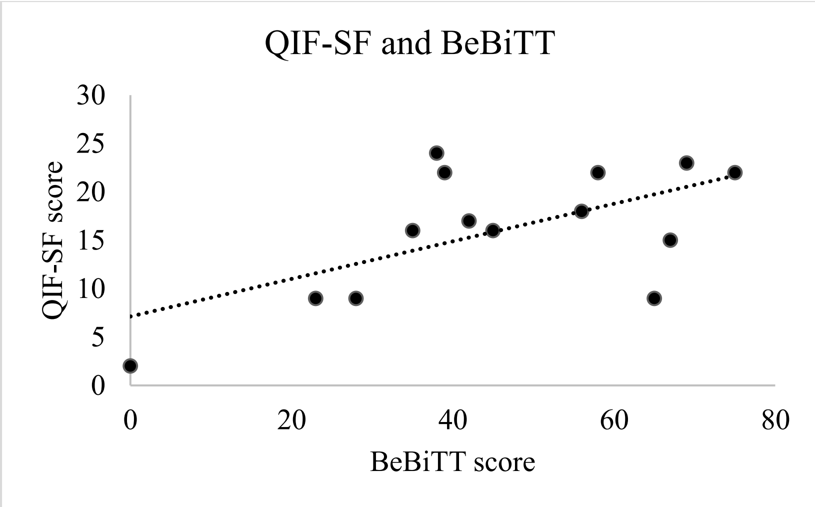

Figure 9: Correlation between BeBiTT scores and QIF-SF scores

Correlation of the Berlin Bimanual Test for Tetraplegia (BeBiTT) scores compared to scores of the Quadriplegia Index of Function – Short Form (QIF-SF) (r = 0.66).

From: Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17

3.2.2 Brain/neural hand exoskeleton use

"On average, participants (n=10) improved significantly in BeBiTT score with use of a B/NHE system (M = 59.8, SD = 17.4) compared to baseline condition (M = 48.2, SD = 17.7), p = 0.029" (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17). Boxplots further illustrate improvement between intervention (median = 55.5, SD = 17.4; q_n (0.25) = 50.3; q_n (0.75) = 70.5) and baseline condition (median = 43.5, SD = 17.4; q_n (0.25) = 38.3; q_n (0.75) = 61.5) (Figure 10).

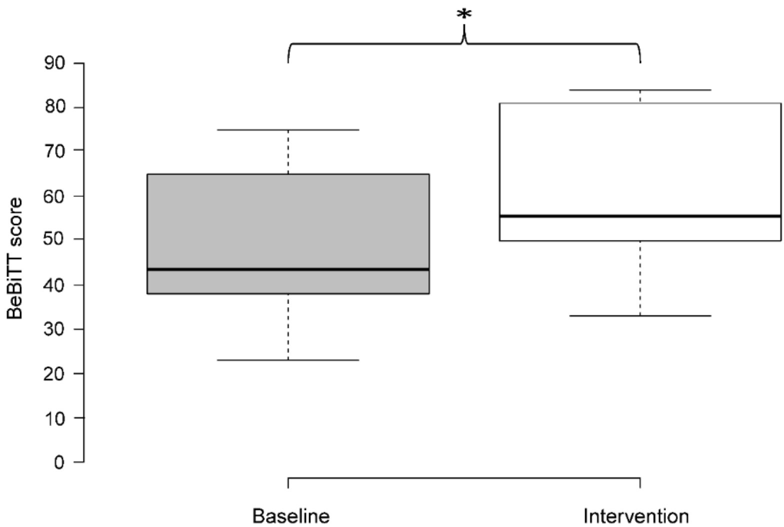

Figure 10: Difference in BeBiTT scores without (baseline) and with use of a B/NHE (intervention)

*Centerlines show the medians. Box limits indicate the 25th and 75th percentiles. Upper and lower whiskers illustrate maximum and minimum, respectively. *p < 0.05*

From: Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17

“The bootstrapped (N = 1000) difference in means was tested for normality and homogeneity of variance and appeared to be normally distributed with skewness of -0.38 (SE = 0.023) and kurtosis of 0.08 (SE = 0.047)” (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17) (Figure 11). Bootstrapped 95% confidence interval (CI) for difference in means was not including zero [6.1;16.4] (Figure 11).

