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Final dissertation

Kinematic analysis of hand movements in patients with Friedreich's ataxia

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ABSTRACT

Reaching and grasping are fundamental motor skills that rely on complex neural circuits, with the cerebellum playing a critical role in coordinating these movements. In neurodegenerative conditions such as Friedreich's ataxia, which involves the progressive degeneration of the nervous system, particularly the cerebellum and spinal cord, fine motor functions are often severely impaired.

This thesis investigates the kinematics of reaching and grasping in patients with Friedreich's ataxia, focusing on how these movements are affected by the disease and the potential for rehabilitation to improve motor function.

The experimental study involved five participants with Friedreich's ataxia and a control group of 10 individuals. The participants with Friedreich's ataxia underwent kinematic analysis on two separate occasions: before and after a four-week multidisciplinary rehabilitation program which included physiotherapy, occupational therapy, manual activities, psychological support, and speech therapy. The control group was tested on a single occasion. The task involved reaching, grasping, and lifting two types of cylindrical objects—one requiring a precision grip and the other a whole-hand grasp—using both their left and right hands across 60 trials.

The kinematic analysis was conducted using the SMART-D optoelectronic motion analysis system, which recorded the participants' movements through six infrared cameras that detected reflective markers placed on their fingertips and wrist.

The results suggest clear differences in the precision grip movement between individuals with Friedreich's ataxia and healthy controls in terms of both spatial and temporal variables, indicating challenges in hand positioning and movement control.

After a four-week multidisciplinary rehabilitation program, Friedreich's ataxia group showed a selective improvement in the time to peak grip aperture. The results of this study indicate that kinematic analysis is a sensitive tool for detecting upper limb motor dysfunction in patients with Friedreich's ataxia and assessing the effectiveness of rehabilitation treatments. This and other future studies could contribute to the development of new bioengineering methods for motor assessment of patients in the clinical setting.

INTRODUCTION

The capacity to reach and grasp objects represents a fundamental motor skill that underlies a significant proportion of human interaction with the environment. This seemingly simple action requires the intricate coordination of multiple neural circuits, with the cerebellum playing a crucial role in the planning, execution, and adjustment of movement. The act of reaching and grasping is characterised by a complex interplay between sensory input, motor output and cognitive processes, which are essential for the attainment of precise and adaptive motor control (Castiello, 2005).

In the context of neurodegenerative diseases such as Friedreich's ataxia, these motor functions can be significantly impaired. Friedreich's ataxia is a hereditary disorder that is characterised by progressive degeneration of the nervous system, with a particular impact on the cerebellum and spinal cord. This results in a range of motor deficits, including difficulties in coordination, balance, and fine motor skills. Given the cerebellum's fundamental role in motor control, understanding how this degeneration impacts reaching and grasping is essential for developing effective therapeutic interventions (Castiello, 1995).

A principal objective of this work is the kinematic analysis of these movements in patients with Friedreich's ataxia. This study specifically examines the effects of rehabilitation treatment of 4 weeks on the kinematic performance of reaching and grasping tasks in patients with Friedreich's ataxia. By analysing pre- and post-treatment data, and comparing these results with a control group, this study aims to elucidate and evaluate the potential for neurorehabilitative treatment to enhance motor function in individuals with cerebellar ataxia.

1. REACHING AND GRASPING MOVEMENT

Every day, as humans we do a lot of common and automatic actions that can appear rather simple, such as taking a bottle or drinking a glass of water. Although these actions don't seem to require a special effort, they need the implementation of complex motor schemes. The act of reaching and grasping an object necessitates the execution of precise and well-coordinated motor movements. Even sophisticated technologies are not able to replicate these types of actions with the same precision as humans. In fact, the human movement is flexible and it adapts to the different qualities of the object.

The act of executing an action requires the coordination of various processes, including the integration of sensory input, the processing of this information by neural mechanisms, and the generation of a motor output.

Hand movements can be differentiated into prehensile and the non-prehensible, based on the way the hand interact with the object. While the first one refers to actions of grasping and holding an object with the hand, the non-prehensile includes all the movements that no require grasping or seizing but include actions such as pushing or pulling.

From the beginning, the study of hand movement has attracted the interest of numerous researchers. An important contribution comes from John Russell Napier, who categorized two fundamental types of prehensile movements, respectively named precision grip and power grip (Napier, 1956). In the precision grip, the object is grabbed between the fingertips, usually from the opposition of the thumb to the finger around the object. This allows for fine manipulation. On the other side, the power grip provides strength and stability, engaging both the fingers and the palm to facilitate secure holding of objects.

The prehensile movement is characterized by two fundamental components: the reaching and the grasping. Reaching is defined as the movement of the hand towards a target. It is

also referred to as the "transport component," and requires the coordination of the shoulder, elbow, and wrist. In contrast, the grasping or “handling component” refers to the opening and closing of the hand around the object.

Initially, it was believed that these two components were independent from each other. This perspective was primarily structured around the assumption that reaching necessitated the engagement of proximal muscles (e.g., shoulder and elbow), whereas grasping required the involvement of distal muscles (e.g., hand and fingers).

In his early work, Jeannerod observed that these two components could be broken down into different segments, each exhibiting different control mechanisms (Jeannerod, 1981). Nowadays, it is known that reaching and grasping are functionally intercorrelated and perfectly synchronized. Although Jeannerod initially suggested the independence of these actions, his later work acknowledged their interdependence.

However, they encode different types of information. The function of reaching is responsible for estimating the spatial location of the object and necessitates sensory feedback to adjust the movement. In contrast, the component of grasping is fundamental to capturing its intrinsic features through the integration of proprioceptive and tactile feedback.

The development of prehensile movement takes place at different stages during ontogeny. The newborn does not possess this capacity at the time of birth; instead, its earliest movements are the result of primary reflex actions. Infants exhibit pre-reaching movements that are disorganized and unintentional. At approximately three months of age, infants begin to reach for objects with intention, and their hands begin to open and close as a result of the gradual disappearance of the grasping reflex (Zoia et al., 2006).

However, it is only at nine months of age that they enhance their grasping abilities, and the hand begins to adapt to the size of the object, differentiating between a precision grip and a whole-hand grasp. In the following months, their abilities are further refined. By the age of 12 months, they have gained better control and can use tools such as cutlery and cups with greater dexterity. Although children are capable of making prehensile movements during the first five years of their lives, these movements exhibit distinct characteristics that differ from those of adults. The final stage of development occurs at the end of the first decade, resulting in the attainment of adult-level coordination (Castiello & Ansuini, 2009).

1.1 Kinematics

The research of motion began in the 19th century with the studies of Muybridge, who captured the movement of animals and humans using multiple sequenced cameras. One of the first important contributions is "The Horse in Motion" (1878), a succession of rapid photographs that made it possible to study a horse's gallop and to demonstrate that the animal during a phase of the gallop lifts all 4 hooves. Some years later, the physiologist Marey invented chronophotography and captured the human gait.

Over time, advances in cinematographic techniques and technology have facilitated research by allowing for repeated viewing of actions or slow-motion examination. However, the study of movement is not merely descriptive, and it encompasses a range of analytical approaches.

Kinematics is the mathematical study of the movements described in terms of time, velocity, trajectory and acceleration. Through the kinematic analysis is possible to translate the movement in a series of mathematical parameters.

The French neuroscientist Marc Jeannerod is the pioneering researcher in the kinematic analysis of reaching and grasping (1981,1984). He classified the object's properties in intrinsic and extrinsic. The intrinsic characteristics encompass all the physical attributes of the object and affect the hand posture. In contrast, the extrinsic ones include all the features situated between the subject and the object, including distance, orientation, and position. These extrinsic characteristics influence the spatial trajectory of the arm.

In addition, using high-speed film, he observed that the maximum grip, defined as the distance between the index finger and the thumb, increases with the object size. Consequently, larger objects necessitate a larger opening of the hand. Since these early studies, the influence of an object's properties in the maximum grip has been widely investigated. Other properties include weight, texture, fragility, shape or even elasticity or rigidity.

Precisely, the maximum grip is modulated by texture and fragility to avoid slippage. Therefore, objects with a smooth texture require a larger grip aperture (Weir et al., 1991) as well as fragile objects, in order to ensure a gentle grasp and prevent the application of excessive force upon these delicate items (Savelsbergh et al., 1996).

Similarly, heavier and irregular shape objects necessitate a larger aperture to be prepared for a stronger grip (Jeannerod, 1984) and for the correct positioning of the fingers around the surface area (Napier, 1956).

It is possible to conclude that reach-to-grasp movements are driven by disparate characteristics of the object which are influenced by visual cues. Consequently, objects with disparate features will result in a distinct choice of grip.

In kinematics, the duration of both the reaching and grasping is identified as “movement time” and corresponds to the entire duration of the action. In this period is possible to differentiate two different curves (Jeannerod, 1984).

The first is the reaching curve which represents the hand moving towards the target and the second involves the grasping, where the fingers start to pre-shape according to the features of the object.

The velocity profile of the reaching movement follows a bell-shaped curve (Fig.1A). Firstly, there is an acceleration phase in which the hand gains speed toward the target. Approximately at half of the total movement time, the peak velocity is reached. Depending on the object's size, form, and distance, the velocity profile changes. Larger or farther away objects, for instance, might need longer acceleration phases and higher peak velocities.

Once the maximum speed has been reached, a deceleration phase occurs, which is essential for adjusting the hand position to guarantee accurate grasping.

The grasping curve begins during the reaching phase when the hand is still moving towards the object. As the hand approaches the object, the fingers begin a pre-shaping process, whereby they begin to open or close in accordance with the dimensions, configuration and position of the object in question (Fig. 1B).

The peak of grip aperture, defined as the maximum opening of the hand, typically occurs when the hand has covered approximately 70-80% of the distance to the object. The peak aperture occurs just before the hand makes contact with the object and its dimensions may vary in accordance with the characteristics of the object to be grasped. In the case of larger objects, the peak will exhibit a wider aperture, whereas, in the case of smaller objects, the aperture will be narrower.

Upon reaching the peak aperture, the fingers begin to close around the object. It is essential that this phase is precisely timed and coordinated with the deceleration phase of the reaching movement in order to guarantee that the hand secures a firm grasp of the object (Jeannerod, 1984; Castiello, 2005).

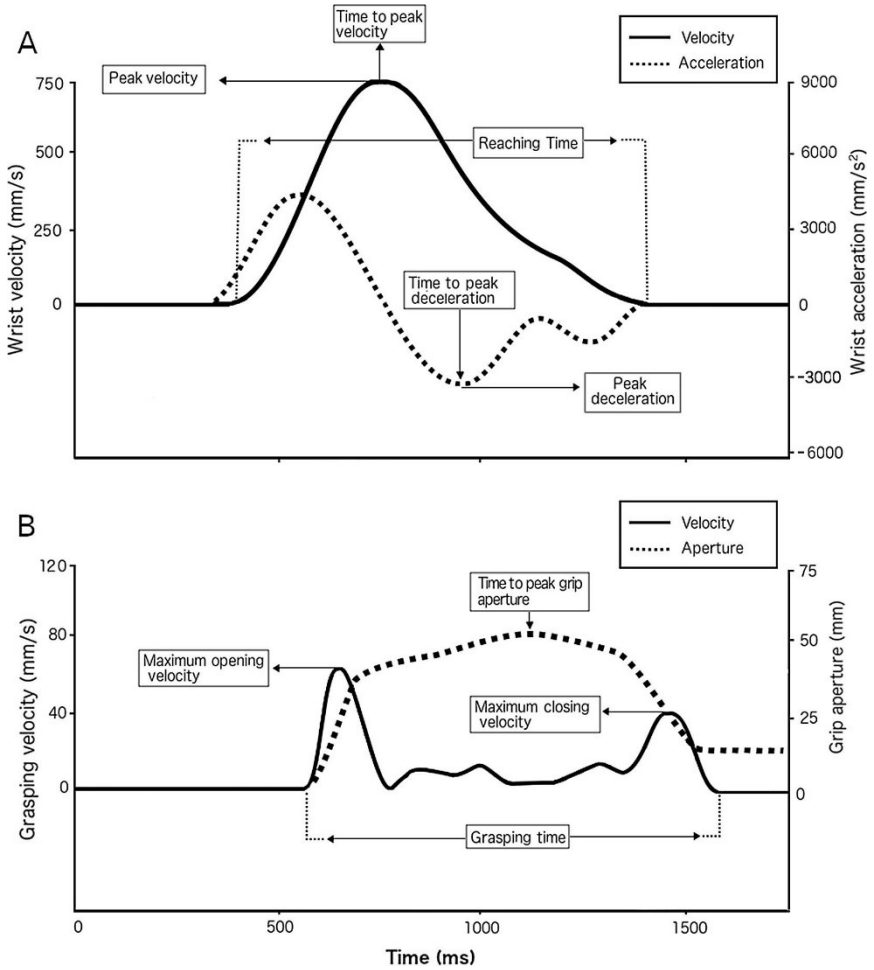

Figure 1. A. Graphical representation of the wrist velocity (solid line) and wrist acceleration (dashed line) during reaching. B. Graphical representation of grasping velocity (solid line) and grip aperture (dashed line). Adapted from: Ceccarini, F., & Castiello, U. (2018). *The grasping side of post-error slowing*. *Cognition*, 179, 1–13.