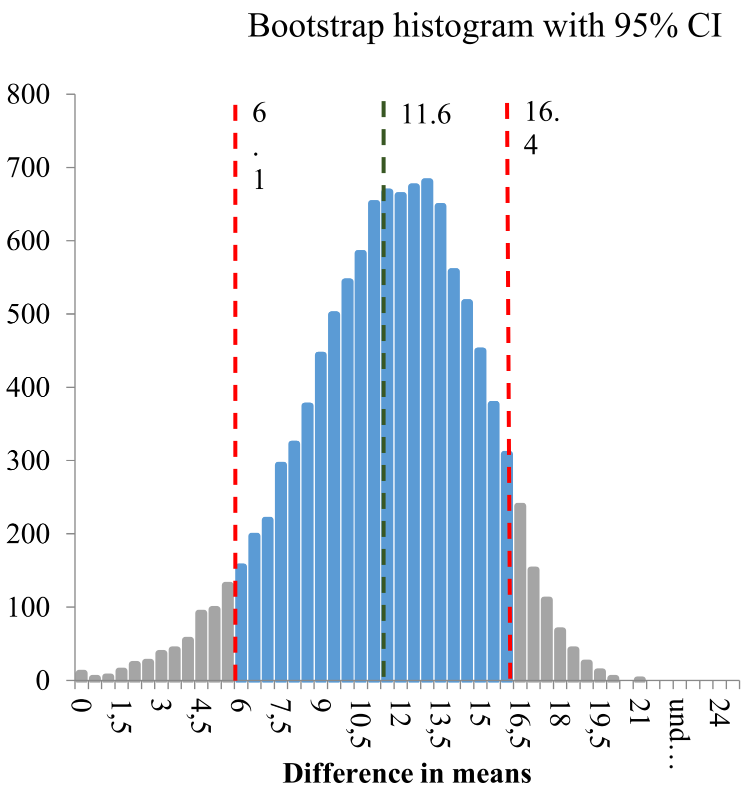

Figure 11: Bootstrapped distribution of difference in means

Bootstrapped difference in means of the baseline condition and intervention (with B/NHE). Lower and upper limits of the 95% confidence interval (CI) are shown with red lines, the mean with green line.

"Among participants, all components of bimanual function (grasping, manipulating, lifting) improved by use of the B/NHE compared to baseline condition [Table 10]. In lifting, the average score improved by more than 50% from 5.8 (SD = 4.3) to 8.8 points (SD = 4.2), $p = 0.048$. Significant improvement was also shown in grasping from baseline (M = 19.8, SD = 4.8) to intervention (M = 27.3, SD = 5.4), $p < 0.001$. Mean score in manipulating slightly but not significantly improved from 22.6 (SD = 9.9) to 23.6 points (SD = 8.5), $p = 0.59$" (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17).

Table 10: Improvement in BeBiTT score for components of bimanual function

Components of bimanual function	BeBiTT score without B/NHE	BeBiTT score with B/NHE	Improvement (%)
Grasping	19.8 ± 4.8	27.3 ± 5.4	37.9
Manipulating	22.6 ± 9.9	23.6 ± 8.5	4.4
Lifting	5.8 ± 4.3	8.8 ± 4.2	51.7

Values are shown as means ± SD, From: Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17

On average, all items of the BeBiTT were scored higher in the intervention (with B/NHE) compared to baseline condition (Table 11). The items *Charge smart phone* showed the largest improvement in score (41.2 %), followed by the item *Open toothpaste* (36.2%) and *Rinse a plate* (34.8%). The items *Open water bottle* and *Pour glass of water* increased moderately in score (31.8%; 29.3%). Little to moderate improvement was detected in the items *Cut meat-like putty* (17.3%) and *Close zipper of a jacket* (14.3%). Little improvement could be seen in the items *Apply toothpaste on toothbrush* (3.6%) and *Take note out of wallet* (6.5%).

Table 11: Improvement in BeBiTT score for all items

Items	BeBiTT score without B/NHE	BeBiTT score with B/NHE
Charge a smart phone	5.10 ± 1.73	7.20 ± 2.25
Open a water bottle	4.40 ± 2.55	5.80 ± 3.29
Pour glass of water	5.80 ± 2.78	7.50 ± 2.64
Rinse a plate	6.60 ± 2.12	8.90 ± 1.37
Cut meat-like putty	5.20 ± 2.35	6.10 ± 2.18
Open toothpaste	4.70 ± 2.95	6.40 ± 2.84
Apply toothpaste on toothbrush	5.50 ± 2.95	5.70 ± 3.50
Take note out of wallet	7.70 ± 1.64	8.20 ± 1.87
Close zipper of a jacket	3.50 ± 2.92	4.00 ± 2.62

Values are shown as means ± SD, From: Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17

Participants with incomplete cSCI (ASIA grade B - D, n=5) improved on average 13.6 points in BeBiTT scores, while participants with complete cSCI (ASIA grade A, n= 5) improve only 8.1 points (Table 12). Participants with more than one-year post injury (n=8), improved on average 15.1 points in the BeBiTT score, whereas participants with less one-year post injury decreased in score (-4.5%) with use of the B/NHE system (Table 12).

Table 12: Improvement in BeBiTT score for demographic features

Demographic features	BeBiTT score without B/NHE	BeBiTT score with B/NHE	Improvement (%)
ASIA grade A	43.7 ± 15.3	51.8 ± 16.7	18.7
ASIA grade B and C	44.0 ± 17.1	57.6 ± 15.9	30.9
> 1 year post injury	49.3 ± 16.4	64.4 ± 15.8	30.7
< 1 year post injury	44.0 ± 29.7	42.0 ± 12.7	-4.5

Values are shown as means ± SD

9 out of 10 participants achieved higher results in the overall BeBiTT score with use of a B/NHE system compared to baseline condition (Table 13). *ID_5SCI* showed the greatest improvement in the BeBiTT score with an improvement of 78.6% from 28 points (baseline) to 50 points (intervention). *ID_4SCI* improved

from initially 38 points in the BeBiTT baseline score to 57 points with use of the B/NHE system (improvement of 50%). *ID_12SCI* and *ID_14SCI* improved their score of approximately 40% (39.7%; 43.5%). Moderate improvement was detected in *ID_1SCI* (21.7%), *ID_2SCI* (33.3%) and *ID_9SCI* (28.6%) and little improvement in *ID_10SCI* (10.7%) and *ID_3SCI* (7.1%). Only *ID_6SCI* performed worse with the use of the B/NHE system. His score decreased by 14 points (-21.5%).

Table 13: Improvement in BeBiTT score among all participants

Participant	**BeBiTT score without N/BHE**	**BeBiTT score with B/NHE**	**Change in score**	**Improvement (%)**
ID_1SCI	69	84	15	21.7
ID_2SCI	45	60	15	33.3
ID_3SCI	42	45	3	7.1
ID_4SCI	38	57	19	50.0
ID_5SCI	28	50	22	78.6
ID_6SCI	65	51	-14	-21.5
ID_9SCI	39	54	15	38.5
ID_10SCI	75	83	8	10.7
ID_12SCI	58	81	23	39.7
ID_14SCI	23	33	10	43.5
Mean	48.2	59.8	11.6	
SD	17.7	17.4	10.9	

From: Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17

To test for agreement in rating within the intervention, ICC was calculated among all rater and participants. For agreement of raters in single values, ICC was “0.950 with a 95% CI from 0.858 to 0.986, F(9,27) = 116.5” (Angerhöfer et al., 2023, J

NeuroEngineering Rehabil 20, 17), p<.001. For agreement of raters in means, ICC was “0.987 with a 95% CI [0.960; 0.997], F(9,27) = 116.5” (Angerhöfer et al., 2023, J NeuroEngineering Rehabil 20, 17), p<.001. Among all participants that participated in the intervention, no safety concerns were expressed while wearing the N/BHE system.

3.3 Discussion

In the present chapter, the psychometric evaluation of the BeBiTT was conducted, indicating excellent reliability and validity. Cronbach’s alpha (0.91) surpassed the threshold for clinical instruments (> 0.9), thereby demonstrating excellent internal consistency of the BeBiTT. We chose to retain the two items (*Pour glass of water* and *Apply toothpaste on toothbrush*) despite their minimal negative impact on the alpha score. Eliminating these items could have slightly enhanced the internal consistency of the BeBiTT. Nevertheless, considering the already exceptional alpha score of 0.91 when all items are included, along with the limited number of items, we opted against removing them. Further, items of the BeBiTT have positive exploratory results, as evidenced by the corrected item-total correlation coefficients $r > 0.30$ for each item.

Interrater reliability was excellent in the baseline condition, as evidenced by an ICC above 0.9, providing further prove of the BeBiTT's reliability. Excellent ICC within the intervention indicates that the BeBiTT can reliably assess state-of-the-art tools in neurotechnology such as a BCI-based hand exoskeleton. The BeBiTT's construct validity is supported by a strong positive correlation between the baseline BeBiTT scores and the SCIM III self-care category as well as the QIF-SF. Considering these findings together with the content validity assessment (chapter 2.3), it can be assumed that the BeBiTT does indeed measure what it is supposed to measure – that is bimanual function in persons with tetraplegia.

Despite the promising results in validity and reliability assessment, psychometric evaluation of the BeBiTT must be consolidated by conducting reliability and validity studies with larger sample sizes. Only by providing further robust psychometric evaluation, the BeBiTT can be established as a commonly used tool in research and clinical environment.

Next to conducting the psychometric evaluation of the BeBiTT, improvement in bimanual function induced by a B/NHE was evaluated among persons with tetraplegia. The BeBiTT scores increased significantly in the intervention, demonstrating that bimanual function substantially improved with the help of the

B/NHE. Given that tetraplegic individuals usually perform passive tenodesis grasp (Johanson & Murray, 2002), a hand exoskeleton that enabled the fingers to actively close and generate a strong grip represented a substantial improvement in bimanual tasks. Further, a firm grip performed by the hand exoskeleton allowed participants to securely lift objects. Thus, bimanual tasks could be comfortably performed in lifted position, resulting in an increased lifting score in the intervention. Manipulating, however, did not significantly improved with the use of the B/NHE. One reasons for this could be that participants may have faced problems to perform fine and complex manipulation task due to the unwieldiness of the device and their inexperience in using a hand exoskeleton.