The time interval between the beginning of the transport phase and the onset of grasping is called "delay" and it is physiological. In healthy people, it occurs after a predictable and consistent amount of time to ensure a successful object manipulation.

This delay worsens when a movement deficit emerges. An altered or prolonged delay in the grip formation reduces the precision and increases the time needed to complete the action. Deviations from the typical kinematic profile may be indicative of neurological impairment.

In Parkinson's disease, the reach-to-grasp movement is significantly altered. In addition to a longer reaction time due to bradykinesia, there is a notable delay in the onset of grip formation, which often initiates much closer to the object or even after the hand has reached the object. The temporal synchronisation between reaching and grasping is disrupted, which results in a less efficient and more segmented movement pattern (Castiello et al., 1993).

Evidence of a disrupted reach-to-grasp movement is also observed in patients with optic ataxia, who demonstrate an abnormally large grip aperture during the transport phase and a lack of correlation between the object's size and the hand's aperture due to their visual deficits and difficulty in visuomotor transformation resulting from lesions of the superior parietal lobe (Jeannerod, 1986).

In a patient with a right cerebellar lesion, the kinematic profile demonstrated a complete absence of coordination between the two components, which prevented the patient from grasping the object. However, the patient was still able to perform the reaching and grasping actions independently. The integration of these actions was impaired, which highlights the essential role of the cerebellum in integrating and coordinating multiple sub-actions within a complex motor task (Haggard et al., 1994).

The nervous system continuously improves performance during the reach-to-grasp movement through corrective actions, called submovements.

Submovements are minor fluctuations that occur during the main movement and are useful in correcting the trajectory towards the target to guarantee that the final position of the hand is as accurate as possible.

They can be classified into three categories (Meyer et al., 1988).

First-type submovements are considered the major corrective actions, that occur when the main movement is considered off-course. They are typically the broadest and take place during the early stage of the movement process.

As the movement progresses towards the target, there are additional adjustments, which are the second-type submovements. They are smaller and more precise compared to the first-type. Third-type submovements are the smallest and most subtle corrective actions, which occur immediately before the end of the movement. They involve highly precise adjustments to finalise the positioning.

The number of submovements during a task, such as reaching or grasping, can indicate how accurately and efficiently the motor system is performing. Fewer submovements are usually required in a precise and well-controlled movement. Conversely, a higher number of submovements might suggest that the motor system is making frequent corrections, which can be a sign of reduced accuracy or difficulties in motor planning. The number of submovements could be useful to differentiate between healthy individuals and those with motor impairments. A study found that individuals with neurological disorders, such as Parkinson's disease or stroke, tend to have a greater number of submovements. This increase can be attributed to the fact that the motor system needs to compensate for impaired control mechanisms with a greater frequency of corrections (Dounskaia et al., 2009).

It is evident that kinematic analysis is a valuable tool for identifying motor impairment in an objective and reliable manner, for monitoring the progression of such impairment, and for evaluating the efficacy of a treatment. Furthermore, it allows clinicians to identify the specific phases of movement that are most affected, thereby enabling them to develop more targeted rehabilitation strategies aimed at improving motor coordination.

1.2 Neural circuits

During the planning phase of reaching and grasping, significant activity occurs in the premotor cortex (PMC) and the posterior parietal cortex (PPC). The premotor cortex is essential for planning based on available information and selecting the appropriate action from potential alternatives. It is divided into the dorsal premotor cortex (PMd) and the ventral premotor cortex (PMv). The PMd is primarily responsible for planning complex sequential movements and integrating sensory information. During reaching it integrates visual cues (target position, and the starting location of the hand and eye) to facilitate the initiation of arm movements. Instead, the PMv is fundamental for transforming sensory input about the object's properties into the appropriate motor commands for grasping, such as shaping the hand (Hoshi & Tanji, 2007). The posterior parietal cortex, formed by the superior parietal lobule (SPL) and the inferior parietal lobule (IPL), plays a key role in sensory-motor integration and supplies the integrated information to both the premotor and primary motor cortices. Within this region, the anterior intraparietal area (AIP) is especially important for integrating visual and/or tactile inputs that guide the configuration of the hand during the reach-to-grasp action (Andersen & Buneo, 2002). Instead, the execution of the movements is associated with the primary motor cortex (M1) and the cerebellum.

The primary motor cortex plays a key role in executing voluntary movements, generating precise motor commands that control the muscles of the arm, hand, and fingers by sending signals directly to the spinal cord and muscles.

Instead, the cerebellum is fundamental to the fine-tuning of motor actions and the coordination of complex movements. It is involved in the temporal and precise organization of the action. Additionally, the cerebellum contributes to adaptive control of movement, enabling corrections in reaction to shifts in the object's position or unexpected interruptions during the grasping or reaching phases. Damage to the cerebellum often results in ataxia, a condition characterised by uncoordinated and imprecise movements, illustrating its role in motor control.

The reach-to-grasp movement depends on the coordination of multiple neural circuits that integrate sensory information with motor commands. These circuits transmit information from the associative visual areas to the frontal cortex. Research on human and non-human primates has shown the presence of specialized circuits for reach-to-grasp movements. (Castiello, 2005). A dichotomy between the two components has been hypothesized, whereby they are encoded by two distinct neural circuits: the dorsomedial and the dorsolateral.

The reaching component appears to occur in the medial parieto-frontal circuit, which mainly involves the medial intraparietal area (mIP) and the superior parieto-occipital cortex (Culham et al.,2006). The medial intraparietal area, situated within the posterior parietal cortex, plays a significant role in spatial processing and the conversion of these processes into motor commands. It facilitates the integration of visual and proprioceptive information, thereby guiding the arm towards a target. The superior parieto-occipital cortex is involved in spatial awareness and visual guidance, thereby supporting the

planning and execution of movements in relation to the spatial environment. It facilitates the coordination of the arm's trajectory, enabling accurate reaching of the object.

The grip component appears to take place in the lateral parietofrontal circuit, with the involvement of the anterior intraparietal area (AIP) and both the dorsal (PMd) and the ventral (PMv) regions of premotor cortex. These areas are more involved in object recognition and fine motor control (Moll & Kuypers, 1977; Raos et al., 2004).

This traditional view that suggests a dichotomy between the reach and grasp components has recently been called into question. According to lesion studies, two other areas, parieto occipital area V6a and dorsal pre-motor area F2, also play an important role in specific aspects of hand posture in prehension (Battaglini et al., 2002).

Overall, the evidence appears insufficient to definitively determine the extent to which grasping and reaching are encoded independently and to what extent they are integrated within the same neural networks.

Recent studies suggest that both components may indeed be coded by the same neural circuit, with differences arising more from the timing of neural activations rather than distinct qualitative processes. This implies that the same regions may be involved in both reaching and grasping, with some neurons showing a stronger preference for one component over the other depending on the phase of the movement. For instance, neurons in the premotor and parietal areas might first contribute to reaching by guiding the arm towards the target, and then, as the hand approaches the object, these same neurons shift to focus on the grip, ensuring precise hand shaping and finger placement.

Additionally, it has been proposed that while these areas are responsive to both reaching and grasping, there may be a significant specialization for one action over the other depending on the context. This preference may become evident on a temporal scale, with

some neurons showing early activation for reaching and later activation for grasping, suggesting a dynamic and context-dependent integration of the two components rather than a strict dichotomy between them (Begliomini et al., 2014).

A fundamental role is played by the cerebellum, which acts as an interface between sensorimotor and cognitive control. It could be considered an instantaneous monitoring system for verifying the success of a movement in progress and for error correction. Without this system, movements would be uncoordinated and inefficient.

1.3 Cerebellum

The cerebellum, often referred to as the "little brain, is the largest part of the hindbrain. Even though it accounts for 10% of the brain's volume, it contains over 50% of the total number of neurons in the brain. It is located in the posterior cranial fossa, behind the pons and the medulla oblongata.

1.3.1 Macroscopic anatomy

From a phylogenetic and anatomo-functional point of view, it is possible to distinguish the archicerebellum, the paleocerebellum and the neocerebellum. The archicerebellum is the most ancient part. The corresponding anatomical part is the flocculo-nodular lobe which is located in the inferior-medial district of the cerebellum.

It is also called vestibulocerebello for its connection with the vestibular system, which is responsible for the sense of balance and motor coordination of hands and eyes.

The principal efferent projections are therefore targeted towards the vestibular nuclei and constitute the initial stage of the cerebellovestibulospinal pathway.

The paleocerebellum comprises the cerebellar vermis and the medial portions of the hemispheres. It is also known as spino-cerebellum due to its strong connection with the spinal cord, from which it receives sensory information about spatial positioning and movement coordination from the body. The spinocerebellum acts on both the extensor and flexor muscles through two different pathways: the cerebellovestibulospinal and cerebellorubro(reticulo)spinal pathways.

The neocerebellum or cerebro-cerebellum includes the cerebellar hemispheres. It is the most evolutionarily advanced part of the cerebellum and is closely connected with the cerebral cortex, particularly through the pontine nuclei. It optimizes the functions of the cerebral cortex by fine-tuning motor commands. Once a motor command is generated by the cerebrum, the neocerebellum receives real-time information to help produce accurate and coordinated movements.

The cerebellum is connected to the brainstem through the cerebellar peduncles.

The inferior cerebellar peduncles (ICP) connect the cerebellum to the medulla and carry sensory information from the periphery of the body. They host spino-cerebellar afferences and carry proprioceptive information about the body's position in space, essential for the coordination of motor commands.

The middle cerebellar peduncles (MCP) are afferent fibers that connect the pons to the cerebellum. They carry cortico-ponto-cerebellar information, which alerts the cerebellum about an impending motor command.

The superior cerebellar peduncles (SCP) are efferent fibers that extend from the cerebellum to the midbrain, transmitting the final output of the cerebellum's integrative processing.

1.3.2 Functions

The cerebellum serves as an interface between the sensorimotor and cognitive control domains. The cerebellum has traditionally been associated with motor control, but in recent years it has been increasingly recognised for its involvement in cognitive functions and affective regulation (Schmahmann, 2019).

The cerebellum is primarily responsible for motor control and coordination, ensuring the accurate execution of voluntary movements by fine-tuning the motor commands that come from the cerebral cortex. This process is fundamental for complex and multi-joint movements, such as reaching or grasping, since it guarantees that the various parts of the body are synchronized.

Additionally, the cerebellum is responsible for maintaining the balance and posture of the body through a series of unconscious muscle movements that allow to keep the station erect while performing an action.

The cerebellum plays a key role in motor learning, which consist in a series of processes associated with the experience that allow to acquire or modify movement skills. This process relies on sensory prediction and error correction, which consist in adjusting the movement in order to reduce the discrepancy between the intended and actual action. Signals coming from the peripheral and central nervous systems are compared at each instant and used to produce an efficient response. In case of discordance between the desired and actual movements, the cerebellum can implement during the execution of the movement corrective measures through a negative feedback mechanism (Tseng et al., 2007).

The repetition of specific motor patterns over time has been demonstrated to modify cerebellar circuits (plasticity), thereby increasing the efficiency of the motor act. This

adaptive learning is essential for tasks that require precise timing and coordination, such as playing a musical instrument or engaging in athletic activities.

Two different types of functional motor models have been proposed: Forward Models and Inverse Models (Wolpert et al., 1998).

The forward model represents a theoretical framework that elucidates how the brain predicts the sensory feedback associated with a given motor command before the actual movement occurs.

For instance, a forward model of the arm is a predictive tool that estimates the subsequent state (e.g., position and velocity) based on the current state and the motor command.

This model is fundamental for fast reaching movements. When the brain initiates a reach, a motor command is sent to the muscles to prompt the movement. At the same time, an efference copy of this command is transmitted to a predictive model. The forward model uses the efference copy to anticipate the sensory consequences of the action, such as the anticipated position of the hand and the anticipated sensory feedback. In fast-reaching movements, the time available to process the feedback and to correct the errors during the movement is often insufficient. For this reason, this model facilitates the process and allow the brain to anticipate the outcome of the movement before its completion. These predictions are useful to guide and adjust the reaching movement in real time.

Finally, during the movement, the actual sensory feedback (such as the position of the hand) is compared with the predicted outcome generated by the forward model.

If there is a discrepancy between them the brain is able to use this information to correct the errors. This process is fundamental to maintain accuracy, particularly in case of unanticipated changes, such as running into an unexpected object. Impairments in the

forward modelling process have been linked to conditions such as cerebellar ataxia, which presents difficulties in controlling precise fast movements (Desmurget & Grafton, 2000). In contrast, inverse models are used to generate pertinent motor commands based on desired outcomes. This is the reverse of the process undertaken by a forward model. For instance, in response to the action of reaching, the inverse model determines the required muscle activations for the movement of the arm to the object's position.

The cerebellum undergoes continuous adaptation of its internal models as a function of experience, thereby enhancing the precision of predictions and the efficacy of motor commands.

Although the cerebellum is most commonly associated with motor control, it plays a significant role in several cognitive functions. For instance, the cerebellum is involved in language production and processing, and damage to this area results in difficulties with speech articulation. Moreover, it seems to play a role in modulating attention and cognitive flexibility, which allows one to focus attention and adapt cognitive strategies in accordance with task demands.