Generally, participants who initially scored below 40 points on the BeBiTT baseline assessment showed the most substantial improvement, with their initial BeBiTT scores increasing by 43.5% up to 78.6%. This finding suggests that tetraplegics with more severely impaired bimanual function benefit the most from the use of a B/NHE. Participants with incomplete cSCI (ASIA B - D) showed a relatively larger improvement in BeBiTT scores compared to participants with complete cSCI (ASIA A). Likewise, this was found for participants with more than one-year post injury compared to participants with less than one year post injury. Although the current work represents a study with the largest sample size that has ever been conducted to assess a BCI-based hand exoskeleton in persons with tetraplegia, larger samples are necessary to draw more general conclusions regarding demographic features such as ASIA classification and time since injury.

Within the assessment of the B/NHE system, confounding variables, such as fatigue and tiredness, were not directly controlled. These parameters, however, influence performance of BCI control significantly (Curran & Stokes, 2003; Myrden & Chau, 2015). Consequently, it would have been desirable to identify poor BCI performance within the study protocol. Poor BCI performance could explain why one participant (ID_6SCI) struggle with the B/NHE, resulted in a worse performance compared to baseline assessment. For future studies, it could be beneficial to assess performance of BCI control by monitoring heart rate variability (HRV), as there are promising results that such biomarker reliably predicts deterioration in sensorimotor rhythm control (Nann et al., 2021). Further, BCI performance can be improved by establishing enhanced classification of EEG signals via machine-learning algorithms (Blankertz et al., 2008; Gao et al., 2016). However, these approaches have so far only been applied offline and real-time application are still missing.

Regarding the study design, the baseline condition was always assessed first, which might have led to learning effects that positively influenced the result of the intervention. Fatigue and tiredness could have worked in the opposite direction. To overcome this limitation, the order of baseline and intervention condition should be randomized in future studies. Beyond that, future studies should explore how wearing exoskeletons on both hands will affect bimanual function in individuals with tetraplegia. Nann et al. (2020) suggested a feasible control paradigm for establishing bimanual hand exoskeleton control, paving the way for such application.

Considering that a B/NHE system enhances the performance of meaningful bimanual tasks provides good reason to apply such system in occupational and physiotherapy. By facilitate the performance of bimanual ADLs, the use of B/NHE can increase therapeutical opportunities and promote motivation to participate in therapy through positive reinforcement. A possible roadmap to integrate BCI-based therapy in neurorehabilitation has already been outlined (Angerhöfer et al., 2021). Also, application of assistive hand exoskeleton in daily life is worth considering to support the performance of ADLs. However, it must be noted that there is still a long way to go for such technology to be applied in a home-based setting (Soekadar & Nann, 2020). So far, mounting and unmounting of the hand exoskeleton and calibrating the EEG system cannot be performed by the user on its own, but requires help of a specially trained instructor. Moreover, hand exoskeletons are difficult to sanitize in daily live situations and cannot be used in moist environment, restricting their application in meaningful ADLs such as self-catheterization, toileting, and body hygiene. Hence, further research must be conducted with the aim of establishing more user-friendly hand exoskeletons. Moreover, commercially available hand exoskeletons are still rather expensive and not individually customized to the user (Mekki et al., 2018). While 3D-print technology and soft robotics allows development of light-weighted and practical hand exoskeletons (Bützer et al., 2020; Yoo et al., 2019), further strategies must be found to lower cost of production and provide individual adjustment to the user's hand.

4. General conclusion

In the present work, the Berlin Bimanual Test for Tetraplegia (BeBiTT) has been introduced as new measurement tool to evaluate bimanual function in persons with tetraplegia. The BeBiTT comprises nine bimanual tasks which are commonly impaired in the daily lives of individuals with tetraplegia. Development of the BeBiTT followed a clear and straightforward structure. Items cover common grasp pattern, account for various types of bimanual actions, and include various categories of ADLs. The BeBiTT is practicable to assess both within research as well as clinical routine. The required equipment can be easily and inexpensively acquired everywhere in the world, paving the way for general acceptance within the research and clinical community. The BeBiTT score reflects level of bimanual function in tetraplegic individuals on a 90-point interval scale. By establishing a standardized scoring protocol, scores are comparable not only between individuals but also between raters, making it a sound tool to monitor progress within rehabilitation interventions. Overall, the BeBiTT represents a reliable and valid measurement tool that thoroughly assesses bimanual function in persons with tetraplegia. By developing such tool, a notable gap within existing hand function tests for the tetraplegic population has been closed.

As evidenced by a significant increase in BeBiTT scores, bimanual function in tetraplegics improved significantly with the use of the B/NHE. This indicates the BeBiTT´s sensitivity to detect improvement in bimanual task performance induced by BCI-based devices. Moreover, these results demonstrate the suitability of B/NHE systems as assistive devices and support their role in restoring hand function following cSCI. By demonstrating the positive effects of a B/NHE system on bimanual function in persons with tetraplegia, it is hoped to encourage further research in modern neurotechnology and contribute to a soon-to-be application in rehabilitation and daily life of persons with tetraplegia. Additionally, this work aims to show the importance of reliably assessing the impact of new technologies. Only by valid and robust evidence, new technologies can be established in broad patient care and ultimately lead to patient benefit.