The cerebellum is also involved in emotional regulation and affective processing. It interacts with limbic structures such as the amygdala and with the prefrontal cortex to modulate the emotional response.

It is hypothesised that the sensorimotor cerebellum is represented in the anterior lobe, with lesions in this area leading to the cerebellar motor syndrome, which presents with ataxia, dysmetria, dysarthria and impaired oculomotor control.

In contrast, the cognitive/limbic cerebellum is located in the cerebellar posterior lobe. Lesions affecting the posterior lobe result in the cerebellar cognitive affective syndrome

(CCAS) which is characterised by deficits in executive function, visual-spatial processing, linguistic skills and affective regulation (Schmahmann, 2019).

2. FRIEDREICH'S ATAXIA

2.1 Definition

Friedreich's ataxia (FRDA) is a progressive spinocerebellar ataxia with multi-system involvement. It is an autosomal recessive neurodegenerative disease that affects the central and peripheral nervous system, the musculoskeletal system, the endocrine pancreas and the myocardium.

Described for the first time by Nicholaus Friedreich in 1863, currently, is the most common progressive hereditary ataxia in the European population, with a prevalence of around 1: 20.000-50.000 inhabitants.

Reduction of balance and coordination are among the initial symptoms, which can make it challenging to perform daily activities such as write, eat, and doing fine motor tasks. Other typical symptoms comprise gait and limb ataxia, dysarthria, dysphagia, oculomotor abnormalities, diabetes, various heart issues and scoliosis.

2.1 Epidemiology

FRDA is the most common inherited ataxia but its prevalence can vary significantly between different geographic regions. It is more common in individuals of European, North African, Middle Eastern, and South Asian descent.

On the other hand, is less frequently observed in populations of East Asian, sub-Saharan African, and indigenous American descent.

The prevalence in the Caucasian population is estimated between 1: 20.000 and 1: 50.000 inhabitants, but it is highly variable going from 1: 21.000 in the North of Spain to 1: 330.000 in Russia.

Is estimated that individuals with one copy of the mutated gene who do not show symptoms are around 1 in 60 to 1 in 110 individuals in populations of European descent. FRDA affects males and females equally, with no significant gender predisposition.

2.2 Etiopathogenesis

The etiopathogenesis of Friedreich's ataxia involves a combination of genetic, molecular, and biochemical mechanisms.

The homozygous GAA triplet repeat expansion in the FXN gene is the primary cause of the disease, and the length of the repeat expansion is correlated with both the severity of the disease and the age at onset. GAA expansion involves silencing the FXN gene and then reducing the gene product, the protein frataxin.

Healthy individuals have 7-22 GAA repeats, while individuals with Friedreich's ataxia typically have 66 to more than 1,000 repeats.

Frataxin is a mitochondrial protein that plays a critical role in iron-sulfur cluster biogenesis, which is essential for the function of various enzymes.

Frataxin deficiency leads to mitochondrial dysfunction characterised by abnormal iron accumulation in cells. This negatively affects tissue with high-energy demand such as neurons and cardiac muscle. This explains why patients often develop hypertrophic cardiomyopathy and undergo to cardiac complications like arrhythmias and heart failure.

The mitochondrial dysfunction also has as a consequence the degeneration of neurones which involves mainly the dorsal root ganglia, spinocerebellar tracts, and the corticospinal tract.

2.3 Clinical features

Symptoms of Friedreich's ataxia typically begin in childhood or adolescence, with the average age of onset around 10 to 15 years. Late onset can occur, with symptoms appearing in adulthood, but this is less common.

The progression of FRDA varies, but it typically leads to severe disability within 10 to 20 years of symptom onset.

Life expectancy is often reduced, primarily due to cardiomyopathy and other complications, with many individuals living into their 40s or 50s. However, some patients may live longer with appropriate medical care and management of symptoms.

The age at which symptoms appear, as well as the disease's progression and severity, differ among patients. These variations are somewhat associated with the size of the shorter GAA repeat expansion in the FXN gene.

One of the earliest and most common signs of FRDA is gait ataxia, which causes difficulty in walking due to poor coordination.

The path becomes unstable in the second decade of life with increased falls and loss of balance. As the disease progresses, walking becomes problematic, and patients require external support. Initially, they support themselves by holding onto external objects or walls or walking alongside others.

In the course of the disease's progression, they transition to using aids such as walkers and frequently must turn to wheelchairs after around 15.5 years from the onset of the symptoms.

Upper limb ataxia generally appears a few years after the onset of gait ataxia, but the progressions vary widely among patients.

Early signs include difficulty with tasks that require fine motor skills, such as writing, using utensils or eating. It impacts coordination and it results in difficulty performing Activities of Daily Living (ADLs) independently.

Patients with Friedreich's ataxia show a reduction in speed and lower peak velocities of reaching movements compared to healthy controls which is hypothesised to result from reduced accuracy and coordination, particularly with regard to movements requiring coordination between several joints. This is thought to be a compensatory strategy employed by the patient, whereby a reduction in movement speed allows for greater precision in execution. The movement is also characterized by a reduction in precision (understood as the distance from a straight-line trajectory) and fluidity of movement, which is fragmented and irregular due to the inefficiency of feedforward control and compensation (Ramos et al., 1997; Maurel et al., 2013; Bonnechère et al., 2018). During reaching there are higher accelerations and decelerations, which are assumed to be related to the reduction of speed. A study by Topka et al. (1998) found that ataxia patients exhibited increased accelerations and decelerations during slow movements, whereas these values were reduced during fast movements. This suggests that even when attempting to move slowly, patients are unable to maintain smooth motion and instead exhibit jerky, irregular bursts of speed.

Individuals may also notice tremors or shakiness and increasing clumsiness during purposeful actions. Additionally, complex movements are decomposed into simpler ones. In Friedreich's ataxia, dysmetria represents a significant symptom, resulting in the inability to control the distance, speed, and range of movement, which cause a notable challenge in accurately reaching for or touching a target.

The later stages of the disease are characterized by progressive pyramidal weakness that is more prominent in the lower limbs compared to the upper.

Some individuals also experience spasticity, which is increased muscle tone and stiffness that contribute to contractures and painful muscle spasms.

Speech can also be affected early in the disease, leading to dysarthria. Dysarthria is characterized by slurred or slow speech resulting from impaired coordination of the muscles used in speaking.

Patients may experience difficulty articulating words clearly, which can make verbal communication challenging. This symptom not only affects social interactions but can also contribute to frustration and social isolation.

Over time, as the disease progresses, speech difficulties may worsen, requiring speech therapy and augmentative communication devices to help maintain effective communication.

Other common symptoms include dysphagia, or difficulty swallowing, which often necessitates dietary modifications.

Additionally, patients may experience oculomotor abnormalities, such as fixation instability, which is interrupted by involuntary saccades or square wave jerks (SWJs). These eye movement issues can impair visual stability and coordination.

Additional neurological symptoms include hearing difficulties, upper (UL) and lower limb (LL) areflexia, reduced muscle tone and muscular weakness.

Overall, cognition in Friedreich's ataxia patients is generally preserved. However, certain cognitive domains can be subtly impacted. Patients often perform worse on tests related to verbal fluency, reaction time, and visuoperceptual capacity.

Non-neurological features comprise cardiac, metabolic and skeletal complications.

Progressive hypertrophic cardiomyopathy, where ventricular walls thicken, is the most common cardiac difficulty in FRDA and it may cause arrhythmias or heart failure.
Heart symptoms, such as shortness of breath, palpitations and fatigue, may develop early but this is poorly correlated with the neurological level of disability.
A significant number of FRDA patients develop diabetes mellitus or glucose intolerance due to mitochondrial dysfunction that affects the production of insulin and the metabolism of glucose. The incidence of diabetes mellitus varies between 8% and 32%.
Regarding skeletal abnormalities, scoliosis is present in nearly all patients. The abnormal curvature of the spine causes back pain, uneven shoulders or hips, and in severe cases, respiratory issues due to reduced lung capacity. High-arched feet, or pes cavus, are also frequent skeletal issues, and together with scoliosis often can anticipate the neurological signs.

2.4 Treatment

Treatment for Friedreich's ataxia focuses on managing symptoms, preventing complications, and improving the patient's quality of life. Guidelines have been published to assist with the management of FRDA (Corben et al, 2014).

2.4.1. Pharmacological interventions

Currently, there are very few treatment options available for FRDA patients. However, in early 2023, Omaveloxolone (Omav), an Nrf2 activator and NF-kB suppressor, was approved as the first pharmacological treatment for FRDA in adults and adolescents aged 16 and older. It improves mitochondrial function, restores redox balance, and reduces

inflammation. The approval of Omav by the European Commission is based on efficacy and safety results from the MOXIe study, where after 48 weeks, patients treated with omaveloxolone significantly improved neurological function and had significantly better scores on the modified Friedreich ataxia rating scale (mFARS) compared to the placebo group.

Antioxidants are believed to mitigate cellular damage caused by harmful “free radicals”. Naturally occurring in foods, these compounds are present at very low levels. Recent research has produced mixed findings regarding the effectiveness of specific antioxidants, such as idebenone, coenzyme Q10, and vitamin E, in treating cardiac issues associated with Friedreich's ataxia.

Their role remains under investigation, with some studies showing potential benefits in reducing cardiac hypertrophy and improving left ventricular mass.

Other pharmacological interventions are primarily aimed at managing symptoms to reduce spasticity, manage cardiopathy, control blood sugar levels or treat neuropathic pain.

2.4.2. Non-pharmacological interventions

Non-pharmacological interventions remain a critical component of FRDA management, encompassing various therapeutic approaches aimed at improving quality of life, addressing the symptoms and maintaining residual functioning (Paparella et al., 2023). These interventions include physical therapy, occupational therapy, speech therapy, and psychological support.

Physical therapy is essential, and it focuses on maintaining mobility, strength, and flexibility. Tailored exercise programs help enhance balance and coordination, reduce the risk of falls, and prevent complications such as scoliosis.

The main goals regard the improvement of the balance, gait pattern, postural control and the stability of the trunk. As trunk stability decreases, the capacity to perform coordinated and precise upper limb movements also diminishes. This is due to the fact that when the trunk is unstable, the arms must provide a counterbalance to the body's core, which often results in uncoordinated and inaccurate movements. It is therefore considered of fundamental importance to work at the trunk level to create at the axial level the stability necessary to free the upper limbs for reaching, relieving them of their support function. For spasticity is useful to do regular stretching to maintain flexibility and prevent contractures.

Regular physiotherapy sessions, combined with home exercise routines adapted to each condition, are designed to address the individual needs of each patient, promoting physical function and independence.

Occupational therapy assists patients in adapting to daily living activities and enhancing their ability to perform tasks independently. Therapists work with patients to develop strategies and utilize adaptive devices that facilitate self-care, work, and leisure activities. This therapy is vital for improving fine motor skills and ensuring that patients can maintain their independence for as long as possible.

Considering that many patients experience difficulties with speech and swallowing due to ataxia affecting the muscles involved, speech therapy focuses on improving communication skills through exercises that enhance speech clarity and volume.

Additionally, speech therapists provide strategies to manage dysphagia, reducing the risk of aspiration and improving nutritional intake.

Furthermore, a balanced diet ensures adequate nutrition to support overall health and vitamin and mineral supplements (e.g., vitamin E) are needed. Additionally, adjustments to food texture and consistency can be useful to prevent aspiration.

Finally, coping with a chronic and progressive condition like FRDA can be emotionally challenging for patients and their families. Psychological support, including counselling and psychotherapy, is crucial for addressing the emotional and mental health needs of patients, especially during those stages of transition that lead the patient to experience new aids such as walkers or wheelchairs.

Support groups and community resources also play a significant role in providing social support, reducing feelings of isolation, and enhancing overall well-being.

A comprehensive, individualized treatment plan addressing these various aspects can significantly improve the quality of life of the patient.

3. PILOT STUDY

3.1 Experimental hypothesis

The primary experimental hypothesis to be tested in this study is that there will be a discernible kinematic profile between participants with Friedreich's ataxia and the control group. In particular, individuals diagnosed with Friedreich's ataxia will initially demonstrate a lack of coordination and efficiency in their fine motor movements. These movements will be characterised by irregular trajectories, an increase in temporal and spatial errors, and inconsistent acceleration profiles.

It is expected that following the four-week multidisciplinary rehabilitation programme, these participants will demonstrate improvements in their kinematic performance. By the second testing session (T2), their kinematic profiles should be more closely aligned with those of the control group, indicating enhanced coordination and efficiency in the reaching and grasping task.

3.2 Materials and Methods

3.2.1 Participants

Five subjects (3 females and 2 males, age range between 16-37, mean age 24 years) took part in the experiment at the Department of General Psychology of the University of Padua. All participants had been diagnosed with Friedreich's ataxia with a GAA trinucleotide expansion or mutation and were in different gravity stages (Table 1). Four of them were right-handed and one left-handed according to the Edinburgh Handedness Inventory (Oldfield 1971).

In addition to these participants, a control group of ten male individuals (age range between 42-55 years, mean age 48 years) was included in the study. All the participants of the control group were right-handed.

The experimental procedure was approved by the Institutional Review Board at the University of Padua in accordance with the Helsinki Declaration (Sixth revision, 2008). All participants and their parents/legal tutors were informed regarding the experimental nature of the study and provided written consent.

Table 1. Demographic and clinical data of recruited patients.

Patient code	**AV**	**EM**	**RB**	**AA**	**CM**
Gender	Female	Male	Male	Female	Female
Age	19	16	37	25	22
Handedness	Left	Right	Right	Right	Right
FARS stage[1]	5	2	4	2	5
Type of aid	Wheelchair	No aid	Walking frame	No aid	Wheelchair

3.2.2 Experimental stimuli

Two different stimuli were used: a small cylinder (15 mm diameter; 140 mm height) for the Precision Grip (PG) and a second larger cylinder (75 mm diameter; 110 mm height) for the Whole-Hand Grasp (WHG) (Fig.2).

[1] Stage 0: Normal, Stage 1.0: No disability, Stage 2.0: Minimal disability, Stage 3.0: Mild disability, Stage 4.0: Moderate disability, Stage 5.0: Severe disability, Stage 6.0: Total disability

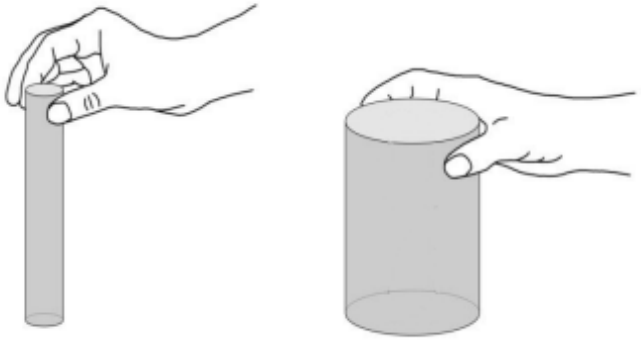

Figure 2. Graphical representation of the experimental stimuli: a small cylinder for the Precision Grip and a larger cylinder for the Whole-Hand Grasp

3.2.3 Procedure

The participants were tested on different days at the Department of General Psychology of the University of Padua.

Following the signing of the informed consent, participants seated at a table with one hand, alternately the left or right, in a designated start position (Fig.3). The hand was positioned with the thumb and the index finger in opposition on a starting pad located at a distance of 35 cm from the cylinder. The task required to reach, grasp and lift the object following the presentation of the Go signal.

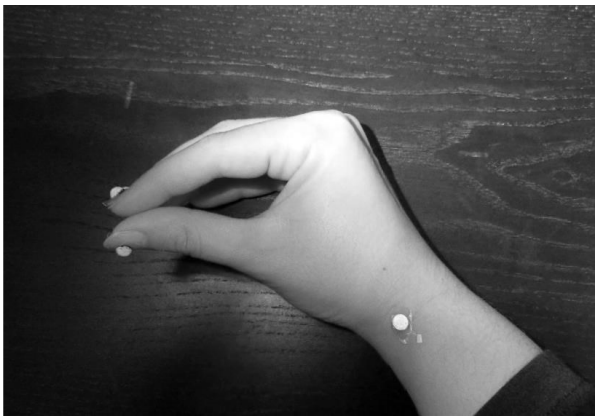

Figure 3. Starting position of the right hand, showing markers on the wrist, thumb and index finger

Depending on the type of object, participants automatically adopted a precision grip for the small cylinder and a whole-hand grasp for the larger one.

A 2x2 factorial design was selected, whereby the two factors, namely the hand to be used and the grip type, were crossed with one another, resulting in four distinct combinations:

1. Right hand and Precision Grip (Right PG)
2. Right hand and Whole-Hand Grasp (Right WHG)
3. Left hand and Precision Grip (Left PG)
4. Left hand and Whole-Hand Grasp (Left WHG)

Each experimental condition was repeated 15 times, resulting in a total of 60 trials (T1). Subsequent to the initial data collection, participants with Friedreich's ataxia underwent a four-week rehabilitation programme at the "Eugenio Medea" Scientific Institute in Pieve di Soligo (Treviso, Italy).

The rehabilitation intervention comprised a multidisciplinary management approach, encompassing physiotherapy, occupational therapy, practical manual activities, psychological support and speech therapy.

Upon the conclusion of the four-week programme, the participants returned to the laboratory to undertake a repetition of the data collection procedure (T2).

The control group participated only in the T1 data collection.

3.2.4 Apparatus

The optoelectronic motion analysis system SMART-D (Bioengineering Technology & Systems, BTS) was used to record reaching and grasping movements. The system comprises six infrared cameras (sampling rate: 60 Hz) positioned in a semicircular

configuration at 1–1.2 metres from the centre of the room, detecting reflective passive markers in a three-dimensional space (Fig.4).

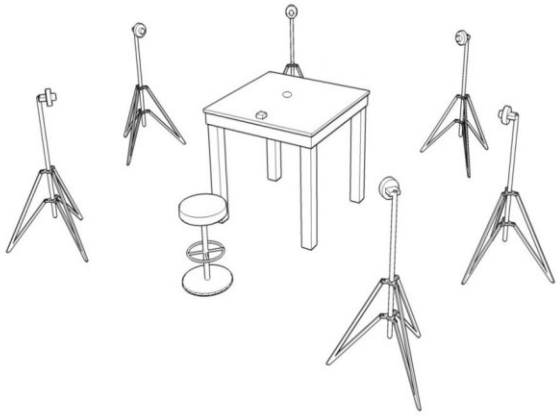

Figure 4. Experimental setting and arrangement of infrared cameras

The markers (6 mm diameter) were attached to the wrists in the radial area, on the tips of each finger of both hands and on the stimuli, using double-sided tape.

Before the collection of data, the cameras were set to obtain the optimal framing, which may entail adjusting the zoom, brightness, and focus.

The system was then calibrated. This procedure consists of two distinct phases. Initially, a dedicated instrument (termed a 'terna') representing the three axes of the Cartesian system was positioned at the centre of the workspace to undertake a static calibration. Subsequently, a dynamic calibration was conducted to delineate the experimental space by moving the wand along three dimensions.

3.3 Rehabilitation intervention

The FRDA programme was based on a multidisciplinary approach, encompassing physiotherapy, occupational therapy, manual activities, psychological support, speech therapy and clinical psychology.

The rehabilitation programme was conducted over a period of four weeks, in accordance with the literature, which suggests that a minimum of four weeks is beneficial for functional improvement in Friedreich's ataxia (Milne et al., 2017).

Each patient participated in 11 weekly physiotherapy sessions, with the programme focusing on improving trunk stability, postural control, and coordination through targeted exercises.

The physiotherapy programme was adapted to align with the severity of the condition. For ambulant patients (able to walk with or without assistance), the focus was on maintaining balance and improving gait. For non-ambulant patients (wheelchair-bound), the emphasis was on enhancing trunk control, upper limb mobility and safe transfer techniques.

Furthermore, patients were engaged in occupational therapy, practical manual activities, and psychological support in order to develop the requisite skills for daily living and to enhance their quality of life. The occupational therapy programme included tasks designed to enhance upper limb and trunk coordination. In addition, practical manual activities were conducted, comprising tasks tailored to the individual patient's severity. Psychological support was provided on three occasions per week, comprising coping strategies and adaptation to aids. Furthermore, all patients underwent neuropsychological assessments and speech therapy during their first week to address swallowing and language difficulties.

3.4 Data Analysis

Once the data acquisition process was completed, each trial was individually tracked using the SMART-Tracker software. The operation consists of assigning the appropriate name (e.g., thumb, index, wrist) to each marker throughout the movement using a specific model that has been previously created. In this way, it was possible to reconstruct the trajectories followed by the hands.

The subsequent processing stage employs the SMART Analyzer software, whereby a comprehensive protocol tailored to the specific experimental procedure was applied to the tracked data to measure the spatial, temporal and acceleration indexes.

Spatial parameters:

- Maximum Grip Aperture (MGA): Maximum distance between thumb and index finger.
- Maximum Trajectory Deviation (MTDev): The maximum deviation of the hand's path to the right or left from a straight line.
- Trajectory Path (TrP): The overall path followed by the hand during movement.

Velocity Parameters:

- Maximum Grip Aperture Velocity (MGAV): The highest speed at which the thumb and index finger move apart.
- Maximum Wrist Velocity (MWV): The highest speed of the wrist during movement.

Temporal Parameters:

- Movement Time (MT): The total time taken to complete the movement.
- Delay Time Reaching-Grasping (Delay RC-GR): The delay time between reaching the target and starting the grip.

- Deceleration Time (DecT): The time spent decelerating before completing the movement.
- Time to Maximum Grip Aperture (TMGA%): The percentage of total movement time taken to reach the maximum grip aperture.
- Time to Maximum Grip Aperture Velocity (TMGAV%): The percentage of total movement time taken to reach the maximum grip aperture velocity.
- Time to Maximum Wrist Velocity (TMWV%): The percentage of total movement time taken to reach the maximum wrist velocity.

Jerk Submovements (JS).

The resulting data were exported to an Excel worksheet

3.5 Statistical Analysis

A statistical analysis was performed to compare the kinematic performance of individuals diagnosed with Friedreich's ataxia (FA) to a control group of ten healthy individuals during reaching and grasping task. The FA group underwent kinematic testing at two time points: before (T1) and after (T2) a four-week multidisciplinary rehabilitation programme, while the control group was tested at a single time point.

Independent Samples T-Tests were used to assess differences between Friedreich's ataxia group and the control group at both T1 and T2.

3.6 Results

This thesis presents data on the Right Hand Precision Grip (PG), which is the most accurate prehension performed with the dominant hand. The results of the other conditions (Right WHG, Left PG and Left WHG) are reported in the Appendix.

SPATIAL PARAMETERS

- Trajectory Path (TrP)

A significant group main effect was observed at T1 ($t_{(13)} = 2.345$, $p = 0.036$, Cohen's $d = 1.284$), with the Friedreich's ataxia group showing longer trajectory paths (M = 350.38 cm, SD = 59.46) compared to the control group (M = 291.58 cm, SD = 38.16).

At T2, this difference remained significant ($t_{(13)} = 2.262$, $p = 0.042$, Cohen's $d = 1.239$), with the FA group still having longer trajectory paths (M = 343.59 cm, SD = 49.50) relative to the controls (Fig. 5).

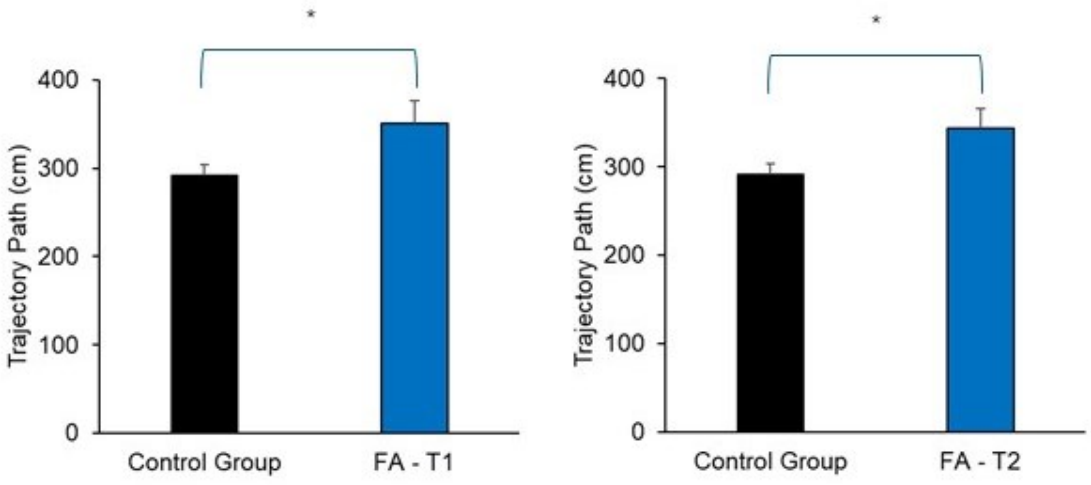

Figure 5. Graphical representation of the mean values of the Trajectory Path for the control group (in black) and Friederich's ataxia group (in blue), before (T1) and after (T2) the rehabilitation intervention. * = $p < .05$.

- Maximum Trajectory Deviation (MTDev)

At T1, a highly significant difference was observed ($t_{(13)}$ = 3.071, p = 0.009, Cohen's d = 1.682), with the Friedreich's ataxia group showing greater movement deviation on the right (M = 55.94 mm, SD = 18.05) compared to controls (M = 32.76 mm, SD = 11.39). A significant difference between the two groups persisted at T2 ($t_{(13)}$ = 2.467, p = 0.028, Cohen's d = 1.351; M = 54.58 mm, SD = 23.59; Fig.6).