5. Summary

5.1 English summary

Introduction

Individuals with cervical spinal cord injury (cSCI) face immense difficulties in daily life. Due to impaired hand function, the performance of activities of daily living are largely restricted. A promising approach in restoration of hand function following cSCI is represented by assistive devices (e.g., hand exoskeletons) controlled via brain-computer interfaces (BCIs). To date, BCI-based hand exoskeletons have only been assessed on their capability to improve unilateral hand function. However, as bimanual tasks are of high relevance in daily life, such devices have yet to demonstrate a positive impact on bimanual function in persons with tetraplegia. Since there are no measurement tools available for such purpose, the Berlin Bimanual Test for Tetraplegia (BeBiTT) was developed in the context of this work and used to assess functional change in bimanual function induced by brain/neural hand exoskeleton (B/NHE) application.

Methods

Items of the BeBiTT were generated with help of patients and experts and selected according to a predefined theoretical

framework. Content validity assessment of items was conducted by an expert panel consisting of nine subject matter field experts. In a feasibility study with five individuals with tetraplegia, items were assessed regarding practicability, comprehensibility, administration time, task difficulty and safety. A scoring system was developed that allows to systemically administer the BeBiTT. Psychometric evaluation of the BeBiTT was conducted based on interrater-reliability, internal consistency, and construct validity. An interventional study with 10 tetraplegic individuals was conducted to evaluate improvement on bimanual function induced by B/NHE application. Here, the BeBiTT was first performed before (baseline) and while wearing a B/NHE (intervention) by the participants. For online brain/neural control of the B/NHE, sensorimotor rhythm-based electroencephalography and electrooculography signals were used and translated in close/open commands of the hand exoskeleton.

Results

The final version of the BeBiTT consists of 9 items representing bimanual tasks that are impaired following cSCI. Items were regarded as content valid by the expert panel. In the feasibility study, items showed to be practical and quick to assess, comprehensible, safe, and affordable. The BeBiTT showed to have excellent interrater reliability and internal consistency. Content and construct validity assessment proved substantial evidence for the BeBiTT's overall validity. Application of the B/NHE showed to significantly increase BeBiTT scores among participants. On average, the performance of all items of the BeBiTT improved with support of the B/NHE.

Conclusion

The BeBiTT represents a reliable and valid test that comprehensively assesses bimanual function in persons with tetraplegia and is suitable to evaluate state-of-the-art tools in neurotechnology. The application of a B/NHE system substantially improves bimanual function in persons with tetraplegia, demonstrated by increased scores in the BeBiTT. These findings highlight the role of modern neurotechnology in restoration of hand function following cSCI.

5.2 German summary

Einleitung

Menschen mit zervikaler Rückenmarksverletzung sind in ihrem täglichen Leben mit immensen Schwierigkeiten konfrontiert. Durch die eingeschränkte Handfunktion ist die Durchführung von

Aktivitäten des täglichen Lebens stark eingeschränkt. Neben chirurgischen Eingriffen zeigen moderne Neurotechnologien vielversprechende Ansätze. Hand-Exoskelette gesteuert über Gehirn-Computer-Schnittstellen (engl. Brain-Computer-Interface (BCI)) können als Hilfsmittel zur Wiederherstellung der Handfunktion bei Tetraplegiker*innen eingesetzt werden. Allerdings wurden diese Hilfsmittel bisher nur auf deren Einfluss auf die unilateralen Handfunktion untersucht. Da bimanuelle Tätigkeiten im täglichen Leben von hoher Relevanz sind, ist es wichtig den Einfluss von BCI-gesteuerten Hand-Exoskelette auf die bimanuelle Handfunktion zu untersuchen. Da es aktuell noch kein geeignetes Messinstrument für diesen Zweck gibt, wurde in dieser Arbeit der Berlin Bimanual Test for Tetraplegia (BeBiTT) entwickelt und eingesetzt, um den Einfluss eines hybriden BCI-gesteuerten Handexoskeletts (ein sog. Brain/Neural Hand Exoskeleton, B/NHE) auf die bimanuelle Funktion bei tetraplegischen Personen zu untersuchen.