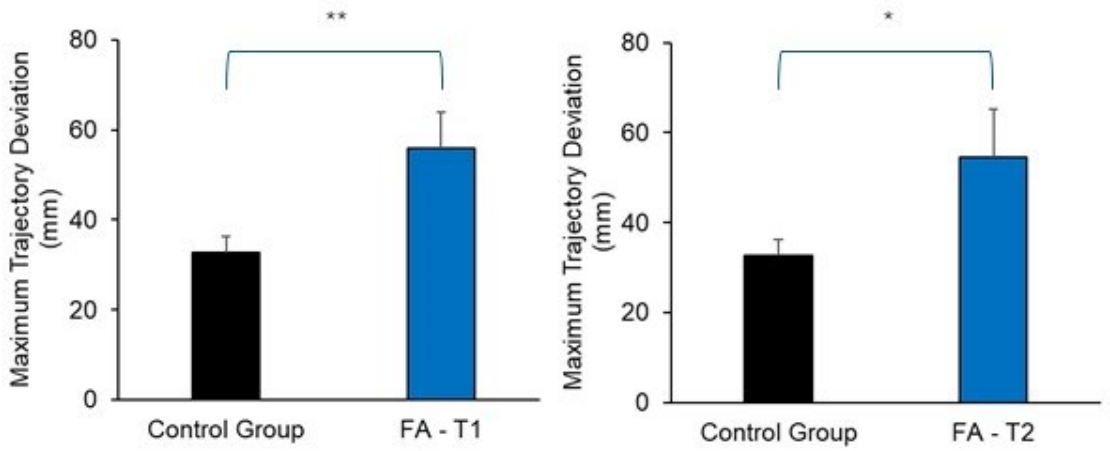

Figure 6. Graphical representation of the mean values of the Maximum Trajectory Deviation on the right for the control group (in black) and Friederich's ataxia group (in blue), before (T1) and after (T2) the rehabilitation intervention. * = $p < .05$, ** = $p < .01$.

- Maximum Grip Aperture (MGA)

The Friedreich's ataxia group showed significantly larger maximum grip aperture at T1 ($t_{(13)}$= 2.897, p = 0.012, Cohen's d = 1.587), with an average of 111.44 mm (SD = 13.68) compared to the control group (M = 90.71 mm, SD = 12.78).

At T2, a highly significant difference was observed (t(13) = 3.999, p = 0.002, Cohen's d = 2.190), with the Friedreich's ataxia group reporting a mean of 115.33 mm and a standard deviation of 6.58 mm (Fig. 7).

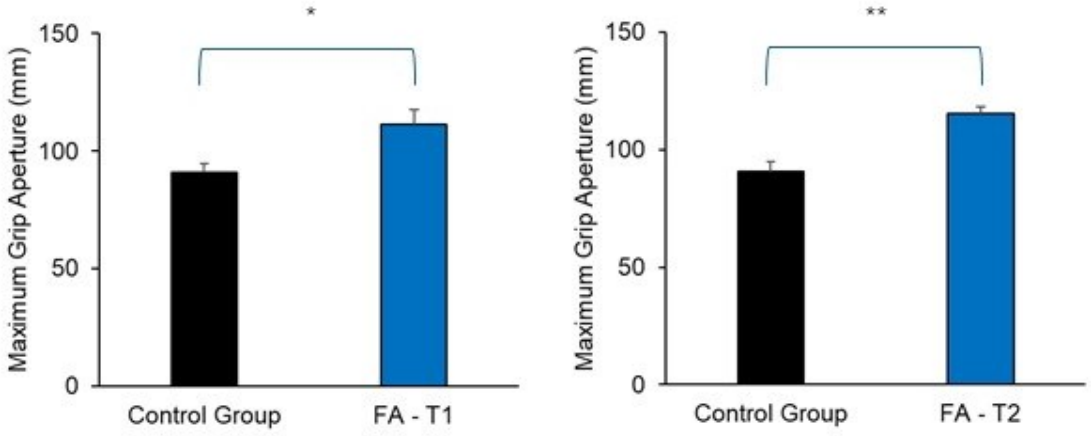

Figure 7. Graphical representation of the mean values of the Maximum Grip Aperture for the control group (in black) and Friederich's ataxia group (in blue), before (T1) and after (T2) the rehabilitation intervention. * = $p < .05$, ** = $p < .01$.

TEMPORAL PARAMETERS

- Movement Time (MT)

A highly significant effect was found at T1 ($t_{(13)}$= 3.601, p = 0.003, Cohen's d = 1.972), with the FA group taking longer to complete the task (M = 2026.03 ms, SD = 796.92) compared to the control group (M = 1001.81 ms, SD = 327.45).

At T2, a highly significant difference persisted ($t_{(13)}$= 3.736, p = 0.002, Cohen's d = 2.046), with the FA group showing a mean movement time of 1828.08 ms and a standard deviation of 537.36 ms (Fig. 8).

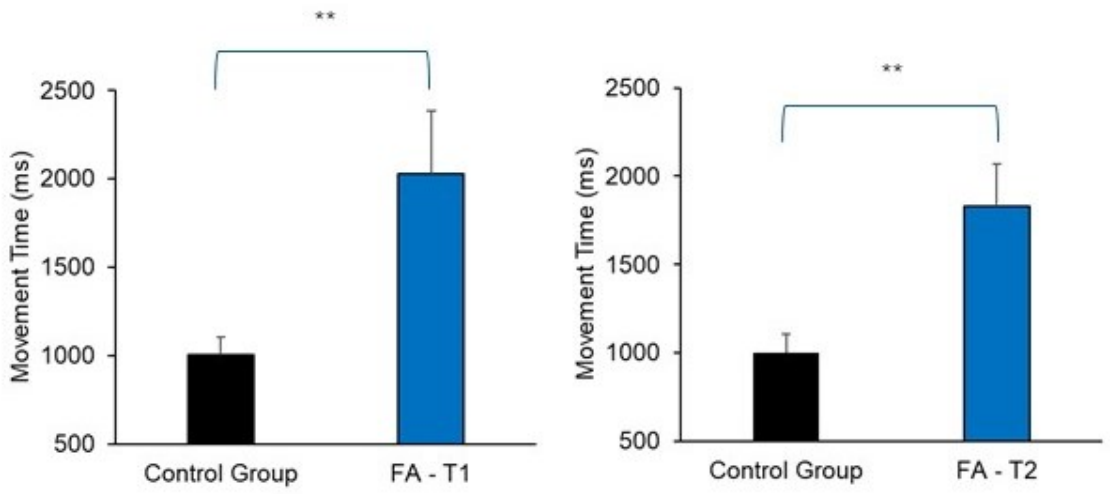

Figure 8. Graphical representation of the mean values of the Movement Time for the control group (in black) and Friederich's ataxia group (in blue), before (T1) and after (T2) the rehabilitation intervention. ** = $p < .01$.

- Delay Time Reaching-Grasping (Delay RC-GR)

At T1, a highly significant group effect was found ($t_{(13)}$= 3.793, p = 0.002, Cohen's d = 2.077), with Friedreich's ataxia group showing longer delay time between the reaching and grasping (M = 240.69 ms, SD = 149.61) compared to the control group (M = 60.66 ms, SD = 30.05).

At T2, a significant difference (t(13) = 2.392, p = 0.033, Cohen's d = 1.310) was found between the control group and the Friedreich's ataxia group (M = 171.10 ms, SD = 145.11). For graphical representation see Figure 9.

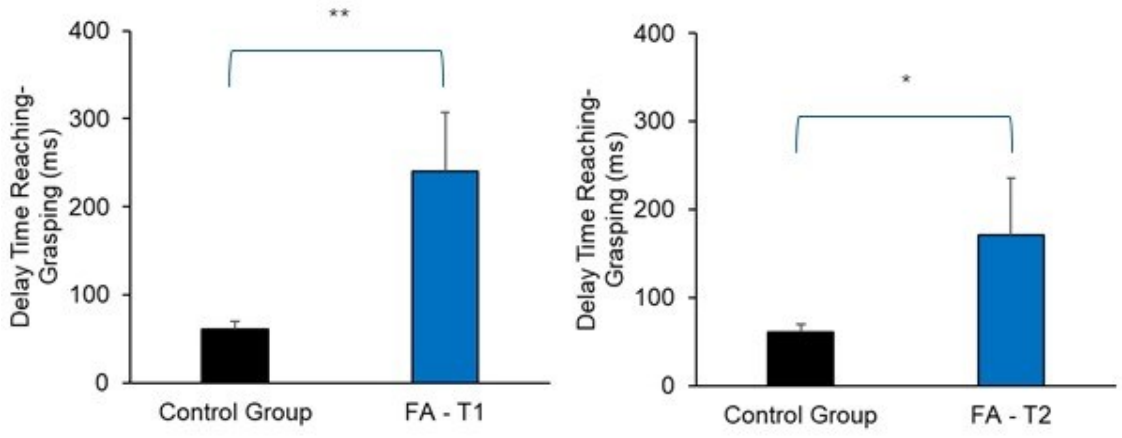

Figure 9. Graphical representation of the mean values of the Delay Time between the Reaching and Grasping for the control group (in black) and Friederich's ataxia group (in blue), before (T1) and after (T2) the rehabilitation intervention. * = $p < .05$, ** = $p < .01$.

- Deceleration Time (DecT)

A highly significant difference was observed at T1 ($t_{(13)}$= 3.810, p = 0.002, Cohen's d = 2.087), with the Friedreich's ataxia group having a longer deceleration phase (M = 1075.90 ms, SD = 368.23) compared to the control group (M = 565.80 ms, SD = 161.44). At T2, the difference remained significant ($t_{(13)}$= 2.793, p = 0.015, Cohen's d = 1.530), with a mean deceleration time of 883.39 ms (SD = 285.27) for the Friedreich's ataxia group (Fig. 10).

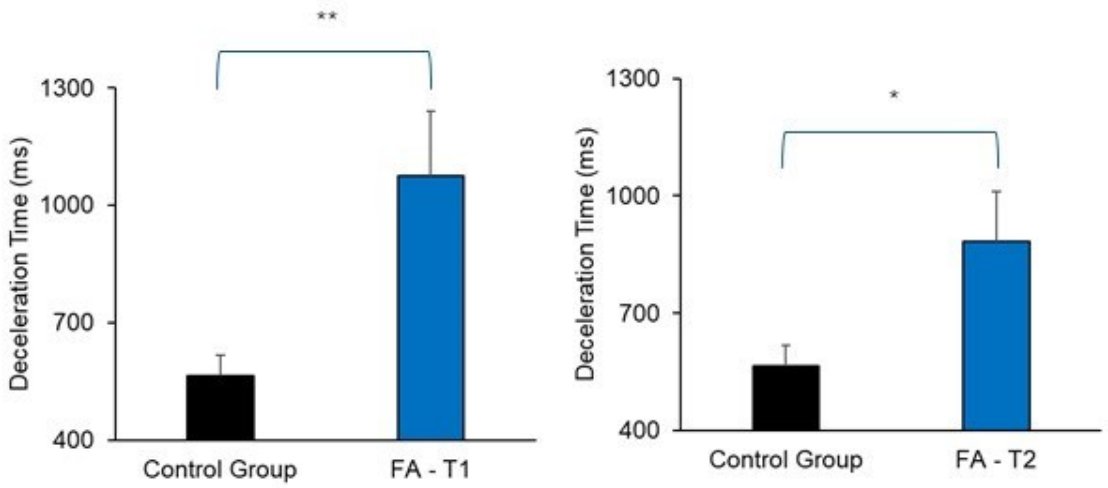

Figure 10. Graphical representation of the mean values of the Deceleration Time for the control group (in black) and Friederich's ataxia group (in blue), before (T1) and after (T2) the rehabilitation intervention. * = $p < .05$, ** = $p < .01$.

- Time to Maximum Grip Aperture (TMGA%)

A significant difference was found at T1 ($t_{(13)}$= -2.469, p = 0.028, Cohen's d = -1.352), with the Friedreich's ataxia group reaching maximum grip aperture earlier in the movement (M = 55.56%, SD = 4.44) compared to the control group (M = 62.33%, SD = 5.24).

At T2, the difference was no longer significant ($t_{(13)}$= -0.948, p = 0.360, Cohen's d = -0.519), with the Friedreich's ataxia group's timing becoming closer to the control group's (M = 59.88%, SD = 3.23). A graphical representation is provided in Figure 11.

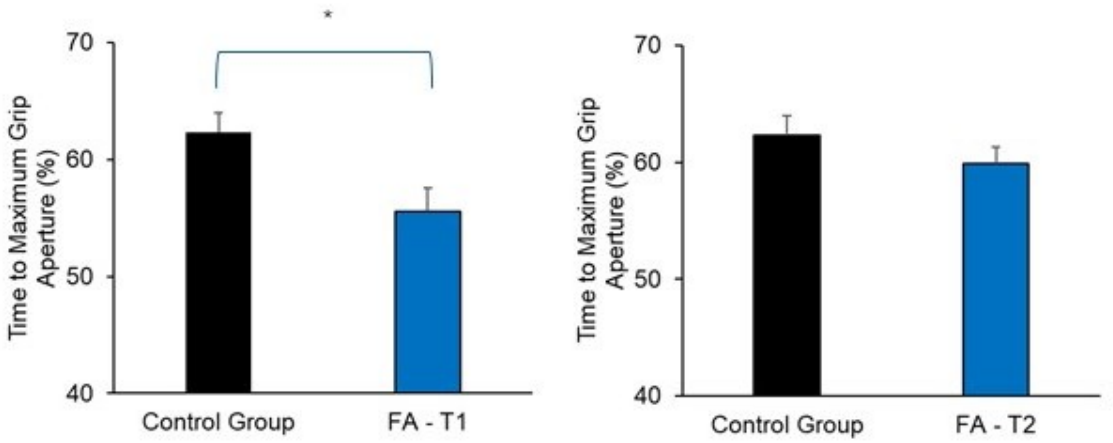

Figure 11. Graphical representation of the mean values of the percentage of the total time taken to reach the Maximum Grip Aperture for the control group (in black) and Friederich's ataxia group (in blue), before (T1) and after (T2) the rehabilitation intervention. * = $p < .05$.

- Time to Maximum Grip Aperture Velocity (TMGAV%)

No significant difference was observed at T1 ($t_{(13)}$= -1.511, p = 0.155, Cohen's d = -0.828), with the Friedreich's ataxia group showing slightly earlier maximum grip aperture velocity (M = 28.94%, SD = 7.42) compared to controls (M = 37.19%, SD = 10.91).

At T2, the difference became significant ($t_{(13)}$ = -2.244, p = 0.043, Cohen's d = -1.229), with the Friedreich's ataxia group reaching maximum velocity earlier (M = 24.62%, SD = 8.50; Fig. 12).

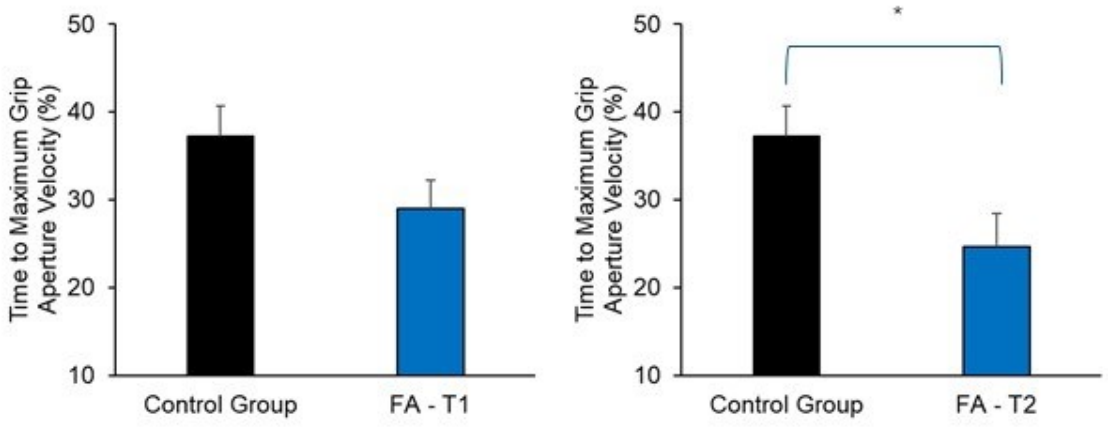

Figure 12. Graphical representation of the mean values of the percentage of the total time taken to reach the Maximum Grip Aperture Velocity for the control group (in black) and Friederich's ataxia group (in blue), before (T1) and after (T2) the rehabilitation intervention. * = $p < .05$.

- Time to Maximum Wrist Velocity (TMWV%)

A highly significant group main effect was observed ($t_{(13)}$= −3.122; p = 0.008, Cohen's d=-1.710), with Friedreich's ataxia group having earlier values in the pre-rehabilitation phase (M = 28.31%; SD = 7.93) compared to the control group (M = 38.10%; SD = 4.40). After the rehabilitation intervention FA group showed significantly earlier values ($t_{(13)}$= −2.181; p= 0.048, Cohen's d = -1.194), which are closer to the control group (M = 31.64%; SD = 7.17; Fig. 13).

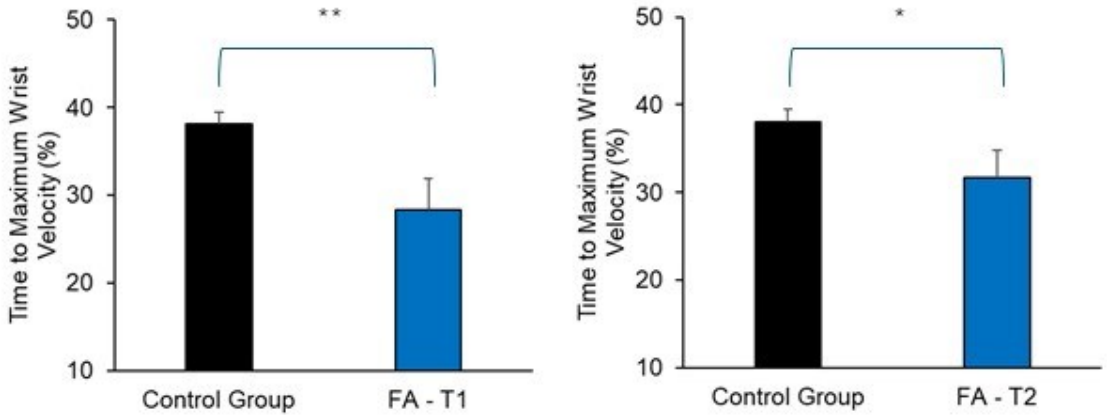

Figure 13. Graphical representation of the mean values of the percentage of the total time taken to reach the Maximum Wrist Velocity for the control group (in black) and Friederich's ataxia group (in blue), before (T1) and after (T2) the rehabilitation intervention. * = $p < .05$, ** = $p < .01$.

VELOCITY PARAMETERS

- Maximum Wrist Velocity (MWV)

A non-significant effect was found at T1 ($t_{(13)}$= -1.759, p = 0.102, Cohen's d = -0.963), with Friedreich's ataxia group showing slightly lower MWV (M = 547.97 mm/s, SD = 149.13) than the control group (M = 698.12 mm/s, SD = 158.73).

At T2, the difference was again non-significant ($t_{(13)}$= -2.065, p = 0.059, Cohen's d = -1.131), with a mean maximum wrist velocity of 515.74 mm/s (SD = 166.80) in the Friedreich's ataxia group (Fig. 14).

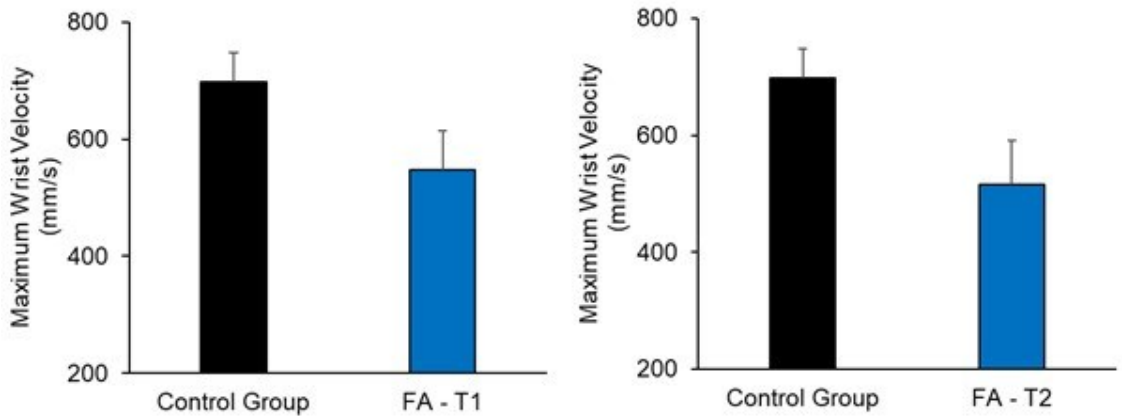

Figure 14. Graphical representation of the mean values of the Maximum Wrist Velocity for the control group (in black) and Friederich's ataxia group (in blue), before (T1) and after (T2) the rehabilitation intervention.

- Maximum Grip Aperture Velocity (MGAV)

There was no significant difference between groups ($t_{(13)}$= -0.106, p = 0.917, Cohen's d = -0.058), with the Friedreich's ataxia group having similar MGAV values at T1 (M = 327.95 mm/s, SD = 121.59) to the control group (M = 334.77 mm/s, SD = 114.99). This lack of significance persisted at T2 ($t_{(13)}$= 0.447, p = 0.663, Cohen's d = 0.245), with the Friedreich's ataxia group having a mean of 360.98 mm/s (SD = 87.02). For graphical representation see Figure 15.

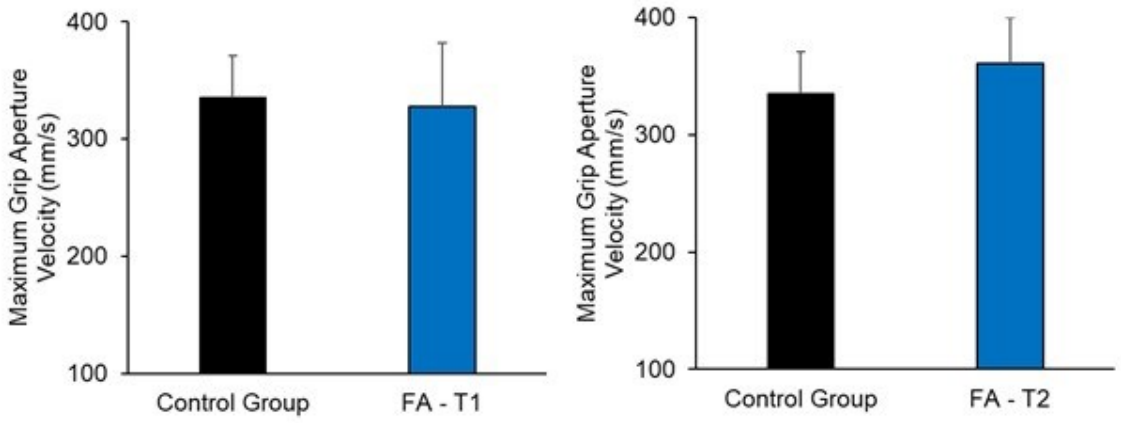

Figure 15. Graphical representation of the mean values of the Maximum Grip Aperture Velocity for the control group (in black) and Friederich's ataxia group (in blue), before (T1) and after (T2) the rehabilitation intervention.

JERK SUBMOVEMENTS (JS)

A significant group main effect was observed (t(13) = 2.553; p = 0.024, Cohen's d = 1.398), with the Friedreich's ataxia group having higher jerk frequency at T1 (M = 7.96; SD = 3.43) compared to the control group (M = 4.62; SD = 1.72).

At T2, the difference remained significant (t(13) = 2.304; p = 0.038, Cohen's d = 1.262), with the FA group having a mean number of submovements of 6.78 (SD = 1.67).

A graphical representation is provided in Figure 16.

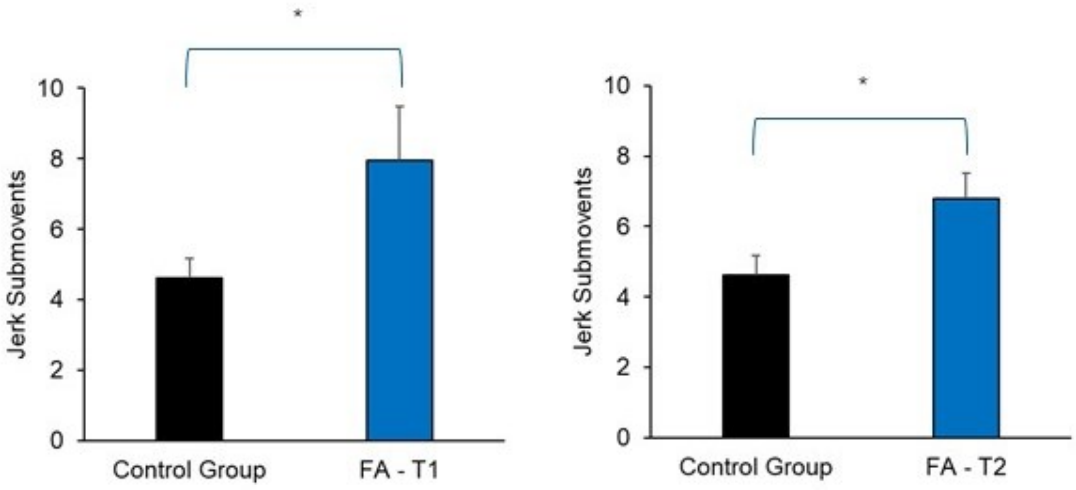

Figure 16. Graphical representation of the mean values of the number of Jerks Submovements for the control group (in black) and Friederich's ataxia group (in blue), before (T1) and after (T2) the rehabilitation intervention. * = $p < .05$, ** = $p < .01$.

4. DISCUSSION

The objective of this experimental study was to analyse the kinematic movements of reaching and grasping in patients with Friedreich's ataxia and to evaluate the potential benefits of a multidisciplinary intervention programme.

The kinematic analysis demonstrated clear differences in reaching and grasping movements of the precision grip between individuals with Friedreich's ataxia and healthy controls. These differences were evident in various spatial and temporal parameters, indicating significant motor dysfunctions in Friedreich's ataxia group (FA).

FA group exhibited significantly longer trajectory paths (TrP), greater maximum trajectory deviation (MTDev – Right), and maximum grip aperture (MGA) compared to the control group at both T1 and T2. These findings indicate that individuals with Friedreich's ataxia are unable to determine the appropriate degree of hand opening in relation to the size of the object to be grasped and to follow a straight-line trajectory. This may be attributed to an inadequacy in the forward model's capacity to predict movement.