Methoden

Items des BeBiTTs wurden mit Hilfe von Betroffenen generiert und anhand vorher festgesetzter Kriterien selektiert. Die Bewertung der Inhaltsvalidität wurde von einem Expertengremium, bestehend aus neun Fachexpert*innen durchgeführt. Im Rahmen einer Machbarkeitsstudie mit fünf

Tetraplegiker*innen wurden die Items des BeBiTT nach den Kriterien Praktikabilität, Verständlichkeit, Durchführungszeit, Aufgabenschwierigkeit und Sicherheit evaluiert. Anschließend wurde ein Bewertungssystem entwickelt, um den BeBiTT standardisiert beurteilen zu können. Weiterhin wurde die Interrater-Reliabilität, internen Konsistenz und Konstruktvalidität des BeBiTT beurteilt. Um Unterschiede in der bimanuellen Funktion bei Personen mit Tetraplegie vor und während der Anwendung eines B/NHE zu quantifizieren, wurde ein interventionelles Studiendesign gewählt, bei dem der BeBiTT ohne Intervention (Baseline-Test) und anschließend mit B/NHE durchgeführt wurde. Die Kontrolle des hybriden B/NHE wurde durch eine Gehirn-Computer-Schnittstelle unter Verwendung von Elektroenzephalographie- und Elektrookulographie-Signalen realisiert.

Ergebnisse

Die finale Version des BeBiTT besteht aus neun Items, die bimanuelle Aufgaben repräsentieren und bei Personen mit Tetraplegie beeinträchtigt sind. Die Items wurden vom Expertengremium als inhaltlich valide eingestuft. In der Machbarkeitsstudie erwiesen sich die Items als praktisch, verständlich und sicher. Der BeBiTT wies eine ausgezeichnete Interrater-Reliabilität und interne Konsistenz auf. Die Bewertung der Inhalts- und Konstruktvalidität lieferte stichhaltige Hinweise für die Gesamtvalidität des BeBiTT. In der Interventionsstudie zeigte sich unter den Probanden eine signifikante Erhöhung des BeBiTT Scores bei Anwendung des B/NHE-Systems. Im Durchschnitt verbesserte sich die Performance bei allen Aufgaben des BeBiTT mit Unterstützung des B/NHE.

Schlussfolgerung

Der BeBiTT ist ein zuverlässiger und valider Test, der die bimanuelle Funktion bei Personen mit Tetraplegie umfassend bewertet sowie geeignet ist, moderne Hilfsmittel der Neurotechnologie wie BCI-basierte Exoskelette zu evaluieren. Die mit Hilfe des BeBiTTs gemessene bimanuelle Funktion verbessert sich bei Personen mit Tetraplegie unter Anwendungen eines hybriden BCI-gesteuerten Hand-Exoskeletts signifikant. Dies untermauert die Rolle moderner Neurotechnologien bei der Wiederherstellung der Handfunktion nach zervikaler Rückenmarksverletzung.

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7. Declaration of contribution

The present work was carried out in the University Hospital for Psychiatry and Psychotherapy Tübingen, Charité - University Medicine Berlin (Campus Mitte) and the Neurological Rehabilitation Clinic Beelitz-Heilstätten under the supervision of Prof. Dr. Surjo Soekadar.

The development of the Berlin Bimanual Test for Tetraplegia (section 2) was performed by me.

The study design of the brain/neural hand exoskeleton assessment (section 3) was performed in collaboration with Mareike Vermehren, Annalisa Colucci, Marius Nann and Prof. Dr. Surjo Soekadar.

The experiments of the brain/neural hand exoskeleton assessment (section 3) were conducted in collaboration with Mareike Vermehren, Annalisa Colucci and Marius Nann.

The statistical analysis was performed by me after consultation with the Institute of Biometry.

I certify that I have written the manuscript independently and that I have not used any sources other than those indicated by me.

Date Signature

8. Publication

Parts of this dissertation have already been published in the following publication:

Angerhöfer C, Vermehren M, Colucci A, Nann M, Koßmehl P, Niedeggen A, Kim WS, Chang WK, Paik NJ, Hömberg V, Soekadar SR. The Berlin Bimanual Test for Tetraplegia (BeBiTT): development, psychometric properties, and sensitivity to change in assistive hand exoskeleton application. J Neuroeng Rehabil. 2023 Jan 27;20(1):17. doi: 10.1186/s12984-023-01137-4. PMID: 36707885; PMCID: PMC9881328.

All text passages and figures that have already been published and used for this dissertation are marked as such with a reference to the original publication.

Appendix A

Interview/survey guideline

1. Introduction

As you know, many activities in daily living require the interaction of both hands to become useful. However, to date, there is no suitable measurement tool that assesses the interaction of both hands in persons with tetraplegia. Thus, it is not yet possible to determine improvements in bimanual function through rehabilitation measures in a uniform and standardized manner.

We, the Applied Neurotechnology Group of the University Hospital of Tübingen, have therefore set ourselves the goal of developing a test that assesses bimanual function in individuals with tetraplegia. For the development we need your help. Your answers will be very useful, since we want to develop the test based on the challenges you face in your daily life.

2. Activities of daily living

Before we start with the actual questions, let me explain what is meant by the term "activities of daily living". Activities of daily living are all activities that are used for self-care. These include personal hygiene, dressing and undressing, eating and drinking, and continence. It also includes food preparation, shopping, household chores, operating a telephone, and using transportation such as the car or public transportation. In our survey, we are primarily interested in activities of daily living that typically require both hands to accomplish.

- In which activities of daily life are you impaired? Please think of those activities that usually require both hands to accomplish.
- How exactly are you impaired?
- To what extent are you impaired? More specifically, do you only have difficulty or are you unable to perform these activities?
- Can you think of any more impaired bimanual activities of daily living in the following categories:
    - Eating and Drinking
    - Dressing
    - Personal hygiene
    - Continence
    - Communication
    - Transportation
    - Managing finances
    - Preparing food
    - House keeping
- Which activities of daily living can you still manage well? Please think of activities that usually require both hands.
- Can you think of any activities of daily living in which you can compensate for your impairment, e.g., opening a bag of chips with your teeth?

3. Demographic features

- Age
- handedness
- Neurological level of injury

- Complete/ incomplete injury
- ASIA classification
- Time since injury

Appendix B

Content validity assessment questionnaire

Dear Sir or Madam,

As you know, individuals with tetraplegia experience difficulties in daily life due to impaired motor function of both hands. However, to date, there is no suitable measurement tool that assesses bimanual function in quadriplegics. Thus, it is not yet possible to determine improvements in bimanual function through rehabilitation measures in a uniform and standardized manner.

We, the Applied Neurotechnology Group of the University Hospital of Tübingen, have therefore set ourselves the goal of developing a test that assesses bimanual function in individuals with tetraplegia. The test is aimed at tetraplegics with neurological level C5 to C8.

To develop a standardized test, we rely on your expertise and experience in persons with tetraplegics. For this reason, we ask you in the following survey to rate the test items in terms of their relevance to the content.

The survey will take about 6 minutes. Thank you very much for your support.

Introduction

With the test we want to assess the performance of bimanual tasks of daily living. By assessing how well or completely the bimanual task can be performed, we would like to draw conclusions about bimanual function in tetraplegics. The evaluation of the execution focuses on the gripping and lifting ability of the hands as well as the interaction of hand and arm movements.

Test subjects are asked to perform a series of test items. These items represent various activities of daily living that normally require both hands to be performed. Test subjects are asked to perform the tasks with their hands only and to refrain from using compensatory strategies, such as using teeth to open a water bottle.

Please evaluate the test tasks in terms of their relevance to the content and consider the following points:

- Does the task represent a relevant bimanual daily activity that is impaired in tetraplegics (C5 - C8)?

- Is the bimanual activity of relevance in motor rehabilitation?

- Does the task seem relevant to you in assessing bimanual function in tetraplegics?

	Highly relevant	Fairly relevant	Little relevant	Not relevant
Cut piece of meat	☐	☐	☐	☐
Open water bottle (screw top)	☐	☐	☐	☐
Pour glass of water	☐	☐	☐	☐
Open beer bottle (crown cap)	☐	☐	☐	☐
Button up trousers	☐	☐	☐	☐
Close zipper of jacket	☐	☐	☐	☐
Put on trousers	☐	☐	☐	☐
Put on socks	☐	☐	☐	☐
Open toothpaste	☐	☐	☐	☐
Put toothpaste and toothbrush	☐	☐	☐	☐
Wring out wash cloth	☐	☐	☐	☐
Charge smart phone	☐	☐	☐	☐
Sign a contract	☐	☐	☐	☐

	Highly relevant	**Fairly relevant**	**Little relevant**	**Not relevant**
Take coins out of wallet	☐	☐	☐	☐
Take note out of wallet	☐	☐	☐	☐
Open coffee tin	☐	☐	☐	☐
Open crisps package	☐	☐	☒	☐
Chop vegetables (e.g. cucumber)	☐	☐	☐	☐
Cut slice of bread	☐	☐	☐	☐
Rinse a plate	☐	☐	☐	☐
Lift up pan	☐	☐	☐	☐

Supplementary questions

Please rate how relevant the set of tasks is to assess bimanual function in quadriplegics?

Select one of the following answers:

- ☐ Very relevant
- ☐ Fairly relevant
- ☐ Somewhat relevant
- ☐ Not Relevant

Do you have any other suggestions for bimanual tasks that are relevant based on your experience**?**

Do you have any other suggestions or comments regarding the test**?**

Please indicate your profession and focus of practice.

How many years have you worked in the treatment of quadriplegics?

Thank you for your participation!

Appendix C

LOEWENSTEIN HOSPITAL REHABILITATION CENTER
Affiliated with the Sackler Faculty of Medicine, Tel-Aviv University
שירותי בריאות כללית
Department IV, Medical Director: Dr. Amiram Catz Tel: 972-9-7709090 Fax: 972-9-7709986 e-mail: amiramc@clalit.org.il

Patient Name: __________________ **ID:** ____________ **Examiner Name:** ________________

(Enter the score for each function in the adjacent square, below the date. The form may be used for up to 6 examinations.)