Temporal analysis revealed that the FA group took significantly longer to complete the tasks, with extended movement time (MT), prolonged delay time between reaching and grasping (Delay RC-GR), and longer deceleration phases (DecT).

Extended movement times in FA patients indicate that they require more time to complete the task, resulting in slower and less efficient movement. The extended delay between reaching and grasping phases suggests a disruption in the coordination of these critical components, leading to fragmented and imprecise movements. Additionally, longer deceleration phases highlight difficulties in fine-tuning movements as the hand approaches the object, causing a slower and less controlled approach. Together with an abnormal frequency of jerk submovements, these temporal deficits reflect significant

challenges in motor coordination and precision for the patients. Following the four-week intervention, the average movement times, delay times, and deceleration phases in the FA group showed a trend toward improvement, with measures getting closer to those of the control group. However, despite these observed improvements, the FA group's performance still does not reach that of the control group.

Interestingly, at T1 the time needed for Friedreich's ataxia group to reach the maximum grip aperture (TMGA%) was anticipated compared to the control group, but this difference was no longer present after the training. Grip anticipation is a classic compensatory strategy in case of difficulties in motor planning, where the hand opens too early to accommodate motor control difficulties later in the movement, and it reflects a disruption in the coordination between the reaching and grasping phases. However, this improvement was achieved by anticipating the time at which the hand reaches maximum opening speed (TMGAV%), unlike in the control group. The patients therefore show that they have acquired a strategy of speed anticipation that allows them to gain time to better calibrate the finalisation phase of the movement.

Although the maximum grip aperture (MGA) is stable between T1 and T2, following the four-week intervention period, the time required to reach it (TMGA%) is postponed and it gets closer to the control group. This ensures that the hand is properly shaped to grasp the object at the appropriate moment, reflecting a well-coordinated motor plan.

The velocity parameters, maximum wrist velocity (MWV) and maximum grip aperture velocity (MGAV), did not demonstrate significant differences between the control and FA groups at both T1 and T2. However, the FA group reached the maximum wrist velocity earlier in time compared to the control group (TMWV%), which again may

indicate compensatory strategies or altered motor planning. After the rehabilitation intervention FA group demonstrated a tendency towards normalisation.

The analysis of jerk submovements (JS), which reflect the smoothness of motion, revealed significantly higher jerk frequencies in the FA group with respect to the control group, indicative of more erratic and less smooth movements.

These findings collectively highlight the profound impact of Friedreich's ataxia on motor function, particularly in the coordination, timing, and smoothness of reaching and grasping movements. Considering the progressive nature of the disease and the average severity of the patient sample, there was substantial maintenance in functions. However, after the multidisciplinary intervention, the reaching component showed a trend toward normalization, indicating that the intervention had a positive effect on this aspect of motor control.

The decision to report only the results of the right hand precision grip can be justified by several factors. Firstly, the precision grip is considered the most critical aspect of motor function in patients with Friedreich's ataxia, providing a clear and specific indicator of motor difficulties and rehabilitation improvements. Additionally, the right hand has been chosen as it is typically the dominant hand in the population. Lastly, given that this is a pilot study with a small sample size of only five patients, focusing on the precision grip of the right hand allowed for a more manageable and focused analysis.

Future research should focus on expanding the sample size to enhance the robustness and generalizability of the findings. Additionally, a larger sample could facilitate subgroup analyses, providing deeper insights into different kinematic profiles of patients at different stages of the disease.

5. CONCLUSIONS

The study's primary aim was to investigate the impact of Friedreich's ataxia, a neurodegenerative disorder that severely affects the nervous system, on the fundamental motor skills of reaching and grasping. Friedreich's ataxia patients experience significant impairments in motor coordination, balance, and fine motor skills, which are associated with difficulties in reaching and grasping. The objective was to evaluate the potential advantages of a four-week multidisciplinary rehabilitation program on kinematic performance. The experimental findings highlighted significant differences in the kinematic parameters between individuals with Friedreich's ataxia and healthy controls, revealing substantial motor dysfunctions in the FA group. These differences were particularly evident in spatial and temporal parameters and in the frequency of submovements. In contrast, velocity parameters did not differ from those observed in the control group.

Notably, Friedreich's ataxia group exhibited less efficient movements, with a pronounced difficulty in executing smooth and coordinated motor actions. The rehabilitation program demonstrated some positive effects, particularly in the reaching component, where the total movement time, the deceleration phase and the delay between reaching and grasping were closer to the control group. Despite these improvements, the motor performance of the FA group does not reach that of the control group, indicating the persistent nature of motor deficits in Friedreich's ataxia patients. However, one notable exception was the time required for the FA group to reach maximum grip aperture, which, after the rehabilitation intervention, no longer showed a significant difference from the control group.

Nevertheless, it is important to reiterate that Friedreich's ataxia is a neurodegenerative condition, meaning that patients experience a progressive worsening of symptoms each year. The primary goal of the intervention is to maintain existing motor functions and to slow down the rate of deterioration, rather than fully reversing the effects of the disease. This study contributes to the growing body of literature on motor control in neurodegenerative diseases, particularly Friedreich's ataxia. It provides evidence that kinematic analysis is a sensitive tool for detecting motor dysfunctions and evaluating rehabilitation outcomes, offering detailed insights into which specific components of movement are most compromised. It offers valuable insights into subtle changes in motor performance that might not be evident through other methods, thereby guiding more targeted and effective rehabilitation strategies.

However, several areas remain unexplored or insufficiently studied. For instance, understanding the kinematic performance of Friedreich's ataxia patients across different stages of the disease, its progression over time and which specific movement components are most affected, could facilitate a more personalized therapeutic approach.

Additionally, integrating the kinematic analysis with standard assessment scales, such as the Scale for Assessment and Rating of Ataxia (SARA), the Friedreich Ataxia Rating Scale (FARS) or the Nine Hole Peg Test (9HPT), could enhance sensitivity to subtle changes in motor performance, offering a more comprehensive evaluation of disease progression and treatment efficacy in the clinical setting.

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APPENDIX

Results Right hand Precision Grip (Right PG) in Friedreich's ataxia group at T1 (Pre-Treatment) vs. control group

Independent Samples T-Test

	t	df	p	Cohen's d	SE Cohen's d
TrP	2.345	13	0.036*	1.284	0.682
MGAV	−0.106	13	0.917	−0.058	0.548
MWV	−1.759	13	0.102	−0.963	0.627
MT	3.601	13	0.003*	1.972	0.830
Delay RC_GR	3.792	13	0.002*	2.077	0.855
DecT	3.810	13	0.002*	2.087	0.858
MGA	2.897	13	0.012*	1.587	0.743
MTDev_DX	3.071	13	0.009*	1.682	0.763
JS	2.552	13	0.024*	1.398	0.704
TMGA%	−2.468	13	0.028*	−1.352	0.695
TMGAV%	−1.511	13	0.155	−0.828	0.607
TMWV%	−3.122	13	0.008*	−1.710	0.770

Descriptives

Group Descriptives

	Group	N	Mean	SD	SE	Coefficient of variation
TrP	Ataxia	5	350.382	59.463	26.593	0.170
	Control	10	291.582	38.164	12.069	0.131
MGAV	Ataxia	5	327.946	121.589	54.376	0.371
	Control	10	334.769	114.992	36.364	0.343
MWV	Ataxia	5	547.970	149.128	66.692	0.272
	Control	10	698.115	158.728	50.194	0.227
MT	Ataxia	5	2026.024	796.918	356.392	0.393
	Control	10	1001.813	327.445	103.547	0.327
Delay RC_GR	Ataxia	5	240.694	149.610	66.908	0.622
	Control	10	60.655	30.047	9.502	0.495
DecT	Ataxia	5	1075.898	368.226	164.676	0.342
	Control	10	565.801	161.442	51.052	0.285
MGA	Ataxia	5	111.434	13.672	6.114	0.123
	Control	10	90.709	12.780	4.041	0.141
MTDev_DX	Ataxia	5	55.936	18.046	8.070	0.323
	Control	10	32.755	11.385	3.600	0.348
JS	Ataxia	5	7.954	3.429	1.534	0.431
	Control	10	4.624	1.723	0.545	0.373
TMGA%	Ataxia	5	55.560	4.439	1.985	0.080
	Control	10	62.328	5.239	1.657	0.084
TMGAV%	Ataxia	5	28.942	7.419	3.318	0.256
	Control	10	37.194	10.912	3.451	0.293
TMWV%	Ataxia	5	28.308	7.933	3.548	0.280
	Control	10	38.100	4.402	1.392	0.116

Results Right hand Precision Grip (Right PG) in Friedreich's ataxia group at T2 (Post-Treatment) vs. control group

Independent Samples T-Test

	t	df	p	Cohen's d	SE Cohen's d
TrP	2.262	13	0.042*	1.239	0.673
MGAV	0.447	13	0.663	0.245	0.553
MWV	−2.065	13	0.059	−1.131	0.654
MT	3.736	13	0.002*	2.046	0.848
DecT	2.793	13	0.015*	1.530	0.731
MGA	3.999	13	0.002*	2.190	0.883
MTDev_DX	2.467	13	0.028*	1.351	0.695
JS	2.307	13	0.038*	1.264	0.678
TMGA%	−0.948	13	0.360	−0.519	0.572
TMGAV%	−2.244	13	0.043*	−1.229	0.672
TMWV%	−2.181	13	0.048*	−1.194	0.665
Delay RC_GR	2.392	13	0.033*	1.310	0.687

Descriptives

Group Descriptives

	Group	N	Mean	SD	SE	Coefficient of variation
TrP	Ataxia	5	343.586	49.505	22.140	0.144
	Control	10	291.582	38.164	12.069	0.131
MGAV	Ataxia	5	360.980	87.013	38.913	0.241
	Control	10	334.769	114.992	36.364	0.343
MWV	Ataxia	5	515.744	166.799	74.595	0.323
	Control	10	698.115	158.728	50.194	0.227
MT	Ataxia	5	1828.080	537.362	240.315	0.294
	Control	10	1001.813	327.445	103.547	0.327
DecT	Ataxia	5	883.390	285.272	127.577	0.323
	Control	10	565.801	161.442	51.052	0.285
MGA	Ataxia	5	115.332	6.580	2.943	0.057
	Control	10	90.709	12.780	4.041	0.141
MTDev_DX	Ataxia	5	54.584	23.593	10.551	0.432
	Control	10	32.755	11.385	3.600	0.348
JS	Ataxia	5	6.780	1.667	0.746	0.246
	Control	10	4.624	1.723	0.545	0.373
TMGA%	Ataxia	5	59.880	3.233	1.446	0.054
	Control	10	62.328	5.239	1.657	0.084
TMGAV%	Ataxia	5	24.618	8.501	3.802	0.345
	Control	10	37.194	10.912	3.451	0.293
TMWV%	Ataxia	5	31.644	7.165	3.204	0.226
	Control	10	38.100	4.402	1.392	0.116
Delay RC_GR	Ataxia	5	171.096	145.111	64.896	0.848
	Control	10	60.655	30.047	9.502	0.495

Results Left hand Precision Grip (Left PG) in Friedreich's ataxia group at T1 (Pre- Treatment) vs. control group

Independent Samples T-Test

	t	df	p	Cohen's d	SE Cohen's d
TrP	1.510	13	0.155	0.827	0.607
MGAV	−1.355	13	0.199	−0.742	0.596
MWV	−2.302	13	0.038*	−1.261	0.678
MT	3.418	13	0.005*	1.872	0.806
DecT	3.084	13	0.009*	1.689	0.765
MGA	2.270	13	0.041*	1.243	0.674
MTDev_DX	1.548	13	0.146	0.848	0.610
JS	2.585	13	0.023*	1.416	0.707
TMGA%	1.101	13	0.291	0.603	0.580
TMGAV%	0.468	13	0.647	0.257	0.554
TMWV%	−2.115	13	0.054*	−1.158	0.659
Delay RC_GR	5.278	13	< .001*	2.891	1.066

Descriptives

Group Descriptives

	Group	N	Mean	SD	SE	Coefficient of variation
TrP	Ataxia	5	352.568	102.724	45.940	0.291
	Control	10	300.640	31.659	10.011	0.105
MGAV	Ataxia	5	302.206	88.705	39.670	0.294
	Control	10	368.606	89.814	28.402	0.244
MWV	Ataxia	5	504.946	201.600	90.158	0.399
	Control	10	736.164	174.622	55.220	0.237
MT	Ataxia	5	2119.366	1069.516	478.302	0.505
	Control	10	957.097	220.246	69.648	0.230
DecT	Ataxia	5	1033.678	510.650	228.370	0.494
	Control	10	521.620	129.724	41.022	0.249
MGA	Ataxia	5	111.390	12.012	5.372	0.108
	Control	10	97.440	10.850	3.431	0.111
MTDev_DX	Ataxia	5	0.174	0.149	0.066	0.854
	Control	10	0.063	0.123	0.039	1.964
JS	Ataxia	5	7.710	4.303	1.924	0.558
	Control	10	4.206	0.785	0.248	0.187
TMGA%	Ataxia	5	62.808	5.795	2.592	0.092
	Control	10	59.704	4.833	1.528	0.081
TMGAV%	Ataxia	5	35.128	8.566	3.831	0.244
	Control	10	32.305	11.930	3.772	0.369
TMWV%	Ataxia	5	31.240	9.855	4.407	0.315
	Control	10	39.780	5.945	1.880	0.149
Delay RC_GR	Ataxia	5	364.366	158.936	71.078	0.436
	Control	10	76.426	55.726	17.622	0.729

Results Left hand Precision Grip (Left PG) in Friedreich's ataxia group at T2 (Post- Treatment) vs. control group

Independent Samples T-Test

	t	df	p	Cohen's d	SE Cohen's d
TrP	0.989	13	0.341	0.542	0.574
MGAV	0.214	13	0.834	0.117	0.549
MWV	−2.780	13	0.016*	−1.522	0.729
MT	4.059	13	0.001*	2.223	0.891
DecT	3.581	13	0.003*	1.962	0.828
MGA	2.778	13	0.016*	1.522	0.729
MTDev_DX	1.039	13	0.318	0.569	0.577
JS	3.125	13	0.008*	1.712	0.770
TMGA%	0.730	13	0.478	0.400	0.562
TMGAV%	0.407	13	0.690	0.223	0.552
TMWV%	−3.261	13	0.006*	−1.786	0.787
Delay RC_GR	3.058	13	0.009*	1.675	0.762

Note. Student's t-test.