SCIM-SPINAL CORD INDEPENDENCE MEASURE

Version III, Sept 14, 2002

EXam 1 2 3 4 5 6

DATE \ \ \ \ \ \ \

Self-Care

1. Feeding (cutting, opening containers, pouring, bringing food to mouth, holding cup with fluid)
0. Needs parenteral, gastrostomy, or fully assisted oral feeding
1. Needs partial assistance for eating and/or drinking, or for wearing adaptive devices
2. Eats independently; needs adaptive devices or assistance only for cutting food and/or pouring and/or opening containers
3. Eats and drinks independently; does not require assistance or adaptive devices

2. Bathing (soaping, washing, drying body and head, manipulating water tap). **A-upper body; B-lower body**

A. 0. Requires total assistance
1. Requires partial assistance
2. Washes independently with adaptive devices or in a specific setting (e.g., bars, chair)
3. Washes independently; does not require adaptive devices or specific setting (not customary for healthy people) (adss)

B. 0. Requires total assistance
1. Requires partial assistance
2. Washes independently with adaptive devices or in a specific setting (adss)
3. Washes independently; does not require adaptive devices (adss) or specific setting

3. Dressing (clothes, shoes, permanent orthoses: dressing, wearing, undressing). **A-upper body; B-lower body**

A. 0. Requires total assistance
1. Requires partial assistance with clothes without buttons, zippers or laces (cwobzl)
2. Independent with cwobzl; requires adaptive devices and/or specific settings (adss)
3. Independent with cwobzl; does not require adss; needs assistance or adss only for bzl
4. Dresses (any cloth) independently; does not require adaptive devices or specific setting

B. 0. Requires total assistance
1. Requires partial assistancewith clothes without buttons, zipps or laces (cwobzl)
2. Independent with cwobzl; requires adaptive devices and/or specific settings (adss)
3. Independent with cwobzl without adss; needs assistance or adss only for bzl
4. Dresses (any cloth) independently; does not require adaptive devices or specific setting

4. Grooming (washing hands and face, brushing teeth, combing hair, shaving, applying makeup)
0. Requires total assistance
1. Requires partial assistance
2. Grooms independently with adaptive devices
3. Grooms independently without adaptive devices

SUBTOTAL (0-20)

Respiration and Sphincter Management

5. Respiration
0. Requires tracheal tube (TT) and permanent or intermittent assisted ventilation (IAV)
2. Breathes independently with TT; requires oxygen, much assistance in coughing or TT management
4. Breathes independently with TT; requires little assistance in coughing or TT management
6. Breathes independently without TT; requires oxygen, much assistance in coughing, a mask (e.g., peep) or IAV (bipap)
8. Breathes independently without TT; requires little assistance or stimulation for coughing
10. Breathes independently without assistance or device

6. Sphincter Management - Bladder
0. Indwelling catheter
3. Residual urine volume (RUV) > 100cc; no regular catheterization or assisted intermittent catheterization
6. RUV < 100cc or intermittent self-catheterization; needs assistance for applying drainage instrument
9. Intermittent self-catheterization; uses external drainage instrument; does not need assistance for applying
11. Intermittent self-catheterization; continent between catheterizations; does not use external drainage instrument
13. RUV <100cc; needs only external urine drainage; no assistance is required for drainage
15. RUV <100cc; continent; does not use external drainage instrument

7. Sphincter Management - Bowel
0. Irregular timing or very low frequency (less than once in 3 days) of bowel movements
5. Regular timing, but requires assistance (e.g., for applying suppository); rare accidents (less than twice a month)
8. Regular bowel movements, without assistance; rare accidents (less than twice a month)
10. Regular bowel movements, without assistance; no accidents

8. Use of Toilet (perineal hygiene, adjustment of clothes before/after, use of napkins or diapers).
0. Requires total assistance
1. Requires partial assistance; does not clean self
2. Requires partial assistance; cleans self independently
4. Uses toilet independently in all tasks but needs adaptive devices or special setting (e.g., bars)
5. Uses toilet independently; does not require adaptive devices or special setting)

SUBTOTAL (0-40)

Quadriplegia Index of Function-Short Form:

Adapted from Marino RJ and Goin JE, Development of a Short-Form Quadriplegia Index of Function Scale, Spinal Cord, 37: 289-296; 1999, Table 2. Used with permission from Nature Publishing.

The Quadriplegia Index of Function-Short Form consists of 6 items, all scored on a scale of 0-4. The clinician observes and evaluates the patient on each item.

Scoring:
4 = independent
3 = independent with devices
2 = supervision
1 = physical assistance
0 = dependent

6 items:
1. Wash/dry hair
2. Turn supine to side in bed
3. Put on lower body clothing
4. Open carton/jar (feeding)
5. Transfer from bed to chair
6. Lock wheelchair

QIF-SF Worksheet:

Patient Name: ______________________ Date: ___________________

Item:	Score (0-4):
Wash/dry hair	
Turn supine to side in bed	
Put on lower body clothing	
Open carton/jar (feeding)	
Transfer from bed to chair	
Lock wheelchair	

Total score: ___________________