Descriptives

Group Descriptives

	Group	N	Mean	SD	SE	Coefficient of variation
TrP	Ataxia	5	323.148	57.919	25.902	0.179
	Control	10	300.640	31.659	10.011	0.105
MGAV	Ataxia	5	381.924	153.772	68.769	0.403
	Control	10	368.606	89.814	28.402	0.244
MWV	Ataxia	5	490.742	125.874	56.292	0.256
	Control	10	736.164	174.622	55.220	0.237
MT	Ataxia	5	1774.602	574.750	257.036	0.324
	Control	10	957.097	220.246	69.648	0.230
DecT	Ataxia	5	813.822	185.087	82.774	0.227
	Control	10	521.620	129.724	41.022	0.249
MGA	Ataxia	5	115.794	14.418	6.448	0.125
	Control	10	97.440	10.850	3.431	0.111
MTDev_DX	Ataxia	5	0.160	0.247	0.111	1.547
	Control	10	0.063	0.123	0.039	1.964
JS	Ataxia	5	6.668	2.309	1.033	0.346
	Control	10	4.206	0.785	0.248	0.187
TMGA%	Ataxia	5	61.520	3.799	1.699	0.062
	Control	10	59.704	4.833	1.528	0.081
TMGAV%	Ataxia	5	34.888	10.750	4.808	0.308
	Control	10	32.305	11.930	3.772	0.369
TMWV%	Ataxia	5	29.892	4.480	2.003	0.150
	Control	10	39.780	5.945	1.880	0.149
Delay RC_GR	Ataxia	5	259.594	178.547	79.849	0.688
	Control	10	76.426	55.726	17.622	0.729

Results Right Hand Whole Hand Grasp (Right WHG) in Friedreich's ataxia group at T1 (Pre-Treatment) vs. control group

Independent Samples T-Test

	t	df	p	Cohen's d	SE Cohen's d
TrP	1.607	13	0.132	0.880	0.614
MGAV	−1.371	13	0.193	−0.751	0.597
MWV	−1.577	13	0.139	−0.864	0.612
MT	3.630	13	0.003*	1.988	0.834
DecT	3.419	13	0.005*	1.873	0.807
MGA	0.477	13	0.641	0.261	0.554
MTDev_DX	2.729	13	0.017*	1.495	0.723
JS	2.770	13	0.016*	1.517	0.728
TMGA%	0.869	13	0.401	0.476	0.568
TMGAV%	−0.824	13	0.425	−0.451	0.566
TMWV%	−1.398	13	0.186	−0.765	0.599
Delay RC_GR	2.311	13	0.038*	1.266	0.678

Descriptives

Group Descriptives

	Group	N	Mean	SD	SE	Coefficient of variation
TrP	Ataxia	5	350.384	74.416	33.280	0.212
	Control	10	303.803	39.802	12.586	0.131
MGAV	Ataxia	5	376.256	134.849	60.306	0.358
	Control	10	466.627	113.257	35.815	0.243
MWV	Ataxia	5	558.432	137.321	61.412	0.246
	Control	10	705.296	182.627	57.752	0.259
MT	Ataxia	5	1832.738	573.656	256.547	0.313
	Control	10	1041.276	287.554	90.932	0.276
DecT	Ataxia	5	950.854	374.942	167.679	0.394
	Control	10	525.957	109.027	34.477	0.207
MGA	Ataxia	5	141.446	15.117	6.760	0.107
	Control	10	138.180	11.154	3.527	0.081
MTDev_DX	Ataxia	5	49.684	21.360	9.553	0.430
	Control	10	28.156	9.842	3.112	0.350
JS	Ataxia	5	7.536	2.555	1.143	0.339
	Control	10	4.736	1.421	0.449	0.300
TMGA%	Ataxia	5	67.130	6.834	3.056	0.102
	Control	10	64.638	4.339	1.372	0.067
TMGAV%	Ataxia	5	28.266	10.288	4.601	0.364
	Control	10	32.437	8.736	2.763	0.269
TMWV%	Ataxia	5	33.168	11.057	4.945	0.333
	Control	10	39.860	7.487	2.368	0.188
Delay RC_GR	Ataxia	5	231.404	203.563	91.036	0.880
	Control	10	71.683	67.654	21.394	0.944

Results Right Hand Whole Hand Grasp (Right WHG) in Friedreich's ataxia group at T2 (Post-Treatment) vs. control group

Independent Samples T-Test

	t	df	p	Cohen's d	SE Cohen's d
TrP	1.815	13	0.093	0.994	0.632
MGAV	−0.020	13	0.984	−0.011	0.548
MWV	−1.641	13	0.125	−0.899	0.617
MT	3.052	13	0.009*	1.672	0.761
DecT	3.116	13	0.008*	1.707	0.769
MGA	0.238	13	0.815	0.130	0.549
MTDev_DX	3.170	13	0.007*	1.737	0.776
JS	2.452	13	0.029*	1.343	0.693
TMGA%	−0.089	13	0.930	−0.049	0.548
TMGAV%	−1.703	13	0.112	−0.933	0.622
TMWV%	−1.623	13	0.129	−0.889	0.616
Delay RC_GR	2.055	13	0.061	1.126	0.653

Descriptives

Group Descriptives

	Group	N	Mean	SD	SE	Coefficient of variation
TrP	Ataxia	5	344.588	43.661	19.526	0.127
	Control	10	303.803	39.802	12.586	0.131
MGAV	Ataxia	5	465.416	99.230	44.377	0.213
	Control	10	466.627	113.257	35.815	0.243
MWV	Ataxia	5	547.128	159.835	71.481	0.292
	Control	10	705.296	182.627	57.752	0.259
MT	Ataxia	5	1660.048	509.038	227.649	0.307
	Control	10	1041.276	287.554	90.932	0.276
DecT	Ataxia	5	835.506	283.112	126.611	0.339
	Control	10	525.957	109.027	34.477	0.207
MGA	Ataxia	5	139.520	7.935	3.549	0.057
	Control	10	138.180	11.154	3.527	0.081
MTDev_DX	Ataxia	5	54.272	22.741	10.170	0.419
	Control	10	28.156	9.842	3.112	0.350
JS	Ataxia	5	6.730	1.620	0.724	0.241
	Control	10	4.736	1.421	0.449	0.300
TMGA%	Ataxia	5	64.404	5.734	2.564	0.089
	Control	10	64.638	4.339	1.372	0.067
TMGAV%	Ataxia	5	24.502	7.965	3.562	0.325
	Control	10	32.437	8.736	2.763	0.269
TMWV%	Ataxia	5	33.232	7.390	3.305	0.222
	Control	10	39.860	7.487	2.368	0.188
Delay RC_GR	Ataxia	5	159.722	97.884	43.775	0.613
	Control	10	71.683	67.654	21.394	0.944

Results Left hand Whole Hand Grasp (Left WHG) in Friedreich's ataxia group at T1 (Pre-Treatment) vs. control group

Independent Samples T-Test

	t	df	p	Cohen's d	SE Cohen's d
TrP	2.355	13	0.035*	1.290	0.683
MGAV	−0.665	13	0.518	−0.364	0.560
MWV	−1.825	13	0.091	−1.000	0.632
MT	3.678	13	0.003*	2.014	0.840
DecT	3.446	13	0.004*	1.887	0.810
MGA	0.527	13	0.607	0.289	0.555
MTDev_DX	1.898	13	0.080	1.040	0.639
JS	2.585	12	0.024*	1.529	0.801
TMGA%	0.002	13	0.998	0.001	0.548
TMGAV%	−0.458	13	0.654	−0.251	0.553
TMWV%	−2.502	13	0.026*	−1.371	0.698
Delay RC_GR	3.188	13	0.007*	1.746	0.778

Descriptives

Group Descriptives

	Group	N	Mean	SD	SE	Coefficient of variation
TrP	Ataxia	5	382.140	83.209	37.212	0.218
	Control	10	311.439	35.546	11.241	0.114
MGAV	Ataxia	5	426.138	174.276	77.938	0.409
	Control	10	483.861	150.932	47.729	0.312
MWV	Ataxia	5	560.472	180.640	80.785	0.322
	Control	10	743.410	184.056	58.204	0.248
MT	Ataxia	5	1882.020	695.693	311.124	0.370
	Control	10	1011.647	233.631	73.881	0.231
DecT	Ataxia	5	964.064	347.554	155.431	0.361
	Control	10	538.891	140.030	44.281	0.260
MGA	Ataxia	5	144.814	11.016	4.926	0.076
	Control	10	141.144	13.389	4.234	0.095
MTDev_DX	Ataxia	5	0.272	0.311	0.139	1.144
	Control	10	0.069	0.109	0.034	1.574
JS	Ataxia	4	6.125	1.555	0.777	0.254
	Control	10	4.613	0.705	0.223	0.153
TMGA%	Ataxia	5	64.924	4.967	2.221	0.077
	Control	10	64.918	5.006	1.583	0.077
TMGAV%	Ataxia	5	29.088	8.632	3.860	0.297
	Control	10	31.354	9.200	2.909	0.293
TMWV%	Ataxia	5	30.214	5.700	2.549	0.189
	Control	10	38.633	6.329	2.001	0.164
Delay RC_GR	Ataxia	5	253.698	160.911	71.962	0.634
	Control	10	73.939	61.637	19.491	0.834

Results Left hand Whole Hand Grasp (Left WHG) in Friedreich's ataxia group at T2 (Post-Treatment) vs. control group

Independent Samples T-Test

	t	df	p	Cohen's d	SE Cohen's d
TrP	1.205	13	0.250	0.660	0.586
MGAV	−0.111	13	0.913	−0.061	0.548
MWV	−2.458	13	0.029*	−1.346	0.694
MT	3.570	13	0.003*	1.956	0.826
DecT	2.738	13	0.017*	1.499	0.724
MGA	0.482	13	0.638	0.264	0.554
MTDev_DX	2.712	13	0.018*	1.486	0.722
JS	3.001	13	0.010*	1.644	0.755
TMGA%	0.808	13	0.434	0.442	0.565
TMGAV%	−0.422	13	0.680	−0.231	0.553
TMWV%	−1.673	13	0.118	−0.916	0.620
Delay RC_GR	2.143	13	0.052	1.174	0.662

Descriptives

Group Descriptives

	Group	N	Mean	SD	SE	Coefficient of variation
TrP	Ataxia	5	338.400	50.769	22.704	0.150
	Control	10	311.439	35.546	11.241	0.114
MGAV	Ataxia	5	474.032	182.207	81.486	0.384
	Control	10	483.861	150.932	47.729	0.312
MWV	Ataxia	5	522.200	107.260	47.968	0.205
	Control	10	743.410	184.056	58.204	0.248
MT	Ataxia	5	1620.304	438.199	195.968	0.270
	Control	10	1011.647	233.631	73.881	0.231
DecT	Ataxia	5	785.972	210.083	93.952	0.267
	Control	10	538.891	140.030	44.281	0.260
MGA	Ataxia	5	144.680	13.433	6.007	0.093
	Control	10	141.144	13.389	4.234	0.095
MTDev_DX	Ataxia	5	0.496	0.491	0.220	0.990
	Control	10	0.069	0.109	0.034	1.574
JS	Ataxia	5	6.376	1.618	0.724	0.254
	Control	10	4.613	0.705	0.223	0.153
TMGA%	Ataxia	5	67.592	7.897	3.532	0.117
	Control	10	64.918	5.006	1.583	0.077
TMGAV%	Ataxia	5	29.028	11.798	5.276	0.406
	Control	10	31.354	9.200	2.909	0.293
TMWV%	Ataxia	5	33.054	5.513	2.466	0.167
	Control	10	38.633	6.329	2.001	0.164
Delay RC_GR	Ataxia	5	187.974	148.798	66.545	0.792
	Control	10	73.939	61.637	19.491	0.834